Noise Activated DNA Translocation for Faster Screening
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Abstract: Nonlinear solid friction between the gel matrix and DNA molecules inhibits the motion of DNA during electrophoresis. We report enhanced mobility of the DNA using external noise to alleviate the effect of solid friction. In presence of noise, the mobility of 1 kbp DNA increases ~86% compared to the conventional gel electrophoresis, whereas the increment is more than ~113% for 6 kbp DNA. At low power of the noise, super Arrhenius kinetics suggest the collective behavior of the activated motion of DNA molecules. Stochastic simulation following modified Langevin equation with the asymmetric pore size distribution of the agarose gel successfully predicts the mobility of DNA molecules and estimates the huge frictional force at the DNA-gel matrix interface.

One-Sentence Summary: Noise-activated electrophoresis results enhanced mobility of DNA by more than 100%.

A child learns to release a stuck (due to some tiny obstacles) toy car on an inclined plank by tapping it, from his/her experience. One can also tap on a horizontal platform having a pile of sand to allow free spreading of the sand from the ‘jammed’ state. The tapping acts as an external perturbation or noise that provides sufficient energy to the system to overcome the surface defects on the plank or the jamming potential barrier in the case of a sand pile. Similar scenarios are encountered almost every day such as the motion of a stuck tiny water droplet either on a windshield of a car on a rainy day or on a shower curtain during a bath. Noise is generated from the random blow of the wind in the former case, whereas, for later, it is the self-excited oscillations due to the condensation of steam and/or coalescence of multiple droplets (1). The potential barriers in such cases originate from the solid friction or its surrogate, - contact angle hysteresis, at the solid-solid or solid-liquid interface, respectively. The solid friction restricts the diffusive as well as biased motion of the nano-micro (2) to the large-scale macroscopic objects (3-5). Burlatsky and Deutch first pointed out that the electrophoretic motion of DNA is hindered by solid friction originates from the DNA-gel matrix interactions along with the viscous dissipation between DNA and the buffer-solvent (6, 7). This solid friction engendered from the adhesive interactions between the pore-wall of the gel matrix and the flexible DNA molecules, rubbing between them, distortion of the gel fibers, and other forms of local kinetic energy dissipation.

To detach from the wall of the gel matrix, an electric field-driven DNA molecule has to overcome these interactions, characterized by critical forces. Constrictions, defined by the dimensions of the pores, govern the solid frictional forces. As the distribution of the pore-size spans over a wide range, one can expect a wide distribution of critical forces. These critical forces can be overcome when enough energy is supplied to the DNA molecules. Here we report a novel
approach for faster transportation of DNA molecules that ensues from the noise-activated subcritical detachment of DNA from the gel matrix in an electrophoretic setting. The experimental configuration promotes rapid screening for DNA or protein fingerprinting.

Fig. 1. Effect of Gaussian noise on electrophoretic separation of DNA. (A) Agarose gel electrophoresis of DNA ladder (1-10 kbp) at 10 V bias for 4 h without any noise (i) and with the noise of different powers (K) depicted on the image. The DNA fragments in the image start from the well (dark rectangle) and then move downward during electrophoresis. The band for 10 kbp is the closest to the well and the band for 5 kbp has maximum brightness. (B) A typical example of a time series of noise as voltage input. (C) Semi log plot of the input noise depicting Gaussian distribution with mean \( \langle V(t) \rangle = 0 \). The symbols indicate the noise input corresponding to the power shown in Fig. (D). (D) Displacement of the 1 kbp to 6 kbp after 4 h of gel electrophoresis without noise and with noise having different powers shown in the inset. To minimize the error, only estimation of the displacement up to 6 kbp was considered. The error bar represents the standard deviation from the results obtained from 9 sets of experiments. (E) % Increment of the displacement was estimated for 1 – 6 kbp at different power of the noise input. The percentage increment in displacement was estimated as \( \% \text{ Increment} = \frac{(x_n - x_c) \times 100}{x_c} \), here \( x_n \) represents displacement for a particular DNA fragment at a particular noise, and \( x_c \) is the displacement of the corresponding DNA fragment from the conventional gel electrophoresis without any noise.

