THERMAL FLUCTUATIONS IN THE SPEED OF LINEAR BIOLOGICAL MOTORS

P.H. HANDEL

Department of Physics and Astronomy, Univ. of Missouri, St. Louis, MO 63121, USA

R. TETZLAFF

Inst. für Angewandte Physik, Universität Frankfurt, Frankfurt a.M., Germany

The speed of linear motors performing the transcription of DNA has recently been shown to change when mechanical tension is applied to the DNA strand being replicated. Large rate fluctuations have also been observed. Here it is shown that based on the measured relation between speed and tension, these linear motors must also exhibit large rate fluctuations of thermal origin. The derived r.m.s. speed fluctuations are proportional to the derivative of the speed/tension relation, and turn out to be considerable, of the order of 8%.

Keywords: DNA Replication Rate, DNA Replication Rate Fluctuations, Molecular Motor Speed Fluctuations, DNA Polymerase Rate Noise, Biothermal Noise, Sequenase Rate Fluctuations, Klenow Fragment Rate Noise, Thermal Noise, Noise in Biology.

Molecular motors are known to run on ATP, generating either rotation, or linear displacement. The latter type is observed in the enzymes that catalyze the replication of DNA. The speed of these linear motors has been measured and shown to depend on the tension applied to the DNA strand.

The linear motor is a DNA-polymerase (DNAp), i.e., an enzyme that runs along a single-strand (ss) DNA molecule [1] and replicates its template base, transforming it to a double-strand (ds) geometry through repeated capture and pairing in of the correct free nucleotides (dNTP). The polymerase then repeats this catalytic process. The mechanical tension is applied during the replication process between the ds and ss ends. One of these ends is fixed at a stationary surface, and the other is attached to a plastic bead. The force creating the tension is applied with optical and magnetic tweezers.

At small applied tension f, below 10 pN, the extension x of ss DNA illustrated qualitatively in Fig. 1 is proportional to f

$$f = Kx, \tag{1}$$

with K ≈ 25 pN/nm taken as random numeric example. We can consider the DNA molecule as a harmonic oscillator, as far as small oscillations of its length are concerned. In thermal equilibrium, the average potential energy of this uniform longitudinal extension mode is

$$W= K\langle x^2/2\rangle = k_BT/2 \tag{2}$$

Using Eq. (1), for small oscillations, we can also write

$$W = \langle(\delta f)^2\rangle/2K =k_BT/2 \tag{3}$$

From here we find the variance of the force acting in thermal equilibrium at 300°K on the DNA molecule, as well as the rms extension

$$\langle(\delta f)^2\rangle =Kk_BT =25\ \mathrm{pN/nm}\cdot k_BT=(25\ \mathrm{pN/nm})\cdot 4\ \mathrm{pN\cdot nm} =100\ \mathrm{pN}^2;\ f_{rms}= 10\ \mathrm{pN}; \tag{4}$$

$$<x^2> = k_BT/K = 4\ pN\cdot nm / (25\ pN/nm) = 0.16\ nm^2;\ \ x_{rms}= 0.4\ nm. \qquad (5)$$

The replication rate k(f), i.e., the speed of the linear motor, has been measured and shown [1] to depend on the tension f applied to the DNA strand. Thermal fluctuations of this force,

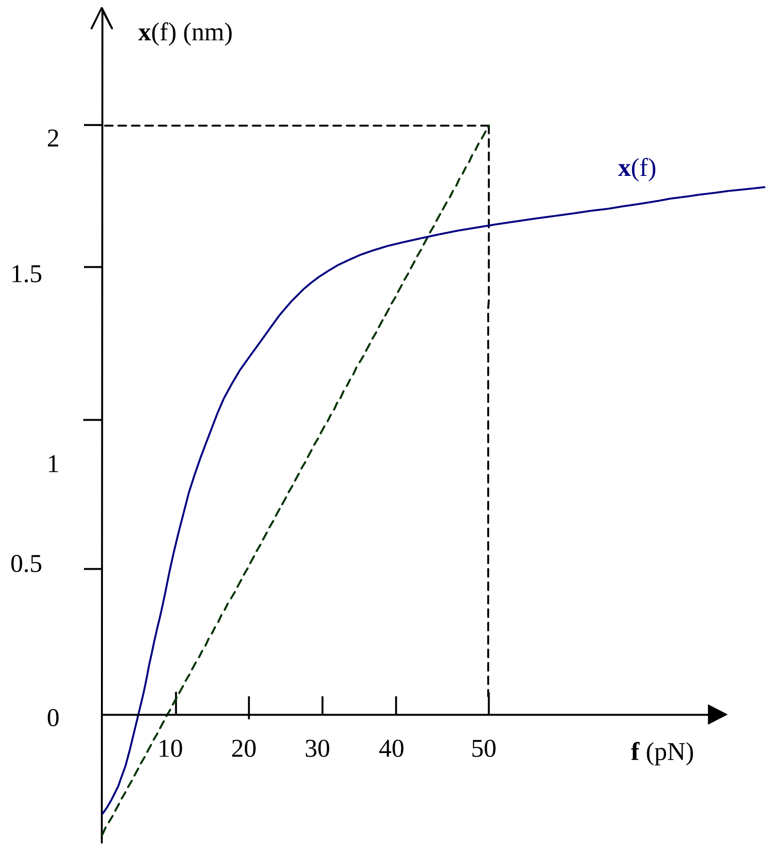

Fig. 1. Typical qualitative extension x vs. force f curve, $x_{ss}(f)$, for ss DNA [1].

