# Diffusion with Localized Traps: Mean First Passage Time, Eigenvalue Asymptotics, and Fekete Points

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# Outline of the Talk

**Some General Considerations:**

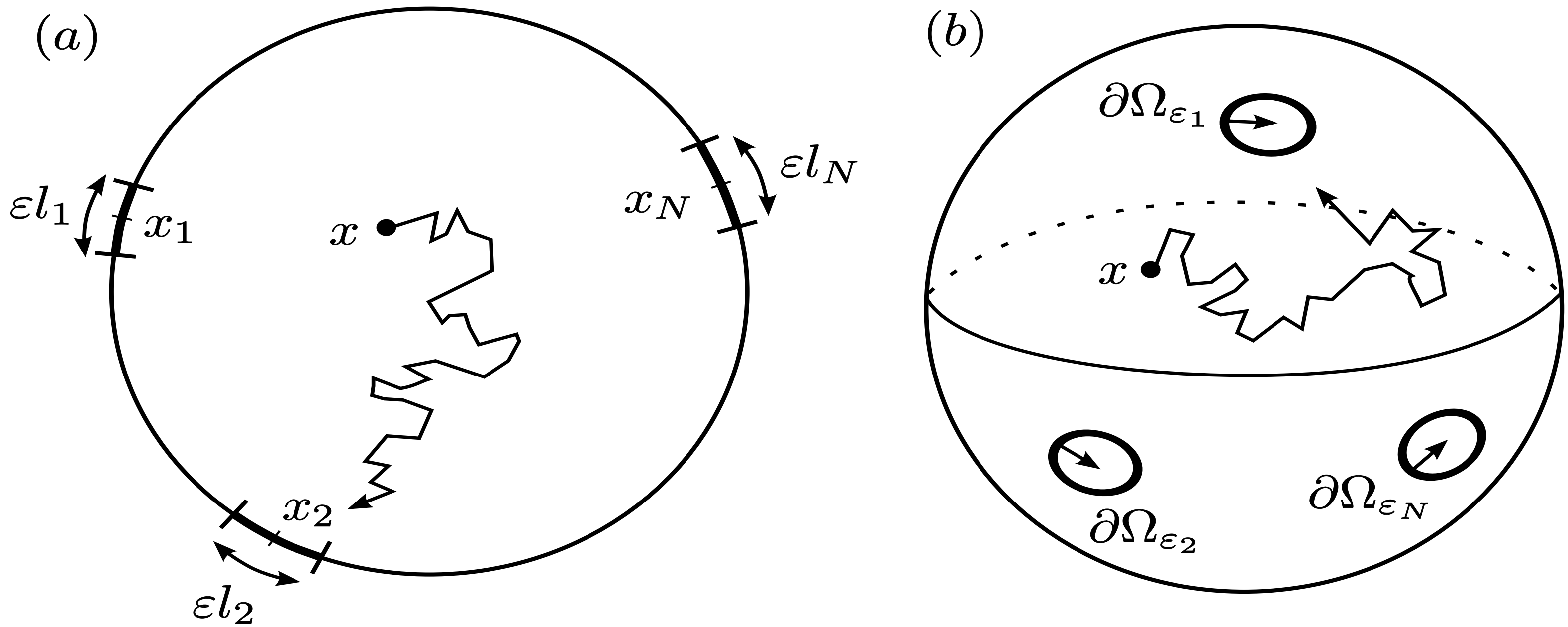
1. Diffusion with Localized Traps (Biological Motivation; from a Mathematician's Viewpoint). The Narrow Escape Problem.
2. Eigenvalue Problems in Perforated Domains and in Domains with Perforated Boundaries. Eigenvalue Optimization and the Mean First Passage Time (General)
3. Fekete Points

**Specific Problems Considered:**

1. Eigenvalue Asymptotics in 2-D or 3-D Perforated Domains.
2. Diffusion on the Surface of a Sphere
3. The Mean First Passage Time for Escape from a Sphere

