Traps, Patches, Spots, and Stripes: Localized Solutions to Diffusive and Reaction-Diffusion Systems

Michael J. Ward (UBC)

BIRS Meeting; Multi-Scale Analysis of Self-Organization in Biology

Collaborators:, R. Straube (Max-Planck, Magdeburg); D. Coombs (UBC); A. Lindsay, S. Pillay (UBC); A. Cheviakov and R. Spiteri (U. Saskatchewan)

Lecture I: Linear Diffusion Problems with Localized Traps or Patches

Outline of the Talk

SOME GENERAL CONSIDERATIONS:

1. Eigenvalue Problems in Perforated Domains and in Domains with Perforated Boundaries (Some Previous Results)
2. Narrow Escape Problem and the Mean First Passage Time (MFPT)
3. Fekete Points

THREE SPECIFIC PROBLEMS CONSIDERED:

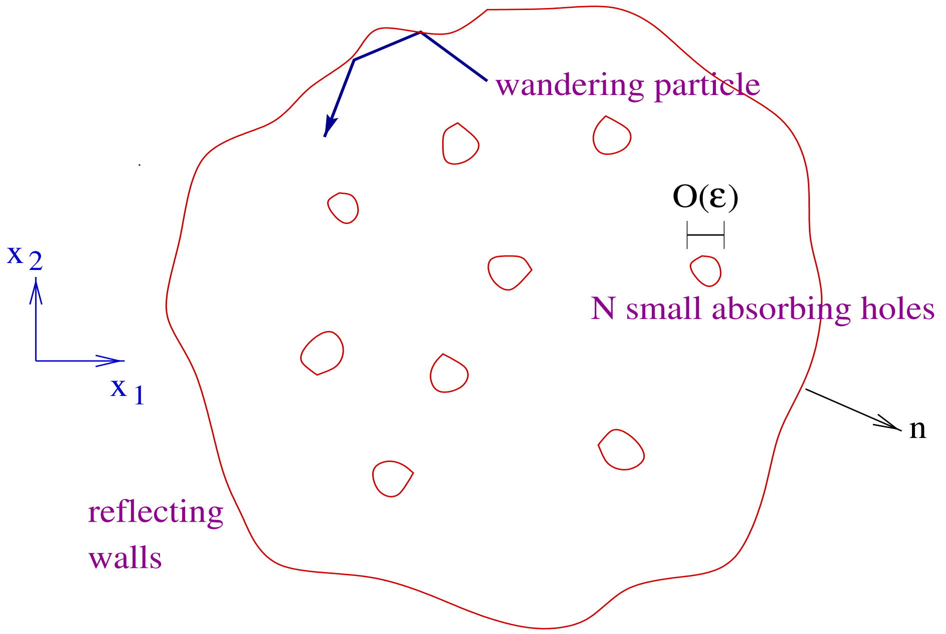
1. Diffusion on the Surface of a Sphere with Traps
2. The Mean First Passage Time for Escape from a Sphere with Localized Absorbing Boundary Patches
3. Persistence Threshold for Diffuse Logistic Model in Highly Patchy Environments

Eigenvalues in Perforated Domains I

For a bounded 2-D or 3-D domain;

$$\Delta u + \lambda u = 0\,, \quad x \in \Omega\backslash\Omega_p\,; \quad \int_{\Omega\backslash\Omega_p} u^2\,dx = 1\,,$$
$$\partial_n u = 0 \quad x \in \partial\Omega\,, \quad u = 0\,, \quad x \in \partial\Omega_p\,.$$

- Here $\Omega_p = \cup_{i=1}^{N} \Omega_{\varepsilon_i}$ are N interior non-overlapping holes or traps, each of 'radius' $O(\varepsilon) \ll 1$.
- Also $\Omega_{\varepsilon_i} \to x_i$ as $\varepsilon \to 0$, for $i = 1, \ldots, N$. The centers x_i are arbitrary.



Eigenvalues in Perforated Domains II

EIGENVALUE ASYMPTOTICS FOR PRINCIPAL EIGENVALUE λ_1:

Previous Studies in 2-D: For the case of N circular holes each of radius $\varepsilon \ll 1$, Ozawa (Duke J., 1981) proved that

$$\lambda_1 \sim \frac{2\pi N\nu}{|\Omega|} + O(\nu^2), \quad \nu \equiv -\frac{1}{\log \varepsilon} \ll 1 \,.$$

Previous Studies in 3-D: For the case of N localized traps, Ozawa (J. Fac. Soc. U. Tokyo, 1983) (see also Flucher (1993)) proved that

$$\lambda_1 \sim \frac{4\pi\varepsilon}{|\Omega|} \sum_{j=1}^{N} C_j + 0(\varepsilon^2) \,.$$

Here C_j is the electrostatic capacitance of the j^{th} trap defined by

$$\Delta_y w = 0 \,, \quad y \notin \Omega_j \equiv \varepsilon^{-1}\Omega_{\varepsilon_j} \,,$$

$$w = 1 \,, \quad y \in \partial\Omega_j \,; \qquad w \sim \frac{C_j}{|y|} \,, \quad |y| \to \infty \,.$$

Eigenvalues in Perforated Domains III

The MFPT: The Mean First Passage Time $v(x)$ for diffusion in a perforated domain with initial starting point $x \in \Omega \backslash \Omega_p$ satisfies (ref. Z. Schuss, (1980))

$$\Delta v = -\frac{1}{D}, \quad x \in \Omega \backslash \Omega_p ;$$
$$\partial_n v = 0 \quad x \in \partial \Omega , \quad v = 0 , \quad x \in \partial \Omega_p .$$

Relationship Between Averaged MFPT and Principal Eigenvalue: is that for $\varepsilon \to 0$

$$\bar{v} \sim \frac{1}{D\lambda_1}, \qquad \bar{v} \equiv \frac{1}{|\Omega|} \int_{\Omega \backslash \Omega_p} v \, dx .$$

Main Goal: Calculate λ_1 and the MFPT on the surface of a sphere that contains N small traps. For $\varepsilon \to 0$ (small hole radius) find the hole locations x_i, for $i = 1, \ldots, N$, that maximizes λ_1, or equivalently minimizes $\bar{v}$. In other words, chose the trap locations to minimize the lifetime of a wandering particle on the sphere.

Key Point: Since the previous results for λ_1 are independent of trap locations x_j, $j = 1, \ldots, N$, need higher order terms in λ_1 to optimize λ_1.

Eigenvalues with Perforated Boundaries I

Let λ_1 be the principal eigenvalue when $\partial\Omega$ is perforated

$$\Delta u + \lambda u = 0\,, \quad x \in \Omega\,; \quad \int_\Omega u^2\, dx = 1\,,$$

$$\partial_n u = 0 \quad x \in \partial\Omega_r\,, \quad u = 0\,, \quad x \in \partial\Omega_a = \cup_{j=1}^{N} \partial\Omega_{\varepsilon_j}\,.$$

- For a 2-D domain with smooth boundary (MJW, Keller, SIAP, 1993)

$$\lambda_1 \sim \frac{\pi N \nu}{|\Omega|} + O(\nu^2), \quad \nu \equiv -\frac{1}{\log \varepsilon} \ll 1\,.$$

- For a 3-D domain with smooth boundary (MJW, Keller, SIAP, 1993)

$$\lambda_1 \sim \frac{2\pi\varepsilon}{|\Omega|} \sum_{j=1}^{N} C_j + 0(\varepsilon^2)\,.$$

