Mathematical Modelling of Narrow Escape Problems

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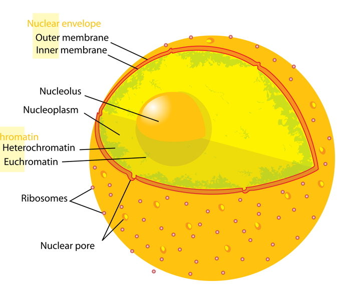
The Narrow Escape Problem

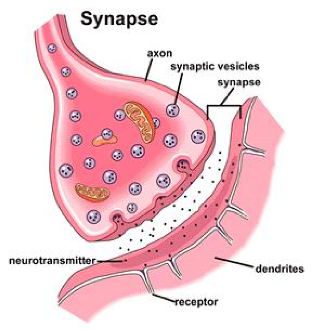
The narrow escape problem concerns the motion of a Brownian particle confined in a bounded domain $\Omega \in \mathbb{R}^d$ ($d = 2, 3$ in two or three space dimensions) whose boundary $\partial\Omega = \partial\Omega_r \bigcup \partial\Omega_a$ is almost entirely reflecting ($\partial\Omega_r$), except for small windows (*traps*, $\partial\Omega_a$), through which the particle can escape.

Applications

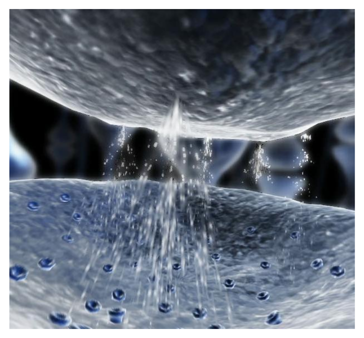
Pores in cell nuclei:



Synaptic receptors on dendrites:



Ion channels in cell membranes:



The Mathematical Model

The **mean first passage time (MFPT)**, $v(x)$, is defined as the expectation value of the time taken for a Brownian particle starting initially from some point x in a domain Ω to escape through any window on the boundary $\partial\Omega$. To find $v(x)$, one must solve the

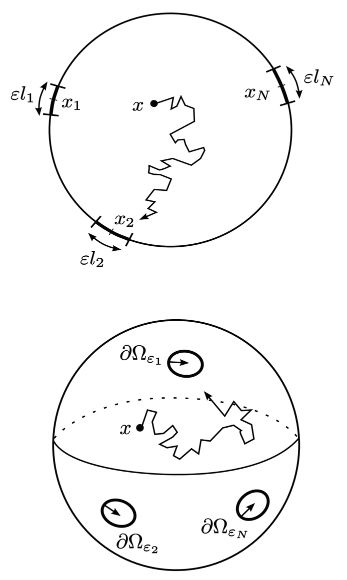
Dirichlet-Neumann boundary problem for MFPT $v(x)$:

$$\triangle v = -\frac{1}{D}, \quad x \in \Omega, \qquad v = 0, \quad x \in \partial\Omega_a = \bigcup_{j=1}^{N} \partial\Omega_{\varepsilon_j}; \qquad \partial_n v = 0, \quad x \in \partial\Omega_r. \tag{1}$$

Where D is the diffusivity coefficient ($D = \text{const}$ or $D = D(x)$). A useful quantity is the average MFPT defined as $\bar{v}$.

- **Average MFPT:**

$$\bar{v} = \frac{1}{|\Omega|} \int_\Omega v(x)\, dx = \text{const.} \tag{2}$$



The Asymptotic Solution

Approximate asymptotic solutions have been obtained for some 2D and 3D domains using the method of ***matched asymptotic expansions***. The method consists of writing separate expansions of $v(x)$ in terms of ε both *near a trap* and *away from a trap*. The expansions are then matched in an intermediate region (see Refs. [1, 2]). Some examples of such solutions are presented here.

- **Assumptions:**
  - Domain size $L = \text{diam}\ \Omega \sim 1$.
  - Small parameter: $\varepsilon \ll 1$; trap sizes $\sim \varepsilon$.
  - Traps are well-separated: $|x_i - x_j| \gg \varepsilon$.

