

## Vibrational shortcut to the mean-first-passage-time problem

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(Received 8 November 2009; published 26 April 2010)

What is the average time a random walker takes to get from A to B on a fractal structure and how does this mean time scale with the size of the system and the distance between source and target? We take a nonprobabilistic approach toward this problem and show how the solution is readily obtained using an analysis of thermal vibrations on fractals. Invariance under scaling and continuity with respect to the spectral dimension are shown to be emergent properties of the solution obtained via vibrational analysis. Our result emphasizes the duality between diffusion and vibrations on fractal structures. Applications to biological systems are discussed.

DOI: 10.1103/PhysRevE.81.040103

PACS number(s): 05.40.Fb, 05.45.Df

In this Rapid Communication we consider a random walker moving on a fractal bounded domain of size  $N$ . We take a nonprobabilistic approach toward a probabilistic problem and find, based on the vibrational properties of the network, an approximate expression for the mean-first-passage time (MFPT)  $T(N, r)$  between two distinct tagged points distanced  $r$  apart,

$$\frac{T(N, r)}{N} \approx \tilde{C} \begin{cases} \frac{1 - (r/a)^{d_f(2/d_s - 1)}}{[d_s/2 - 1]} & d_s > 2 \\ d_f \ln(r/a) & d_s = 2 \\ \frac{-1 + (r/a)^{d_f(2/d_s - 1)}}{[1 - d_s/2]} & d_s < 2 \end{cases} . \quad (1)$$

Here  $a$  is the distance between nearest neighbors,  $d_s$  and  $d_f$  are the network spectral and fractal dimensions, respectively, and  $\tilde{C}$  is a constant to be defined later in the Rapid Communication. The joint domain in which the approximation is valid is given by:  $\{N \gg 1, a \ll r \leq R_g\}$  where  $R_g$  is the radius of gyration. The spectral dimension  $d_s$  governs the density of low-frequency normal modes of a fractal. More precisely, denoting the density of modes  $g(\omega)$ , the scaling relation  $g(\omega) \sim \omega^{d_s - 1}$  holds for low frequencies. Describing the mass fractal dimension  $d_f$  is most convenient using a three-dimensional example. Draw a sphere of radius  $r$  enclosing some lattice points in space and calculate their mass  $M(r)$ , increase  $r$ , and calculate again. Do this several times and if  $M(r)$  scales as  $r^{d_f}$  the exponent  $d_f$  is called the fractal dimension. We note that the ratio  $d_s/2d_f$  is just the Hurst exponent of the random-walk mean-square displacement in time [1].

It is important to notice that in general the MFPT between two points on a finite, anisotropic, and inhomogeneous structure may depend specifically on the identity of the source and target points. Equation (1) was hence written for the disorder average (average over all pairs distanced  $r$  apart) of the MFPT. The main conclusion from Eq. (1) is that as a function of the source-target distance  $r$  the normalized MFPT either grows like a power law ( $d_s < 2$ ) or saturates

toward a limiting constant ( $d_s > 2$ ). In its domain of validity Eq. (1) covers both the numerically dominant part and the nonanalytic part of the MFPT. For  $d_s < 2$  the nonanalytic part is the numerically dominant one, while for  $d_s > 2$  it is not. We note that a result similar to Eq. (1) was obtained via probabilistic methods in a recent paper by Condamin *et al.* [2]. Other relations between first-passage-time statistics and the spectral dimension can be found in [3–5].

Deriving Eq. (1), we start by solving the analogous vibrational problem using scaling arguments. We then continue with a more direct treatment which leads to additional insights regarding the solution. Consider an elastic network (EN) of masses coupled by harmonic springs in the framework of what is known as the scalar elasticity model or the Gaussian network model (GNM) when applied for proteins [6,7]. The same network can be thought of as a network of nodes connected by edges (which we will refer to as RN) and we will alternate between these representations as we go (see Fig. 1). Let us now couple the EN to a thermal bath and consider a MFPT problem on the RN where at every time step the random walker on the RN performs a random jump to a nearest neighbor without preference. Consider two nodes on the RN,  $i$  and  $j$ , characterized by an Euclidean distance  $r$  between them. What is the MFPT  $T(i, j)$  for motion between sites  $i$  and  $j$ ? [If the MFPT depends on the direction of travel, we define  $T(i, j)$  to be the average for the two directions.] On the EN the distance between mass  $i$  and  $j$  is not fixed due to thermal fluctuations. From the way we have constructed the EN (Fig. 1) it follows that the equilibrium (ensemble-average) distance is  $r$ , and we will denote the instantaneous distance by  $r_{ij}$ . It turns out that there is a relation between the thermal variance in  $r_{ij}$  and the MFPT  $T(i, j)$  [8],