Here C_j is the capacitance of the electrified disk problem

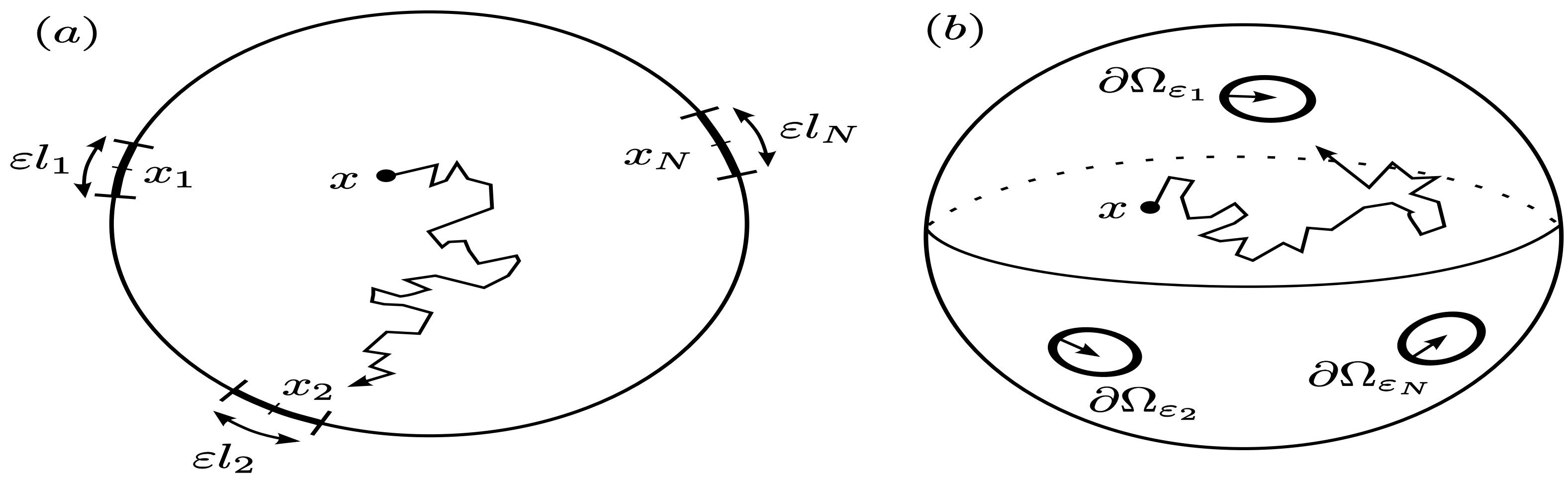
$$\Delta_y w = 0\,, \quad y_3 \geq 0, \quad -\infty < y_1, y_2 < \infty\,,$$

$$w = 1\,, \quad y_3 = 0\,, (y_1, y_2) \in \partial\Omega_j\,; \; \partial_{y_3} w = 0\,, \quad y_3 = 0\,, (y_1, y_2) \notin \partial\Omega_j\,;$$

$$w \sim C_j/|y|\,, \quad |y| \to \infty\,.$$

Eigenvalues with Peforated Boundaries II

Narrow Escape: Brownian motion with diffusivity D in Ω with $\partial\Omega$ insulated except for an (multi-connected) absorbing patch $\partial\Omega_a$ of measure $O(\varepsilon)$. Let $\partial\Omega_a \to x_j$ as $\varepsilon \to 0$ and $X(0) = x \in \Omega$ be initial point for Brownian motion.



The MFPT $v(x) = E\left[\tau | X(0) = x\right]$ satisfies (Z. Schuss (1980))

$$\Delta v = -\frac{1}{D}, \quad x \in \Omega; \qquad \bar{v} \equiv \frac{1}{|\Omega|}\int_\Omega v\, dx,$$

$$\partial_n v = 0, \quad x \in \partial\Omega_r; \quad v = 0, \quad x \in \partial\Omega_a = \cup_{j=1}^{N} \partial\Omega_{\varepsilon_j}.$$

The average MFPT is related to the fundamental eigenvalue λ_1 by

$$\bar{v} \sim \frac{1}{D\lambda_1}, \quad \text{for } \varepsilon \to 0.$$

Eigenvalues with Peforated Boundaries III

KEY GENERAL REFERENCES:

- Z. Schuss, A. Singer, D. Holcman, *The Narrow Escape Problem for Diffusion in Cellular Microdomains*, PNAS, **104**, No. 41, (2007), pp. 16098-16103.
- O. Bénichou, R. Voituriez, *Narrow Escape Time Problem: Time Needed for a Particle to Exit a Confining Domain Through a Small Window*, Phys. Rev. Lett, **100**, (2008), 168105.
- S. Condamin, et al., Nature, **450**, 77, (2007)
- S. Condamin, O. Bénichou, M. Moreau, Phys. Rev. E., **75**, (2007).

RELEVANCE OF NARROW ESCAPE TIME PROBLEM IN BIOLOGY:

- time needed for a reactive particle released from a specific site to activate a given protein on the cell membrane
- biochemical reactions in cellular microdomains (dendritic spines, synapses, microvesicles), consisting of a small number of particles that must exit the domain to initiate a biological function.
- determines reaction rate in Markov model of chemical reactions

Eigenvalues with Peforated Boundaries IV

RECENT 2-D and 3-D RESULTS:

- In $\Omega \in \mathbb{R}^2$, (**Ref:** D. Holcman, et al., J. Stat. Phys., **117**, (2004).)

$$v(x) = \frac{|\Omega|}{\pi D} \left[-\log \varepsilon + O(1) \right] , \quad \text{for} \;\; \varepsilon \to 0 \,.$$

  The $O(1)$ term was determined for the unit disk **Ref:** A. Singer, Z. Schuss, D. Holcman, J. Stat. Phys. **122**, (2006), and was fit to Brownian simulations for the case of two traps, **Ref:** D. Holcman et al., J. of Phys. A: Math Theor., **41**, (2008), 155001.

- For one circular trap of radius ε on the unit sphere Ω

$$\bar{v} \sim \frac{|\Omega|}{4\varepsilon D} \left[1 - \frac{\varepsilon}{\pi} \log \varepsilon + O\left(\varepsilon\right) \right] , \qquad |\Omega| = 4\pi/3 \,.$$

  Ref: A. Singer et al. J. Stat. Phys., **122**, No. 3, (2006).

- For arbitrary $\Omega \in \mathbb{R}^3$ with smooth $\partial\Omega$ and one circular trap at $x_0 \in \partial\Omega$

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

  Here H is the mean curvature of $\partial\Omega$ at $x_0 \in \partial\Omega$. **Ref:** A. Singer, Z. Schuss, D. Holcman, Phys. Rev. E., **78**, No. 5, 051111, (2009).

Eigenvalues and Fekete Points

Main Goal: Calculate a higher-order expansion as $\varepsilon \to 0$ in 3-D to determine the effect on $\bar{v}$ of the spatial configuration $\{x_1, \cdots, x_N\}$ of multiple absorbing boundary traps for a fixed trap area fraction. Minimize $\bar{v}$ wrt $\{x_1, \cdots, x_N\}$.

- **3-D (Fekete Points):** Let Ω be the unit sphere with N-circular absorbing patches on $\partial\Omega$ of a common radius. Is minimizing $\bar{v}$ equivalent to minimizing the Coulomb energy $\mathcal{H}_C(x_1, \ldots, x_N)$ defined by

$$\mathcal{H}_C(x_1, \ldots, x_N) = \sum_{j=1}^{N} \sum_{k>j}^{N} \frac{1}{|x_j - x_k|}, \quad |x_j| = 1 .$$

  (Ref: J.J. Thomson, E. Saff, N. Sloane, A. Kuijlaars etc..)

- **2-D (Elliptic Fekete Points):** minimum point of the logarithmic energy $\mathcal{H}_L$

$$\mathcal{H}_L(x_1, \ldots, x_N) = -\sum_{j=1}^{N} \sum_{k>j}^{N} \log |x_j - x_k| , \quad |x_j| = 1 .$$

  (Ref: Smale and Schub, Saff, Sloane, Kuijlaars, etc..) Are these points related to optimizing the MFPT for diffusion on the surface of the sphere with localized traps?

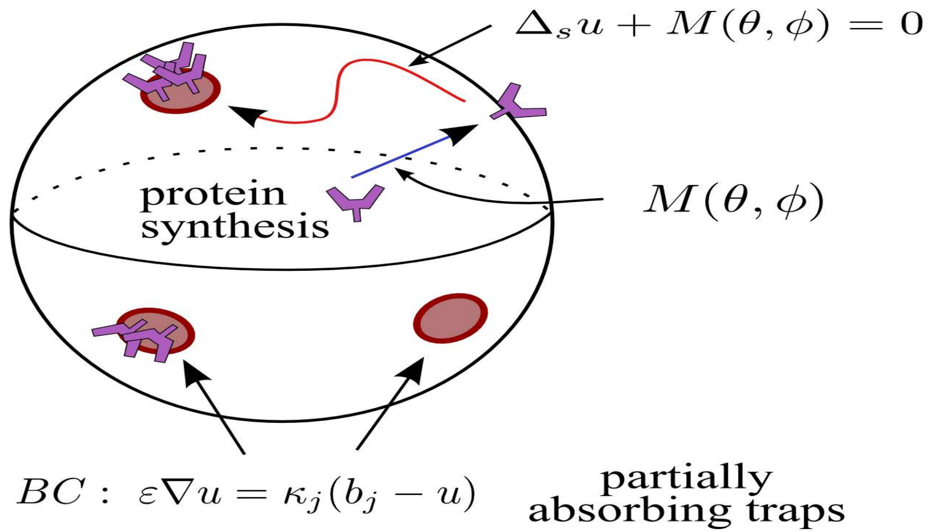
Three Specific Problems: Common Features

1. Diffusion on the Surface of a Sphere with Traps
2. The Mean First Passage Time for Escape from a Sphere with Localized Absorbing Boundary Patches
3. Persistence Threshold for Diffuse Logistic Model in Highly Patchy Environments

Common Features:

- **Eigenvalue Problems:** singularly perturbed eigenvalue problems with local expansions needed to resolve solution in $O(\varepsilon)$ regions near traps or patches, and match to global solution, which changes slowly as $\varepsilon \to 0$. **Method of matched asymptotic expansions.**
- **Neumann Green's Function:** Calculation of the principal eigenvalue requires the Neumann Green's function for the Laplacian.
- **Discrete Optimization Problems:** For the MFPT we want to maximimze λ_1 for a fixed number of traps wrt the configuration $\{x_1, \ldots, x_N\}$. For the persistence problem, we want to minimize λ_1.
- **Formal Asymptotic Analysis:** Treatment by matched asymptotic analysis; need of a rigorous theory.