as shown in Eq. (4), will cause thermal equilibrium fluctuations δk in the rate k

$$\delta k(f) = (\partial k/\partial f)\delta f \qquad (6)$$

The variance of the rate k caused by thermal fluctuations can thus be obtained in the form

$$<(\delta k)^2> = (\partial k/\partial f)^2<(\delta f)^2> = \underline{(\partial k/\partial f)^2 K k_B T} \qquad (7)$$

The derivative of the rate k can be obtained by differentiating the curves k(f)/k(0) exemplified in Fig. 2 for a typical enzyme for which measurements were performed. For instance, denoting $k(0)=k_o$ and assuming just for numerical example a rate $k=k_0(1/30pN)$, at small f close to zero, one would obtain

$$<(\delta k)^2> =(\partial k/\partial f)^2 K k_B T =k_o^2(1/30pN)^{2}\cdot 25\ pN/nm\cdot 4\ pN\cdot nm =2.776\cdot 10^{-2}k_o^2; \qquad (8)$$

$$\delta k_{rms}= 0.166k_o. \qquad (9)$$

These are large fluctuations. However,

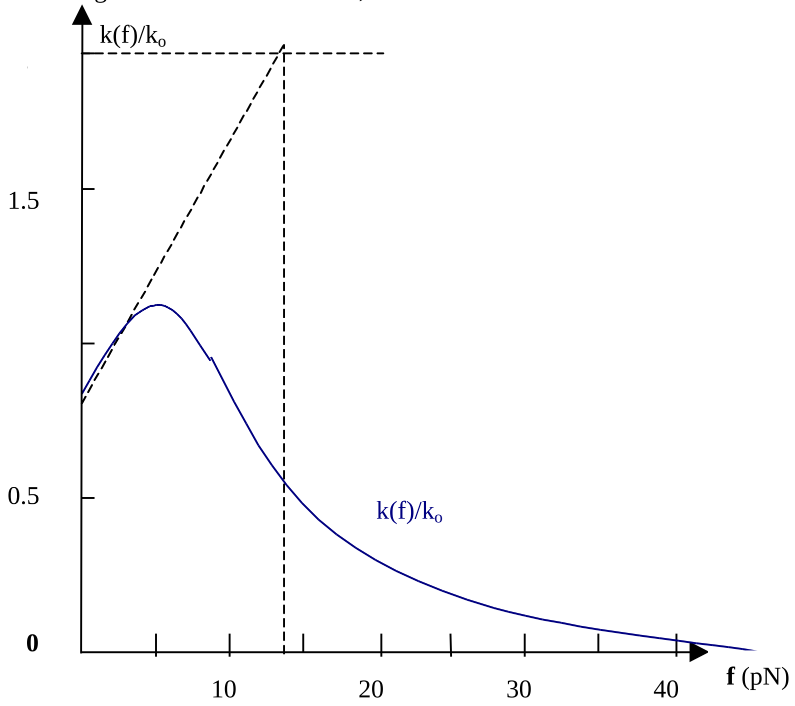

Fig. 2. Typical result [1]-[4] of replication rate measurements as a function of applied tension f on the DNA during the replication process.

the fluctuations present in Fig. 2 are considerably larger than 17%. This implies that measurement errors may be involved, and also that excess noise may be present, to various degrees, in the speed of the three motors considered. That excess noise may include the quantum 1/f effect that modulates the cross sections and process rates defining the speed of the transcription process.

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References

[1] A. Goel, T. Ellenberger, M. D. Frank-Kamenetskii and D. Herschbach, J. Biomolecular Structure & Dynamics **19**, 1-14 (2002); jbsdonline.com

[2] A. Goel, M. D. Frank-Kamenetskii, T. Ellenberger, D. Herschbach, Proc. Natl. Acad. Sci. USA 98, 8485-8489 (2001).

[3] G.J.L. Wuite, S.B. Smith, M. Young, D. Keller, & C. Bustamante, Nature **404**, 103-106 (2000).

[4] B. Mayer, D. Bensimon and V. Croquette, Proc. Natl. Acad. Sci. USA **97**, 12002-12007 (2000).