The Asymptotic MFPT in a 2D Domain

The leading-term asymptotic behaviour for the MFPT in a 2D domain Ω with N equal length ε sized traps located at $x_1, ..., x_N$, is given by [1]:

$$v(x) \sim \bar{v} - \frac{|\Omega|}{ND} \sum_{i=1}^{N} G(x; x_i), \tag{3}$$

$|\Omega|$ is the measure of Ω, and $G(x; x_i)$ is the corresponding *surface Neumann Green's function*. In the vicinity of the trap x_i, the 2D Green's function behaves like

$$G(x; x_i) \sim -\frac{1}{\pi} \log|x - x_i| + R(x_i; x_i).$$

Here $R(x_i; x_i)$ is the regular part of the Green's function. Let

$$\mathcal{G} \equiv \begin{pmatrix} R_1 & G_{12} & \cdots & G_{1N} \\ G_{21} & R_2 & \cdots & G_{2N} \\ \vdots & \vdots & \ddots & \vdots \\ G_{N1} & \cdots & G_{N,N-1} & R_N \end{pmatrix}$$

be the symmetric Green's function matrix; $G_{ij} \equiv G(x_i; x_j)$; $R_i \equiv R(x_i; x_i)$. Then the average MFPT $\bar{v}$ for $\epsilon \ll 1$ is given by

$$\bar{v} \sim \frac{|\Omega|}{\pi N D \mu} + \frac{|\Omega|}{N^2 D} p(x_1, ..., x_N) + \mathcal{O}(\mu), \quad \mu \equiv -\frac{1}{\log(\varepsilon\ell/4)}, \tag{4}$$

where the leading term depends on the total trap size, and in the second term

$$p(x_1, ..., x_N) = \sum_{i=1}^{N} \sum_{j=1}^{N} \mathcal{G}_{ij}$$

is an ***interaction term***, dependent on the mutual arrangement of traps. The above results may be generalized for situations involving traps of ***non-equal sizes*** (see Refs. [1,2]).

Asymptotic Results: Unit Circle, Unit Square

- For the ***unit circle***, the surface Green's function and its regular part are given by

$$G(x; x_i) \sim -\frac{1}{\pi} \log|x - x_i| + \frac{|x|^2}{4\pi} - \frac{1}{8\pi}, \quad R(x_i; x_i) = \frac{1}{8\pi}, \quad |x_i| = 1.$$

- For the ***unit square***, both $G(x; x_i)$ and $R(x_i; x_i)$ can be expressed as rapidly converging infinite sums of logarithmic terms (see Ref. [1]).

3D Domains: The Unit Sphere

In [2], it has been independently shown that the mean first passage time (MFPT) formula (3), also applies to 3-dimensional domains. For N identical circular windows of radius ε located at points x_i on the unit sphere ($|x_i| = 1$), the MFPT and the average MFPT for a Brownian particle are given by

$$v(x) \sim \bar{v} - \frac{|\Omega|}{ND} \sum_{i=1}^{N} G_s(x; x_i),$$

Where the spherical surface Neumann-Green's function is given by:

$$G_s(x_i; x_j) = -\frac{9}{20\pi} + \frac{1}{2\pi}\left(\frac{1}{|x_i - x_j|} - \frac{1}{2}\log\left[\sin^2\left(\frac{\gamma_{ij}}{2}\right) + \sin\left(\frac{\gamma_{ij}}{2}\right)\right]\right), \quad \cos(\gamma_{ij}) = x_i \cdot x_j$$

.

The average MFPT has the leading-term behaviour,

$$\bar{v} = \frac{|\Omega|}{4\varepsilon D N}\left[1 + \frac{\varepsilon}{\pi}\log\left(\frac{2}{\varepsilon}\right) + \frac{\varepsilon}{\pi}\left(-\frac{9N}{5} + 2(N-2)\log 2 + \frac{3}{2} + \frac{4}{N}\mathcal{H}\right) + \mathcal{O}(\varepsilon^2 \log\varepsilon)\right]. \tag{5}$$

The *interaction term* (interaction energy) $\mathcal{H} = \mathcal{H}(x_1, \ldots, x_N)$ (depending on the mutual arrangement of traps) is defined by

$$\mathcal{H}(x_1, \ldots, x_N) = \sum_{i=1}^{N} \sum_{j=i+1}^{N} \left(\frac{1}{|x_i - x_j|} - \frac{1}{2}\log|x_i - x_j| - \frac{1}{2}\log(2 + |x_i - x_j|)\right). \tag{6}$$

The above results may be generalized for non-equally sized traps (see Ref. [2]). In particular, the interaction energy (6) is a linear combination of Coulonb potential, logarithmic potential and an addtional logarithmic term.

