Narrow Escape Problems in Three-Dimensional Domains

Daniel Gomez and Alexey F. Shevyakov
Department of Mathematics and Statistics, University of Saskatchewan

NSERC CRSNG

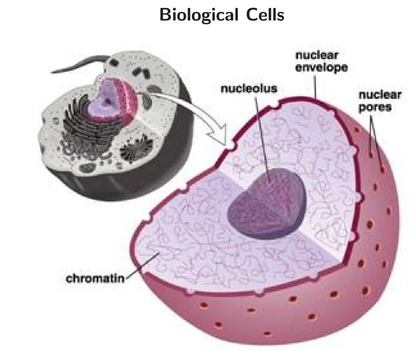
Motivation/Application

Numerous biological processes involve the transport of particles from a cell through its membrane:

- RNA transport through nuclear pores.
- Passive diffusion of molecules (e.g. CO_2 and O_2) through cell membrane.
- Diffusion of ions through protein channels (e.g. Na-K-Cl co-transporter in blood cells).

Typical size of transport regions is $\sim 0.1\%$ relative to overall cell size.

Biological Cells



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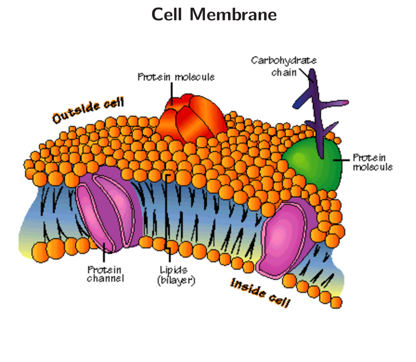
Cell Membrane



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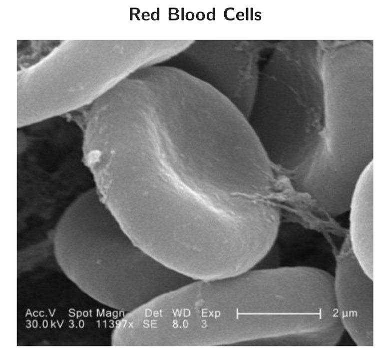
Red Blood Cells



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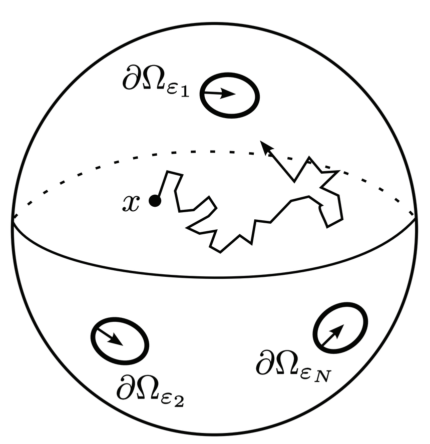
The Narrow Escape Problem (NEP)



- Three-Dimensional domain Ω.
- Boundary traps: $\partial\Omega_{\epsilon_j}$ $(j=1,\dots,N)$.
- Brownian motion.
- Mean first passage time (MFPT): $v(\mathbf{x})$.
- Average MFPT: $\bar{v}\equiv\frac{1}{|\Omega|}\int_\Omega v(\mathbf{x})\,d^3\mathbf{x}$.
- Dirichlet-Neumann Boundary Value Problem [3]:

$$\begin{aligned}&\Delta v(\mathbf{x})=-\frac{1}{D},\quad \mathbf{x}\in\Omega;\\ &\partial_n v(\mathbf{x})=0,\quad \mathbf{x}\in\partial\Omega\setminus\textstyle\bigcup_j\partial\Omega_{\epsilon_j};\\ &v(\mathbf{x})=0,\quad \mathbf{x}\in\textstyle\bigcup_j\partial\Omega_{\epsilon_j}.\end{aligned}\tag{1}$$

Asymptotic Solutions

- The problem (1) does not admit a known analytic solution.
- It is difficult to solve numerically due to its highly heterogeneous boundary conditions.