The experimental setup was similar to the conventional agarose gel electrophoresis under the influence of a constant bias voltage with a provision for introducing Gaussian noise as time-dependent voltage input (fig. S1) (8). A function generator, along with an amplifier, was attached with a bias DC voltage source in a series connection, and the resultant potential was applied across a gel in an electrophoretic set-up through a pair of Pt electrodes and Tris Acetate-EDTA (TAE) buffer (8). Under the influence of a bias voltage, the negatively charged DNA fragments slither through the gel having the network of porous tortuous tubes, the birth of which itself is engendered
by the lateral transport of DNA through the matrix (9). Keeping the bias voltage fixed at 10 V, the intensity of the Gaussian noise was controlled by amplifying the voltage amplitude of the noise. Under the influence of the noise having power, $K = 5.15 \times 10^6 \text{m}^2/\text{s}^3$ (8), almost 20% enhancement in the mobility of 1kbp DNA over the conventional gel electrophoresis was achieved. The mobility of 1kbp DNA increased further up to 86% with the amplified noise having the power of $K = 7.5 \times 10^7 \text{m}^2/\text{s}^3$. This increment of mobility was found more than 113% for 6 kbp DNA at the power of $K = 7.5 \times 10^7 \text{m}^2/\text{s}^3$ (Fig. 1).

As reported by Burlatsky et al. screening of the negatively charged DNA fragments based on the molecular weight is only possible in an electrophoretic setting because of solid friction offered by the gel (6). Otherwise, free electrophoresis only in a buffer, without the gel, shows similar mobility towards a positive electrode for the large DNA molecules (having base pairs larger than ~ 400 bp) (10, 11). This suggests that the linear kinematic friction is not sufficient to screen the large DNA fragments. It is the general notion that displacement fluctuation of a free Brownian particle in a thermal bath exhibits Gaussian distribution. This is true when the particle experiences linear kinematic friction where the cause of friction is coupled with the source of the noise, the heat bath. However, the non-Gaussian asymmetric tail of the displacement distribution, especially at the larger fluctuations, is observed when a particle/object interacting with a surface through Coulombic friction (5). A similar observation is also reported in the case of a colloidal particle diffuses along a lipid bilayer tube or diffuses through the entangled F-actin network (12). The use of external Gaussian noise alleviates the effect of the nonlinear solid friction ("Noise-lubricity") and enhances the mobility retaining the screening characteristics of the gel. An earlier report suggests similar subcritical detachment of a soft elastic body from a rigid contacor in presence of mechanical noise that promotes diffusive exploration of different states in an energy landscape and selects the least action pathway(13).

The noise used here is the time-dependent accelerations $\gamma(t) = \frac{qV(t)}{md}$, experienced by each base pair unit (8). Here $m$ is the average mass of a unit base pair, $q$ is the total charge of a base pair, $d$ is the distance between the two electrodes, and $V(t)$ is the delta correlated time-dependent voltage. The distribution of the noise pulses is Gaussian. This noise-induced drifted motion of the DNA molecules can be approximated by a modified Langevin equation:

$$\frac{d\theta}{dt} + \frac{\theta(t)}{\tau_L} + \sigma(\theta)\Delta(x) = \tilde{\gamma} + \gamma(t), \tag{1}$$

Here, $\tilde{\gamma} = \frac{Eq}{m}$ is the bias driving force per unit base pair with $E = \frac{V}{d}$ being the electric field, pertinent to the applied constant bias voltage $V$. $\Delta(x)$ is the space-dependent nonlinear solid friction associated with a signum function, $\sigma(\theta) = \frac{\theta}{|\theta|}$, that defines the direction of the solid friction opposite to that of the instantaneous velocity, $\theta$. $\tau_L$ being the Langevin relaxation time accounts for the linear kinematic friction. We have considered the translocation of the center of mass of DNA neglecting its curvilinear conformations. However, the dynamic frictional change due to its time-dependent conformations (coiled, stretched, etc.) will be interesting to consider. Apart from this, as evident from the FESEM image of the gel, the pore size ($\alpha$) is distributed over space (Fig. 2A). As the solid friction is related to the constriction, defined by the pore walls, the variation of $\Delta$, as a function of the space is thus justified. The allometric decay of the pore size
(Fig. 2B) readily suggests the frequency of encounters with the high solid friction (small pore) by a DNA molecule is more than the number of encounters with the low solid friction (large pore).