Diffusion on the Surface of a Sphere: I



Let S be the unit sphere, Ω_{ε_j} be a circular trap of radius $O(\varepsilon)$ on S centered at x_j with $|x_j| = 1$. Then, the **The MFPT** v satisfies

$$\triangle_s v = -\frac{1}{D}\,, \quad x \in S_\varepsilon \equiv S \backslash \cup_{j=1}^{N} \Omega_{\varepsilon_j}\,; \quad v = 0\,, \quad x \in \partial\Omega_{\varepsilon_j}\,.$$

Eigenvalue Problem: The corresponding eigenvalue problem on S is

$$\triangle_s \psi + \sigma \psi = 0\,, \quad x \in S_\varepsilon\,; \qquad \psi = 0\,, \quad x \in \partial\Omega_{\varepsilon_j}\,.$$

For $\varepsilon \to 0$ then $\bar{v} \sim 1/(D\sigma_1)$.

Diffusion on the Surface of a Sphere: II

Principal Result: *Consider N perfectly absorbing circular traps of a common radius $\varepsilon a \ll 1$ centered at x_j, for $j = 1, \ldots, N$ on S. Then, the asymptotics for the MFPT v in the "outer" region $|x - x_j| \gg O(\varepsilon)$ for $j = 1, \ldots, N$ is*

$$v(x) = -2\pi \sum_{j=1}^{N} A_j G(x; x_j) + \chi\,, \quad \chi \equiv \frac{1}{4\pi} \int_S v\, ds\,,$$

where A_j for $j = 1, \ldots, N$ with $\mu = -1/\log(\varepsilon a)$ satisfies

$$A_j = \frac{2}{ND} \left[1 + \mu \sum_{\substack{j=1 \\ j \neq i}}^{N} \log|x_i - x_j| - \frac{2\mu}{N} p(x_1, \ldots, x_N) + O(\mu^2) \right] .$$

The average MFPT $\bar{v} = \chi$ and the principal eigenvalue $\sigma(\varepsilon)$ satisfy

$$\bar{v} = \chi = \frac{2}{ND\mu} + \frac{1}{D} \left[(2\log 2 - 1) + \frac{4}{N^2} p(x_1, \ldots, x_N) \right] + O(\mu)\,,$$

$$\sigma(\varepsilon) \sim \frac{\mu N}{2} + \mu^2 \left[-\frac{N^2}{4} (2\log 2 - 1) - p(x_1, \ldots, x_N) \right] + O(\mu^3)\,.$$

Diffusion on the Surface of a Sphere: III

Here the discrete energy $p(x_1, \ldots, x_N)$ *is the logarithmic energy*

$$p(x_1, \ldots, x_N) \equiv -\sum_{i=1}^{N} \sum_{j>i}^{N} \log |x_i - x_j| \, .$$

The Green's function $G(x; x_0)$ that appears satisfies

$$\triangle_s G = \frac{1}{4\pi} - \delta(x - x_0) \, , \quad x \in S \, ; \quad \int_S G \, ds = 0 \, ,$$

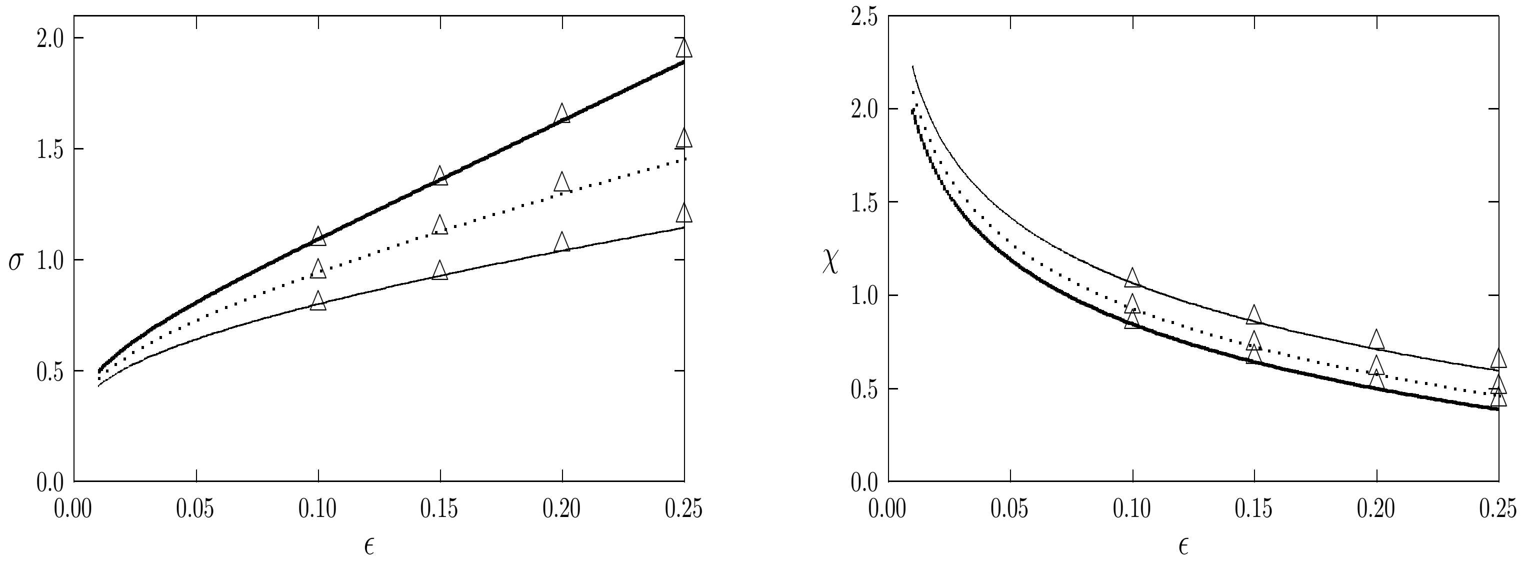
and is given analytically by

$$G(x; x_0) = -\frac{1}{2\pi} \log |x - x_0| + R \, , \qquad R \equiv \frac{1}{4\pi} \left[2 \log 2 - 1 \right] \, .$$

- G occurs in study of fluid vortices on a sphere (P. Newton, S. Boatto)
- Can also treat the case of N partially absorbing traps of different radii.
- **Key Point:** $\sigma(\varepsilon)$ is maximized and $\bar{v}$ minimized at the minumum point of p, i.e. at the elliptic Fekete points.
- **Reference:** D. Coombs, R. Straube, MJW, *"Diffusion on a Sphere with Traps..."*, SIAM J. Appl. Math., Vol. 70, No. 1, (2009), pp. 302–332.

Diffusion on the Surface of a Sphere: IV

EFFECT OF SPATIAL ARRANGEMENT OF $N = 4$ IDENTICAL TRAPS:



Note: $\varepsilon = 0.1$ corresponds to 1% trap surface area fraction.

Plots: Results for $\sigma(\varepsilon)$ (left) and $\chi(\varepsilon)$ (right) for three different 4-trap patterns with perfectly absorbing traps and a common radius ε. **Heavy solid:** $(\theta_1, \phi_1) = (0, 0)$, $(\theta_2, \phi_2) = (\pi, 0)$, $(\theta_3, \phi_3) = (\pi/2, 0)$, $(\theta_4, \phi_4) = (\pi/2, \pi)$; **Solid:** $(\theta_1, \phi_1) = (0, 0)$, $(\theta_2, \phi_2) = (\pi/3, 0)$, $(\theta_3, \phi_3) = (2\pi/3, 0)$, $(\theta_4, \phi_4) = (\pi, 0)$; **Dotted:** $(\theta_1, \phi_1) = (0, 0)$, $(\theta_2, \phi_2) = (2\pi/3, 0)$, $(\theta_3, \phi_3) = (\pi/2, \pi)$, $(\theta_4, \phi_4) = (\pi/3, \pi/2)$. The marked points are computed from finite element package COMSOL.