The Unit Cube

For the unit cube, assuming that (3) holds, one needs to find the corresponding surface Neumann Green's function to determine the essential behaviour of the MFPT. For a single trap located at a point $(0, y_0, z_0)$ in the plane $x = 0$, the Green's function satisfies the problem

$$\triangle G_c = 1 - 2\delta(x)\delta(y - y_0)\delta(z - z_0), \quad -1 < x < 1,\ 0 < y, z < 1;$$

$$\partial_r G_c = 0 \ at \ x = \pm 1, \text{ or } y = 0, 1 \text{ or } z = 0, 1,$$

$$\int_{-1}^{1} dx \int_0^1 dy \int_0^1 dz\, G_c = 0.$$

The solution can be found in terms of a triple cosine Fourier series expansion in the double domain, and subsequently converted into a double summation for faster convergence, using trigonometric identities (see Ref. [3]).

Asymptotic Solution: Applicability Study

For several 2D and 3D domains, we compare known asymptotic solutions of both the mean first passage time (MFPT) and average MFPT with full numerical finite-difference solutions to experimentally establish applicability limits of the asymptotic solutions.

We are interested in determining the

- maximal trap sizes,
- minimal trap separation distances,

for which the asymptotic solutions hold within reasonable precision.

For example, in the term $\mathcal{O}(\mu)$ in formula (4), $\mu \sim 0.01$ only when $\varepsilon \lesssim 10^{-40}$; in the term $\mathcal{O}(\varepsilon^2 \log\varepsilon)$ in formula (5), $\epsilon^2 \log\epsilon \sim 0.01$ only when $\varepsilon \lesssim 0.06$. We test whether the asymptotic formulas still hold outside these predicted ranges of ε.

The Numerical Method

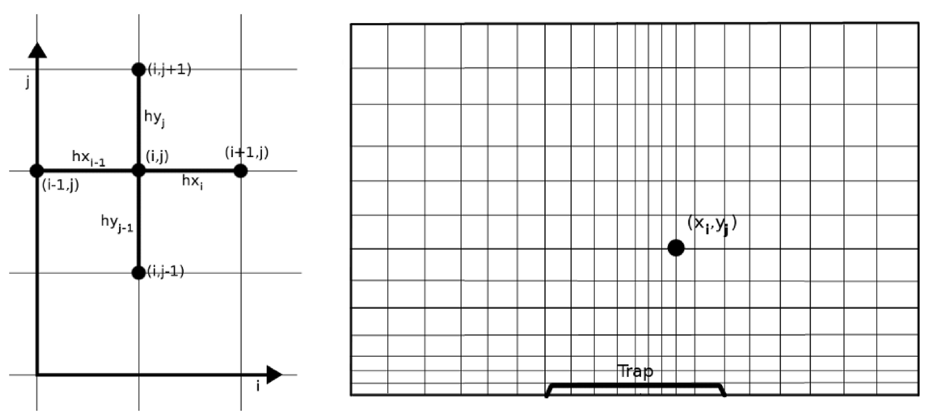
We solve problem (1) in two and three dimensions numerically, using a variable-step first-order finite-difference numerical method. For example, in the case of the unit square, the approximate solution at a grid point (x_i, y_j) is given by $v_{ij} \approx v(x, y)$. The Laplacian differential operator is approximated by a *finite difference operator*:

$$\triangle v(x, y) \equiv \left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2}\right) v(x, y) \approx (\Lambda_{xx} + \Lambda_{yy})[v_{ij}],$$

$$\Lambda_{xx}[v_{ij}] \equiv \frac{(h^x)_i^{-1}(v_{i\,j+1} - v_{ij}) - (h^x)_{i-1}^{-1}(v_{ij} - v_{i\,j-1})}{0.5((h^x)_i + (h^x)_{i-1})}, \quad \text{similar for } \Lambda_{yy}[v_{ij}].$$

