Asymptotic Analysis of Narrow Escape Problems in Non-Spherical 3D Domains

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Outline

1. Narrow Escape Problems, Mean First Passage Time (MFPT)

2. Asymptotic Results for Small Traps; Higher-Order MFPT for the Sphere

3. Asymptotic Analysis of the MFPT Problem for Non-Spherical Domains

4. Asymptotic vs. and Numerical Average MFPT for Non-Spherical Domains
   - Oblate Spheroid
   - Prolate Spheroid
   - Biconcave Disk–Blood Cell Shape

5. Towards Higher-order MFPT Asymptotics

6. Highlights and Open Problems
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6 Highlights and Open Problems
A Brownian particle escapes from a bounded domain through small windows.

Examples of applications:

- Pores of cell nuclei.
- Synaptic receptors on dendrites.
- Ion channels in cell membranes.
- Typical cell sizes: $\sim 10^{-5}$ m; pore sizes $\sim 10^{-9}...10^{-8}$ m.
Mathematical Formulation

Given:

- A Brownian particle confined in a domain $\Omega \in \mathbb{R}^3$.
- Initial position: $x \in \Omega$.
- Mean First Passage Time (MFPT): $\nu(x)$.
- Domain boundary: $\partial \Omega = \partial \Omega_r$ (reflecting) $\cup \partial \Omega_a$ (absorbing).
- $\partial \Omega_a = \bigcup_{i=1}^{N} \partial \Omega_{\varepsilon_i}$: small absorbing traps (size $\sim \varepsilon$).

Figure 1: A Schematic of the Narrow Escape Problem in a 2-D and a 3-D domain.
Problem for the MFPT $\nu = \nu(x)$ \cite{Holcman, Schuss (2004)}:

\[
\begin{cases}
\Delta \nu = -\frac{1}{D}, & x \in \Omega, \\
\nu = 0, & x \in \partial\Omega_a; \quad \partial_n \nu = 0, & x \in \partial\Omega_r.
\end{cases}
\]

Average MFPT: $\bar{\nu} = \frac{1}{|\Omega|} \int_{\Omega} \nu(x) \, dx = \text{const.}$
The Mathematical Problem

Boundary Value Problem:
- Linear;
- Strongly heterogeneous Dirichlet/Neumann BCs;
- Singularity perturbed:
  \[ \varepsilon \to 0^+ \quad \Rightarrow \quad \nu \to +\infty \quad \text{a.e.} \]

Problem for the MFPT:

\[
\begin{cases}
\Delta \nu = -\frac{1}{D}, & x \in \Omega, \\
\nu = 0, & x \in \partial \Omega_a = \bigcup_{j=1}^{N} \partial \Omega_{\varepsilon_j}, \\
\partial_n \nu = 0, & x \in \partial \Omega_r.
\end{cases}
\]
Some General Results

Arbitrary 2D domain with smooth boundary; one trap \([\textit{Holcman et al (2004, 2006)}]\)

\[ \bar{v} \sim \frac{|\Omega|}{\pi D} \left[ - \log \varepsilon + O(1) \right] \]

Unit sphere; one trap \([\textit{Singer et al (2006)}]\)

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

Arbitrary 3D domain with smooth boundary; one trap \([\textit{Singer et al (2009)}]\)

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

\(H\): mean curvature at the center of the trap.
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Matched Asymptotic Expansions (Illustration for the Unit Sphere)

- **Outer expansion**, defined at $\mathcal{O}(1)$ distances from traps:
  \[
  v_{out} \sim \varepsilon^{-1} v_0(x) + v_1(x) + \varepsilon \log \left(\frac{\varepsilon}{2}\right) v_2(x) + \varepsilon v_3(x) + \cdots.
  \]

- **Inner expansion** of solution near trap centered at $x_j$ uses scaled coordinates $y$:
  \[
  v_{in} \sim \varepsilon^{-1} w_0(y) + \log \left(\frac{\varepsilon}{2}\right) w_1(y) + w_2(y) + \cdots.
  \]