# Narrow Escape Problem I

**Narrow Escape:** Brownian motion with diffusivity $D$ in $\Omega$ 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))

$$\Delta v = -\frac{1}{D}\,, \quad x \in \Omega\,,$$

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

# Narrow Escape Problem II

**Key General References:**

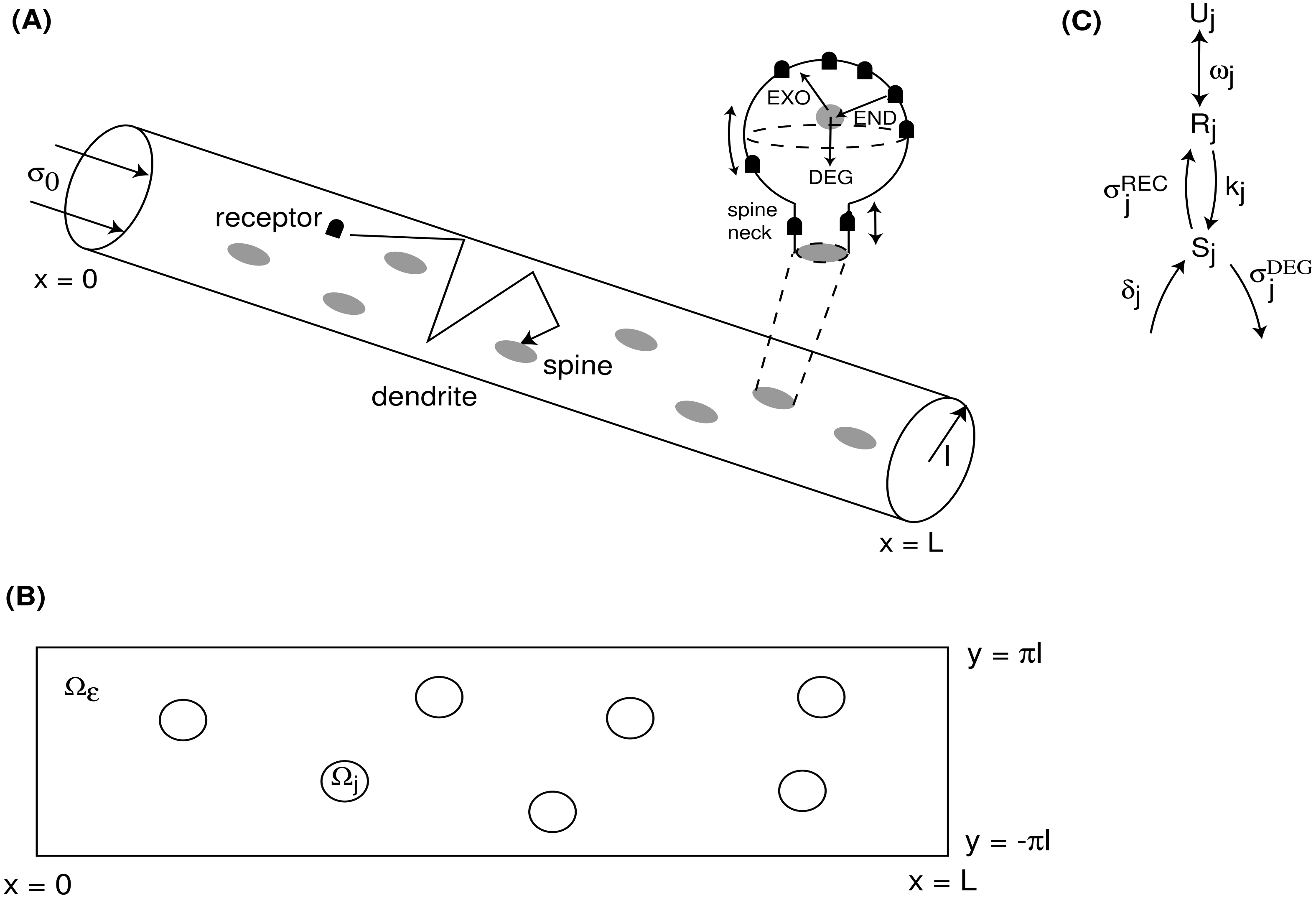
- Z. Schuss, A. Singer, D. Holcman, *The Narrow Escape Problem for Diffusion in Cellular Microdomains*, PNAS, **104**, No. 41, (2007), pp. 16098-16103.
- O. Bénichou, R. Voituriez, *Narrow Escape Time Problem: Time Needed for a Particle to Exit a Confining Domain Through a Small Window*, Phys. Rev. Lett,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

**Relevance of Narror Escape Time Problem in Biology:**

- time needed for a reactive particle released from a specific organelle to activate a given protein on the cell membrane
- biochemical reactions in cellular microdomains, like dendritic spines, synapses, or microvesicles. Such submicron domains often contain a small amount of particles that must first exit domain to fullfill a biological function.