Diffusion on the Surface of a Sphere: V

For $N \to \infty$, the optimal energy for elliptic Fekete points gives

$$\max\left[-p(x_1,\ldots,x_N)\right] \sim \frac{1}{4}\log\left(\frac{4}{e}\right)N^2 + \frac{1}{4}N\log N + l_1 N + l_2\,, \qquad N \to \infty\,,$$

with $l_1 = 0.02642$ and $l_2 = 0.1382$.

Reference: E. A. Rakhmanov, E. B. Saff, Y. M. Zhou, (1994); B. Bergersen, D. Boal, P. Palffy-Muhoray, J. Phys. A: Math Gen., **27**, No. 7, (1994).

This yields a key scaling law for the minimum of the averaged MFPT as

Principal Result: *For $N \gg 1$, and N circular disks of common radius εa, and with small trap area fraction $N\varepsilon^2 a^2 \ll 1$ with $|S| = 4\pi$, then*

$$\min \bar{v} \sim \frac{1}{ND}\left[-\log\left(\frac{\sum_{j=1}^{N}|\Omega_{\varepsilon_j}|}{|S|}\right) - 4l_1 - \log 4 + O(N^{-1})\right]\,.$$

Diffusion on the Surface of a Sphere: VI

Application: Estimate the averaged MFPT T for a surface-bound molecule to reach a molecular cluster on a spherical cell.

Physical Parameters: The diffusion coefficient of a typical surface molecule (e.g. LAT) is $D \approx 0.25\mu$m^2/s. Take $N = 100$ (traps) of common radius 10nm on a cell of radius 5μm. This gives a 1% trap area fraction:

$$\varepsilon = 0.002\,, \qquad N\pi\varepsilon^2/(4\pi) = 0.01\,.$$

Scaling Law: The scaling law gives an asymptotic lower bound on the averaged MFPT. For $N = 100$ traps, the bound is 7.7s, achieved at the elliptic Fekete points.

One Big Trap: As a comparison, for one big trap of the same area the averaged MFPT is 360s, which is very different.

Bounds: Therefore, for any other arrangement, 7.7s $< T < 360$s.

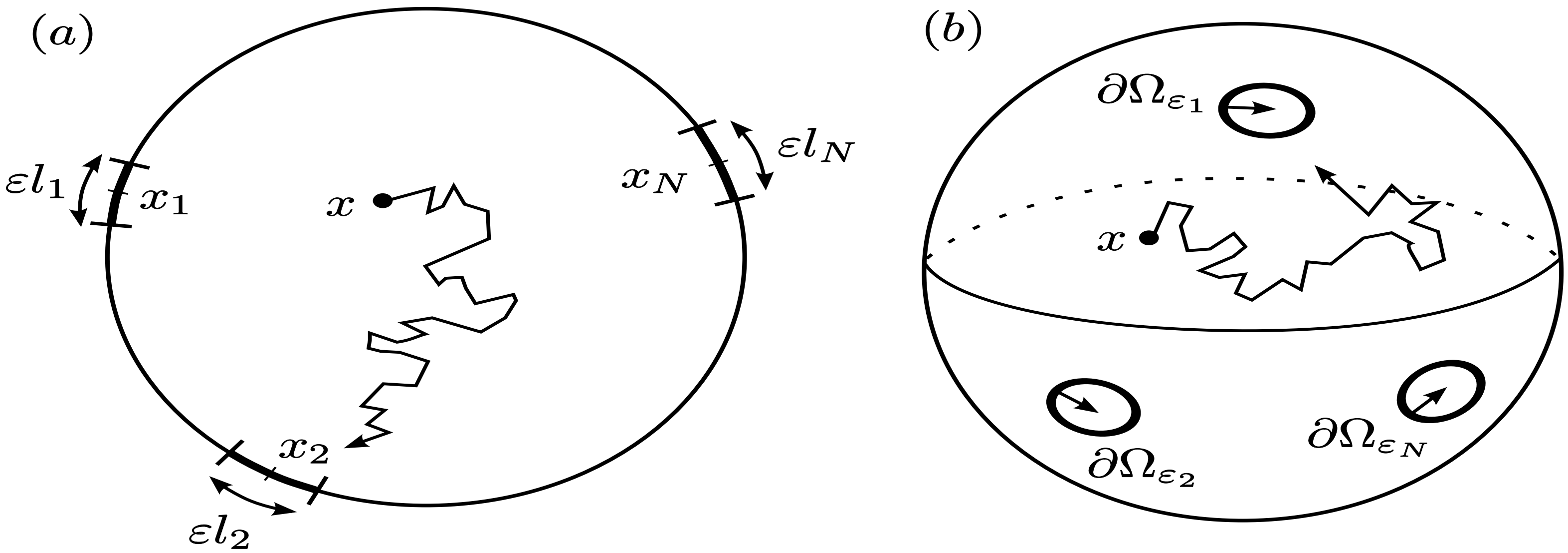
Conclusion: Both the Spatial Distribution and Fragmentation Effect of Localized Traps are Rather Significant even at Small Trap Area Fraction

MFPT and Narrow Escape From a Sphere I

Narrow Escape Problem for MFPT $v(x)$ and averaged MFPT $\bar{v}$:

$$\Delta v = -\frac{1}{D}, \quad x \in \Omega; \qquad \bar{v} \equiv \frac{1}{|\Omega|} \int_\Omega v \, dx,$$

$$\partial_n v = 0 \quad x \in \partial\Omega_r; \quad v = 0, \quad x \in \partial\Omega_a = \cup_{j=1}^N \partial\Omega_{\varepsilon_j}.$$



Key Question: What is effect of spatial arrangement of traps on the unit sphere? Relation to Fekete Points? Need high order asymptotics.

Reference: S. Pillay, M.J. Ward, A. Pierce, R. Straube, T. Kolokolnikov, *An Asymptotic Analysis of the Mean First Passage Time for Narrow Escape Problems*, submitted, SIAM J. Multiscale Modeling, (2009).

MFPT and Narrow Escape From a Sphere II

The surface Neumann G-function, G_s, is central:

$$\triangle G_s = \frac{1}{|\Omega|}\,, \quad x \in \Omega\,; \qquad \partial_r G_s = \delta(\cos\theta - \cos\theta_j)\delta(\phi - \phi_j)\,, \quad x \in \partial\Omega\,,$$

__**Lemma**__: *Let* $\cos\gamma = x \cdot x_j$ *and* $\int_\Omega G_s\, dx = 0$. *Then* $G_s = G_s(x; x_j)$ *is*

$$G_s = \frac{1}{2\pi|x - x_j|} + \frac{1}{8\pi}(|x|^2 + 1) + \frac{1}{4\pi}\log\left[\frac{2}{1 - |x|\cos\gamma + |x - x_j|}\right] - \frac{7}{10\pi}\,.$$

Define the matrix $\mathcal{G}_s$ using $R = -\frac{9}{20\pi}$ and $G_{sij} \equiv G_s(x_i; x_j)$ as

$$\mathcal{G}_s \equiv \begin{pmatrix} R & G_{s12} & \cdots & G_{s1N} \\ G_{s21} & R & \cdots & G_{s2N} \\ \vdots & \vdots & \ddots & \vdots \\ G_{sN1} & \cdots & G_{sN,N-1} & R \end{pmatrix}\,,$$

Remark: As $x \to x_j$, G_s has a subdominant logarithmic singularity:

$$G_s(x; x_j) \sim \frac{1}{2\pi|x - x_j|} - \frac{1}{4\pi}\log|x - x_j| + O(1)\,.$$

MFPT and Narrow Escape From a Sphere III

Principal Result: *For $\varepsilon \to 0$, and for N circular traps of radii εa_j centered at x_j, for $j = 1, \ldots, N$, the averaged MFPT $\bar{v}$ satisfies*

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

$$\left. - \frac{\varepsilon}{N\bar{c}} \sum_{j=1}^{N} c_j \kappa_j + O(\varepsilon^2 \log \varepsilon) \right] .$$

Here $c_j = 2a_j/\pi$ is the capacitance of the j^{th} circular absorbing window of radius εa_j, $\bar{c} \equiv N^{-1}(c_1 + \ldots + c_N)$, $|\Omega| = 4\pi/3$, and κ_j is defined by

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

Moreover, $p_c(x_1, \ldots, x_N)$ is a quadratic form in terms $\mathcal{C}^t = (c_1, \ldots, c_N)$

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

Remarks: 1) A similar result holds for non-circular traps. 2) The logarithmic term in ε arises from the subdominant singularity in G_s.