- **Matching condition**: when $x \to x_j$ and $y = \varepsilon^{-1}(x - x_j) \to \infty$,
  \[
  v_{in} \sim v_{out}.
  \]
Higher-Order Asymptotic MFPT for the Sphere

Given:

- Sphere with \( N \) traps located at \( \{x_j\} \).
- Trap radii: \( r_j = a_j \varepsilon, \quad j = 1, \ldots, N \); capacitances: \( c_j = 2a_j/\pi \).

MFPT and average MFPT \([A.C., M. Ward, R. Straube (2010)]\):

\[
\nu(x) = \bar{\nu} - \frac{|\Omega|}{DN\bar{c}} \sum_{j=1}^{N} c_j G_s(x; x_j) + O(\varepsilon \log \varepsilon)
\]

\[
\bar{\nu} = \frac{|\Omega|}{2\pi \varepsilon DN\bar{c}} \left[ 1 + \varepsilon \log \left( \frac{2}{\varepsilon} \right) \frac{\sum_{j=1}^{N} c_j^2}{2N\bar{c}} + \frac{2\pi \varepsilon}{N\bar{c}} p_c(x_1, \ldots, x_N) - \frac{\varepsilon}{N\bar{c}} \sum_{j=1}^{N} c_j \kappa_j + O(\varepsilon^2 \log \varepsilon) \right]
\]

- \( G_s(x; x_j) \): spherical Neumann Green’s function (known).
- \( \bar{c} \): average capacitance; \( \kappa_j = \text{const} \).
- \( p_c(x_1, \ldots, x_N) \): trap interaction term involving \( G_s(x_i; x_j) \).
Applications of the MFPT Formula for the Sphere

**MFPT and average MFPT:**

\[
\nu(x) = \bar{\nu} - \frac{|\Omega|}{DN\bar{c}} \sum_{j=1}^{N} c_j G_s(x; x_j) + O(\varepsilon \log \varepsilon)
\]

\[
\bar{\nu} = \frac{|\Omega|}{2\pi\varepsilon DN\bar{c}} \left[ 1 + \varepsilon \log \left( \frac{2}{\varepsilon} \right) \sum_{j=1}^{N} \frac{c_j^2}{2N\bar{c}} + \frac{2\pi\varepsilon}{N\bar{c}} p_c(x_1, \ldots, x_N) - \frac{\varepsilon}{N\bar{c}} \sum_{j=1}^{N} c_j \kappa_j + O(\varepsilon^2 \log \varepsilon) \right]
\]

**Applications:**

- Fast MFPT computations.
- Optimal \(N\)-trap arrangements – local and global optimization.
- Dilute trap limit – homogenization limit for of \(N \gg 1\) small traps \([A.C., M. Ward, & R. Straube (2010); A.C. & D. Zawada (2013)]\)
Dilute Trap Fraction Limit; \( N = 802, \varepsilon = 0.0005 \)

one makes the homogenization MFPT \( \bar{v}_h \) (5.5) become
\[
\bar{v}_h = \pi \varepsilon \frac{1}{12} D \sigma + \frac{1}{15} D,
\]
(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
\[
f(\varepsilon) = \varepsilon + \alpha \varepsilon^2 \log \varepsilon + \beta \varepsilon^2,
\]
\[
\kappa(\sigma) = \frac{4}{\pi} \sigma + \gamma \sqrt{\sigma}.
\]
(5.10)
The homogenization MFPT (5.5) consequently becomes
\[
\bar{v}_h = \pi \varepsilon \frac{1}{12} D \sigma + \pi \varepsilon^2 \frac{1}{12} D \sigma (\beta + \alpha \log \varepsilon) + \frac{1}{15} D + \gamma \varepsilon \frac{1}{12} D \sqrt{\sigma} + Q(\varepsilon, \sigma),
\]
(5.11)
where
\[
Q(\varepsilon, \sigma) = \gamma \varepsilon \frac{1}{12} D \sigma (\beta + \alpha \log \varepsilon).
\]
(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
\[
\alpha = -\frac{1}{\pi}, \beta = \frac{1}{\pi} \log 2, \gamma = \frac{8}{b}.
\]
(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
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A General Class of 3D Domains

- \((\mu, \nu, \omega)\): an orthogonal coordinate system in \(\mathbb{R}^3\).

