Narrow-escape problem for the unit sphere: Homogenization limit, optimal arrangements of large numbers of traps, and the N^2 conjecture

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A narrow-escape problem is considered to calculate the mean first passage time (MFPT) needed for a Brownian particle to leave a unit sphere through one of its N small boundary windows (traps). A procedure is established to calculate optimal arrangements of $N \gg 1$ equal small boundary traps that minimize the asymptotic MFPT. Based on observed characteristics of such arrangements, a remarkable property is discovered, that is, the sum of squared pairwise distances between optimally arranged N traps on a unit sphere is integer, equal to N^2. It is observed for $2 \leqslant N \leqslant 1004$ with high precision. It is conjectured that this is the case for such optimal arrangements for all N. A dilute trap limit of homogenization theory when $N \to \infty$ can be used to replace the strongly heterogeneous Dirichlet-Neumann MFPT problem with a spherically symmetric Robin problem for which an exact solution is readily found. Parameters of the Robin homogenization problem are computed that capture the first four terms of the asymptotic MFPT. Close agreement of asymptotic and homogenization MFPT values is demonstrated. The homogenization approach provides a radically faster way to estimate the MFPT since it is given by a simple formula and does not involve expensive global optimization to determine locations of $N \gg 1$ boundary traps.

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I. INTRODUCTION

Narrow-escape problems, where a Brownian particle attempts to escape from a bounded domain through small absorbing windows on the boundary, arise in various contexts. In such problems, one is interested in determining the mean first passage time (MFPT), which is the expected time needed for the particle to escape from the domain starting from a given point. In particular, narrow-escape problems arise in the modeling of escape kinetics in chemistry [1], as well as in cell biology, where the motion of ions, molecules, or receptors is modeled using Brownian motion [2–5]. Such problems have recently attracted significant attention from the point of view of mathematical and numerical modeling.

For a domain with absorbing traps located on the boundary, with the rest of the boundary being reflective, it is well known that the mean first passage time for the Brownian particle starting from a given point x satisfies a time-independent boundary value problem for the Poisson equation [2]. Let $X(t)$, with $X(0) = x$, describe the path of the particle in a bounded domain $\Omega \in \mathbb{R}^d$, $d = 2,3$, where the boundary $\partial\Omega$ contains small traps centered at the points $x_j \in \partial\Omega$, $j = 1, \ldots, N$ (Fig. 1).

In such a setting, the MFPT $v(x)$ satisfies the mixed Dirichlet-Neumann problem (cf. [2])

$$\begin{aligned} &\triangle v = -\frac{1}{D}, \quad x \in \Omega; \\ &v = 0, \quad x \in \partial\Omega_a = \bigcup_{j=1}^{N} \partial\Omega_{\varepsilon_j}, \\ &\partial_n v = 0, \quad x \in \partial\Omega_r = \partial\Omega \backslash \partial\Omega_a, \end{aligned} \tag{1.1}$$

where $D = \text{const}$ is the diffusivity coefficient. An important integral characteristic of escape times from a domain with a prescribed trap arrangement is the average MFPT, given by

$$\bar{v} = \frac{1}{|\Omega|} \int_{\Omega} v(x) dx, \tag{1.2}$$

where $|\Omega|$ is the volume of Ω [in the three-dimensional (3D) setting] or its area (in two dimensions).

For two-dimensional domains, a number of asymptotic results have been derived over time. In particular, the leading term for the MFPT $v(x)$ for a two-dimensional domain with smooth boundary with one small window of length $O(\varepsilon)$ as $\varepsilon \to 0$ was derived in Refs. [2,6]. The second term for $v(x)$ for the unit disk with one and two absorbing windows on the boundary was computed in Refs. [6,7], respectively. In Ref. [8], two terms of the asymptotic expansion of the MFPT $v(x)$ were derived for an arbitrary two-dimensional domain with any number of small well-separated traps, using the method of matched asymptotic expansions. In particular, the second term of the expansion for the average MFPT $\bar{v}$ is dependent on the respective trap locations.

For an arbitrary three-dimensional bounded domain with one locally circular absorbing window of radius ε on its smooth boundary, it was shown in Ref. [9] that

$$\bar{v} \sim \frac{|\Omega|}{4\varepsilon D}\left[1 - \frac{\varepsilon}{\pi} H \log \varepsilon + O(\varepsilon)\right], \tag{1.3}$$

where H denotes the mean curvature of the domain boundary at the center of the absorbing window. In Ref. [10], this result was substantially extended for the case when Ω is a unit sphere in $\mathbb{R}^3$; in the assumption of small well-separated boundary traps, three-term asymptotic expressions for the MFPT and the average MFPT were derived through matched asymptotic expansions. The formula is valid for equal and nonequal traps, and has the general form

$$v(x) \sim \bar{v} + \sum_{j=1}^{N} k_j \, G(x; x_j) + O(\varepsilon \log \varepsilon), \tag{1.4}$$

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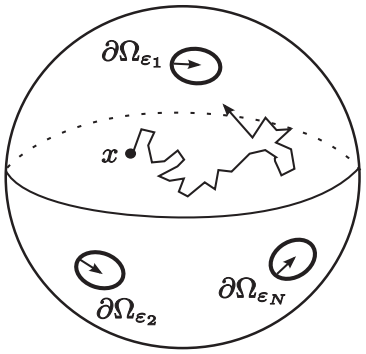


FIG. 1. Schematic of the narrow-escape problem in a 3D domain.

where k_j for $j = 1, \ldots, N$ are certain constants, and $G(x; x_j)$ is the Neumann Green's function for the spherical domain Ω with a singularity at $x_j \in \partial\Omega$. Importantly, the third term in the formula for $\bar{v}$, i.e., the *trap interaction energy*, depends on mutual locations of the boundary traps, which allows for a global optimization of the average MFPT through the computation of optimal arrangements of trap positions on the boundary of the unit sphere. (This result is discussed in Sec. II below.) In a recent paper [11], the results of [10] have been justified rigorously.

The computation of globally optimal arrangements of N point particles on the surface of a smooth domain, which repel to minimize a certain interaction energy, is a complicated problem that has recently attracted attention (e.g., [12–14]). Putative optimal configurations of $4 \leqslant N \leqslant 282$ particles have been computed in Ref. [15] for the Coulombic interaction potential.

The minimization of the average escape time $\bar{v}$ with respect to positions of N small equal traps on a unit sphere involves the global optimization of the trap interaction energy function, which contains Coulombic and logarithmic terms. Such globally optimal arrangements were computed numerically in Ref. [10] for $N \leqslant 65$ using global optimization software packages; these arrangements were compared with optimal arrangements for purely Coulombic and purely logarithmic pairwise trap interactions up to $N \leqslant 20$. Moreover, an asymptotic scaling law for the trap interaction energy for $N \gg 1$ was derived. In Ref. [16], optimal arrangements of configurations containing traps of two kinds were computed.

In Ref. [16], a numerical solution of (1.1) was compared to the asymptotic formula (1.4), and the corresponding formula for the average MFPT $\bar{v}$. It was shown for circular, rectangular, and spherical domains that the asymptotic formulas closely match the numerical results even when the traps are relatively large or close to each other.

The "brute force" approach to numerically find optimal spherical trap arrangements involves numerical global optimization of the trap interaction energy function in $(2N-3)$-dimensional space. Even the fastest available software can take a very long time (weeks to months) to compute a trap arrangement for N over one hundred. Results obtained using LIPSCHITZ-CONTINUOUS GLOBAL OPTIMIZER (LGO) software for $N \leqslant 200$ are listed in Sec. IV of this paper.

In Secs. III and IV, we develop a heuristic algorithm to find the optimal arrangement of $N + k$ traps from a known optimal arrangement of N traps. It is motivated by the concept of the topological derivative introduced in Ref. [17]. In Sec. III, we derive a change in the total trap interaction energy due to an addition of one trap to a given N-trap spherical configuration ("Principal result 1"). This result is used in the algorithm of Sec. IV, where additional traps are introduced at minima of the topological derivative of the trap interaction energy. The trap configuration is subsequently evolved via a dynamical system driven by forces that are gradients of the trap interaction energy function. Using the proposed method, putative optimal locations of $N \leqslant 1004$ traps are computed.

In order to verify the validity of the putative optimal spherical trap arrangements obtained in Sec. IV, two approaches are used. First, the computed minimal interaction energy values are compared with an asymptotic scaling law of [10], and demonstrate close agreement. Second, the putative optimal trap arrangements were tested against the N^2 *conjecture* (Sec. IV C). This remarkable property was initially found for the known optimal trap arrangements for $N \leqslant 200$; it says that the sum of pairwise squared distances between optimally located traps is equal to N^2.

In Sec. V, the dilute trap fraction limit of homogenization theory is considered for the unit sphere. A similar approach has been used in Ref. [18] for a unit disk. The homogenization theory framework provides a simplified approximate description of the MFPT problem (1.1) for the unit sphere in the case of $N \gg 1$ small boundary traps. In the homogenized problem, the strongly heterogeneous boundary conditions of (1.1) are replaced with Robin boundary conditions. The "Principal result 2" of Sec. V contains asymptotic expressions for the Robin boundary condition; it is obtained using the asymptotic average MFPT formula of [10]. The resulting Robin problem for the sphere is solved analytically. For a sample optimal arrangement of $N = 802$ traps, a good agreement is demonstrated between the asymptotic and the homogenization MFPT values throughout the sphere, except for, as expected, the neighborhoods of the actual boundary traps.