MFPT and Narrow Escape From a Sphere IV

- **One Trap:** Let $N = 1$, $c_1 = 2/\pi$, $a_1 = 1$, (compare with Holcman et al)

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

- **N Identical Circular Traps:** of common radius ε:

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

with discrete energy $\mathcal{H}(x_1,\ldots,x_N)$ given by

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

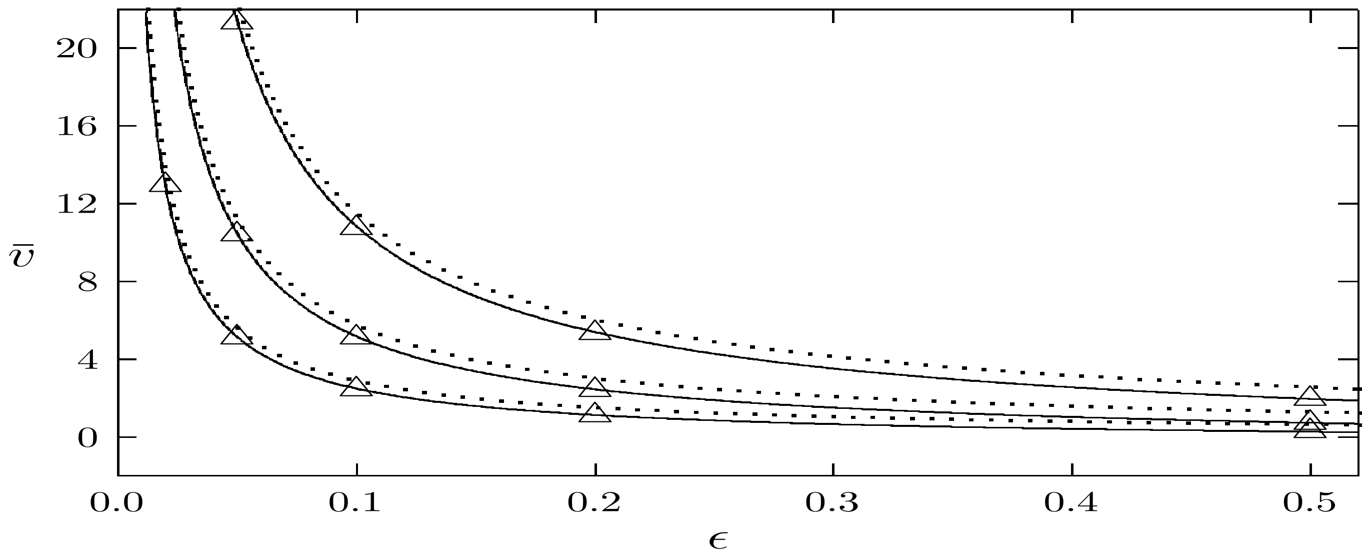
- **Key point:** Minimizing $\bar{v}$ corresponds to minimizing $\mathcal{H}$. This discrete energy is a generalization of the purely Coulombic or logarithmic energies associated with Fekete points.

MFPT and Narrow Escape From a Sphere V

KEY STEPS IN DERIVATION OF MAIN RESULT

- The Neumann G-function has a subdominant logarithmic singularity on the boundary (related to surface diffusion)
- Tangential-normal coordinate system used near each trap.
- Asymptotic expansion of global (outer) solution and local (inner solutions near each trap.
- Leading-order local solution is electrified disk problem in a half-space, with capacitance c_j.
- Logarithmic switchback terms in ε needed in global solution (ubiquitous in Low Reynolds number flow problems)
- Need corrections to the tangent plane approximation in the inner region, i.e. near the trap. This determines κ_j.
- Asymptotic matching and solvability conditions (Divergence theorem) determine v and $\bar{v}$

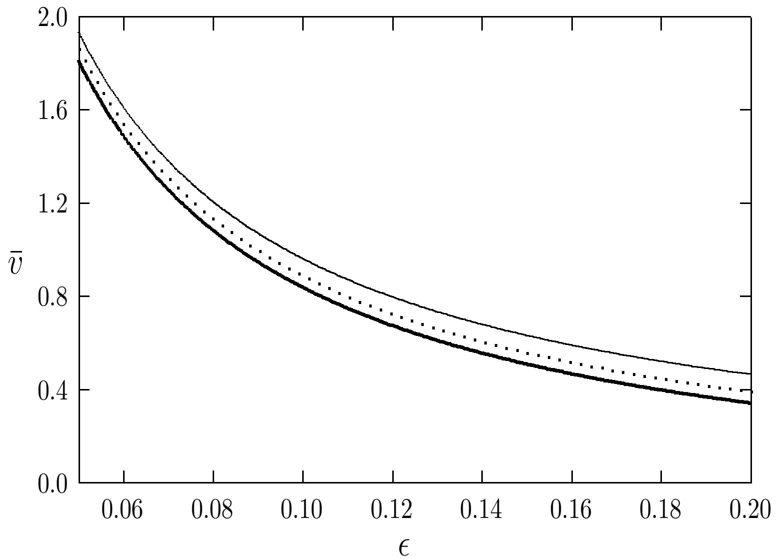
MFPT and Narrow Escape From a Sphere VI

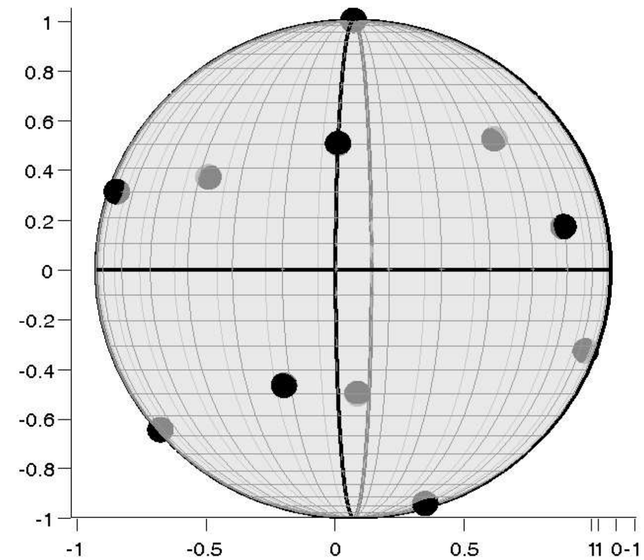


Plot: $\bar{v}$ vs. ε with $D = 1$ and either $N = 1, 2, 4$ equidistantly spaced circular windows of radius ε. **Solid:** 3-term expansion. **Dotted:** 2-term expansion. **Discrete:** COMSOL. **Top:** $N = 1$. **Middle:** $N = 2$. **Bottom:** $N = 4$.

	$N=1$			$N=2$			$N=4$		
ε	$\bar{v}_2$	$\bar{v}_3$	$\bar{v}_n$	$\bar{v}_2$	$\bar{v}_3$	$\bar{v}_n$	$\bar{v}_2$	$\bar{v}_3$	$\bar{v}_n$
0.02	53.89	53.33	52.81	26.95	26.42	26.12	13.47	13.11	12.99
0.05	22.17	21.61	21.35	11.09	10.56	10.43	5.54	5.18	5.12
0.10	11.47	10.91	10.78	5.74	5.21	5.14	2.87	2.51	2.47
0.20	6.00	5.44	5.36	3.00	2.47	2.44	1.50	1.14	1.13
0.50	2.56	1.99	1.96	1.28	0.75	0.70	0.64	0.28	0.30