An asymptotic approximation is beneficial because it offers fast computation times, and gives properties of the solution that would otherwise be hidden by numerical data. One considers asymptotic expansion of the form

$$v(\mathbf{x})\sim\epsilon^{-1}v_0(\mathbf{x})+v_1(\mathbf{x})+\epsilon\log\left(\frac{\epsilon}{2}\right)v_2(\mathbf{x})+\epsilon v_3(\mathbf{x})+\dots.$$

where ϵ is the trap size parameter. Using the method of matched asymptotic expansions one then obtains the average MFPT of the form

$$v(\mathbf{x})=\bar{v}+\sum_{j=1}^{N}k_jG_s(\mathbf{x};\mathbf{x}_j),\tag{2}$$

where k_j are particular constants. The function $G_s(\mathbf{x};\mathbf{x}_j)$ is known as the surface Neumann Green's function and it satisfies the boundary value problem

$$\begin{aligned}&\Delta G_s(\mathbf{x};\mathbf{x}_j)=\frac{1}{|\Omega|}, && \mathbf{x}\in\Omega;\\ &\partial_n G_s(\mathbf{x};\mathbf{x}_j)=\delta_s(\mathbf{x}-\mathbf{x}_j), && \mathbf{x}\in\partial\Omega;\\ &\textstyle\int_\Omega G_s(\mathbf{x};\mathbf{x}_j)d^3\mathbf{x}=0.\end{aligned}\tag{3}$$

The Unit Sphere

When Ω is the unit sphere with N holes of radii ϵa_j located at $\mathbf{x}_j$ respectively, it was found in [1] that

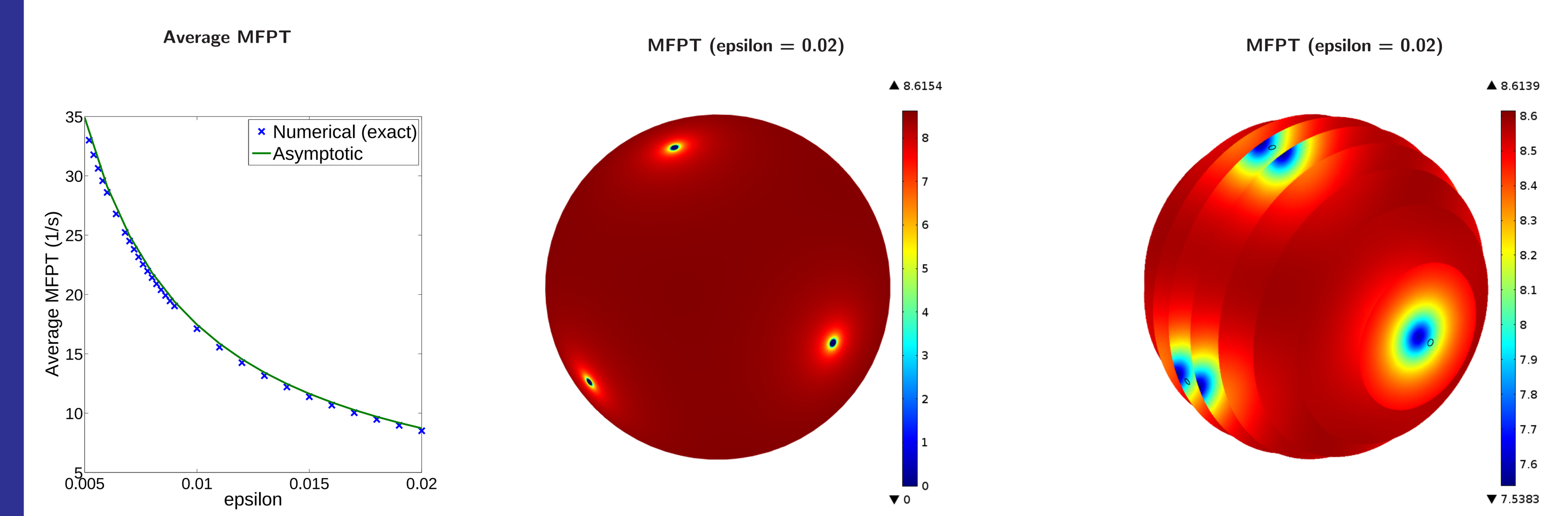
$$\bar{v}=\frac{|\Omega|}{2\pi\epsilon DN\bar{c}}\left[1+\epsilon\log\left(\frac{2}{\epsilon}\right)\frac{\sum_{j=1}^N c_j^2}{2N\bar{c}}+\frac{2\pi\epsilon}{N\bar{c}}p_c(\mathbf{x}_1,\dots,\mathbf{x}_N)-\frac{\epsilon}{N\bar{c}}\sum_{j=1}^{N}c_j\kappa_j+O(\epsilon^2\log\epsilon)\right].\tag{4}$$

In this expression $p_c(\mathbf{x}_1,\dots,\mathbf{x}_N)$ depends on the hole sizes and their relative distances, the constants κ_j depend only on the hole radii a_j, and the c_j are known as the trap capacitance and are given by

$$c_j=\frac{2a_j}{\pi}.\tag{5}$$

Such a high order asymptotic expansion for the average MFPT is made possible by the explicit knowledge of the surface Neumann Green's function for the sphere. Unfortunately this is not the case for non-spherical domains.