# Diffusion of Protein Receptors: I

Diffusion of protein receptors on a cylindrical dendritic membrane $\Omega = \{|x| < L, |y| < 2\pi l\}$, with partially absorbing traps.



# Diffusion of Protein Receptors: II

**Model: Localized Traps** and $\sigma > 0$ is protein receptors influx from the soma:

$$U_t = \Delta U \,, \quad \mathbf{x} \in \Omega \backslash \Omega_p \,, \quad \Omega_p = \cup_{j=1}^{N} \Omega_{\varepsilon_j} \,,$$
$$\partial_x U(-L, y) = -\sigma \,, \quad \partial_x U(L, y) = 0 \,; \quad U \,, \; \partial_y U \,, \quad 2\pi l \text{ periodic in } y \,,$$
$$\varepsilon \partial_n U = -\kappa_j \left( U - T_j \right) \,, \quad \mathbf{x} \in \partial \Omega_{\varepsilon_j} \,, \quad j = 1, \ldots, N \,.$$

Define the average concentration $U_j$ on the $j^{\text{th}}$ spine boundary

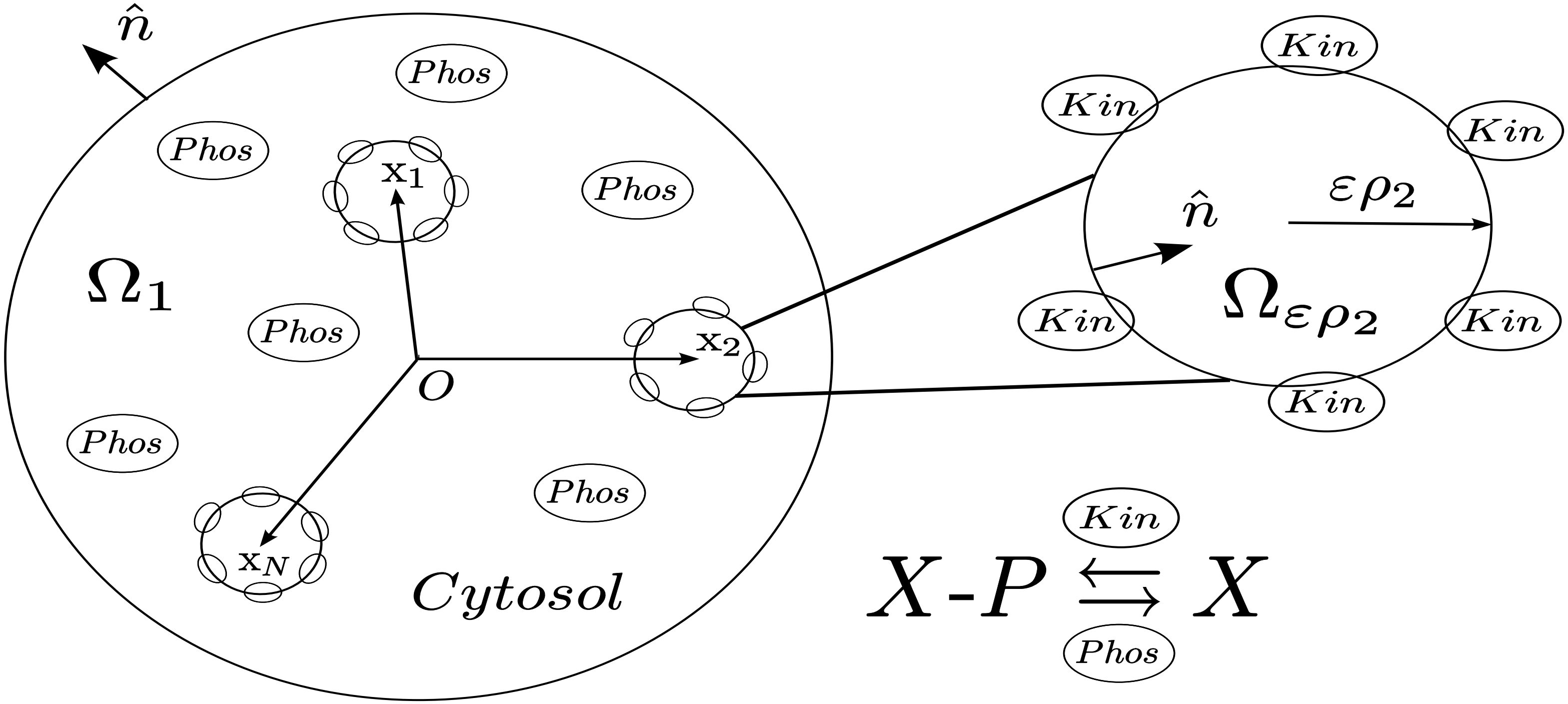
$$U_j = \frac{1}{2\pi\varepsilon} \int_{\partial \Omega_{\varepsilon_j}} U \, d\mathbf{x} \,.$$