Consider \(\Omega\) defined by

\[ \Omega \equiv \{(\mu, \nu, \omega) | 0 \leq \mu \leq \mu_0, 0 \leq \nu \leq \nu_0, 0 \leq \omega \leq \omega_0\}, \]

\[ \partial \Omega \equiv \{(\mu, \nu, \omega) | \mu = \mu_0, 0 \leq \nu \leq \nu_0, 0 \leq \omega \leq \omega_0\}. \]

At the boundary: \(\partial n|_{\partial \Omega} = \partial \mu|_{\mu=\mu_0}\).

Scale factors:

\[ h_{\mu_j} = h_\mu(x_j), \quad h_{\nu_j} = h_\nu(x_j), \quad h_{\omega_j} = h_\omega(x_j). \]

Local stretched coordinates (centered at the \(j^{th}\) trap):

\[ \eta = -h_{\mu_j} \frac{\mu - \mu_j}{\varepsilon}, \quad s_1 = h_{\nu_j} \frac{\nu - \nu_j}{\varepsilon}, \quad s_2 = h_{\omega_j} \frac{\omega - \omega_j}{\varepsilon}. \]

Example: axially symmetric domains.
The Laplacian in Local Stretched Coordinates

Laplacian in orthonormal coordinates \((\mu, \nu, \omega)\):

\[
\Delta \Psi = \frac{1}{h_\mu h_\nu h_\omega} \left[ \frac{\partial}{\partial \mu} \left( \frac{h_\nu h_\omega}{h_\mu} \frac{\partial \Psi}{\partial \mu} \right) + \frac{\partial}{\partial \nu} \left( \frac{h_\mu h_\omega}{h_\nu} \frac{\partial \Psi}{\partial \nu} \right) + \frac{\partial}{\partial \omega} \left( \frac{h_\mu h_\nu}{h_\omega} \frac{\partial \Psi}{\partial \omega} \right) \right].
\]

Leading terms:

\[
\Delta = \frac{1}{\varepsilon^2} \Delta_{(\eta, s_1, s_2)} + \frac{1}{\varepsilon} L_\Delta + O(1),
\]

where

\[
\Delta_{(\eta, s_1, s_2)} \equiv \frac{\partial^2}{\partial \eta^2} + \frac{\partial^2}{\partial s_1^2} + \frac{\partial^2}{\partial s_2^2},
\]

and

\[
L_\Delta \equiv \Lambda_\eta \frac{\partial^2}{\partial \eta^2} + \Lambda_{s_1} \frac{\partial^2}{\partial s_1^2} + \Lambda_{s_2} \frac{\partial^2}{\partial s_2^2} + \lambda_\eta \frac{\partial}{\partial \eta} + \lambda_{s_1} \frac{\partial}{\partial s_1} + \lambda_{s_2} \frac{\partial}{\partial s_2}.
\]

\(\Lambda_\alpha, \lambda_\alpha\): rather complicated expressions in terms of scale factors \(h_\beta\).
The Surface Neumann Green’s Function

Green’s Function problem:

\[ \Delta G_s(x; x_j) = \frac{1}{|\Omega|}, \quad x \in \Omega, \quad \partial_n G_s(x; x_j) = \delta_s(x - x_j), \quad x \in \partial \Omega, \]

\[ \int_{\Omega} G \, dx = 0. \]
Green’s Function problem:

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\[ \int_{\Omega} G \, dx = 0. \]

Expression for a general domain [A. Singer, Z. Schuss & D. Holcman (2008)]:

\[ G_s(x; x_j) = \frac{1}{2\pi|\Omega|} - \frac{H(x_j)}{4\pi} \log |x - x_j| + v_s(x; x_j). \]

- \( H(x_j) \): the mean curvature of \( \partial \Omega \) at \( x_j \).
- \( v_s(x; x_j) \): a bounded function of \( x \) and \( x_j \) in \( \Omega \).
The Surface Neumann Green’s Function

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- \( H(x_j) \): the mean curvature of \( \partial \Omega \) at \( x_j \).
- \( v_s(x; x_j) \): a bounded function of \( x \) and \( x_j \) in \( \Omega \).

Asymptotic expansion:

\[ G_s(\eta, s_1, s_2) = \frac{1}{2 \pi \rho} \frac{1}{\varepsilon} - \frac{H(x_j)}{4 \pi} \log \frac{\varepsilon}{2} + g_0(\eta, s_1, s_2) + g_1(\eta, s_1, s_2) \varepsilon \log \frac{\varepsilon}{2} + O(\varepsilon), \]

\[ \rho = \sqrt{\eta^2 + s_1^2 + s_2^2}. \]
Matched Asymptotic Expansions

- **Inner expansion** of solution near trap centered at $x_j$ uses stretched coordinates:

$$v_{in} = w(\eta, s_1, s_2) \sim \frac{1}{\varepsilon} w_0 + \log \left( \frac{\varepsilon}{2} \right) w_1 + w_2 + \cdots.$$ 

- **Outer expansion** far from each of the boundary traps $x_j$, $|x - x_j| = \mathcal{O}(1)$:

$$v_{out} \sim \frac{1}{\varepsilon} v_0 + v_1 + \varepsilon \log \left( \frac{\varepsilon}{2} \right) v_2 + \varepsilon v_3 + \cdots.$$ 

- **Matching condition**: as $x \to x_j$ and as $\rho = \sqrt{\eta^2 + s_1^2 + s_2^2} \to \infty$,

$$\frac{1}{\varepsilon} v_0 + v_1 + \varepsilon \log \left( \frac{\varepsilon}{2} \right) v_2 + \varepsilon v_3 + \cdots \sim \frac{1}{\varepsilon} w_0 + \log \left( \frac{\varepsilon}{2} \right) w_1 + w_2 + \cdots.$$
The Average MFPT Asymptotic Expression

Average MFPT for a general domain:

- Under the assumption $g_1 = 0$ in the Green’s function, as it is for the sphere, matched solutions for first terms of the asymptotic expansions can be computed.

- Average MFPT expression in the outer region $|x - x_j| \gg O(\varepsilon)$:

$$
\bar{v} = \frac{|\Omega|}{2\pi D N \bar{c} \varepsilon} \left[ 1 - \left( \frac{1}{2N\bar{c}} \sum_{i=1}^{N} c_i^2 H(x_i) \right) \varepsilon \log \left( \frac{\varepsilon}{2} \right) + O(\varepsilon) \right]
$$
The Average MFPT Asymptotic Expression

**Average MFPT for a general domain:**

- Under the assumption \( g_1 = 0 \) in the Green’s function, as it is for the sphere, matched solutions for first terms of the asymptotic expansions can be computed.