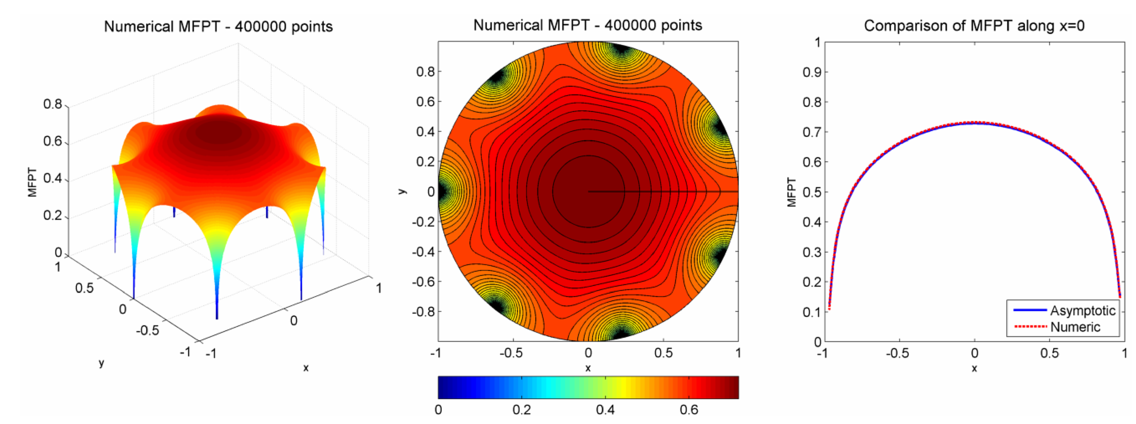
The step sizes $\{(h^x)_i\}$, $\{(h^y)_j\}$, $i = 1, ..., n$, $j = 1, ..., m$, are chosen so that more grid points are produced near each trap than far from traps. Normally, near 100 points per trap were taken.

Mesh refinement illustration for a 2D square domain:

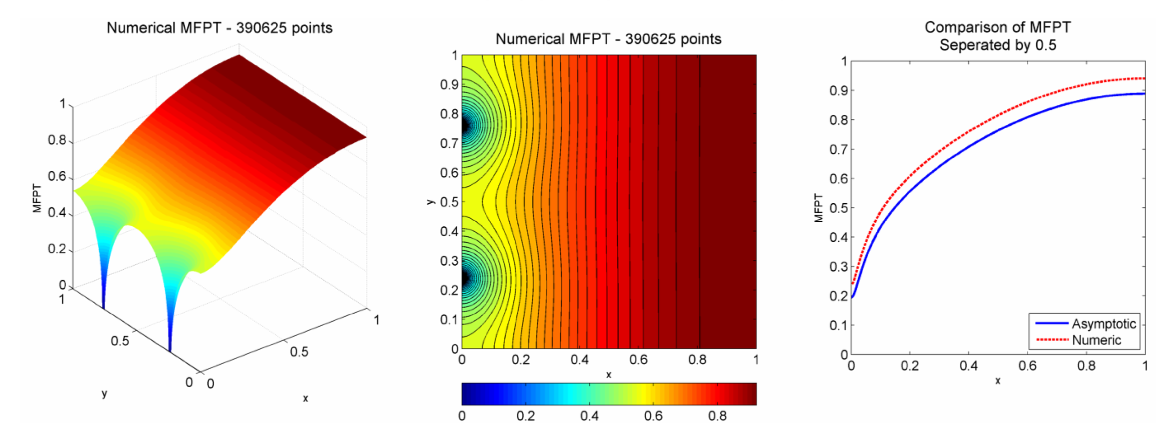


Computations and plotting were done in Matlab.