Asymptotic and Numerical MFPT for Unit Sphere with Six Identical Traps



Singer, Schuss, and Holcman Approximation

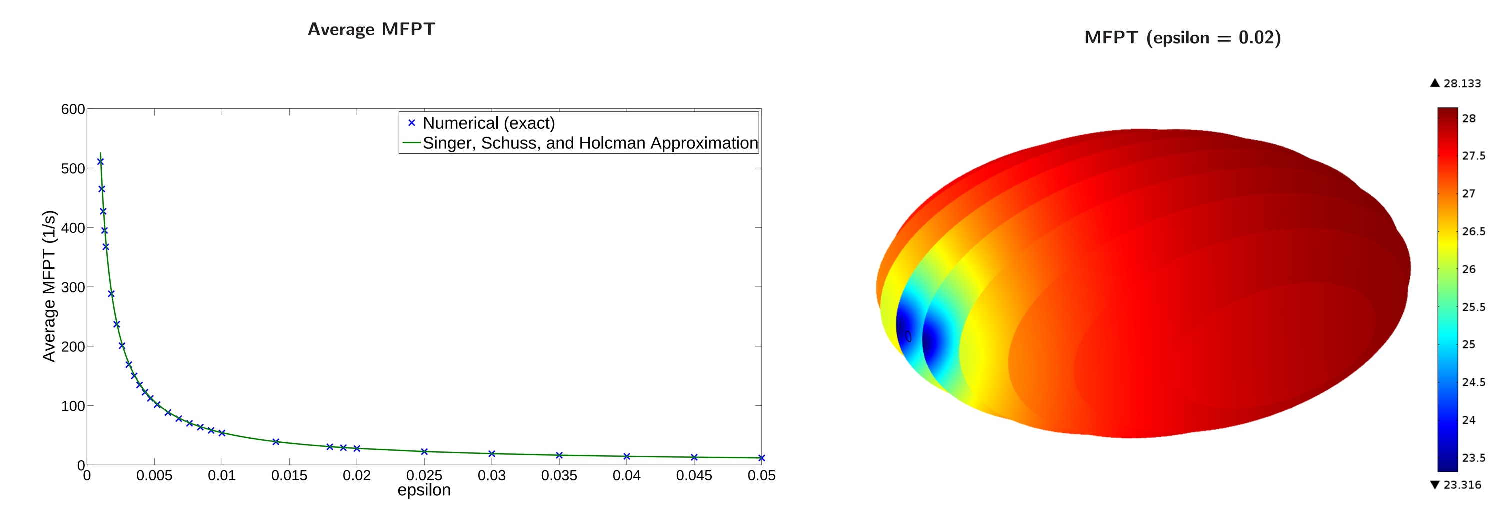
For non-spherical domains the surface Neumann-Green's function is not explicitly known. Nevertheless, for such a domain, Ω, with exactly one circular trap of radius ϵ centred at $\mathbf{x}_0$ the average MFPT is given in [4] by

$$\bar{v}\equiv\frac{|\Omega|}{4\epsilon D}\left[1+\frac{H(\mathbf{x}_0)}{\pi}\epsilon\log\epsilon+O(\epsilon)\right]^{-1},\tag{6}$$

where $H(\mathbf{x}_0)$ is the mean curvature of $\partial\Omega$ at $\mathbf{x}_0$. While this formula approximates the average MFPT for an arbitrary domain, its limitations are:

- Only valid for one absorbing window.
- Error bound is $O(\epsilon)$ as opposed to $O(\epsilon^2\log\epsilon)$ found for sphere.

Oblate Spheroid with One Trap



Multi-Trap Generalization

Comparison between the Singer, Schuss, and Holcman approximation (6) and the asymptotic formula for the sphere (4) suggests the introduction of a modified trap capacitance

$$\tilde{c}_j=\frac{2a_jH(\mathbf{x}_j)}{\pi},$$

where $H(\mathbf{x}_j)$ is the mean curvature at the jth trap location. With the modified trap capacitance the proposed multi-trap average MFPT approximation takes on the form

$$\bar{v}=\frac{|\Omega|}{4\epsilon D\sum_{j=1}^N a_j}\left[1+\frac{\epsilon}{2}\log\epsilon\frac{\sum_{j=1}^N\tilde{c}_j^2}{\sum_{j=1}^N\tilde{c}_j}+O(\epsilon)\right]^{-1}.\tag{7}$$

Testing Procedure and COMSOL

Used oblate spheroid, prolate spheroid, and biconcave disk geometries.