- Average MFPT expression in the outer region \(|x - x_j| \gg \mathcal{O}(\varepsilon)|\):

\[
\bar{v} = \frac{|\Omega|}{2\pi DN\bar{c}\varepsilon} \left[ 1 - \left( \frac{1}{2N\bar{c}} \sum_{i=1}^{N} c_i^2 H(x_i) \right) \varepsilon \log \left( \frac{\varepsilon}{2} \right) + \mathcal{O}(\varepsilon) \right]
\]

**Compare to the spherical MFPT formula:**

\[
\bar{v} = \frac{|\Omega|}{2\pi DN\bar{c}\varepsilon} \left[ 1 - \left( \frac{1}{2N\bar{c}} \sum_{j=1}^{N} c_j^2 \right) \varepsilon \log \left( \frac{\varepsilon}{2} \right) + \frac{2\pi \varepsilon}{N\bar{c}} p_c(x_1, \ldots, x_N) - \frac{\varepsilon}{N\bar{c}} \sum_{j=1}^{N} c_j \kappa_j + \ldots \right]
\]

- \( \mathcal{O}(1) \) term for the sphere depends on *trap positions*.

- A similar expression of the same order for a general domain can be derived, with some details still missing...
The Average MFPT: Comparison of Asymptotic and Numerical Results

- Numerical solver: COMSOL Multiphysics 4.3b
- Compare numerical and asymptotic average MFPT for three distinct geometries
- $N = 3$ and $N = 5$ traps
- Relative error:
  \[
  \text{R.E.} = 100\% \times \frac{\bar{v}_{\text{numerical}} - \bar{v}_{\text{asymptotic}}}{\bar{v}_{\text{numerical}}}
  \]
- “Extremely fine” and “fine” mesh regions:

![Mesh Regions](image-url)
Sample COMSOL MFPT Computations for the Unit Sphere

MFPT (epsilon = 0.02)

MFPT (epsilon = 0.02)
Oblate Spheroid

- \( x = \rho \cosh \xi \cos \nu \cos \phi, \quad y = \rho \cosh \xi \cos \nu \sin \phi, \quad z = \rho \sinh \xi \sin \nu \)
- \( \xi \in [0, \infty), \quad \nu \in [-\pi/2, \pi/2], \quad \phi \in [0, 2\pi) \)
- \( \partial \Omega: \quad \xi = \xi_0 = \tanh^{-1}(0.5), \quad \rho = (\cosh \xi_0)^{-1} \)

Figure 4: Plots of (a) comparison of numerical (circles) and two-term asymptotic expression for average MFPT, and (b) relative error (see (22)) for an oblate spheroid with \( N = 5 \).

Figure 5: Three-dimensional (transparent) plots of the numerical MFPT for the oblate spheroid at \( \varepsilon = 0.02 \) with (a) \( N = 3 \) and (b) \( N = 5 \) traps. The trap parameters are given in Table 1.

\[ x = \rho \cosh \xi \cos \nu \cos \phi, \quad y = \rho \cosh \xi \cos \nu \sin \phi, \quad z = \rho \sinh \xi \sin \nu \]
\[ \xi \in [0, \infty), \quad \nu \in [-\pi/2, \pi/2], \quad \phi \in [0, 2\pi) \]
\[ \partial \Omega: \quad \xi = \xi_0 = \tanh^{-1}(0.5), \quad \rho = (\cosh \xi_0)^{-1} \]
**Oblate Spheroid**

- Trap radii: \( r_j = a_j \epsilon \)

<table>
<thead>
<tr>
<th>Number of Traps</th>
<th>( a )</th>
<th>( \nu )</th>
<th>( \phi )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N = 3 )</td>
<td>1</td>
<td>(-3\pi/8)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0</td>
<td>( \pi )</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>( \pi/2 )</td>
<td>0</td>
</tr>
<tr>
<td>( N = 5 )</td>
<td>1</td>
<td>0</td>
<td>( \pi/2 )</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>( \pi/4 )</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>(-\pi/2)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>(-\pi/4)</td>
<td>( \pi/4 )</td>
</tr>
<tr>
<td></td>
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</tr>
</tbody>
</table>

Trap locations and relative radii for oblate and prolate spheroids
Figure 4: Plots of (a) comparison of numerical (circles) and two-term asymptotic expression for average MFPT, and (b) relative error (see (22)) for an oblate spheroid with $N = 5$.