$$\frac{T(i, j)}{N} = \frac{z\gamma}{6k_B T} \langle (r_{ij} - r)^2 \rangle = \frac{z\gamma}{6k_B T} \langle \Delta r_{ij}^2 \rangle, \quad (2)$$

where  $\gamma$  is the network spring constant and  $z$  is the mean coordination number of a node in the RN. See Fig. 1 for an explanation and visual illustration of this result. One way to evaluate  $T(i, j)$  is via direct evaluation of the thermal variance  $\langle \Delta r_{ij}^2 \rangle$ . We return to this approach later on. Our current

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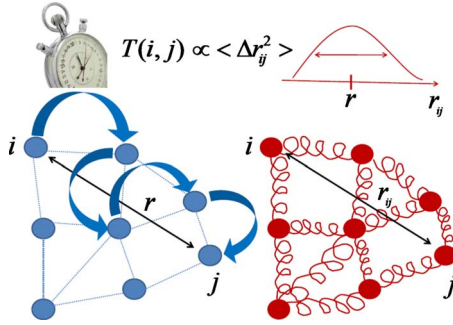


FIG. 1. (Color online) Left: a network of nodes connected by edges (RN); right: an analogs elastic network of masses coupled by harmonic springs (EN). One can transform a RN to an EN by transforming nodes to masses and edges to springs. We study the relation between a random walk on the RN and the thermal vibrations of the EN. Consider two nodes on the RN,  $i$  and  $j$ , characterized by an Euclidean distance  $r$  between them. On the EN the distance between mass  $i$  and  $j$  is not fixed due to thermal fluctuations. From the way we have constructed the EN it follows that the equilibrium (ensemble-average) distance is  $r$ , and we will denote the instantaneous distance by  $r_{ij}$ . The MFPT a random walker takes to get from node  $i$  to node  $j$  [if the MFPT depends on the direction of travel, we define  $T(i, j)$  to be the average for the two directions] on a RN is proportional to the thermal variance in the distance between mass  $i$  and mass  $j$  on an EN coupled to a thermal bath.

efforts concentrate on an alternative route. A rearranged version of Eq. (2),

$$k_B T = \frac{Nz\gamma}{6T(i, j)} \langle \Delta r_{ij}^2 \rangle \equiv \frac{1}{2} k_r^{eff} \langle \Delta r_{ij}^2 \rangle, \quad (3)$$

immediately lends itself to an effective inverse spring constant interpretation of  $T(i, j)$ . The higher the MFPT  $T(i, j)$ , the softer the effective spring connecting sites  $i$  and  $j$ ; the softer the spring, the higher the magnitude of the fluctuations. We note here that a similar analogy was made between  $T(i, j)$  and the point to point resistivity  $\rho(i, j)$  in the analogous electrostatic problem [9,10]. Defining  $T(N, r)$  as the average of  $T(i, j)$  over all pairs with an equilibrium distance  $r$ , we conclude that the effective spring constant associated with this distance is

$$k_r^{eff} = \frac{Nz\gamma}{3T(N, r)}, \quad (4)$$

In deriving the scaling of  $k_r^{eff}$  for fractal structures we follow Alexander [11] and associate a length scale with a vibrational frequency. Consider the isolation of a fractal blob of size  $r$  from an original larger fractal. High-frequency modes for which  $\omega \gg \omega(r)$  will not be effected by this isolation; on the other hand, low-frequency modes for which  $\omega \ll \omega(r)$  will disappear from the spectrum due to the disconnection of the blob. By construction the crossover will occur at  $\omega(r)$  the frequency we have associated with  $r$ . In the domain:  $a \ll r \ll R_g$ , this frequency was shown to scale as  $\omega(r) \sim r^{-d_f/d_s}$  [11] and we note that this is nothing but the appropriate dispersion relation for a fractal elastic network. Let us now use this result in order to associate a length scale

with an effective spring constant. Coarse graining the original fractal as we collapse all blobs of size  $r$  to points of mass  $M(r) \sim r^{d_f}$ , we construct a new network on this scale. Preserving the self-similarity we require that the basic frequency (highest) in the coarse-grained fractal would be  $\omega(r)$ , and it follows that the spring constant of the springs connecting the newly adjacent points should be [11]