Finally, Sec. VI contains conclusions and discusses open problems.

II. ASYMPTOTIC EXPRESSIONS FOR THE MFPT AND THE AVERAGE MFPT

Consider a unit sphere with N nonequal small well-separated circular boundary traps of radii εa_j, $j = 1, \ldots, N$, $\varepsilon \ll 1$, centered at points $x_j \in \partial\Omega$, $|x_j| = 1$. In Ref. [10], an asymptotic solution to the problem (1.1) in the limit $\varepsilon \to 0$ was derived using the method of matched asymptotic expansions. It has the general form

$$v(x) = \bar{v} - \frac{|\Omega|}{DN\bar{c}} \sum_{j=1}^{N} c_j G_s(x; x_j) + O(\varepsilon \log \varepsilon). \quad (2.1)$$

In Eq. (2.1), $|\Omega| = 4\pi/3$ is the volume of the spherical domain, $c_j = 2a_j/\pi$ are constant trap capacitances, $\bar{c} = N^{-1}(c_1 + \cdots + c_N)$ is the average capacitance, and $G(x; x_j)$ is the Neumann Green's function for the domain Ω with a singularity at $x_j \in \partial\Omega$. The Green's function $G(x; \xi)$ is the

unique solution to the problem

$$\begin{aligned} \triangle G &= \frac{1}{|\Omega|}, \quad x \in \Omega; \quad \partial_n G = 0, \\ x &\in \partial\Omega\backslash\{\xi\}; \quad \int_\Omega G dx = 0, \end{aligned} \tag{2.2}$$

with the prescribed singularity behavior

$$G(x;\xi) = \frac{1}{2\pi\,|x-\xi|} + R(x;\xi) \tag{2.3}$$

and the regular part $R(x;\xi)$. For the unit sphere, $G(x;\xi)$ has a closed form given by

$$\begin{aligned} G(x;\xi) = &\frac{1}{2\pi\,|x-\xi|} + \frac{1}{8\pi}(|x|^2+1) \\ &+ \frac{1}{4\pi}\log\left(\frac{2}{1-|x|\cos\gamma+|x-\xi|}\right) - \frac{7}{10\pi}, \end{aligned} \tag{2.4}$$

where γ is the angle between the vectors $\boldsymbol{x} \in \Omega$ and $\boldsymbol{\xi} \in \partial\Omega$, defined by $|x|\cos\gamma = \boldsymbol{x}\cdot\boldsymbol{\xi}$ with $|\xi| = 1$.

A three-term asymptotic formula for the average MFPT $\bar{v}$ (1.2) for the sphere has also been derived in Ref. [10]. It contains terms of the order of $O(\varepsilon^{-1})$, $O[\log(\varepsilon)]$, and $O(1)$, and is given by

$$\begin{aligned} \bar{v} = \frac{|\Omega|}{2\pi\varepsilon D N\bar{c}}\Bigg[1 + \varepsilon\log\left(\frac{2}{\varepsilon}\right)\frac{\sum_{j=1}^N c_j^2}{2N\bar{c}} + \frac{2\pi\varepsilon}{N\bar{c}}\,p_c(x_1,\ldots,x_N) \\ - \frac{\varepsilon}{N\bar{c}}\sum_{j=1}^N c_j\kappa_j + O(\varepsilon^2\log\varepsilon)\Bigg], \end{aligned} \tag{2.5}$$

where

$$\kappa_j = \frac{c_j}{2}\left[2\log 2 - \frac{3}{2} + \log a_j\right] = \text{const.}$$

The quantity

$$p_c(x_1,\ldots,x_N) \equiv \mathcal{C}^T\mathcal{G}\mathcal{C}$$

is given in terms of the capacitance vector $\mathcal{C} = (c_1,\ldots,c_N)^T$ and the Green's function matrix defined in terms of $G(x_i;x_j)$ by

$$\begin{aligned} \mathcal{G} &\equiv \begin{pmatrix} R & G_{12} & \cdots & G_{1N} \\ G_{21} & R & \cdots & G_{2N} \\ \vdots & \vdots & \ddots & \vdots \\ G_{N1} & \cdots & G_{N,N-1} & R \end{pmatrix}, \\ R &= -\frac{9}{20\pi}, \quad G_{ij} \equiv G(x_i;x_j). \end{aligned} \tag{2.6}$$

The two leading terms of the average MFPT $\bar{v}$ (2.5) depend only on trap sizes; the third term includes the information about the mutual trap arrangement on the sphere, through the "*interaction energy*" $p_c(x_1,\ldots,x_N)$. Thus the minimization of the average MFPT for a given set of trap sizes is equivalent to finding an *optimal trap arrangement* that minimizes the interaction energy.

In Ref. [10], it has also been shown that the optimal trap arrangement that minimizes the average MFPT $\bar{v}$ simultaneously maximizes the asymptotic expression of the principal eigenvalue of the Laplacian. The physical meaning of this is, for example, the maximization of heat escape or diffusion rate out of the domain Ω by arranging the "windows" on an otherwise reflecting boundary in the optimal way.

In the current paper, we restrict to a particularly important case of N equal traps of radius ε (all $a_j = 1$). For this case, the formula (2.5) reduces to

$$\begin{aligned} \bar{v} = \frac{|\Omega|}{4\varepsilon DN}\Bigg\{1 + \frac{\varepsilon}{\pi}\log\left(\frac{2}{\varepsilon}\right) + \frac{\varepsilon}{\pi}\Bigg[-\frac{9N}{5} + 2(N-2)\log 2 \\ + \frac{3}{2} + \frac{4}{N}\mathcal{H}(x_1,\ldots,x_N)\Bigg] + O(\varepsilon^2\log\varepsilon)\Bigg\}, \end{aligned} \tag{2.7}$$

where the interaction energy $\mathcal{H}(x_1,\ldots,x_N)$ is defined by

$$\begin{aligned} \mathcal{H}(x_1,\ldots,x_N) = \sum_{i=1}^N\sum_{j=i+1}^N\Bigg[\frac{1}{|x_i-x_j|} - \frac{1}{2}\log|x_i-x_j| \\ - \frac{1}{2}\log(2+|x_i-x_j|)\Bigg]. \end{aligned} \tag{2.8}$$

The interaction energy (2.8) is the sum of pairwise interaction energies between particles (traps) located on the sphere; it consists of a sum of the classical Coulombic and logarithmic energy terms and an additional logarithmic term.

In a setting with a large number of equal traps, assuming that the traps are spread "homogeneously" throughout the sphere, one may derive a scaling law for $\mathcal{H} = \mathcal{H}(N)$ as $N \to +\infty$. The leading terms of the scaling law are given by [10]

$$\begin{aligned} \mathcal{H} \approx \mathcal{F}(N) = \frac{N^2}{2}(1-\log 2) + b_1 N^{3/2} + b_2 N\log N + b_3 N \\ + b_4\sqrt{N} + b_5\log N + b_6 + o(1), \end{aligned} \tag{2.9a}$$

where

$$\begin{aligned} &b_1 = -\tfrac{1}{2}, \quad b_2 = -\tfrac{1}{8}, \quad b_3 = \tfrac{1}{2}\left(\log 2 - \tfrac{1}{4}\right), \\ &b_4 = \tfrac{1}{4}, \quad b_5 = \tfrac{1}{24}, \quad b_6 = -\tfrac{1}{16} - \tfrac{1}{6}\log 2. \end{aligned} \tag{2.9b}$$

The derivation of (2.9), somewhat more general than in Ref. [10], is given in the Appendix.

In Sec. IV below, we numerically compute putative optimal trap arrangements that minimize the average MFPT $\bar{v}$ (2.7).

Subsequently, in Sec. V, formulas (2.7) and (2.8) are used to estimate the leading-order terms in the boundary conditions of a Robin problem describing a dilute trap fraction limit of the homogenization theory for the unit sphere.

III. THE CHANGE IN THE AVERAGE MFPT FOR THE SPHERE AT AN ADDITION OF A SINGLE TRAP

Consider a prescribed configuration of N equal traps located on the boundary of the unit sphere at the points $x_j \in \partial\Omega$, $j = 1,\ldots,N$. Let the MFPT $v(x)$ be the solution of the corresponding problem (1.1), and $\bar{v} = \bar{v}(x_1,\ldots,x_N)$ be the corresponding asymptotic average MFPT given by (1.2). We now analyze the change in the asymptotic average MFPT $\bar{v}$ when a trap is added to the existing configuration.