MFPT and Narrow Escape From a Sphere VII

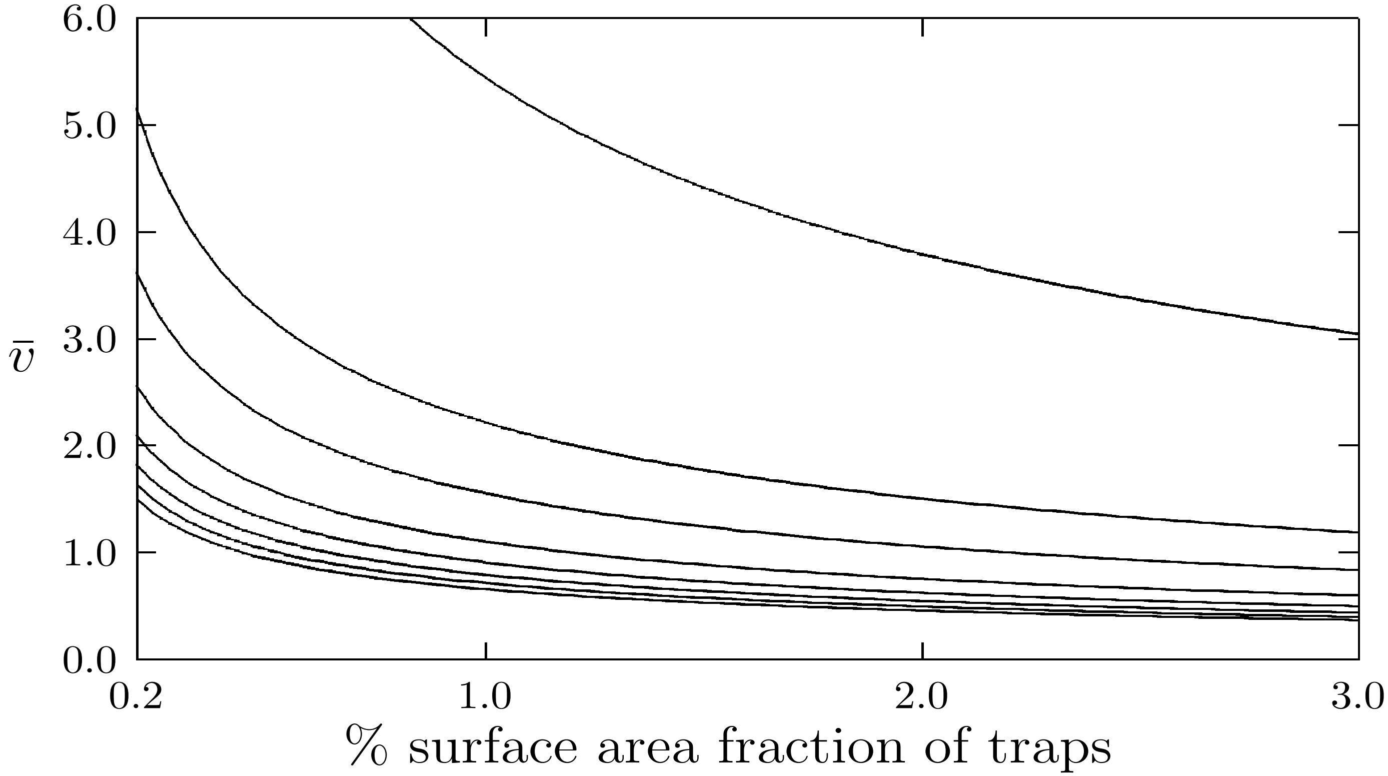




Plot: $\bar{v}(\varepsilon)$ for $D = 1$, $N = 11$, and three trap configurations. **Heavy:** global minimum of $\mathcal{H}$ (right figure). **Solid:** equidistant points on equator. **Dotted:** random.

- Table: $\bar{v}$ agrees well with COMSOL even at $\varepsilon = 0.5$. For $\varepsilon = 0.5$ and $N = 4$, absorbing windows occupy $\approx 20\%$ of the surface. Still, the 3-term asymptotics for $\bar{v}$ differs from COMSOL by only $\approx 7.5\%$.
- For $\varepsilon = 0.1907$, $N = 11$ traps occupy $\approx 10\%$ of surface area; optimal arrangement gives $\bar{v} \approx 0.368$. For a single large trap with a 10% surface area, $\bar{v} \approx 1.48$; a result 3 times larger.

MFPT and Narrow Escape From a Sphere VIII



Plot: averaged MFPT $\bar{v}$ versus % trap area fraction for $N = 1, 5, 10, 20, 30, 40, 50, 60$ (top to bottom) at optimal trap locations.

- **fragmentation** effect of traps on the sphere is a significant factor.
- **only marginal decrease in** $\bar{v}$ by increasing N when N is already large.

MFPT and Narrow Escape From a Sphere IX

Numerical Computations: to compare optimal energies and point arrangements of $\mathcal{H}$ with those of classic Coulomb or Logarithmic energies

$$\mathcal{H}_{\rm C} = \sum_{i=1}^{N} \sum_{j>i}^{N} \frac{1}{|x_i - x_j|}, \quad \mathcal{H}_{\rm L} = -\sum_{i=1}^{N} \sum_{j>i}^{N} \log |x_i - x_j|.$$

(A. Cheviakov, R. Spiteri, MJW).

Numerical Methods:

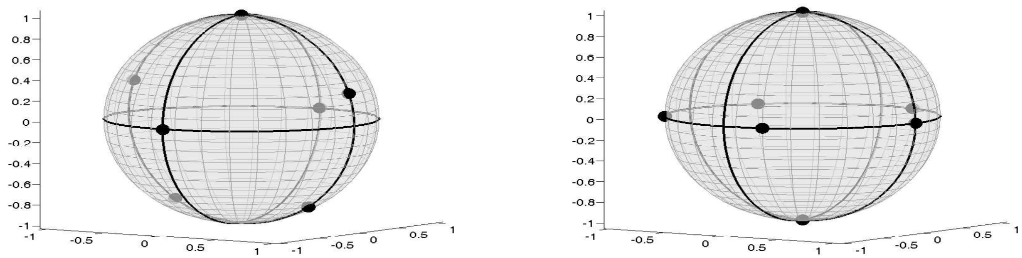
- **Extended Cutting Angle method (ECAM).** (cf. G. Beliakov, Optimization Methods and Software, **19** (2), (2004), pp. 137-151).
- **Dynamical systems – based optimization (DSO).** (cf. M.A. Mammadov, A. Rubinov, and J. Yearwood, (2005)).
- Our computational results obtained by using the open software library GANSO where both the ECAM and DSO methods are implemented.

Results for Small N:

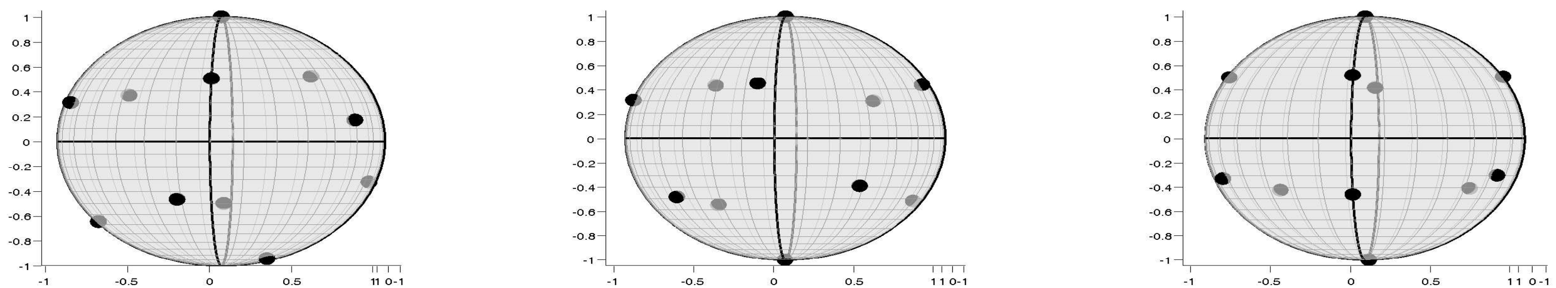
- For $N = 5, 6, 8, 9, 10$ and 12, optimal point arrangments coincide
- Some differences for $N = 7, 11, 16$.

MFPT and Narrow Escape From a Sphere X

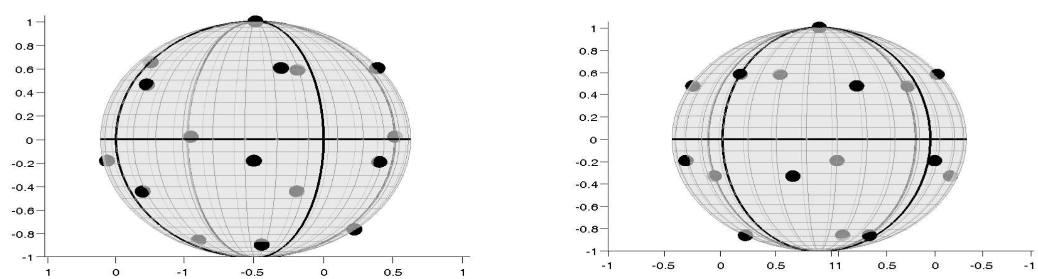
N=7: Left: $\mathcal{H}$. Right: $\mathcal{H}_C$ and $\mathcal{H}_L$.



N=11: Left: $\mathcal{H}$. Middle: $\mathcal{H}_C$. Right: $\mathcal{H}_L$.



N=16: Left: $\mathcal{H}$ and $\mathcal{H}_L$. Right: $\mathcal{H}_C$.



MFPT and Narrow Escape From a Sphere XI

OPTIMAL ENERGIES: (Computations by R. Spiteri and A. Cheviakov)

N	$\mathcal{H}$	$\mathcal{H}_{\mathrm{C}}$	$\mathcal{H}_{\mathrm{L}}$
3	-1.067345	1.732051	-1.647918
4	-1.667180	3.674234	-2.942488
5	-2.087988	6.474691	-4.420507
6	-2.581006	9.985281	-6.238324
7	-2.763658	14.452978	-8.182476
8	-2.949577	19.675288	-10.428018
9	-2.976434	25.759987	-12.887753
10	-2.835735	32.716950	-15.563123
11	-2.456734	40.596450	-18.420480
12	-2.161284	49.165253	-21.606145
16	1.678405	92.911655	-36.106152
20	8.481790	150.881571	-54.011130
25	21.724913	243.812760	-80.997510
30	40.354439	359.603946	-113.089255
35	64.736711	498.569272	-150.192059
40	94.817831	660.675278	-192.337690
45	130.905316	846.188401	-239.453698
50	173.078675	1055.182315	-291.528601
55	221.463814	1287.772721	-348.541796
60	275.909417	1543.830401	-410.533163
65	336.769710	1823.667960	-477.426426

Open Questions:

- **Q1:** Derive a rigorous scaling law for the optimal energy for large N?
- **Q2:** Does the result approach a homogenization theory result in the dilute trap area limit?