$$k_r^{eff} \equiv M(r)\omega^2(r) \sim r^{d_f(1-2/d_s)}. \quad (5)$$

Substituting into Eq. (4) we obtain the correct scaling dependence of the normalized MFPT on the intersite distance,

$$\begin{cases} \frac{T(N, r)}{N} \sim r^{d_f(2/d_s-1)} & d_s \neq 2 \\ \frac{T(N, r)}{N} \sim \ln r & d_s = 2 \end{cases}, \quad (6)$$

where in the case of a vanishing exponent we have assumed a logarithmic correction. Equation (6) gives the dependence up to an unknown additive constant  $A$  and an unknown multiplicative constant  $B$ . The sign of the multiplicative constant  $B$  is determined by the rather intuitive requirement from the averaged MFPT to be a monotonically increasing function of the distance. It follows that the sign is a step function of the spectral dimension and that

$$\begin{cases} B < 0 & d_s > 2 \\ B > 0 & d_s \leq 2 \end{cases}. \quad (7)$$

We now provide a more direct derivation of the same result. This time we will start from Eq. (2) and directly evaluate  $\langle \Delta r_{ij}^2 \rangle$ . First we denote by  $\vec{r}_i^0$  and  $\vec{u}_i$  the equilibrium position of the  $i$ th mass and the instantaneous deviation from this position, respectively. It follows that the instantaneous distance separating any given pair is:  $r_{ij} \equiv \sqrt{(\vec{r}_j^0 + \vec{u}_j - \vec{r}_i^0 - \vec{u}_i)^2}$ . If the equilibrium distance between mass  $i$  and  $j$  is  $r$  it is straight forward to show that

$$\frac{T(i, j)}{N} = \frac{z\gamma}{6k_B T} \langle (r_{ij} - r)^2 \rangle = \frac{z\gamma}{6k_B T} \langle \vec{u}_j^2 + \vec{u}_i^2 - 2\vec{u}_i \cdot \vec{u}_j \rangle, \quad (8)$$

using the fact that  $\langle r_{ij} \rangle = r$ , and  $\langle \vec{u}_j \rangle = \langle \vec{u}_i \rangle = 0$ . In order to proceed we average over all the  $N_r$  pairs distanced  $r$  apart and get

$$\frac{T(r)}{N} \simeq \frac{z\gamma}{3k_B T} \left[ \frac{1}{N} \sum_{i=1}^N \langle \vec{u}_i^2 \rangle - \frac{1}{N_{r \text{ pairs}}} \sum \langle \vec{u}_i \cdot \vec{u}_j \rangle \right] \quad (9)$$

where we have further assumed that the pairs average over the first two terms in the right-hand side of Eq. (8) is well represented by the average mean-square displacement [first term in Eq. (9)]. Calculating the thermal average we may consider the contribution of each normal mode separately. We consider two limits [12,13], normal modes with frequencies  $\omega \ll \omega(r)$  result in a correlated movement (on average) of pairs separated  $r$  apart ( $\vec{u}_i \cdot \vec{u}_j \simeq \vec{u}_i^2$ ), and hence in this limit,

$$\frac{1}{N} \sum_{i=1}^N \langle \vec{u}_i^2 \rangle - \frac{1}{N_r \text{ pairs}} \sum \langle \vec{u}_i \cdot \vec{u}_j \rangle \approx 0. \quad (10)$$

Conversely, for normal modes with frequencies  $\omega \gg \omega(r)$ , the terms in the second sum add up incoherently and this term can hence be neglected. In this limit we get

$$\frac{1}{N} \sum_{i=1}^N \langle \vec{u}_i^2 \rangle - \frac{1}{N_r \text{ pairs}} \sum \langle \vec{u}_i \cdot \vec{u}_j \rangle \approx \frac{1}{N} \sum_{i=1}^N \langle \vec{u}_i^2 \rangle. \quad (11)$$

We are left with the high-frequency contribution to  $\frac{1}{N} \sum_{i=1}^N \langle \vec{u}_i^2 \rangle$  and it is reasonable to sum only over relevant modes and approximate

$$\frac{T(r)}{N} \approx \frac{z\gamma}{3k_B T} \int_{\omega(r)}^{\omega(a)} \frac{3k_B T g(\omega)}{mN \omega^2} d\omega = \frac{z}{N} \int_{l(r)}^{l(a)} \frac{g(l)}{l} dl. \quad (12)$$