A. Addition of an infinitesimal trap: The topological derivative

In the spirit of [17], define the *topological derivative* of $\bar{v}$,

$$\mathcal{T}(x^*) = \lim_{\alpha\to 0} \frac{\bar{v}(x_1,\ldots,x_N,x^*) - \bar{v}(x_1,\ldots,x_N)}{\alpha}, \quad (3.1)$$

as the rate of change of $\bar{v}$ with respect to the size of the $(N+1)$st trap of radius $\alpha\varepsilon$, located at the point x^* on the unit sphere, computed at $\alpha = 0$. The leading terms of the topological derivative can be calculated directly from the expression (2.5); the computation yields

$$\mathcal{T}(x^*) \sim \frac{\pi}{3D\varepsilon N^2}\left[-1+\frac{\varepsilon}{\pi}\left(-1+4\log 2-2\log\frac{2}{\varepsilon}\right)\right.$$
$$\left.-\frac{8\varepsilon}{\pi}\sum_{i,j=1}^{N} G_{ij} + 8\varepsilon\sum_{i=1}^{N} G(x_i,x^*)\right]. \quad (3.2)$$

It follows that it is optimal to introduce an additional infinitesimally small trap at the point x^* that minimizes $\mathcal{T}(x^*)$, i.e., leads to the largest relative decrease of the average MFPT $\bar{v}$ (3.1).

It is only the last term in Eq. (3.2) that depends on the position x^* of the new trap; the topological derivative is thus minimized through minimization of the interaction term $\sum_{i=1}^{N} G(x_i,x^*)$ or, equivalently, the quantity

$$\mathcal{M}(x^*) = \sum_{i=1}^{N}\left[\frac{1}{|x_i-x^*|} - \frac{1}{2}\log|x_i-x^*|\right.$$
$$\left.-\frac{1}{2}\log(2+|x_i-x^*|)\right]. \quad (3.3)$$

The optimal location x^* of an additional infinitesimal trap thus is the global minimum of the function (3.3) that depends on two spherical coordinates.

B. Addition of a trap of an arbitrary size comparable to existing traps

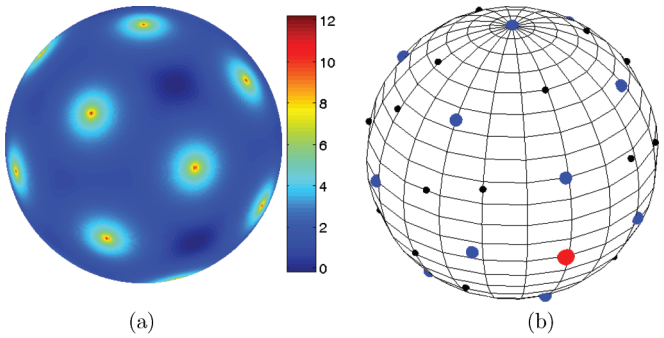
The above calculation can be generalized to treat the addition of a trap of arbitrary radius $\alpha\varepsilon$ (comparable to given traps, so that asymptotic formulas remain valid). The following statement holds.

Principal result 1. Consider a prescribed configuration of N equal traps of radii ε located on the unit sphere at the points $x_j \in \partial\Omega$, $j = 1,\ldots,N$. Consider an additional trap of radius $\alpha\varepsilon$, located at $x^* \in \partial\Omega$, $x^* \neq x_j$, $j = 1,\ldots,N$. The difference between the asymptotic average MFPT values $\bar{v}_{N+1}(x_1,\ldots,x_N,x^*)$ for the $N+1$-trap configuration and $\bar{v}_N(x_1,\ldots,x_N)$ for the N-trap configuration is given by

$$\Delta v(x^*) \equiv \bar{v}_{N+1}(x_1,\ldots,x_N,x^*) - \bar{v}_N(x_1,\ldots,x_N)$$
$$\sim \frac{8\pi}{DN}\left\{\frac{1}{3}\frac{\alpha}{N} - 2\left(\frac{\alpha}{N}\right)^2 + \left(\frac{\alpha}{N}\right)^3\right.$$
$$\left.-\frac{4}{3}\left(\frac{\alpha}{N}\right)^4 + O\left[\left(\frac{\alpha}{N}\right)^5\right]\right\}\mathcal{M}(x^*) + \mathcal{K}, \quad (3.4)$$

where $\mathcal{M}(x^*)$ is given by (3.3), and the quantity $\mathcal{K}$ does not depend on the location x^* of the additional trap.

Formula (3.4) is derived directly using the expression (2.5). Depending on the sign of the square bracket in Eq. (3.4), the optimal location x^* of the additional trap is either a global minimum or a global maximum of $\mathcal{M}(x^*)$ (3.3).



(a) (b)

FIG. 2. (Color online) The topological derivative for an optimal arrangement of 17 equal traps on a unit sphere. (a) The value of $\log[\mathcal{M}(x^*)]$ (3.3) on the surface of the unit sphere. The darker (dark blue) color corresponds to low values of $\mathcal{M}(x^*)$ [equivalently, of the topological derivative $\mathcal{T}(x^*)$ (3.2) and the function $\Delta v(x^*)$ (3.4)]. Red and lighter colors correspond to higher values of $\log[\mathcal{M}(x^*)]$ that occur close to existing traps. (b) The 17 optimally arranged traps (medium-sized blue markers), the local minima of the function $\mathcal{M}(x^*)$ (3.3) (small black markers), and the global minimum of $\mathcal{M}(x^*)$ (large red marker).

In subsequent sections, we consider the question of finding optimal arrangements of large numbers of equal traps. Formula (3.4) will be used to seek putative optimal configurations of $N+k$ traps starting from a known putative optimal N-trap configuration. When $\alpha = 1$, $k = 1$, and $N \gg 1$, the bracketed expression in Eq. (3.4) is positive, hence the optimal location x^* of one new trap will correspond to the global minimum of the function (3.3) on the surface of the unit sphere.

An illustration showing local minima and the global minimum of the function $\mathcal{M}(x^*)$ for a unit sphere with 17 optimally arranged traps is given in Fig. 2. (The optimal arrangement has been computed in Ref. [10].)

IV. COMPUTATION OF OPTIMAL ARRANGEMENTS OF LARGE NUMBERS OF TRAPS ON A SPHERE

A. The global optimization problem

The general problem of finding a global minimum of a function

$$F(x_1,\ldots,x_N) = \sum_{i=1}^{N}\sum_{j=i+1}^{N} f(|x_i-x_j|),$$
$$|x_k| = 1, \quad k = 1,\ldots,N, \quad (4.1)$$

that depends only on distances between pairs of N traps on the unit sphere has recently received a lot of attention on its own. For some particular dimensions and number of traps, there exist universally optimal configurations that minimize (4.1) for some class of functions f [19]. For example, an icosahedron on $S^2 \in \mathbb{R}^3$ is universally optimal. However, generally, for a given N, a universally optimal configuration on $S^2 \in \mathbb{R}^3$ may not exist. This is proven to be the case, for example, for five points on S^2 (see [19]). Hence, in general, computations have to be done separately for every specific form of the pairwise interaction function f.

A number of putative global energy minimizing configurations for the Coulomb potential $f = |x_i - x_j|^{-1}$ and the logarithmic potential $f = \log|x_i - x_j|$ have been computed in Refs. [12,15]. In a similar fashion, global minima of the average MFPT $\bar{v}$ obtained as global minima of the interaction energy $\mathcal{H}(x_1,\ldots,x_N)$ (2.8) for $2 \leqslant N \leqslant 65$ were computed in Ref. [10]. We now attempt to compute trap configurations corresponding to global minima of the energy $\mathcal{H}(x_1,\ldots,x_N)$ (2.8) for $N \lesssim 1000$. We refer to such configurations as *optimal arrangements*.

B. The numerical global optimization problem

On a unit sphere, location x_j of every trap is defined by spherical coordinates (θ_j,ϕ_j), where θ_j is the azimuthal angle and ϕ_j is the polar angle. To eliminate the effect of the rotational symmetries of the sphere, we fix the first trap x_1 at the north pole, i.e., $(\theta_1,\phi_1) = (0,0)$, and we let $\phi_2 = 0$ for the second trap centered at x_2. Then, for N traps on the unit sphere, the global optimization problem involves $2N-3$ parameters in the range $0 < \theta_j \leqslant \pi$ for $j = 2,\ldots,N$, and $0 \leqslant \phi_j < 2\pi$ for $j = 3,\ldots,N$.

Various numerical methods for global optimization are available (cf. [20–22]), including methods for nonsmooth optimization and optimization with constraints. A number of commercial and public domain implementations exist for various platforms and programming environments. Software designed for higher-dimensional problems normally uses heuristic strategies. The majority of free packages tested by the authors could not be used for efficient computations with 50 and more degrees of freedom. Some details are now provided for optimization software used in the current work.

LIPSCHITZ-CONTINUOUS GLOBAL OPTIMIZER (*LGO*). This is a commercial global optimization software program available for a number of software and hardware platforms, including C++ and MATLAB. The software is based on a combination of rigorous (theoretically convergent) global minimization strategies and a number of local minimization strategies [20]. To date, there exists no parallelized version of LGO software.