MFPT and Narrow Escape From a Sphere XII

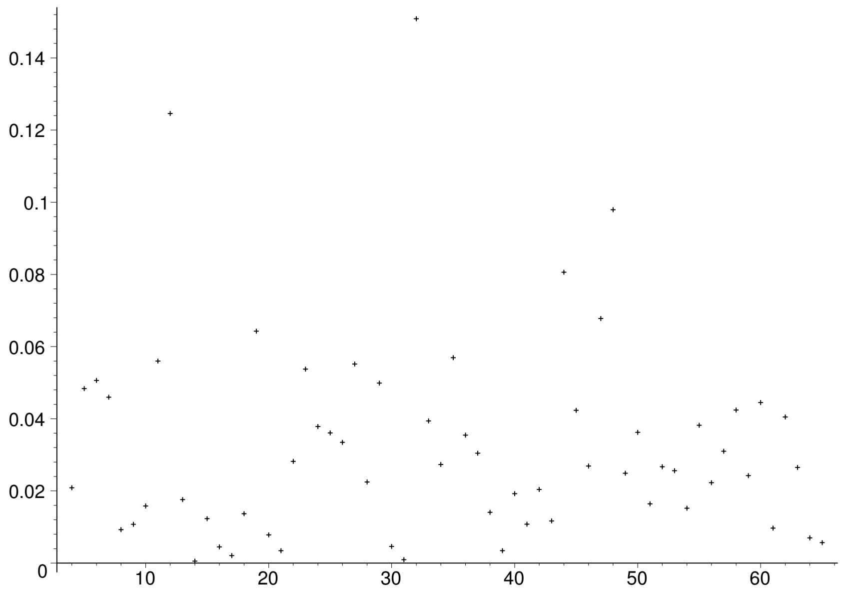
For $N \gg 1$, the optimal $\mathcal{H}$ has the form

$$\mathcal{H} \approx \mathcal{F}(N) = \frac{N^2}{2}(1-\log 2) + b_1 N^{3/2} + b_2 N \log N + b_3 N + b_4 N^{1/2} + b_5 \log N + b_6 \,,$$

where we least-squares fit the coefficients to the data as

$$b_1 \approx -0.5668\,, \quad b_2 \approx 0.0628\,, \quad b_3 \approx -0.8420\,,$$
$$b_4 \approx 3.8894\,, \quad b_5 \approx -1.3512\,, \quad b_6 \approx -2.4523\,.$$

Caption: Scatter plot of the error $|\mathcal{F}(N) - \mathcal{H}|$ vs. N



Persistence in Patchy Environments I

Consider the diffusive logistic equation for $u(x,t)$ with $x \in \Omega \in \mathbb{R}^2$

$$u_t = \Delta u + \lambda u \left[m_\varepsilon(x) - c(x) u \right] \,, \quad x \in \Omega \,; \quad \partial_n u = 0 \,, \quad x \in \partial\Omega \,.$$

Linearize around the zero solution with $u = e^{\mu t}\phi(x)$ and set $\mu = 0$

$$\Delta\phi + \lambda m_\varepsilon(x)\phi = 0 \,, \quad x \in \Omega \,; \quad \partial_n \phi = 0 \,, \quad x \in \partial\Omega \,.$$

- Threshold for species persistence is determined by the stability border to the extinct solution $u = 0$, with $\lambda = 1/D$, and D the diffusivity.
- Growth rate m_ε changes sign $\rightarrow$ indefinite weight eig. problem.

Key Previous Result I: Assume that $\int_\Omega m_\varepsilon \, dx < 0$, but that $m_\varepsilon > 0$ on a set of positive measure. Then, there exists a positive principal eigenvalue λ, with corresponding positive eigenfunction ϕ (Brown and Lin, (1980))

Goal: Minimize λ_1 wrt $m_\varepsilon(x)$, subject to a given $\int_\Omega m_\varepsilon \, dx < 0$: i.e. determine the largest D that can still allow for the persistence of the species. (Cantrell and Cosner 1990's, Lou and Yanagida, (2006); Kao, Lou, and Yanagida, (2008); Roques and Stoica, (2007); Berestycki et al. (2005)).

Persistence in Patchy Environments II

Key Previous Result II: The optimal growth rate $m_\varepsilon(x)$ is of bang-bang type. (Theorem 1.1 of Lou and Yanagida, 2006, for 2-D).

Patch Model: The eigenvalue problem for the persistence threshold is

$$\Delta\phi + \lambda\, m_\varepsilon(x)\phi = 0\,, \quad x \in \Omega; \quad \partial_n\phi = 0\,, \quad x \in \partial\Omega\,; \quad \int_\Omega \phi^2\, dx = 1\,,$$

where the growth rate $m_\varepsilon(x)$ is defined as

$$m_\varepsilon(x) = \begin{cases} m_j/\varepsilon^2\,, & x \in \Omega_{\epsilon_j} \equiv \{x \,|\, |x - x_j| = \varepsilon\rho_j \;\cap\; \Omega\}\,, \quad j = 1,\ldots,n\,, \\ -m_b\,, & x \in \Omega \backslash \bigcup_{j=1}^n \Omega_{\varepsilon_j}\,. \end{cases}$$

Remarks and Terminology:

- Patches Ω_{ε_j} are portions of small circular disks strictly inside Ω.
- The constant m_j is the local growth rate of the j^{th} patch, with $m_j > 0$ for a favorable habitat and $m_j < 0$ for a non-favorable habitat.
- The constant $m_b > 0$ the background bulk decay rate.
- The boundary $\partial\Omega$ is piecewise smooth, with possible corner points.

Persistence in Patchy Environments III

Remarks and Terminology:

- Define $\Omega^I \equiv \{x_1, \ldots, x_n\} \cap \Omega$ to be the set of the centers of the interior patches, while $\Omega^B \equiv \{x_1, \ldots, x_n\} \cap \partial\Omega$ is the set of the centers of the boundary patches. We assume patches are well-separated, i.e. $|x_i - x_j| \gg \mathcal{O}(\varepsilon)$ for $i \neq j$ and that $\text{dist}(x_j, \partial\Omega) \gg \mathcal{O}(\varepsilon)$ if $x_j \in \Omega^I$.
- To accommodate a boundary patch, we put with each x_j for $j = 1, \ldots, n$, an angle $\pi\alpha_j$ representing the angular fraction of a circular patch that is contained within Ω. More specifically, $\alpha_j = 2$ whenever $x_j = \Omega^I$, and $\alpha_j = 1$ when $x_j \in \Omega^B$ and x_j is a point where $\partial\Omega$ is smooth, and $\alpha_j = 1/2$ when $x_j \in \partial\Omega$ is at a $\pi/2$ corner of $\partial\Omega$, etc.

The condition $\int_\Omega m_\varepsilon \, dx < 0$ is asymptotically equivalent for $\varepsilon \to 0$ to

$$\int_\Omega m_\varepsilon \, dx = -m_b |\Omega| + \frac{\pi}{2} \sum_{j=1}^{n} \alpha_j m_j \rho_j^2 + \mathcal{O}(\varepsilon^2) < 0 \, .$$

Assumption I: Assume that this holds, and that one m_j is positive.

Then, there exists a positive principal eigenvalue λ.

Persistence in Patchy Environments IV

Goal: Calculate the positive principal eigenvalue λ as $\varepsilon \to 0$, and determine the patch distribution for a fixed $\int_\Omega m_\varepsilon \, dx$ than minimizes λ. The parameter set is $\{m_1, \ldots, m_n\}$, $\{\rho_1, \ldots, \rho_n\}$, $\{x_1, \ldots, x_n\}$, and $\{\alpha_1, \ldots, \alpha_n\}$.