Fig. 2. Agarose gel pore size and solid friction. (A) SEM image of the 0.8% agarose gel. The gel was initially frozen at – 20 °C for overnight and then vacuum dried at 20 mTorr and – 103 °C in a Lyophilizer for 24 h before the SEM analysis (B) Open-source ImageJ software was used to estimate the pore size (inset image showing the thresholding of the image). The probability distribution function \( P(\alpha) \) of the pore size (\( \alpha \)) (open blue circle) is fitted with the allometric regression of the form \( \sim \alpha^{-2.2} \). (C) Extreme value distribution of solid friction \( \Delta \) used for the numerical simulation of the Langevin Eq. 1.

Thus, one can qualitatively assume the ‘Extreme value’ distribution of the \( \Delta \) values:

\[
P(\Delta) = \frac{1}{\sigma} \exp\left(\frac{\Delta - \Delta_m}{\sigma}\right) \exp\left[-\exp\left(\frac{\Delta - \Delta_m}{\sigma}\right)\right]
\]

randomly distributed over the space. Here, \( \Delta_m \) is the magnitude of \( \Delta \) with the maximum occurrence, and \( \sigma \) as the scale parameter of the distribution. (Fig. 2C). While the DNA molecules slither through the pores, this random space-dependent \( \Delta \) inherently takes into account the time-dependency of the molecular conformations. Granick’s group reported an interesting observation while imaging a single DNA molecule transporting through an agarose gel(14). They demonstrated that the trailing end and the leading end of a DNA molecule are stuck at the same position of an agarose matrix for quite some time before leaving the position. This observation straightaway suggests that there is a distribution of constrictions throughout the gel matrix, which encouraged us to consider the random distribution of \( \Delta \) as a function of position. For the longer duration of the electrophoresis with a large number of DNA molecules, one can still assume an approximate average \( \Delta \) value for a particular gel with a specific agarose concentration. Considering the linear approximation of Eq. 1 and from the Fokker-Planck solution in the velocity space, one can estimate the average drift velocity as (3, 15):

\[
\vartheta_d = \frac{\bar{\gamma} \tau_L}{1 + \frac{\Delta^2 \tau_L}{K}}
\]

(2)

This approximate drift velocity (\( \vartheta_d \)) agrees well with the experimental drift velocity of the DNA molecules with \( \Delta \sim n^{0.1} \) and \( \tau_L \sim n^{0.4} \) (fig. S2).

Although the approximate Eq. 2 describes the drift velocity reasonably well, its validity is somewhat dubious in the present scenario. From the fitting of the drift velocity using Eq. 2, the
Langevin relaxation time $\tau_L$ is found to be of the order of $10^{-13}$ s, which is much smaller than the sampling time, $dt$, of the external noise input $\left(\frac{\tau_L}{dt} \sim 10^{-3}\right)$. Ideally, the Langevin relaxation time, $\tau_L$, should be longer than the noise correlation time scale, $\tau_c$, for Eq. 2 to be applicable. However, the power spectra of the noise, reveal that the noise is white till $f_c = 2.5 \times 10^7$ Hz (fig. S3)(8). Considering this $f_c$ as the corner frequency, the approximate correlation time constant, $\tau_c \sim 6$ ns, (from the equation, $\tau_c = \frac{1}{2\pi f_c}$). The estimation of $f_c$ is however limited by the experimental sampling rate of the noise data collection. Thus, one can expect actual $\tau_c$ may be much smaller than the 6 ns as the $f_c > 2.5 \times 10^7$ Hz. In support of this smaller noise correlation, numerical simulation of the Langevin equation (Eq. 1) following Gillespie (16), satisfactorily agrees with the experimental drift velocity with $\frac{\tau_L}{dt} \sim 10$ (Fig. 3C).

Fig. 3. Simulation results from the Langevin equation. (A) Typical simulated trajectories of the DNA fragments (color code is shown in the inset) in gel electrophoretic setting at a particular noise $K = 2.1 \times 10^7$ m$^2$/s$^3$. (B) Simulated trajectories of 6 kbp DNA fragment at different powers of the noise shown in the figure. Inset shows 4 different trajectories of 6 kbp DNA fragments at low power ($K = 3.0 \times 10^4$ m$^2$/s$^3$) of the noise depicting the randomness and fluctuations during translocation. (C) Comparison of the drift velocity obtained from the 30 simulations for each case (solid curves) and the experiments (solid symbols). The error bar for the experimental data depicts the standard deviation of the results obtained from 9 sets of experiments in each case.