GLOBAL AND NONSMOOTH OPTIMIZATION TOOLBOX (*GANSO*). The GANSO software package for MAPLE [23] includes a number of routines for global and local optimization. At each step, global optimization routines normally execute several local optimization steps. The extended cutting angle method (ECAM) within the GANSO software package uses a deterministic global optimization technique and is applicable to Lipschitz-continuous functions. Within the algorithm, a sequence of piecewise linear lower approximations to the objective function is constructed. The sequence of the corresponding solutions to these relaxed problems converges to the global minimum of the objective function [24]. A different method provided within the GANSO package is the dynamical systems based optimization method (DSO), in which a dynamical system is constructed, using a number of sampled values of the objective function to introduce "forces." The corresponding evolution leads to lower values of the objective function; the sampling continues until a stationary point is reached [25]. The GANSO code is also nonparallelized.

For computations of optimal trap arrangements, it was realistic to use GANSO software for numbers of traps $N \leqslant 20$, and LGO software for $N \leqslant 200$, after which each computation took more than a week to complete.

C. A heuristic algorithm to find the optimal arrangement of $N + k$ traps from the optimal arrangement of N traps

It has been observed that for large N, there exist a large number of locally optimal N-trap arrangements whose relative energy difference from the globally optimal arrangement is small, and quickly decreases as N becomes larger.

A second important observation that was made for optimal arrangements of $2 \leqslant N \leqslant 65$ traps computed in Ref. [10] is now formulated as a conjecture.

The N^2 conjecture. For an optimal arrangement of $N \geqslant 2$ traps that minimizes the interaction energy $\mathcal{H}$ (2.8) and the asymptotic average MFPT $\bar{v}$ (2.7), the sum of squares of pairwise distances between traps is equal to N^2:

$$\mathcal{Q}(x_1,\ldots,x_N) \equiv \sum_{i=1}^{N}\sum_{j=i+1}^{N} |x_i - x_j|^2 = N^2. \qquad (4.2)$$

The following arguments can be used to support the conjecture:

(1) It is easy to show that the conjecture holds for $N = 2$ (two traps in poles), $N = 3$ (traps in vertices of an equilateral triangle on an equator), and $N = 4$ (traps in vertices of a tetrahedron).

(2) For $5 \leqslant N \leqslant 200$, as shown in Table I in Sec. IV D, the conjecture is numerically supported for up to 10 significant digits.

(3) The conjecture is supported by an asymptotic scaling law estimate of $\mathcal{Q}(x_1,\ldots,x_N)$ as $N \to \infty$, performed in Sec. A 2 of the Appendix.

We remark that the numerical global maximization of $\mathcal{Q}(x_1,\ldots,x_N)$ (4.2) performed for $N \lesssim 30$ spherical traps indicated that, indeed, $\max \mathcal{Q}(x_1,\ldots,x_N) = N^2$; however, the trap arrangement that maximizes $\mathcal{Q}$ is not unique. In particular, N traps placed on the equator (unit circle) in the vertices of a regular polygon also yield $\mathcal{Q} = N^2$. It has also been observed that the values of $\mathcal{Q}$ are noticeably below N^2 for arrangements close to the arrangement minimizing the MFPT $\bar{v}$ (i.e., when one or more traps are slightly displaced from the optimal positions).

We now outline an algorithm to seek putative globally optimal trap arrangements of $N \gg 1$ traps, which is based on introducing additional traps in "optimal" locations (Sec. III), and a subsequent local optimization.

1. A local optimization method

Consider a nonoptimal arrangement of $N \gg 1$ traps on the surface of the unit sphere, which is close to a globally optimal arrangement. Representing the N traps as moving particles, a dynamical system approach can be used, where the interaction energy minimum corresponds to an equilibrium state. Since the problem consists of minimizing the total interaction energy $\mathcal{H}$ (2.8), one may compute the force exerted on the ith trap by all

TABLE I. Values of the interaction energy $\mathcal{H}$ (2.8) and sums of squared distances between traps $\mathcal{Q}$ (4.2) for putative globally optimal arrangements of N equal traps on a unit sphere surface. The optimal arrangements were computed with using the LGO global optimization package for $2 \leqslant N \leqslant 90$, and a combination of the LGO package and the local optimization technique (see Sec. IV C1) for $95 \leqslant N \leqslant 200$. Numbers are given with eight significant digits for $\mathcal{H}$, and 10 significant digits for $\mathcal{Q}$. The LGO computations were performed by Spiteri and Richards [27].

N	$\mathcal{H}$	$\mathcal{Q}$	N	$\mathcal{H}$	$\mathcal{Q}$	N	$\mathcal{H}$	$\mathcal{Q}$
2	−0.53972077	4.000000000	33	54.295972	1089.000000	64	324.08963	4096.000000
3	−1.0673453	9.000000000	34	59.379488	1156.000000	65	336.76971	4225.000000
4	−1.6671799	16.00000000	35	64.736711	1225.000000	70	403.83089	4900.000000
5	−2.0879876	25.00000000	36	70.276097	1296.000000	75	477.36359	5625.000000
6	−2.5810055	36.00000000	37	76.066237	1369.000000	80	557.23154	6400.000000
7	−2.7636584	49.00000000	38	82.080300	1444.000000	85	643.77234	7225.000000
8	−2.9495765	64.00000000	39	88.329560	1521.000000	90	736.65320	8100.000000
9	−2.9764336	81.00000000	40	94.817831	1600.000000	95	836.12537	9025.000000
10	−2.8357352	100.0000000	41	101.56854	1681.000000	100	942.12865	10000.00000
11	−2.4567341	120.9999505	42	108.54028	1764.000000	105	1054.8688	11025.00000
12	−2.1612842	144.0000000	43	115.77028	1849.000000	110	1174.1103	12100.00000
13	−1.3678269	168.9999763	44	123.16343	1936.000000	115	1300.1081	13225.00000
14	−0.55259278	196.0000000	45	130.90532	2025.000000	120	1432.6666	14400.00000
15	0.47743760	225.0000000	46	138.92047	2116.000000	125	1572.0271	15625.00000
16	1.6784049	256.0000000	47	147.15035	2209.000000	130	1718.0039	16900.00000
17	3.0751594	289.0000000	48	155.41742	2304.000000	135	1870.6706	18225.00000
18	4.6651247	324.0000000	49	164.21746	2401.000000	140	2030.3338	19600.00000
19	6.5461714	361.0000000	50	173.07868	2500.000000	145	2196.5017	21025.00000
20	8.4817896	400.0000000	51	182.26664	2601.000000	150	2369.6548	22500.00000
21	10.701320	441.0000000	52	191.72428	2704.000000	155	2549.6182	24025.00000
22	13.101742	484.0000000	53	201.38475	2809.000000	160	2736.2180	25600.00000
23	15.821282	529.0000000	54	211.28349	2916.000000	165	2929.8023	27225.00000
24	18.581981	576.0000000	55	221.46381	3025.000000	170	3130.1596	28900.00000
25	21.724913	625.0000000	56	231.85398	3136.000000	175	3337.4168	30625.00000
26	25.010031	676.0000000	57	242.51803	3249.000000	180	3551.5021	32400.00000
27	28.429699	729.0000000	58	253.43460	3364.000000	185	3772.5761	34225.00000
28	32.192933	784.0000000	59	264.57186	3481.000000	190	4000.3892	36100.00000
29	36.219783	841.0000000	60	275.90942	3600.000000	195	4235.2645	38025.00000
30	40.354439	900.0000000	61	287.62114	3721.000000	200	4477.0669	40000.00000
31	44.757617	961.0000000	62	299.48031	3844.000000			
32	49.240949	1024.000000	63	311.65585	3969.000000			

other traps as

$$\mathbf{F}_i = -\nabla_i \mathcal{H} = \sum_{j \neq i} \left[\frac{1}{|x_i - x_j|^2} + \frac{1}{2|x_i - x_j|} + \frac{1}{2(2 + |x_i - x_j|)} \right] \mathbf{e}_{ji}, \tag{4.3}$$

where $\mathbf{e}_{ji}$ is a unit vector from trap j to trap i. The algorithm consists of moving each trap in the direction of the force, and proceeds as follows:

(1) Compute the total force (4.3) acting on each trap.

(2) Move each particle a small distance proportional to the force in that direction. The proportionality constant is a user specified parameter.

(3) Project the position of each particle back onto the surface of the unit sphere.

After a number of iterations (in our computations, 500), the tangential components of the force acting on each particle are computed, and if the sum of the absolute values of these is less than a user specified tolerance level, the program is stopped.

2. *An algorithm to compute a putative globally optimal arrangement of $N + k$ traps*

Suppose that the globally optimal N-trap arrangement that minimizes the interaction energy (2.8) is known. We wish to introduce k additional traps and compute the corresponding putative globally optimal arrangement of $N + k$ traps. The procedure used in the current paper can be outlined as follows:

(1) For the current N-trap configuration, compute all local minima of the function $\mathcal{M}(x^*)$ (3.3) on the surface of the unit sphere. [These local minima are computed by numerically solving the equation $\operatorname{grad} \mathcal{M}(x^*) = 0$ in the vicinity of a center of each triangle formed by three adjacent traps in the given N-trap arrangement.]

(2) Order the local minima of $\mathcal{M}(x^*)$ starting from the lowest; refer to these points as $x_{m1}, x_{m2}, \ldots$.