Within each spine $T_j(t)$ and $S_j(t)$ for $j = 1, \ldots, N$ satisfy coupled ODE's

$$T_j' = \mathcal{F}_j \left( T_j, S_j, U_j \right) \,, \qquad S_j' = \mathcal{H}_j \left( T_j, S_j \right) \,.$$

- Model due to **Bressloff and Earnshaw (Phys. Rev. E. (2007), J. Neuroscience (2006)). The 1-D steady-state problem studied.**
- **2-D** steady state problem studied in **Bressloff, Earnshaw, MJW**, SIAP (2008).

# Cell Signalling From Small Compartments




**Model of Straube, MJW (SIAP, 2009):** Spatial gradients of activated signalling molecules from small compartments inside a cell. Stationary concentration for fraction $c = c_a/c_t$ of such molecules:

$$\Delta c - \alpha^2 c = 0\,, \quad x \in \Omega \backslash \cup_{j=1}^{N} \Omega_{\varepsilon_j}\,; \quad \partial_n c = 0\,, \quad x \in \partial\Omega$$

$$\varepsilon \partial_n c = \begin{cases} \sigma_j\,,\ x \in \partial\Omega_{\varepsilon_j} & \text{saturated enzyme}\,, \\ \kappa_j(1-c)\,,\ x \in \partial\Omega_{\varepsilon_j} & \text{un-saturated enzyme}\,, \end{cases}$$