As discussed above, the energy barrier, $E_o$, originates from the nonlinear interactions of DNA molecules with the gel matrix. Solid friction, $\Delta$, being the significant contributor to the nonlinear interactions, one can assume the scaling of energy barrier $E_o \sim \Delta$ as the first approximation. The rate of the detachment of DNA molecules from the gel matrix manifests in the drift velocity of the molecules and can be represented as:

$$\vartheta = \vartheta_o \exp \left[ -\frac{C(\Delta - \overline{\vartheta})}{MK\tau_L} \right],$$

Here $C$ is a numerical constant and $\vartheta_o$ is the critical velocity while the biased force per unit mass, $\overline{\vartheta}$, is sufficient to transcend the energy barrier, i.e. $\overline{\vartheta} \approx \Delta$. The energy supplied through the
external noise, \( MK\tau_L \), represents the mechanical analog to thermal energy \( k_B T \), where M is the MW of DNA. While \( \ln \left( \frac{\vartheta}{\vartheta_0} \right) \) is plotted against \( \frac{(\Delta - \bar{\gamma})}{MK\tau_L} \), all the velocity data for different DNA fragments merges into a single master curve with the same average \( \Delta \) values used for the approximate Eq. 2 (Fig. 4). Although at the high power of the noise (K), the velocity follows the Arrhenius-Eyring (15, 17) like equation (black dash-dot line in Fig. 4), it exhibits Super-Arrhenius-like behavior (pink dashed line in Fig. 4) at a low power of the noise.

Fig. 4. Arrhenius/Non-Arrhenius-like behavior. The velocity data for all the fragments (1 – 6 kbp) are plotted following Eq. 3 having \( \Delta \sim n^{0.1} \) and \( \tau_L \sim n^{-0.4} \). The blue shaded (high K) region shows noise-activated Arrhenius-like behavior and is represented with a black dash-dot line. Whereas, the yellow shaded (low K) region depicts Super-Arrhenius behavior, – the velocity obtained is much higher (shown with a pink dash line) than that expected from Arrhenius prediction (black dash-dot line).

Arrhenius expression for a kinetic process implicitly assumes a single and well-defined rate-limiting energy barrier to transcend. However, the free energy landscape of gel electrophoresis is populated with multiple metastable states separated by saddle points. Thus a process in which a particle or molecule maneuvers through these pathways overcoming the multiple saddle points, bypassing the pinnacles of the energy barriers, exhibits Non-Arrhenius kinetics.

The super Arrhenius behavior is often observed in thermally activated viscous slowing down of a weakly bonded glass-forming liquid in a super-cooled regime (18). At a higher temperature than a characteristic temperature \( T^* \) for a liquid, its viscosity follows roughly the Arrhenius behavior with temperature. Whereas at \( T<T^* \), its dependency is faster than the Arrhenius (Super-Arrhenius). This is attributed to the collective and cooperative behavior for the thermally activated system at low temperature (\( T<T^* \)) for a weakly bonded system.

At the low power of the noise (analogous to low temperature), super Arrhenius behavior indicates that the dynamics are influenced by the cooperative motion of DNA, affected by prominent non-linear friction. The magnitude of this friction is distributed over a wide range and is the source of space-dependent energy barriers. Langevin simulation at a very low power of the noise shows considerable ‘stick’ states in the trajectories of DNA molecules at some high \( \Delta \) value.
DNA molecule translocates through the different pathways meandering downhill of the energy landscape towards the global equilibrium. In this quest, DNA may stick to a local energy pit until and unless a high-energy noise pulse rescues it. However, the overall motion of the DNA is collectively emerging as space averaged drift velocity. At a high power of the noise, the effect of the nonlinear friction is alleviated by frequent such rescue events. Thus, free-flowing yet noise-activated Arrhenius characteristics emerge at high athermal energy.