(3) Introduce additional k traps at the k smallest local minima $x_{m1}, x_{m2}, \ldots, x_{mk}$ of $\mathcal{M}(x^*)$.

(4) Run the local optimization routine described in Sec. IV C1 to adjust positions of all the $N + k$ equal traps

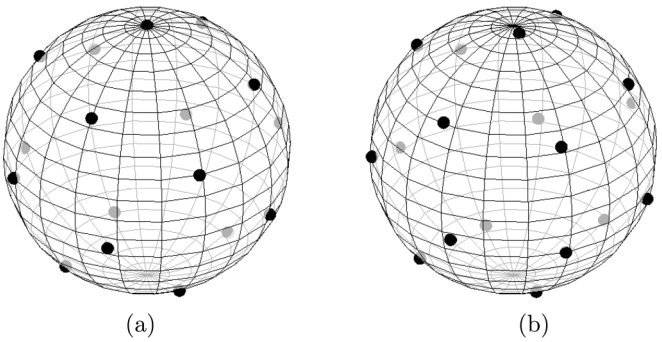


FIG. 3. The application of the global optimization algorithm of Sec. IV C2 to the (a) optimal arrangement of 17 equal traps on a unit sphere to obtain a (b) putative optimal arrangement of 18 traps. The latter coincides with the globally optimal 18-trap arrangement [10].

to a configuration that minimizes the trap interaction energy (2.8), and thus maximizes the average MFPT.

(5) Test the N^2 conjecture (4.2).

The algorithm, in fact, seeks local optimal $(N+k)$-trap arrangements; however, at large N, the differences between energy values at such local minima and the global energy minimum quickly decrease. Hence, we refer to the results as putative globally optimal configurations.

Though originally designed for $N \gg 1$, $k \gg 1$, the above algorithm can be used for smaller values of N and k. As an example, taking $N = 17$, $k = 1$ produces a putative optimal 18-trap arrangement from the known optimal 17-trap arrangement. The corresponding color diagram of $\mathcal{M}(x^*)$ and its global minimum for the 17-trap arrangement are shown in Fig. 2. The initial 17-trap and the resulting 18-trap arrangements are given in Fig. 3. It is straightforward to verify that the thus obtained 18-trap arrangement coincides, up to a rotation, with the globally optimal 18-trap arrangement computed in Ref. [10].

For the global configurations that were obtained using the above method in the following sections, the N^2 conjecture has been tested and holds within 10 significant digits or more. This is used as an indication of the proximity of each putative global minimum of the average MFPT to the actual global minimum. It should be noted that the "conditioning number" for such a test is, in fact, unknown, i.e., it remains an open question whether a small difference between the sum of squared distances and N^2 indeed corresponds to a small difference between a given and a globally optimal trap arrangement. However, the authors believe that such a conditioning number is not extremely large. In particular, we have observed that the sum of squared distances between traps before Step 4 in the above algorithm is several percent below N^2.

D. Putative globally optimal arrangements of $N \leqslant 200$ traps

To compute globally optimal trap configurations for $3 \leqslant N \leqslant 200$ traps, the LGO software was used. The values of the corresponding energy minima are given in Table I. For $3 \leqslant N \leqslant 20$, these minimum values were verified using the GANSO software package for MAPLE [23], where two different global optimization routines (ECAM and DSO) returned the same results.

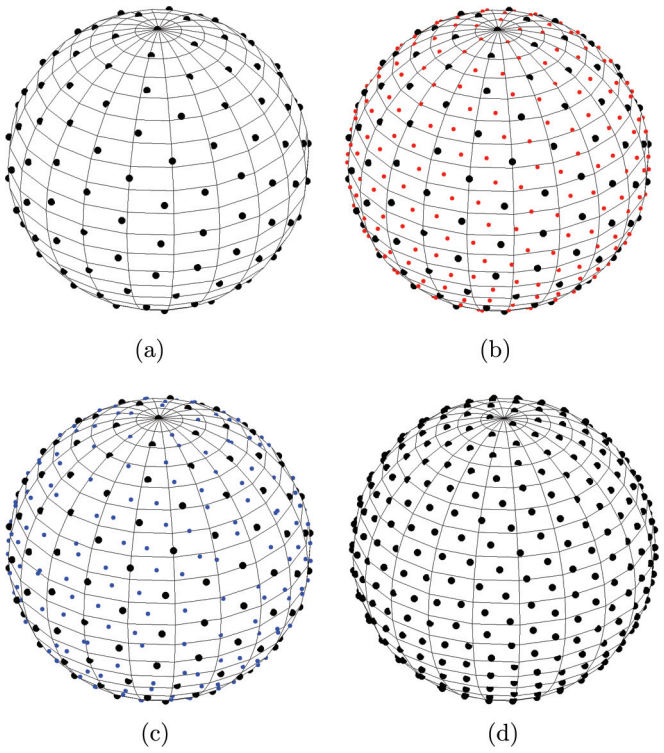


FIG. 4. (Color online) An illustration of the algorithm to compute putative optimal arrangements of $N+k$ traps starting from an N-trap arrangement (Sec. IV C2). (a) A putative optimal 160-trap arrangement. (b) Same as (a), with centers of triangle formed by triples of adjacent traps shown with small red markers. (c) Same as (a), with local minima of the function $\mathcal{M}(x^*)$ (3.3) shown with small blue markers. (d) The new 436-trap arrangement obtained by introducing additional traps at all local minima of $\mathcal{M}(x^*)$ and subsequent local optimization (Sec. IV C2, Step 4).

After the execution of global LGO optimization, the local optimization algorithm (Sec. IV C1) was applied. For some cases within the range $95 \leqslant N \leqslant 200$, it yielded lower energy minima in the sixth significant digit.

E. Putative globally optimal arrangements of $200 < N \leqslant 1004$ traps

For $N > 200$ traps, the algorithm described in Sec. IV C2 was used. For each of the previously known optimal arrangements with $N \leqslant 200$, $k = K$ traps were added, where K is the number of local minima of the function $\mathcal{M}(x^*)$ (3.3) for each corresponding arrangement. Then the procedure was repeated on the new putative optimal arrangements.

An example of the algorithm application to a putative optimal 160-trap arrangement to obtain a putative optimal 436-trap arrangement is given in Fig. 4.

The resulting set of energies and sums of squared distances for the new putative optimal arrangements up to $N = 1004$ is presented in Table II. The data supports the N^2 conjecture in each case within at least 10 significant digits.

In Fig. 5, the numerical data of Tables I and II for the interaction energies $\mathcal{H}$ (2.8) of the putative optimal arrangements of traps is presented in comparison with the asymptotic scaling law (2.9a) and (2.9b). The curves demonstrate a close agreement.

TABLE II. Values of the interaction energy $\mathcal{H}$ (2.8) and sums of squared distances between traps $\mathcal{Q}$ (4.2) for globally optimal arrangements of N equal traps on a unit sphere surface, $200 \leqslant N \leqslant 1004$, computed using the algorithm of Sec. IV C2. Numbers are given with eight significant digits for $\mathcal{H}$ and 10 significant digits for $\mathcal{Q}$.

N	$\mathcal{H}$	$\mathcal{Q}$	N	$\mathcal{H}$	$\mathcal{Q}$	N	$\mathcal{H}$	$\mathcal{Q}$
206	4776.8410	42436.00000	406	20535.947	164836.0000	650	55251.870	422500.0000
219	5459.4441	47961.00000	413	21292.863	170569.0000	697	63918.659	485809.0000
248	7151.7851	61504.00000	424	22511.130	179776.0000	704	65263.714	495616.0000
253	7466.6853	64009.00000	436	23879.932	190096.0000	764	77386.805	583696.0000
260	7920.1793	67600.00000	437	23996.280	190969.0000	778	80361.722	605284.0000
268	8455.6701	71824.00000	442	24579.608	195364.0000	781	81008.459	609961.0000
272	8729.6105	73984.00000	449	25409.395	201601.0000	802	85602.707	643204.0000
291	10094.183	84681.00000	462	26987.790	213444.0000	850	96587.973	722500.0000
308	11401.557	94864.00000	480	29251.492	230400.0000	868	100878.53	753424.0000
310	11560.554	96100.00000	529	35888.599	279841.0000	891	106503.70	793881.0000
333	13471.931	110889.0000	536	36896.959	287296.0000	922	114327.22	850084.0000
337	13819.916	113569.0000	546	38354.222	298116.0000	928	115873.47	861184.0000
368	16669.611	135424.0000	548	38648.578	300304.0000	992	133031.24	984064.0000
369	16766.235	136161.0000	577	43063.555	332929.0000	1004	136383.69	1008016.000
380	17846.466	144400.0000	618	49718.287	381924.0000			
382	18045.887	145924.0000	636	52794.233	404496.0000			

V. DILUTE TRAP FRACTION LIMIT OF HOMOGENIZATION THEORY FOR THE UNIT SPHERE

The homogenization theory approach is now used to provide a simplified approximate description of the MFPT problem (1.1) for the unit sphere in the case of a large number of small boundary traps, distributed "homogeneously" over the sphere and known to occupy a certain given surface area fraction.