2D Domain: Numerical vs. Asymptotic Results

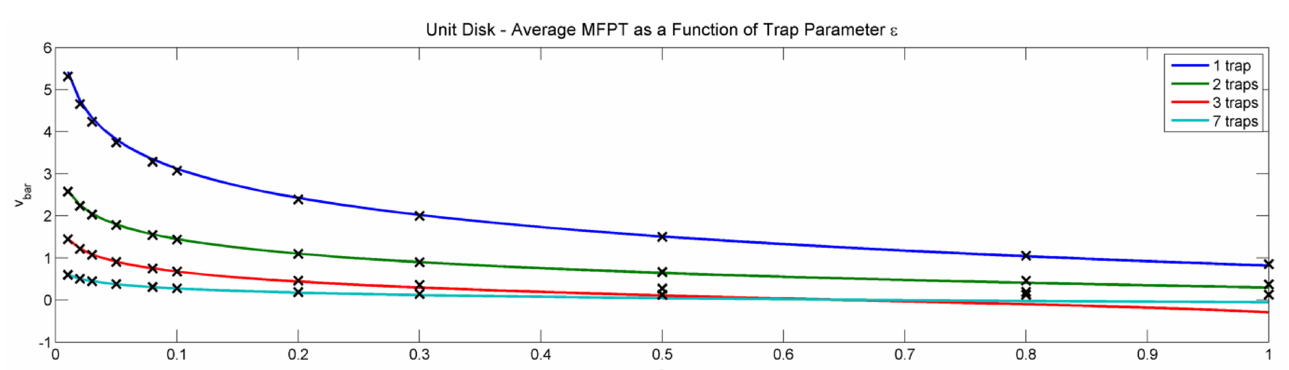


Unit disk with seven equally spaced traps, each with a width of $2\epsilon = 0.02$.



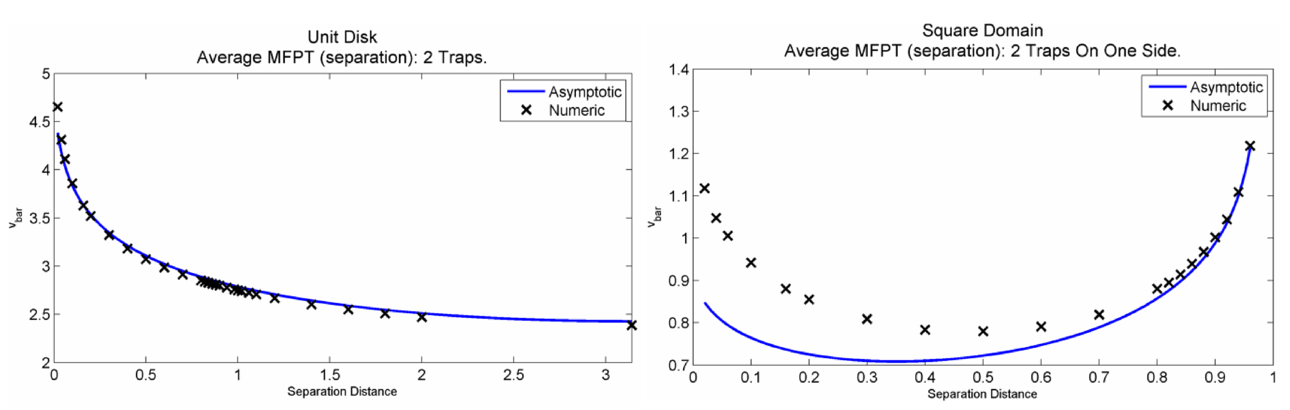
Unit square with two traps separated by 0.5, each with a width of $2\epsilon = 0.02$.