Our experimental results demonstrate that the mobility of DNA molecules in gel electrophoretic settings can be significantly faster (~ 100 % or more) than the conventional gel electrophoresis (19) with the aid of external Gaussian noise. The drift velocity of the DNA induced by activated “noise-lubricity”, follows the Arrhenius-Eyring-like escape rate at the high power of the external noise. Whereas, at the low power, the cooperative dynamics of the DNA molecules impart super Arrhenius-like behavior. A modified Langevin simulation successfully predicts the drift velocity for an applied bias and noise along with the consideration of space-dependent nonlinear solid friction, originating from the wide distribution of the gel pore size. In contrast to the conventional notion, this study reveals the enormous amount of solid friction (~ 10^7 m^2/s^3) is operative at the interface of the DNA-gel matrix. This work suggests strategies for noise-activated faster DNA fingerprinting and set up the basis for advanced research on resonance-induced super mobility for the isolation of a specific protein fragment from a crowd.

References and Notes

1. S. Daniel, M. K. Chaudhury, J. C. Chen, Fast drop movements resulting from the phase change on a gradient surface. Science. 291, 633–6 (2001).

2. V. Bormuth, V. Varga, J. Howard, E. Schäffer, Protein friction limits diffusive and directed movements of kinesin motors on microtubules. Science. 325, 870–3 (2009).

3. P.-G. De Gennes, Brownian Motion with Dry Friction. J. Stat. Phys. 119, 953–962 (2005).

4. P. S. Goohpattader, M. K. Chaudhury, Diffusive motion with nonlinear friction: apparently Brownian. J. Chem. Phys. 133, 024702 (2010).

5. P. S. Goohpattader, S. Mettu, M. K. Chaudhury, Experimental investigation of the drift and diffusion of small objects on a surface subjected to a bias and an external white noise: roles of coulombic friction and hysteresis. Langmuir. 25, 9969–79 (2009).

6. S. Burlatsky, J. Deutch, Influence of solid friction on polymer relaxation in gel electrophoresis. Science. 260, 1782–1784 (1993).

7. S. F. Burlatsky, J. M. Deutch, Solid friction in gel electrophoresis. J. Chem. Phys. 103, 8216 (1995).

8. See supplementary materials.

9. P. G. de Gennes, Reptation of a Polymer Chain in the Presence of Fixed Obstacles. J. Chem. Phys. 55, 572 (1971).
10. B. M. Olivera, P. Baine, N. Davidson, Electrophoresis of the nucleic acids. Biopolymers. 2, 245–257 (1964).

11. N. C. Stellwagen, Electrophoresis of DNA in agarose gels, polyacrylamide gels and in free solution. Electrophoresis. 30, 1–14 (2009).

12. B. Wang, S. M. Anthony, S. C. Bae, S. Granick, Anomalous yet Brownian. Proc. Natl. Acad. Sci. U. S. A. 106, 15160–4 (2009).

13. M. K. Chaudhury, P. S. Goohpattader, Noise-activated dissociation of soft elastic contacts. Eur. Phys. J. E. 35, 131 (2012).

14. J. Guan, B. Wang, S. C. Bae, S. Granick, Modular stitching to image single-molecule DNA transport. J. Am. Chem. Soc. 135, 6006–6009 (2013).

15. P. S. Goohpattader, M. K. Chaudhury, Random motion with interfacial contact: driven diffusion vis-à-vis mechanical activation. Eur. Phys. J. E. Soft Matter. 35, 67 (2012).

16. D. T. Gillespie, The mathematics of Brownian motion and Johnson noise. Am. J. Phys. 64, 225–240 (1996).

17. H. Eyring, Viscosity, Plasticity, and Diffusion as Examples of Absolute Reaction Rates. J. Chem. Phys. 4, 283 (1936).

18. G. Tarjus, D. Kivelson, P. Viot, The viscous slowing down of supercooled liquids as a temperature-controlled super-Arrhenius activated process: a description in terms of frustration-limited domains. J Phys. Condens. Matter. 12, 6497 (2000).

19. O. Smithies, Zone electrophoresis in starch gels: group variations in the serum proteins of normal human adults. Biochem. J. 61, 629–641 (1955).