A. Homogenization theory for the unit disk and the unit sphere

For a two-dimensional version of the narrow-escape problem (1.1) formulated for a unit disk, the homogenization theory limit has been considered in Ref. [18]. It has been shown that in the dilute trap fraction limit, i.e., when the number of traps

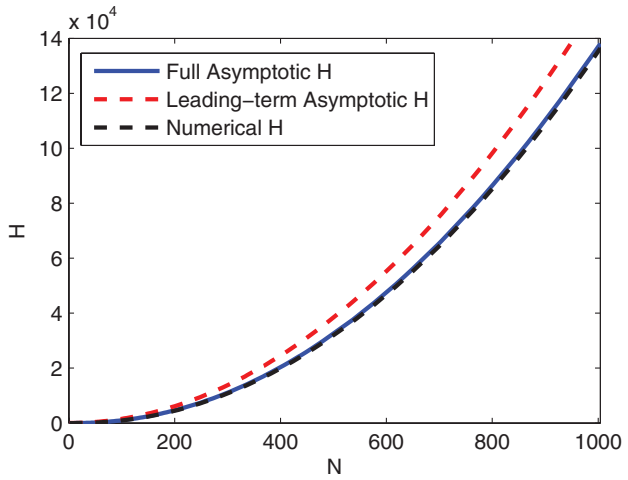


FIG. 5. (Color online) The asymptotic scaling law (2.9a), its leading term $\mathcal{H} \sim \frac{N^2}{2}(1 - \log 2)$, and the numerically computed trap interaction energies $\mathcal{H}$ (2.8) for putative optimal arrangements of $2 \leqslant N \leqslant 1004$ traps on the unit sphere.

$N \to +\infty$, with the total trap length fraction $\sigma = 2\varepsilon N/(2\pi)$ kept constant, the mixed Dirichlet-Neumann problem (1.1) for the MFPT $v(x)$ can be approximated by a Robin problem for $v_h(x) \simeq v(x)$ given by

$$\begin{aligned} &\triangle v_h = -\frac{1}{D}, \quad r = |x| < 1; \quad \varepsilon \partial_r v_h + \kappa(\sigma) v_h = 0, \\ &r = 1, \end{aligned} \tag{5.1}$$

where the boundary condition factor $\kappa(\sigma)$ is given by

$$\kappa = -\frac{\pi\sigma}{2}\left\{\log\left[\sin\left(\frac{\pi\sigma}{2}\right)\right]\right\}^{-1}.$$

In Ref. [8], an asymptotic solution was constructed for a two-dimensional MFPT problem with an arbitrary number of small well-separated traps on the boundary of a unit disk. It has also been demonstrated in Ref. [8] that in the limit $N \to +\infty$ with the total trap length fraction $\sigma \ll 1$ kept constant, the asymptotic solution indeed corresponds to the solution of the problem (5.1) described in Ref. [18].

The homogenization transition in the problem for a sphere in three dimensions with equal traps is significantly different from that for a 2D disk. Indeed, for a unit disk, an optimal arrangement of N equal boundary traps evidently corresponds to the N values of $\sqrt[N]{1}$ in the complex plane. Conversely, locations of N optimally placed traps on a unit sphere are not regular, neither are they given by analytical formulas.

As discussed in Sec. IV above, such optimal arrangements can be approximately computed by global minimization of the average asymptotic MFPT (2.7), which is highly computationally intensive. In the current section, we show that in spite of this difficulty, it is still possible to make an association between the asymptotic MFPT result (2.7) and a solution to a homogenization theory-type boundary value problem, and thus obtain high-precision approximations of the average MFPT with minimal computations, avoiding global optimization.

B. The Robin problem for the unit sphere

Consider the narrow-escape problem (1.1) for the case of N equal traps of radius ε. The total trap area fraction is given by $\sigma = \pi\varepsilon^2 N/(4\pi) = N\varepsilon^2/4$. Suppose that in the dilute trap limit,

$$N \gg 1, \quad \varepsilon \ll 1, \quad \sigma = \text{const}, \tag{5.2}$$

with traps "homogeneously" distributed over the unit sphere, the MFPT $v(x)$ can be approximated by a solution $v_h(x)$ of a Robin problem

$$\begin{aligned} \triangle v_h &= -\frac{1}{D}, \quad \rho = |x| < 1; \\ f(\varepsilon)\partial_r v_h + \kappa(\sigma) v_h &= 0, \quad \rho = 1, \end{aligned} \tag{5.3}$$

involving the boundary condition factors $f(\varepsilon)$ and $\kappa(\sigma)$. Due to the symmetry, the MFPT solution is dependent only on the spherical radius ρ, and is readily found to be given by a quadratic function

$$v_h(\rho) = \frac{f(\varepsilon)}{3D\kappa(\sigma)} + \frac{1-\rho^2}{6D}, \tag{5.4}$$

with the average MFPT given by

$$\bar{v}_h = \frac{f(\varepsilon)}{3D\kappa(\sigma)} + \frac{1}{15D}. \tag{5.5}$$

In order to estimate the unknown functions $f(\varepsilon)$ and $\kappa(\sigma)$, we use the asymptotic formula (2.7).

1. *Leading-order estimates of the homogenization parameters $f(\varepsilon)$ and $\kappa(\sigma)$*

The expression (2.7) is valid when its terms are properly ordered; in particular, one has to have $\varepsilon \ll 1$ and $N \ll O(\log\varepsilon)$. We will assume the large number of traps $N \gg 1$. Substituting the leading terms of $\mathcal{H}$ for large N from the scaling law (2.9a) into the asymptotic expression (2.7), and keeping the proper term ordering, one obtains

$$\begin{aligned} \bar{v} = {} & \frac{\pi}{3\varepsilon DN} + \frac{1}{3DN}\log\frac{2}{\varepsilon} + \frac{1}{15D} + \frac{4}{3}\frac{b_1}{D\sqrt{N}} + \frac{4}{3}\frac{b_2\log N}{DN} \\ & + \frac{1}{DN}\left[\frac{1}{2} + \frac{4}{3}(b_3 - \log 2)\right] + o\left(\varepsilon^0 + \frac{1}{N}\right). \end{aligned} \tag{5.6}$$

Upon the substitution of $N = 4\sigma/\varepsilon^2$, one has

$$\begin{aligned} \bar{v} = {} & \frac{\pi\varepsilon}{12D\sigma} + \frac{\varepsilon^2}{12D\sigma}\log\frac{2}{\varepsilon} + \frac{1}{15D} + \frac{2\varepsilon b_1}{3D\sqrt{\sigma}} + A(\varepsilon,\sigma) \\ & + B(\varepsilon,\sigma) + o\left(\varepsilon^0 + \frac{1}{N}\right), \end{aligned} \tag{5.7}$$

where

$$\begin{aligned} A(\varepsilon,\sigma) &= \frac{\varepsilon^2 b_2}{3D\sigma}\log\frac{4\sigma}{\varepsilon^2} \sim \frac{\log N}{N}, \\ B(\varepsilon,\sigma) &= \frac{\varepsilon^2}{D\sigma}\left(\frac{1}{8} - \frac{1}{3} - \log 2 + \frac{b_3}{3}\right) \sim \frac{1}{N}. \end{aligned}$$

In the situation with a large number of traps, clearly $A(\varepsilon,\sigma) \gg O[B(\varepsilon,\sigma)]$.