2D Domain: Effects of Trap Size



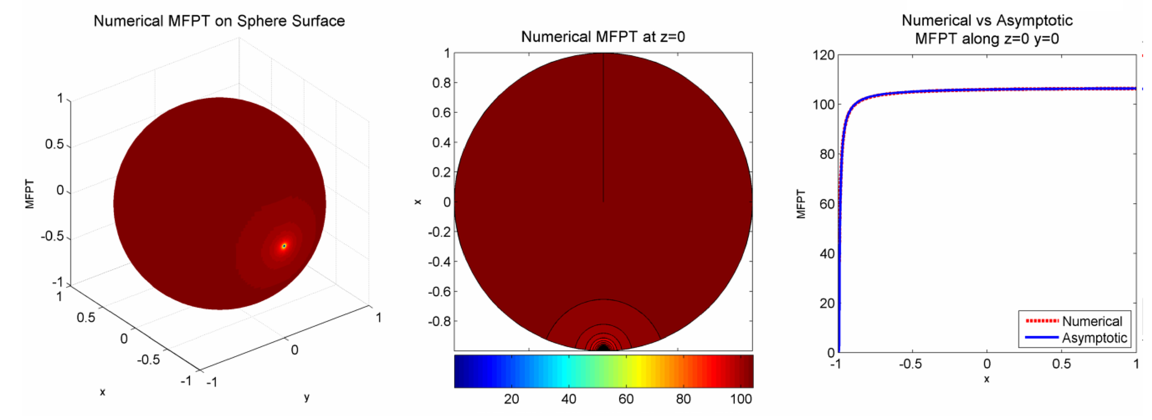
Average MFPT for unit disk with one, two, and seven equally spaced traps with width $2\epsilon = 0.02$. For the three trap curve, two traps have width $2\epsilon = 0.02$ centred at $\pi/2$ and $3\pi/2$ and one trap has width $6\epsilon = 0.06$ centred at π.

2D Domain: Effects of Trap Separation

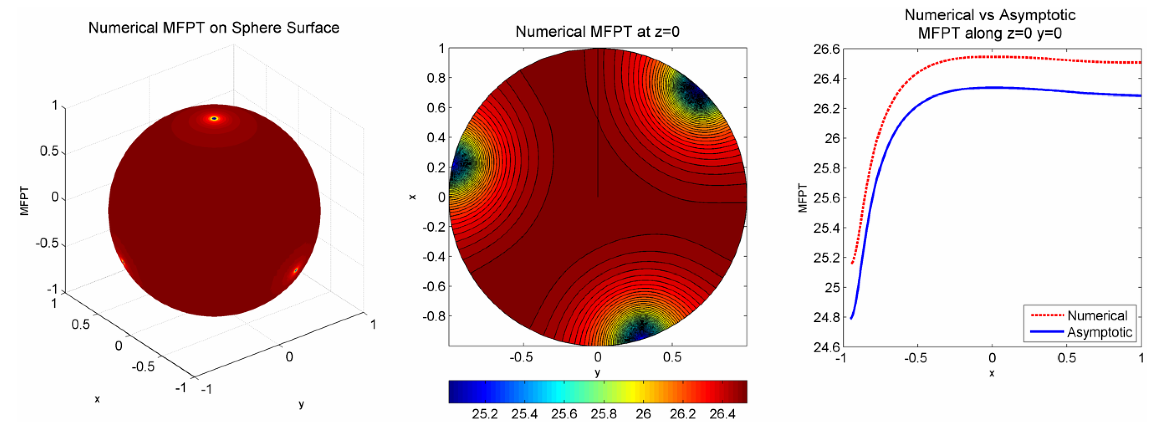


For polar domain, separation distance is arc length. For square domain, separation distance is measured along one side.

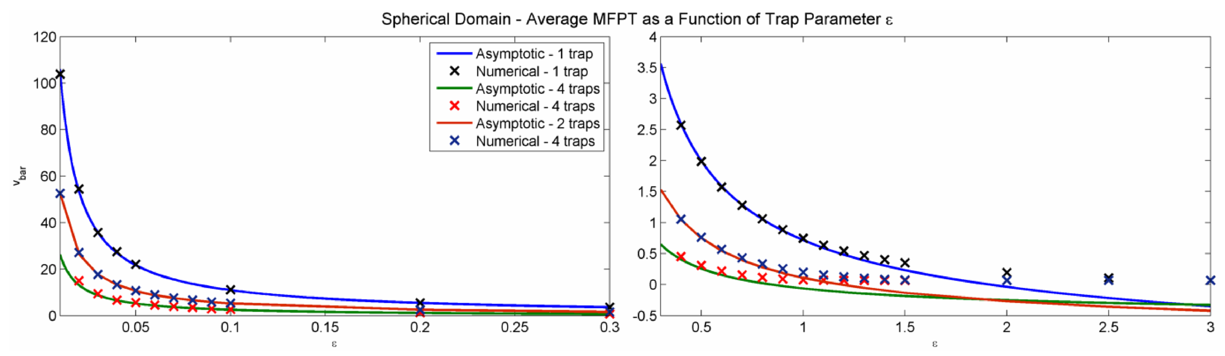
3D Sphere and Effects of Trap Size



MFPT for unit sphere with one circular trap with radius $\epsilon = 0.01$.