Modified G-Function: Define the modified G-function G_m by

$$G_m(x; x_j) \equiv G(x; x_j) \,, \quad x_j \in \Omega \,; \qquad G_m(x; x_j) \equiv G_s(x; x_j) \,, \quad x_j \in \partial\Omega \,.$$

Here $G(x; x_j)$ is the unique Neumann Green's function satisfying

$$\Delta G = \frac{1}{|\Omega|} - \delta(x - x_j) \,, \quad x \in \Omega \,; \quad \partial_n G = 0 \,, \quad x \in \partial\Omega \,; \qquad \int_\Omega G \, dx = 0 \,,$$

$$G(x; x_j) \sim -\frac{1}{2\pi} \log|x - x_j| + R(x_j; x_j) \,, \quad \text{as} \quad x \to x_j \,,$$

while $G_s(x; x_j)$ is the unique surface Neumann Green's function

$$\triangle G_s = \frac{1}{|\Omega|} \,, \quad x \in \Omega \,; \quad \partial_n G_s = 0 \,, \qquad x \in \partial\Omega \backslash \{x_j\} \,; \qquad \int_\Omega G_s \, dx = 0 \,,$$

$$G_s(x; x_j) \sim -\frac{1}{\alpha_j \pi} \log|x - x_j| + R_s(x_j; x_j) \,, \quad \text{as } x \to x_j \in \partial\Omega \,.$$

Persistence in Patchy Environments V

Principal Result: *In the limit $\varepsilon \to 0$, the positive principal eigenvalue λ has the following two-term asymptotic expansion*

$$\lambda = \mu_0 \nu - \mu_0 \nu^2 \left(\frac{\kappa^t \left(\pi \mathcal{G}_m - \mathcal{P} \right) \kappa}{\kappa^t \kappa} + \frac{1}{4} \right) + \mathcal{O}(\nu^3) \,, \quad \nu = -1/\log \varepsilon \,.$$

Here $\kappa = (\kappa_1, \ldots, \kappa_n)$ and $\mu_0 > 0$ is the first positive root of $\mathcal{B}(\mu_0) = 0$

$$\mathcal{B}(\mu_0) \equiv -m_b |\Omega| + \pi \sum_{j=1}^{n} \sqrt{\alpha_j} \kappa_j \,, \qquad \kappa_j \equiv \frac{\sqrt{\alpha}_j m_j \rho_j^2}{2 - m_j \rho_j^2 \mu_0} \,.$$

Finally, the $n \times n$ matrix $\mathcal{G}_m$ and diagonal matrix $\mathcal{P}$ are defined by

$$\mathcal{G}_{mij} = \sqrt{\alpha_i \alpha_j} G_{mij} \,, \quad i \neq j \,; \quad \mathcal{G}_{mjj} = \alpha_j R_{mjj} \,; \quad \mathcal{P}_{jj} = \log \rho_j \,.$$

Principal Result: *There exists a unique root μ_0 to $\mathcal{B}(\mu_0) = 0$ on the range* $0 < \mu_0 < \mu_{0u} \equiv 2/(m_J \rho_J^2)$, *where* $m_J \rho_J^2 = \max_{m_j > 0} \{ m_j \rho_j^2 | \, j = 1, \ldots, n \}$.

Proof: $\mathcal{B}(0) < 0$ by Assumption I; $\mathcal{B}(\mu_0) \to +\infty$ as $\mu_0 \to \mu_{0u}^-$, and $\mathcal{B}'(\mu_0) > 0$ on $0 < \mu_0 < \mu_{0u}$. Hence, there exists a unique root $\mu_0 > 0$.

Persistence in Patchy Environments VI

By optimizing **the leading-order coefficient** μ_0 subject to $\int_\Omega m_\varepsilon dx < 0$ and fixed we obtain:

Qualitative Result I: *The movement of either a single favorable or unfavorable habitat to the boundary of the domain is advantageous for the persistence of the species.*

Qualitative Result II: *The fragmentation of one favorable interior habitat into two separate favorable interior habitats is not advantageous for species persistence. Similarly, the fragmentation of a favorable boundary habitat into two favorable boundary habitats, with each centered at a smooth point of $\partial\Omega$, is not advantageous.*

Persistence in Patchy Environments VII

<u>**Qualitative Result III**</u>: *The fragmentation of one favorable interior habitat into a new smaller interior favorable habitat together with a favorable boundary habitat, is advantageous for species persistence when the boundary habitat is sufficiently strong in the sense that*

$$m_k \rho_k^2 > \frac{4}{2-\alpha_k} m_j \rho_j^2 > 0\,.$$

Such a fragmentation of a favorable interior habitat is not advantageous when the new boundary habitat is too weak in the sense that

$$0 < m_k \rho_k^2 < m_j \rho_j^2\,.$$

Finally, the clumping of a favorable boundary habitat and an unfavorable interior habitat into one single interior habitat is not advantageous for species persistence when the resulting interior habitat is still unfavorable.

Persistence in Patchy Environments VIII

These qualitative results shows that, given some fixed amount of favorable resources to distribute, the optimal strategy is to clump them all together at a point on the boundary of the domain, and more specifically at the corner point of the boundary (if any are present) with the smallest angle. This strategy will minimize μ_0, thereby maximizing the chance for the persistence of the species.

Principal Result: *For a single boundary patch centered at x_1 on a smooth boundary $\partial\Omega$, μ_0 is minimized at the global maximum of the regular part $R_s(x_1; x_1)$ of the surface Neumann Green's function.*

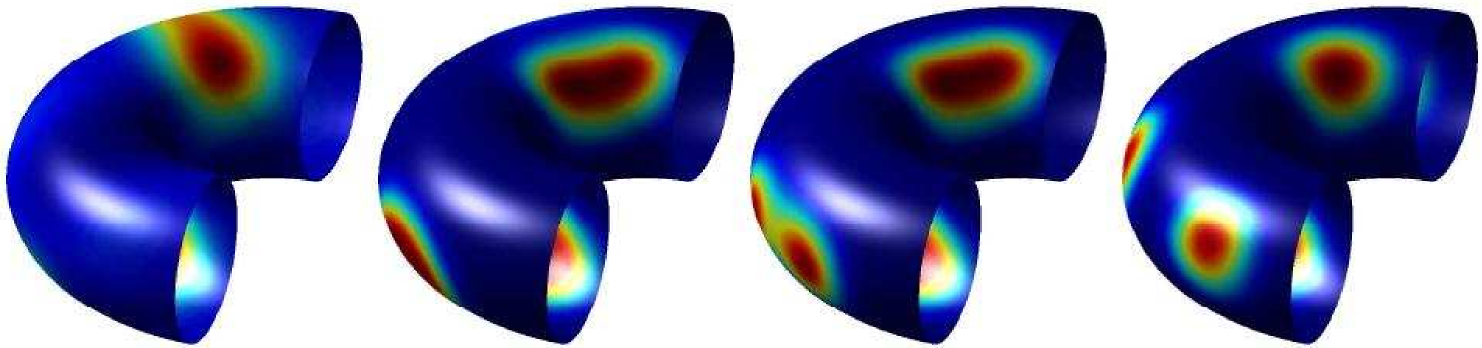
Question: For $\partial\Omega$ smooth, is the global maximum of $R_s(x_1; x_1)$ obtained at the global maximum of the boundary curvature κ? (No; we can find a counterexample for smooth perturbations of the unit disk, by deriving a perturbation formula for R_s)

Remark: Given a pre-existing patch distribution, the optimal location of a new favorable habitat may require optimizing the $\mathcal{O}(\nu^2)$ term.

Further Directions and Open Problems

- Narrow escape problems in arbitrary 3-d domains: require Neumann G-functions in 3-D with boundary singularity
- Surface diffusion on arbitrary 2-d surfaces: require Neumann G-function and regular part on surface.
- Include chemical reactions occurring within each trap, with binding and unbinding events. Can diffusive transport between traps influence stability of steady-state of time-dependent localized reactions (ode's) valid inside each trap? Yields a new Steklov-type eigenvalue problem.
- Couple surface diffusion to diffusion processes within the cell.
- Analysis of localized spot patterns for RD systems in 2-D planar domains (**Lecture II**) and on manifolds (open).
- Rigorous results for persistence threshold with localized patches?

Schnakenburg model on a Manifold: S. Ruuth (JCP, 2008)



References

Available at: http://www.math.ubc.ca/ ward/prepr.html

- D. Coombs, R. Straube, M.J. Ward, *Diffusion on a Sphere with Localized Traps: Mean First Passage Time, Eigenvalue Asymptotics, and Fekete Points*, SIAM J. Appl. Math., Vol. 70, No. 1, (2009), pp. 302–332.
- S. Pillay, M.J. Ward, A. Pierce, R. Straube, T. Kolokolnikov, *An Asymptotic Analysis of the Mean First Passage Time for Narrow Escape Problems*, submitted, SIAM J. Multiscale Modeling, (2009).
- A. Lindsay, M.J. Ward, *An Asymptotic Analysis of the Persistence Threshold for the Diffusive Logistic Model in Spatial Environments with Localized Patches*, to be submitted, DCDS-B, (30 pages).