Figure 5: Three-dimensional (transparent) plots of the numerical MFPT for the oblate spheroid at $\varepsilon = 0.02$ with (a) $N = 3$ and (b) $N = 5$ traps. The trap parameters are given in Table 1.

Table 1: Trap locations and relative radii for in sample MFPT computations for oblate and prolate spheroids.
Oblate Spheroid

- Numerical vs. asymptotic average MFPT for the oblate spheroid, \( N = 5 \):
Prolate Spheroid

- \( x = \rho \sinh \xi \cos \nu \cos \phi \), \( y = \rho \sinh \xi \cos \nu \sin \phi \), \( z = \rho \cosh \xi \sin \nu \)
- \( \xi \in [0, \infty), \nu \in [-\pi/2, \pi/2], \) and \( \phi \in [0, 2\pi) \)
- \( \partial \Omega: \xi_0 = \tanh^{-1}(1/1.5) \) and \( \rho = (\sinh \xi_0)^{-1} \)
Prolate Spheroid

- Numerical vs. asymptotic average MFPT for the prolate spheroid, \( N = 3 \):

\[
\begin{align*}
\text{Average MFPT} & \quad \text{Relative Error (\%)} \\
\end{align*}
\]

\[
\begin{align*}
0 & \quad 0 \\
\cdots & \quad \cdots \\
0.05 & \quad \cdots \\
\end{align*}
\]
Numerical vs. asymptotic average MFPT for the prolate spheroid, $N = 5$: 

- **Figure 7**: Plots of (a) comparison of numerical (circles) and two-term asymptotic expression for average MFPT, and (b) relative error (see (22)) for a prolate spheroid with $N = 5$.

- **Figure 8**: Three-dimensional (transparent) plots of the numerically calculated MFPT (in seconds) for the prolate spheroid at $\varepsilon = 0.02$ with (a) $N = 3$ and (b) $N = 5$ traps.
Shape obtained by rotating the following curve about the z-axis:

\[ x = a\alpha \sin \chi, \quad z = a\frac{\alpha}{2} \left(b + c \sin^2 \chi - d \sin^4 \chi\right) \cos \chi, \quad \chi \in [0, \pi]. \]

Common parameters [Pozrikidis (2003)]:

\[ a = 1, \quad \alpha = 1.38581994, \quad b = 0.207, \quad c = 2.003, \quad d = 1.123. \]
Biconcave Disk (Blood Cell Shape)

**Trap radii:** \( r_j = a_j \varepsilon \)

<table>
<thead>
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<td>( \pi )</td>
<td>0</td>
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<tr>
<td></td>
<td>2</td>
<td>( \pi/2 )</td>
<td>( \pi/2 )</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>( \pi/2 )</td>
<td>( \pi )</td>
</tr>
</tbody>
</table>

Trap locations and relative radii for biconcave disk (blood cell)
Biconcave Disk (Blood Cell Shape)

- Numerical vs. asymptotic average MFPT for the biconcave disk, $N = 3$: 

  ![Graphs showing numerical vs. asymptotic average MFPT for a biconcave disk](image)

  - **Left**: Comparison of numerical (circles) and two-term asymptotic expression for average MFPT.
  - **Right**: Relative error (see (22)) for a biconcave disk with $N = 5$.

Conjecture 4.1:

For the problem (1) have the following asymptotic expressions:

$$
\text{MFPT} \approx C \left( \frac{1}{\epsilon} \right)^n + D
$$

where $C$, $D$, and $n$ are constants. The above expressions are in rather similar to the ones for the unit sphere obtained in [4].
Numerical vs. asymptotic average MFPT for the biconcave disk, $N = 5$:
Numerous biological processes involve the transport of particles from a cell through its membrane: by SIAM. Unauthorized reproduction of this article is prohibited.