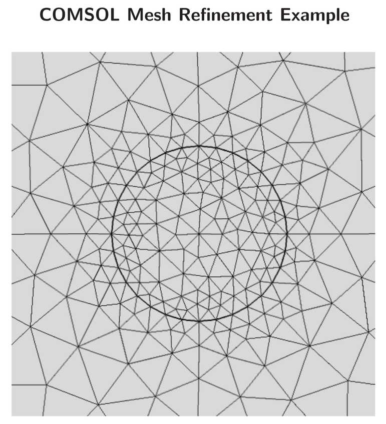
- Provide range of local curvatures.
- Represent different biological cells.

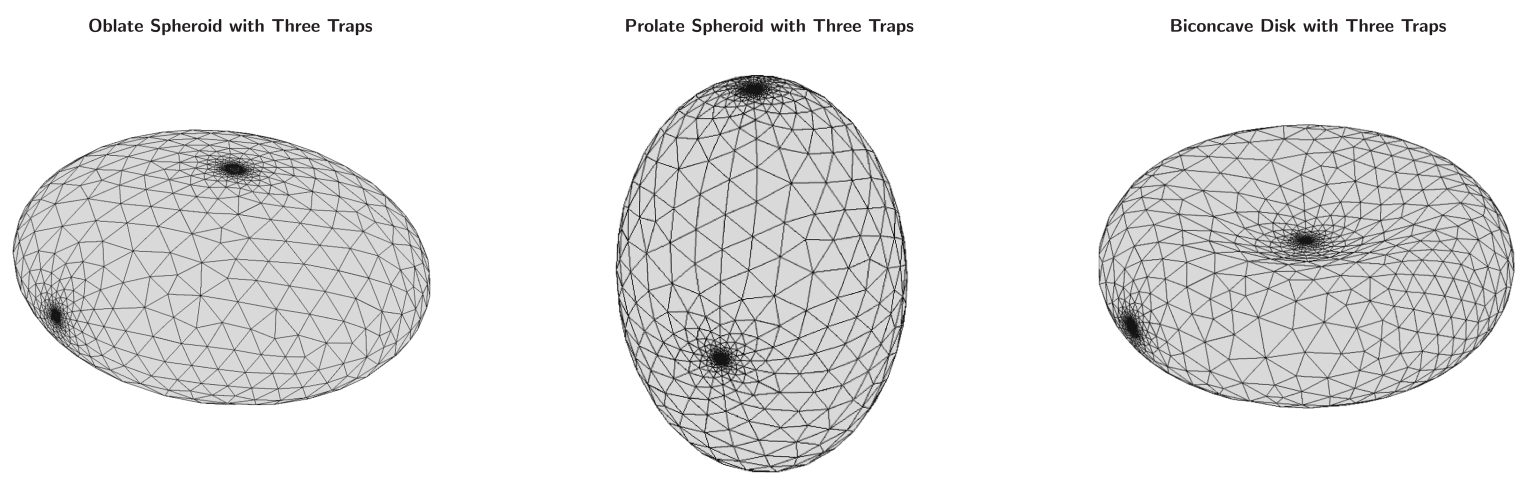
COMSOL Multiphysics 4.3b software used for numerical results.

- Finite element PDE solver.
- Tetrahedral mesh.

Numerical results for two and three traps of equal and different sizes compared to proposed multi-trap approximation in MATLAB.