20. H. A. Kramers, Brownian motion in a field of force and the diffusion model. Phys. 7, 284–304 (1940).

21. H. Risken, The Fokker-Planck Equation: Methods of Solution and Applications. (Springer-Verlag, Berlin, ed. 2nd, 1989), vol. 18.
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Supplementary Materials
Materials and Methods
Supplementary Text
Figs. S1 to S4
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Supplementary Materials for

Noise Activated DNA Translocation for Faster Screening
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Materials and Methods

Preparation of Gel:

0.8% (w/v) Agarose was prepared by dissolving agarose powder (Loba Chemie) in 50X Tris Acetate-EDTA (TAE) buffer (Himedia) and 1% (w/v) of 0.5 mg/ml Ethidium bromide (Loba Chemie). A homogeneous solution was prepared by mixing vigorously and then boiling in a microwave oven for 1 min. The solution was then cooled down to room temperature before casting in the horizontal gel platform. A gel comb was placed at one end of the gel platform to form the wells into which the DNA would be loading before electrophoresis. The casted agarose gel was allowed to set at room temperature for 2 h. TAE buffer was used to maintain the pH of the solution at ~ 8 and EtBr, which chelates in between two strands of DNA, was added to facilitate the detection of the same under UV illumination.

Experimental Methodology:

The DNA 1 kbp to 10 kbp molecular weight ladder (Takara Bio Inc.) was loaded into the wells of the gel. Any bubble formation during loading of the DNA was avoided carefully. The gel was run at 10 V DC Voltage (constant current of ~ 1 mA) across a separation distance of d = 13 cm between two Pt electrodes. The duration of the electrophoresis was 4 h. The temperature of the gel and the TAE buffer was maintained at ~23 °C. Visualization of the DNA fragments was done using Gel Doc (Chemidoc XRS+) instrument. The system software captures the images at various modes of magnification. Gaussian white noise was generated and amplified using a Function Waveform Generator (SIGLENT SDG-1062X) and a Noise Amplifier (Q44 Keysight 33502A 2-Channel Isolated Amplifier Power Amplifier), respectively and connected in series with a DC voltage source (Genei Electrophoresis Power Supply) as schematically shown in Fig. S1. To characterize the noise, the output from the voltage source via the amplifier was connected to an oscilloscope (RIGOL DS1052E) and the noise data are stored. The stored data then was extracted for further analysis. The minimum interval for the sampling data was 40 ns. The images of the DNA bands after electrophoretic separation were analyzed using the open-source ImageJ software.

Supplementary Text

Power of the noise:

The power of the noise is calculated per base pair of the nucleotide as follows:

Time-dependent random acceleration per base-pair \( \gamma(t) = \frac{2\times C \times V(t)}{d \times m} \); where

\( C \) = Charge of an electron,
\( d \) = Distance between two electrodes of the electrophoretic chamber,
\( m \) = mass of a base pair,
\( V(t) \) = time-dependent voltage generated by function waveform generator,

The mean of the noise input, \( \langle \gamma \rangle = 0 \),

The power of the noise then calculated as \( K = \langle \gamma^2 \rangle \tau_c \),

The \( \langle \gamma^2 \rangle \) denotes the mean square acceleration.
Approximate drift velocity from the linearization of Langevin equation:

\[ \mathcal{G}_d = \frac{\bar{\gamma} \tau_L}{1 + \Delta^2 \tau_L / K} , \]

(S1)

Here, \( \bar{\gamma} = \frac{E \eta}{m} \) is the bias driving force per unit base pair. \( \tau_L \) is the Langevin relaxation time and \( \Delta \) is the average solid friction force per unit base pair. The approximate drift velocity is estimated from the stationary solution of the Fokker Planck equation in velocity space (3, 15). The drift velocity obtained from equation (S1) is shown in Fig. S2.

The power spectrum of the experimental input noise:

The power spectrum of the input noise is shown in Fig. S3. The power spectrum of the noise, having total bandwidth (-f_{max} to +f_{max}, \( f_{max} \) being the maximum frequency) of 50 MHz, is reasonably flat indicating the noise can be considered a white noise up to the maximum frequency \( f_{max} \). However, this is limited by the data sampling frequency with \( dt = 40 \) ns. The actual bandwidth of the input noise might be larger than this 50 MHz.

Details of the Numerical Simulation:

A numerical simulation of the modified Langevin Equation (Eq. 2 in the manuscript):

\[ \frac{d\mathcal{G}}{dt} + \frac{\mathcal{G}(t)}{\tau_L} + \sigma(\mathcal{G}) \Delta(x) = \bar{\gamma} + \gamma(t) , \]

(S2)

was carried out following the methodology of Gillespie (16) using MATLAB. The DNA molecule is assumed as a point mass at the center of gravity of the molecule at any point in time. Random noise is generated as a volt signal using an inbuilt random number generator having Gaussian distribution. The simulations were carried out with an integration time step of \( dt = 0.04 \) ps so that the ratio of \( \frac{\tau_L}{dt} \approx 10 \).