Here  $g(\omega)$  denotes the density of states,  $\omega(a)$  and  $\omega(r)$  are the frequencies associated with the mean spacing between nearest neighbors  $a$  and the distance  $r$ , respectively,  $m$  is the mass of a single bead in the elastic network,  $\gamma$  is the spring constant,  $l \equiv m\omega^2/\gamma$  is a dimensionless variable, and the factor 3 appears due to the threefold degeneracy of the scalar elasticity model. In order to evaluate the integral we recall that  $\omega(r) \sim r^{-d_f/d_s}$ . On the other hand  $\omega(a)$  is the basic frequency in the system and is hence of order  $\sqrt{\gamma/m}$ ; it follows that  $l(r) = C(r/a)^{-2d_f/d_s}$  where  $C$  is a numeric constant of order unity. The scaling of the density of states  $g(l) \sim l^{d_s/2-1}$  is easily found by a change in variable when we recall that:  $g(\omega) \sim \omega^{d_s-1}$ . Preserving normalization,  $\int_{l(2R_g)}^{l(a)} g(l) dl = N$ , one gets

$$g(l) = \frac{Nd_s}{2C^{d_s/2} [1 - (2R_g/a)^{-d_f}]} l^{d_s/2-1}, \quad (13)$$

where  $R_g$  is the radius of gyration. Substituting into Eq. (12) we integrate and obtain Eq. (1) where  $\tilde{C} = \frac{zd_s}{2C[1 - (2R_g/a)^{-d_f}]}$ . We note that the expression we have obtained is clearly missing an additive constant since for a random walker traveling to a nearest neighbor ( $r=a$ ) it predicts zero MFPT.

Examining Eq. (1) more closely shows that the solution obtained via vibrational analysis complies with two basic requirements demanded from any solution of this problem: invariance under scaling and continuity with respect to the spectral dimension. Clearly if we were to take our RN and inflate/shrink it, creating an exact magnified/miniature copy of it, the MFPT between two sites will not be affected. This

is so because the MFPT is only affected by the transition probabilities between sites and by construction these were left unchanged. It follows that  $T(N, r)$  must be invariant under a scaling transformation that inflates/shrinks all lengths by a factor of  $\alpha$ ; Eq. (1) is clearly invariant under this transformation. Another thought experiment we could do is to think of a system whose spectral dimension is a tunable parameter. Examining the MFPT between two sites as we continuously vary the value of  $d_s$ , we would expect a continuous behavior of  $T(N, r)$ . Indeed, taking the limit  $d_s \rightarrow 2$  (from above/below) in Eq. (1) demonstrates the continuity of  $T(N, r)$  with respect to the spectral dimension.

In this Rapid Communication we have introduced a vibrational shortcut to the solution of the MFPT problem on fractal structures and showed how the solution is readily obtained without the use of probabilistic arguments. Effective inverse spring constant interpretation of the MFPT allowed us to obtain the desired solution via scaling arguments. Direct calculation of the thermal variance in the distance between two tagged masses provides another route to the solution. Invariance under scaling and continuity with respect to the spectral dimension were shown to be emergent properties of the solution obtained via vibrational analysis. Our result emphasizes the duality between diffusion and vibrations on fractal structures. The study of diffusion and vibrations is essential to the understanding of biological systems where fractals were shown to naturally emerge. From the 3D structure and dynamics of single proteins [14–16] through the 3D organization of chromatin in the nucleus [17,18] and up to the entire cell level [19], fractals appear time and time again. As we have demonstrated above, when studying diffusion it is sometimes much more effective to tackle the dual problem of vibrations and vice versa. Even in the case where such a transformation does not carry with it an immediate computational gain, the insights gained from considering the analogous problem may be of interest. In Ref. [16] we discuss how such a procedure sheds new light regarding the fractal-like nature of proteins. In particular we utilize the inverse spring constant interpretation of the MFPT in the analysis of conformational changes in proteins.

S.R. acknowledges support from the Converging Technologies program of the Israeli Council for higher education. R.G. and J.K. acknowledge support from the Israel Science Foundation. R.G. acknowledges the Ilse Katz Center for Meso and Nanoscale Science and Technology and the Reimund Stadler Minerva Center for Mesoscale Macromolecular Engineering.

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