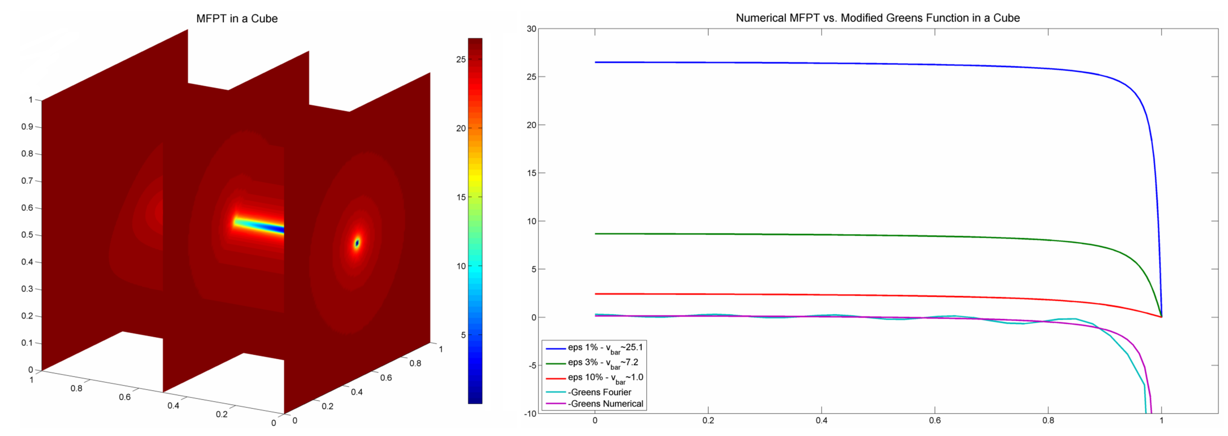


MFPT for unit sphere with four optimally placed circular traps with radius $\epsilon = 0.01$.



Numerical average MFPT vs. asymptotic average MFPT given by (4).

Narrow Escape from a 3D Cube

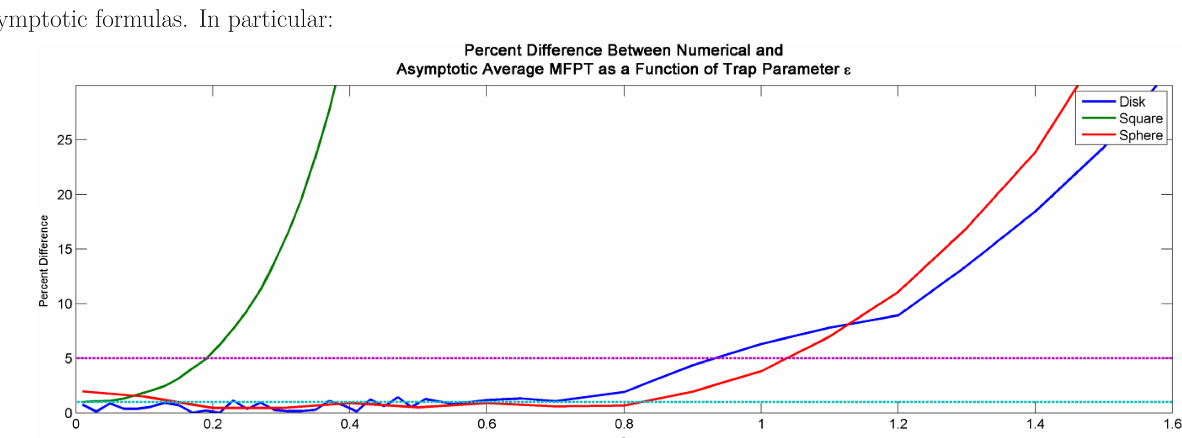


Left: *Numeric MFPT.* ***Right:*** *Numeric MFPT vs. Truncated Fourier Series of Green's Function.*