Space dependent \( \Delta \):

To introduce the space-dependent \( \Delta \), first, a set of random \( \Delta \) values are generated that follows Extreme value distribution: \( P(\Delta) = \sigma^{-1} \exp \left( \frac{\Delta - \Delta_m}{\sigma} \right) \exp \left( -\exp \left( \frac{\Delta - \Delta_m}{\sigma} \right) \right) \). Then each \( \Delta \) value is assigned to the position \( X \) in such a manner so that over a random length (l) of space the same \( \Delta \) value will be experienced. This length (l) also follows a normal distribution.
Specific conditions for $|\Delta| > |\bar{\gamma} + \gamma(t)|$:

At any instance, if the velocity of the DNA molecule is zero and the $|\Delta| > |\bar{\gamma} + \gamma(t)|$, the velocity will remain as zero unless, at a later time, one pulse of the noise $\gamma(t)$ will be sufficient enough so that the total acceleration $|\bar{\gamma} + \gamma(t)|$ surpasses the magnitude of the $\Delta$. If at any instance, the velocity is small and less than a critical value $\theta_0$ along with the $|\Delta| > |\bar{\gamma} + \gamma(t)|$, exponential decay of the velocity with the Langevin time scale $\tau_L$ is assumed. Otherwise, full Eq. 1 is integrated numerically.

Displacement distribution:

From the trajectory, at different time steps, the displacement jumps were calculated. The probability density function (PDF) of the displacement $\bar{x}$ are depicted for 1 kbp and 10 kbp in Fig. S4A and S4B with a peak shift of $\left(\bar{x} = \left(x - x_p\right)\right)$. Here $x_p$ denotes the displacement value having maximum count in the distribution of $x$. Due to the presence of non-linear friction, the distribution is asymmetric and having a non-Gaussian exponential tail. Assuming average solid friction $\Delta$, from the steady-state solution of the Klein-Kramers equation (20, 21) the PDF of the velocity distribution can be obtained as:

$$P(\theta) = P_o \exp \left(-\frac{\theta^2}{K\tau_L} - \frac{2|\theta|\Delta}{K} + \frac{2\theta E q}{K m}\right)$$

(S3)

The presence of the 2nd and 3rd terms within the argument of the exponential function impart the asymmetric non-Gaussian tail in the velocity distribution that is evident from the displacement PDF. Simulation with $\Delta = 0$ must give rise to symmetric Gaussian distribution according to equation S3, and thus depicted in Fig S4C for 1 kbp DNA.
**Fig. S1. Schematic representation of the experimental set-up.** The function waveform generator is connected with a signal amplifier. The output from the amplifier is connected in series with a constant DC voltage source and the resultant output is applied across the agarose gel in the electrophoretic chamber. The arrow with the symbol $\theta$ denotes the direction of the DNA band motion.
**Fig. S2. Drift velocity of the DNA fragments.** Comparison between the experimental drift velocity (symbols) and the velocity predicted by the Eq. S1 for different DNA fragments.
**Fig. S3. Power Spectra of the input noise.** A typical power spectrum of the time-dependent voltage $V(t)$ as the noise input. The spectrum shows that the spectrum is reasonably flat up to the frequency $f_c = 2.5 \times 10^7 \text{Hz}$. As this estimation is limited by the sampling time $dt = 40 \text{ ns}$ one can expect the noise is white over a larger frequency domain than $2.5 \times 10^7 \text{Hz}$. 
**Fig. S4. PDF of displacement fluctuation.** The PDF of the displacement fluctuation in semi-log plot at different time windows (0.001, 0.01, and 0.05 ns) for 1 kbp (A) and 10 kbp (B) with space-dependent $\Delta$. The peak position of the distribution is shifted to zero by $x = (x - x_p)$. The tails of these distributions are asymmetric and exponential. (C) The PDF of the displacement fluctuation for 1 kbp DNA with $\Delta = 0$ shows Gaussian distribution.