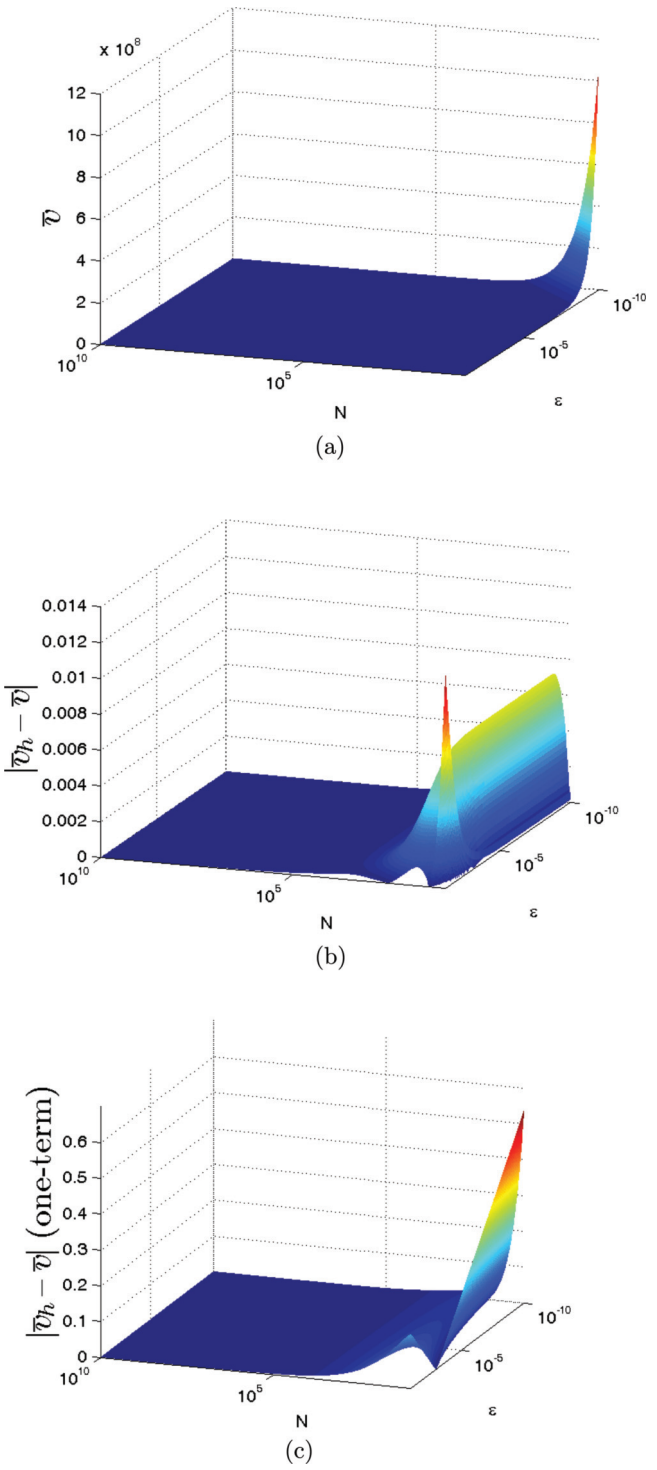


FIG. 6. (Color online) (a) The plot of the asymptotic average MFPT $\bar{v}$ (2.7) for $10^1 \leqslant N \leqslant 10^{10}$ and $10^{-10} \leqslant \varepsilon \leqslant 10^{-1}$. (b) The absolute difference between the asymptotic average MFPT $\bar{v}$ (2.7) and the full homogenization MFPT $\bar{v}_h$ (5.5) and (5.14). (c) The absolute difference between the asymptotic average MFPT $\bar{v}$ (2.7) and the one-term homogenization MFPT (5.8) and (5.9).

Comparing the asymptotic MFPT expression (5.7) with the homogenization solution (5.5), it is clear that by taking

$$f(\varepsilon) = \varepsilon, \quad \kappa(\sigma) = \frac{4\sigma}{\pi}, \tag{5.8}$$

one makes the homogenization MFPT $\bar{v}_h$ (5.5) become

$$\bar{v}_h = \frac{\pi\varepsilon}{12D\sigma} + \frac{1}{15D}, \tag{5.9}$$

which contains the correct first and third terms of the asymptotic MFPT (5.7).

In order to match additional terms of (5.7), one can consider the coefficients $f(\varepsilon)$ and $\kappa(\sigma)$ of the extended form

$$f(\varepsilon) = \varepsilon + \alpha\varepsilon^2\log\varepsilon + \beta\varepsilon^2, \quad \kappa(\sigma) = \frac{4\sigma}{\pi + \gamma\sqrt{\sigma}}. \tag{5.10}$$

The homogenization MFPT (5.5) consequently becomes

$$\bar{v}_h = \frac{\pi\varepsilon}{12D\sigma} + \frac{\pi\varepsilon^2}{12D\sigma}(\beta + \alpha\log\varepsilon) + \frac{1}{15D} + \frac{\gamma\varepsilon}{12D\sqrt{\sigma}} + Q(\varepsilon,\sigma), \tag{5.11}$$

where

$$Q(\varepsilon,\sigma) = \frac{\gamma\varepsilon^2}{12D\sigma}(\beta + \alpha\log\varepsilon). \tag{5.12}$$

The form (5.11) of the homogenization MFPT can be used to match the first four leading terms of (5.7) upon choosing

$$\alpha = -\frac{1}{\pi}, \quad \beta = \frac{1}{\pi}\log 2, \quad \gamma = 8b_1. \tag{5.13}$$

A direct computation shows that under the choice of parameters (5.13), the additional term $Q(\varepsilon,\sigma)$ (5.12) is small compared to both of the higher-order terms $A(\varepsilon,\sigma)$ and $B(\varepsilon,\sigma)$ in the limit $\varepsilon \to 0$, $N \ll O(\log\varepsilon)$. We have thus arrived at the following result.

Principal result 2. Consider an arrangement of $N \gg 1$ equal small traps on a unit sphere. Suppose that this arrangement is optimal, i.e., it minimizes the interaction energy (2.8). Then, in an asymptotic limit $\varepsilon \to 0$, $N \ll O(\log\varepsilon)$, the asymptotic expression for the MFPT $v(x)$ (2.1) and the average

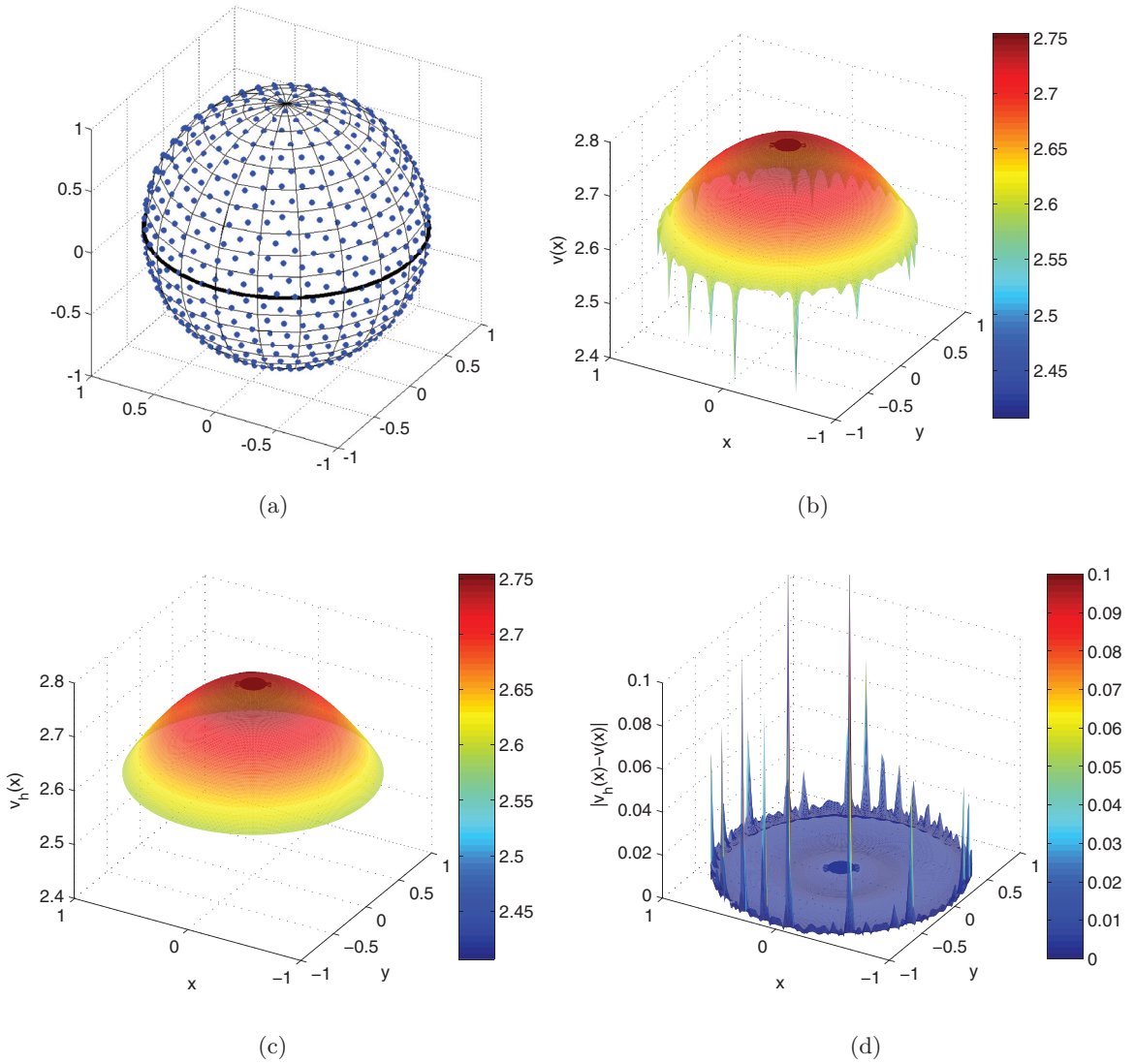


FIG. 7. (Color online) MFPT comparison plots for $N = 802$ traps with $\varepsilon = 0.0005$. (a) The putative optimal trap arrangement. (b) The equatorial cross section ($z = 0$) of the asymptotic MFPT $v(x)$ (2.1). (c) The equatorial cross section of the homogenization MFPT $v_h(\rho)$ (5.4). (d) The absolute difference $|v_h(\rho) - v(x)|$.

MFPT $\bar{v}$ (2.7) for such a configuration can be approximated, within the four leading terms, by a solution (5.4) and (5.5) of the Robin boundary value problem (5.3) with parameters

$$f(\varepsilon) = \varepsilon - \frac{\varepsilon^2}{\pi}\log\varepsilon + \frac{\varepsilon^2}{\pi}\log 2,$$
$$\kappa(\sigma) = \frac{4\sigma}{\pi + 8b_1\sqrt{\sigma}}, \quad b_1 = -\frac{1}{2} \tag{5.14}$$

[cf. (2.9b)]. In particular, the values of the asymptotic MFPT $v(x)$ and the asymptotic average MFPT $\bar{v}$ can be approximately computed without the computation of trap coordinates of the actual globally optimal trap arrangement.