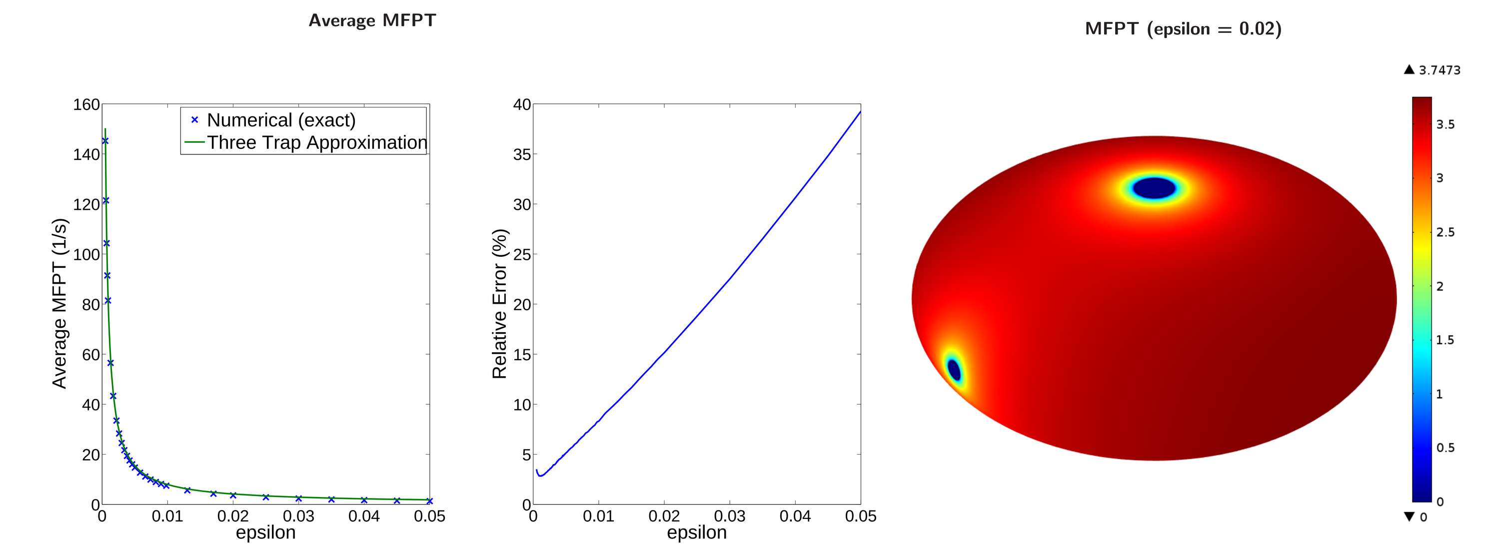
COMSOL Mesh Refinement Example



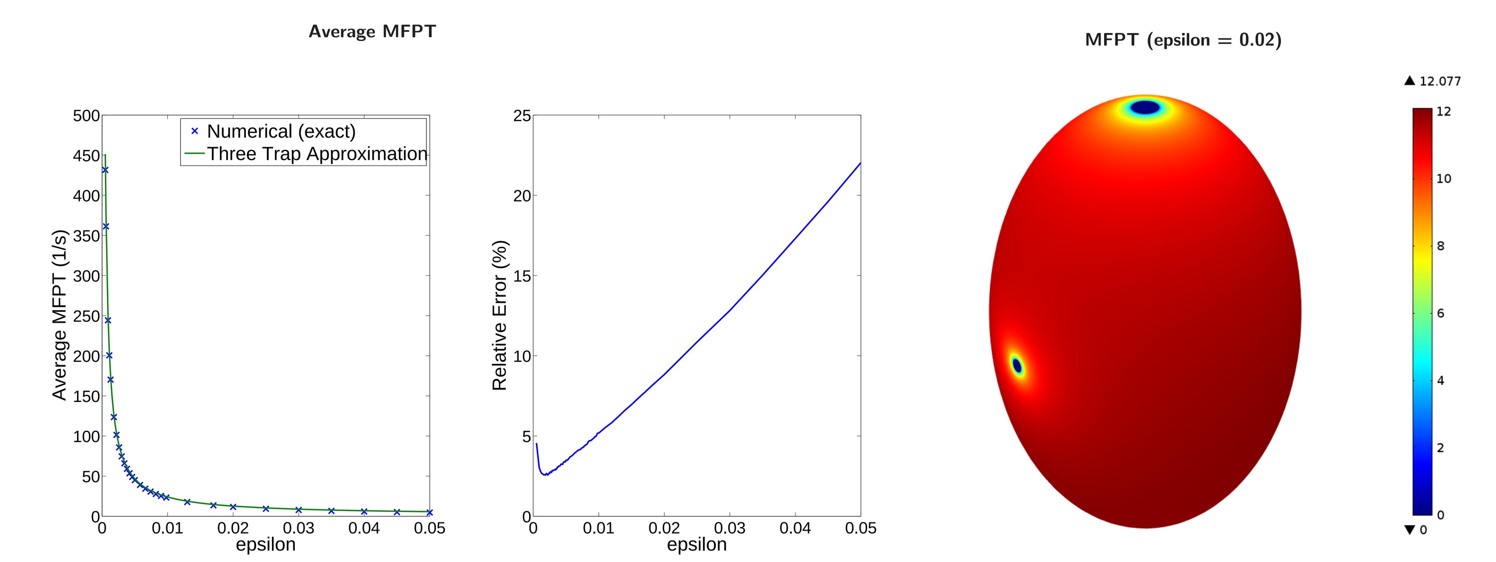


Results for Three Different Sized Traps

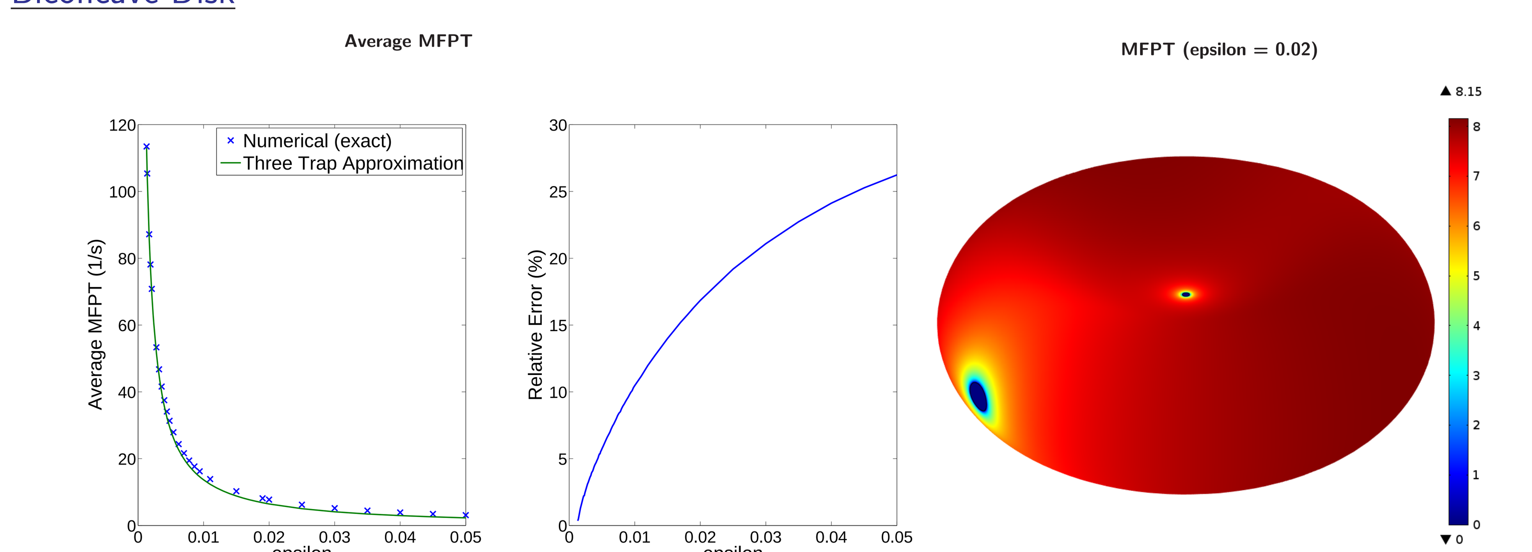
Oblate Spheroid



Prolate Spheroid



Biconcave Disk



Conclusions

- A multi-trap generalization of (6) was proposed and tested.
- Relative error remained below 10% for $\epsilon\leq 0.01$ for tested geometries (numerical error $\sim 1\%$).

Future Research

- Comparison of numerical simulation to proposed formula for greater number of traps on more varied geometries.
- Asymptotic methods for narrow escape problems with non-constant diffusivity.
- Determination of surface Neumann Green's function and derivation of higher-order asymptotic expansions for non-spherical domains.
- Study of dilute trap limit of homogenization theory for non-spherical domains [2].

References

[1] Alexei F. Cheviakov, Michael J. Ward, and Ronny Straube.
An asymptotic analysis of the mean first passage time for narrow escape problems. II. The sphere.
Multiscale Model. Simul., 8(3):836–870, 2010.

[2] Cyrill B. Muratov and Stanislav Y. Shvartsman.
Boundary homogenization for periodic arrays of absorbers.
Multiscale Model. Simul., 7(1):44–61, 2008.

[3] Zeev Schuss.
Theory and applications of stochastic differential equations.
John Wiley & Sons Inc., New York, 1980.
Wiley Series in Probability and Statistics.

[4] A. Singer, Z. Schuss, and D. Holcman.
Narrow escape and leakage of Brownian particles.
Phys. Rev. E (3), 78(5):051111, 8, 2008.