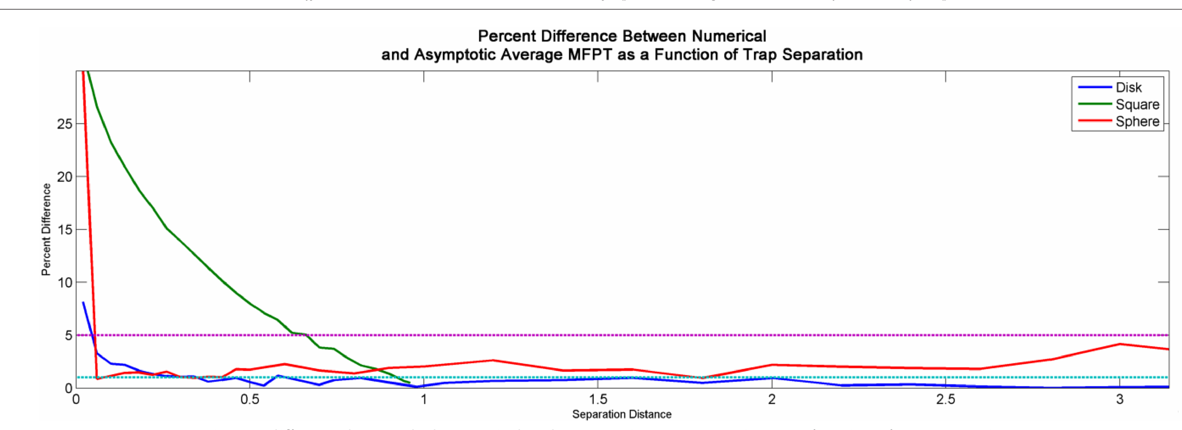
The asymptotic MFPT and asymptotic average MFPT are given by (2.43) and (2.44) respectively in [2]. The average MFPTs were calculated using the difference between Green's Numerical and each numerical MFPT.

Conclusions

1. From the comparison of numerical and asymptotic solutions for 2D and 3D problems, it was determined that for the considered examples, the asymptotic formulas have **applicability ranges much wider** than one might expect from the asymptotic formulas. In particular:



Percent difference between both numerical and asymptotic average MFPTs as a function of trap size.



Percent difference between both numerical and asymptotic average MFPTs as a function of trap separation.

- The MFPT predicted by formulas (3), (4) in 2D **agrees within $\sim$ 1%** of the numerical solution when **total trap arclength is $\lesssim$ 0.1 for the unit square** and **$\lesssim$ 0.6 for the unit disk**. [The difference between the square and the sphere can be attributed to effects of corners.]
- The MFPT predicted by formulas (3), (5) in 3D **agrees within $\sim$ 1%** of the numerical solution when **total trap area $\lesssim$ 0.8 for the unit sphere**.
- For **two traps**, the MFPT for the 2D disk and 3D spherical domain predicted by formulas (3), (4), and (5) **agree within $\sim$ 5%** of the numerical solution **when total separation distance $\gtrsim$ 10 times the size of traps** as governed by above conclusions.

  For the **square domain**, the formulas **agree within $\sim$ 5%** of the numerical solution when **total separation distance $\gtrsim$ 0.6**.

2. We showed that **the results for the 3D sphere can be generalized for a *unit cube***. It has been shown that the MFPT for the cubic domain can be approximately computed using both the truncated 3D Fourier series for the surface Neumann Green's function for the cube and formula (3).

References

[1] S. Pillay, M. J. Ward, A. Peirce, and T. Kolokolnikov. *An asymptotic analysis of the mean first passage time for narrow escape problems: Part I: two-dimensional domains*, Multiscale Model. Simul. **8** (3), 803–835 (2010).

[2] A. F. Cheviakov, M. J. Ward, and R. Straube. *An asymptotic analysis of the mean first passage time for narrow escape problems: Part II: the sphere*, Multiscale Model. Simul. **8** (3), 836–870 (2010).

[3] A. S. Reimer and A. F. Cheviakov. Manuscript in preparation.