Asymptotic approximations are of the form

\[ \text{Numerical (exact)} \]

\[ \Singer, Schuss, and Holcman Approximation \]

\[ \text{Three Trap Approximation} \]

\[ \text{Relative Error (%)} \]

\[ \epsilon = 0.02 \]

\[ \epsilon = 0.03 \]

\[ \epsilon = 0.04 \]

\[ \text{Retrieved Aug. 13, 2013 from: } \]

\[ \text{http://www.sciencedaily.com/releases/2007/11/071126201333.htm} \]

\[ \text{NARROW ESCAPE FROM A SPHERE } 837 \]

\[ \text{the ... equations resulting from } \]

\[ \text{a separation of variables approach. A similar result for } \]

\[ \bar{v} \]

\[ \text{was obtained in [41] for the } \]

\[ \text{problem, and the matching condition. } \]

\[ \text{depends only on } \]

\[ s, v, \]

\[ \nu \]

\[ \omega \]

\[ \bar{v} \]

\[ \bar{p} \]

\[ \epsilon \]

\[ \text{trap capacitance} \]

\[ c \]

\[ \mu_0, \nu_j, \omega_j \]

\[ \eta \]

\[ s_1, s_2 \]
Based on certain assumptions, higher terms in MFPT formulas can be written, generalizing those for the unit sphere:

$$\bar{v} = \frac{\left| \Omega \right|}{2\pi \epsilon DN\bar{c}} \left[ 1 - \frac{1}{2N\bar{c}} \sum_{j=1}^{N} c_j^2 H(x_j) \epsilon \log \frac{\epsilon}{2} \right. \right.$$  

$$\left. + \frac{\epsilon}{N\bar{c}} \left( \sum_{j=1}^{N} b_j + p_c(x_1, \ldots, x_N) \right) + O(\epsilon^2 \log \epsilon) \right].$$

$$v(x) = \bar{v} - \frac{\left| \Omega \right|}{DN\bar{c}} \sum_{j=1}^{N} c_j G_s(x; x_j),$$

The “interaction energy”:

$$p_c(x_1, \ldots, x_N) \equiv 2\pi \sum_{j=1}^{N} \sum_{i \neq j} c_j c_i G_s(x_j; x_i).$$

Ingredients still required: $G_s(x; x_j), b_j$. 

Towards Higher-order MFPT Asymptotics
Outline

1. Narrow Escape Problems, Mean First Passage Time (MFPT)
2. Asymptotic Results for Small Traps; Higher-Order MFPT for the Sphere
3. Asymptotic Analysis of the MFPT Problem for Non-Spherical Domains
4. Asymptotic vs. and Numerical Average MFPT for Non-Spherical Domains
   - Oblate Spheroid
   - Prolate Spheroid
   - Biconcave Disk–Blood Cell Shape
5. Towards Higher-order MFPT Asymptotics
6. Highlights and Open Problems
Results

- For the average MFPT $\bar{v}$, a two-term asymptotic expansion is derived for a wide class of non-spherical domains.
- Directly generalizes the results for the sphere.
- Full finite-element MFPT numerical calculations have been performed to compare average MFPT with asymptotic expansions – close agreement observed for small $\varepsilon$.
- Steps towards the derivation of a higher-order formula for $v(x)$, $\bar{v}$ involving trap positions are taken.

Open problems

- Assumptions on surface Neumann Green’s function expansion have been made – justification or modification is required.
- The trap interaction term for non-spherical domains requires further work...
- ... when clarified, global optimization of the average MFPT with respect to trap locations may be performed.
Some References

A. Singer, Z. Schuss, and D. Holcman,

A. F. Cheviakov, M. J. Ward, and R. Straube,

A. F. Cheviakov, A. S. Reimer, and M. J. Ward,

A. F. Cheviakov and D. Zawada,

D. Gomez and A. F. Cheviakov,
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Thank you for attention!