2. *A numerical comparison of asymptotic and homogenization MFPT formulas*

For a first comparison, we analyze the difference of the asymptotic average MFPT $\bar{v}$ (2.7) and the homogenization average MFPT $\bar{v}_h$ (5.5) and (5.14), for a range of parameters ε, N. As remarked above, the expressions for $\bar{v}$ and $\bar{v}_h$ are simultaneously valid when $\varepsilon \ll 1, N \gg 1$, and $N \ll O(\log\varepsilon)$.

We wish, however, to analyze the quality of approximation provided by the homogenization theory formula in a wider range of parameters; for that purpose, we take $10^1 \leqslant N \leqslant 10^{10}$ and $10^{-10} \leqslant \varepsilon \leqslant 10^{-1}$. The plots in Fig. 6 provide the values of the asymptotic $\bar{v}$ (2.7) and the absolute differences between the asymptotic $\bar{v}$ and the homogenization MFPT $\bar{v}_h$ given by the full formulas (5.5) and (5.14), and the one-term approximation (5.8) and (5.9). The figure clearly justifies the benefit of using higher-order terms (5.14) as opposed to the leading-order terms (5.8) in the boundary conditions of the Robin problem.

As a second comparison, consider a specific example of a previously computed putative optimal arrangement. We take an arrangement of $N = 802$ traps (cf. Table II). The trap arrangement and the equatorial cross sections of the asymptotic MFPT $v(x)$ (2.1), the homogenization MFPT $v_h(\rho)$ (5.4), and the absolute difference $|v_h(\rho) - v(x)|$ are given in Fig. 7 for $\varepsilon = 0.0005$.

As expected, the homogenization solution provides an acceptable description of the asymptotic MFPT $v(x)$ away from the boundary, since it does not take into account particular traps.

VI. CONCLUSIONS

In the current contribution, the narrow-escape problem (1.1) for the unit sphere was considered, concentrating on the case of a large number $N \gg 1$ of equal boundary traps.

The asymptotic solution of the problem (1.1) in the case of small well-separated traps was reviewed in Sec. II. In particular, the asymptotic MFPT $v(x)$ depends on the constant average MFPT $\bar{v}$ and variable terms involving the spherical Neumann Green's function. The asymptotic expression (2.7) for the average MFPT contains a special term (the trap interaction energy) $\mathcal{H}(x_1, \ldots, x_N)$ that explicitly depends on mutual trap locations.

In Sec. III, an expression for the increment of the average MFPT $\bar{v}$, for the case when a trap is added at a specific location, was derived. The result was subsequently used to formulate a method to compute putatively optimal arrangements of $N + k$ traps from a known arrangement of N traps (Sec. IV). The method consists of adding k traps to the existing N-trap configuration at points corresponding to the lowest minima of the increment of $\bar{v}$, and then evolving all traps according to a dynamical system that minimizes $\bar{v}$. As examples of the suggested algorithm, putative optimal spherical arrangements were computed for $N \leqslant 1004$ traps, well beyond the ability of any available global optimization software package. The results were verified by the comparison with available scaling law estimates, as well as by using the N^2 conjecture, which states that the sum of squares of pairwise distances between traps in an optimal configuration of N traps is equal to N^2. This conjecture was shown to hold with remarkable precision for known optimal trap arrangements; additionally, a scaling law argument was presented that supports the conjecture for large N.

The second part of the current paper was concerned with the dilute trap fraction limit of homogenization theory for the unit sphere, where the strongly heterogeneous Dirichlet-Neumann problem (1.1) is replaced by an effective Robin boundary condition. Parameters involved in that boundary condition were derived using the available asymptotic MFPT expression. The Robin problem is subsequently solved exactly to yield a spherically symmetric homogenization MFPT expression $v_h(\rho)$ (5.4). MFPT computations for $N \gtrsim 800$ using the homogenization theory result and the approach of Sec. IV were shown to give rather close MFPT values for the internal points of the sphere.

It remains an open problem to derive an exact expression for, or to rigorously justify and improve, the asymptotic formula (5.10) for the coefficients in the effective Robin boundary condition in the homogenization limit. Progress in this direction will require more detailed information about MFPT-minimizing spherical arrangements of $N \gg 1$ traps.

Further extensions of the model considered in the current work may include the consideration of nonspherical domains, variable diffusivity coefficients, nonreflective domain boundaries, and imperfect or dynamic transmission properties of boundary traps. Such extensions are required, in particular, for models arising in cell biology.

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APPENDIX: SOME SCALING LAW ESTIMATES

1. An estimate of the MFPT interaction energy $\mathcal{H}$ (2.8)

Following the idea of [12,26], assume that one has $N \gg 1$ traps, distributed "homogeneously" on the sphere. Without loss of generality, place the first trap at the north pole. As per (2.8), the interaction energy H_{1i} with the ith other trap is given by

$$h_{1i} = \frac{1}{r_{1i}} - \frac{1}{2}\log r_{1i} - \frac{1}{2}\log(2 + r_{1i}),$$
$$r_{1i} = |x_1 - x_i| = \sqrt{2(1 - \cos\theta)},$$

where θ is the azimuthal angle of the particle located at x_i.

There is no charge in the azimuthal neighborhood $0 \leqslant \theta < \theta_0$ of the north pole, where $\theta_0 \ll 1$. It follows that the number density of charges is given approximately by

$$P(\theta,\phi) = \begin{cases} \frac{N}{4\pi} & \text{for} \quad \theta_0 < \theta < \pi \\ 0 & \text{for} \quad 0 < \theta < \theta_0. \end{cases}$$

The angle θ_0 satisfies the condition that $\int_0^{2\pi}\int_{\theta_0}^{\pi} P(\theta,\phi) \sin\theta\, d\theta\, d\phi = N-1$, which yields

$$\theta_0 = \arccos\left(1 - \frac{2}{N}\right). \tag{A1}$$

The interaction energy of the north-pole charge with the remaining charges is approximated via replacing the sum with an integral:

$$\mathcal{H}_1 = \sum_{i=2}^{N} h_{1i} \simeq \int_0^{2\pi}\int_{\theta_0}^{\pi} P(\theta,\phi)\, h_{1i} \sin\theta d\theta d\phi, \tag{A2}$$

which can be calculated analytically, yielding a closed-form expression after the substitution of (A1). In order to calculate the total energy and avoid counting traps twice, the expression (A2) is multiplied by $N/2$. The resulting scaling law estimate for $\mathcal{H}$ (2.8) with (A1) is given by

$$\mathcal{H} \simeq \frac{N^2}{2}(1-\log 2) - \frac{N^{3/2}}{4} + \frac{N^2}{4}\log\frac{\sqrt{N}}{\sqrt{N}+1} + \frac{N}{4}\log\frac{\sqrt{N}+1}{N} + \frac{N}{4}(2\log 2 - 1). \tag{A3}$$

The leading terms in the expansion of (A3) as $N \to +\infty$ are readily computed to be

$$\mathcal{H} \simeq \frac{N^2}{2}(1-\log 2) - \frac{N^{3/2}}{2} - \frac{1}{8}N\log N + \frac{N}{2}\left(\log 2 - \frac{1}{4}\right) + \frac{\sqrt{N}}{4} + \frac{1}{24}\log N - \frac{1}{16} - \frac{1}{6}\log 2 + o(1). \tag{A4}$$

We note that a formula analogous to (A3) can be derived for an arbitrary θ_0; the leading term in such a formula is given by $\frac{N^2}{2}(1-\log 2)$ and does not depend on the form of θ_0, whereas all subsequent terms do. In particular, all terms in Eq. (A4) except for the leading term vanish if one sets $\theta_0 = 0$.

2. An estimate of the sum of squared distances between traps

We now use the same technique to obtain a scaling law for the sum of squared distances (4.2),

$$\mathcal{Q} = \sum_{i=1}^{N}\sum_{j=i+1}^{N} |x_i - x_j|^2,$$

between traps, assuming that $N \gg 1$ are arranged optimally. For one trap located at the north pole,

$$\mathcal{Q}_1 = \sum_{i=2}^{N} |x_1 - x_j|^2 \simeq 2\int_0^{2\pi}\int_{\theta_0}^{\pi} P(\theta,\phi)(1-\cos\theta)\sin\theta d\theta d\phi. \tag{A5}$$

Computing the integral, one finds

$$\mathcal{Q}_1 = \frac{N}{2}(3 + 2\cos\theta_0 - \cos^2\theta_0). \tag{A6}$$

For θ_0 given by (A1), one obtains $\mathcal{Q}_1 = 2N - 2/N$. Multiplying by $N/2$ to count each trap pair once, one has an asymptotic estimate

$$\mathcal{Q} \simeq N^2 - 1. \tag{A7}$$

Note that taking $\theta_0 = 0$ in Eq. (A6), one would obtain

$$\mathcal{Q} \simeq N^2. \tag{A8}$$

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