**General:** B Kholodenko, *Cell-Signalling Dynamics in Time and Space*, Nat Rev Mol Cell Biol, (2006).

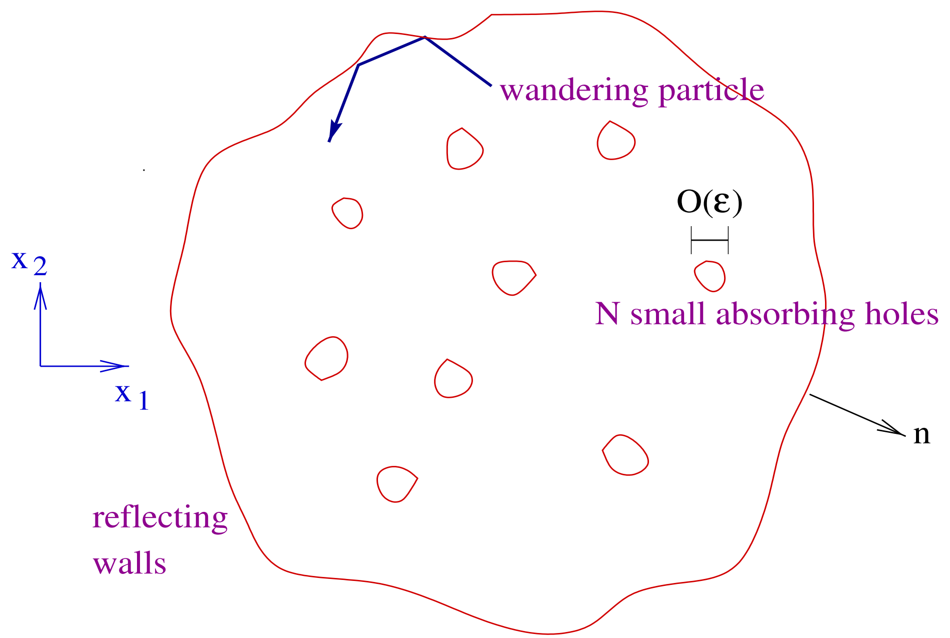
# Eigenvalues in Perforated Domains I

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 $\lambda_1$:**

**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

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

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

**Remark:** problem dates back to Szego 1930's.

# 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 $\varepsilon \to 0$

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

- **Goal:** Let $\lambda_1 > 0$ be the fundamental eigenvalue. For $\varepsilon \to 0$ (small hole radius) find the hole locations $x_i$, for $i = 1, \ldots, N$, that maximize $\lambda_1$.
- In other words, chose the trap locations to minimize the lifetime of a wandering particle in $\Omega$. Maximizing $\lambda_1$ is equivalent to minimizing $\bar{v}$.
- **Goal:** Extend planar 2-D case to a manifold; surface of a sphere.
- **Key Point:** Since the previous results for $\lambda_1$ are independent of trap locations $x_j$, $j = 1, \ldots, N$, we need higher order terms to optimize $\lambda_1$.

# Eigenvalues and Narrow Escape I

For $\varepsilon \to 0$, $\bar{v} \sim 1/(D\lambda_1)$, where $\lambda_1$ is the first eigenvalue of

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

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

- 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 and Narrow Escape II

SOME RECENT WORK IN 2-D

- For $\varepsilon \to 0$,

$$v(x) = \frac{|\Omega|}{\pi D}\left[-\log\varepsilon + O(1)\right] .$$

**Ref:** D. Holcman, Z. Schuss, J. Stat. Phys., **117**, (2004), pp. 975–1014.

- For the unit disk, with $x_1 = (1,0)$

$$v(0) = E\left[\tau | X(0) = 0\right] \sim \frac{|\Omega|}{\pi D}\left[-\log\varepsilon + \log 2 + \frac{1}{4}\right] .$$

**Ref:** A. Singer, Z. Schuss, D. Holcman, J. Stat. Phys. **122**, (2006), pp. 465-489.

- Analysis of $v(x)$ for two traps on the unit disk or unit sphere (up to undertermined $O(1)$ terms fit through Brownian particle simulations). **Ref:** D. Holcman, Z. Schuss, J. of Phys. A: Math Theor., **41**, (2008), 155001.

# Eigenvalues and Narrow Escape III

SOME RECENT WORK IN 3-D

- For one circular trap of radius $\varepsilon$ on the unit sphere $\Omega$ with $|\Omega| = 4\pi/3$,

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

  **Ref:** A. Singer, Z. Schuss, D. Holcman, R. S. Eisenberg, J. Stat. Phys., **122**, No. 3, (2006), pp. 437–463.

- For arbitrary $\Omega$ with smooth boundary and one circular trap

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

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

# Eigenvalues and Fekete Points: I

**Main Goal:** Calculate higher-order expansions for $v(x)$ and $\bar{v}$ as $\varepsilon \to 0$ in 2-D and 3-D to determine the signficant effect on $\bar{v}$ of the spatial configuration $\{x_1, \cdots, x_N\}$ of absorbing boundary traps for a fixed area fraction of traps. Optimize $\bar{v}$ with respect to $\{x_1, \cdots, x_N\}$.

**One Specific Question in 3-D:**

- Let $\Omega$ be the unit sphere with $N$-circular absorbing patches on $\partial\Omega$ of a common radius. Is minimizing $\bar{v}$ equivalent to minimizing the discrete energy $\mathcal{H}_c(x_1, \ldots, x_N)$ defined by

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

  Such points are **Fekete points.** They correspond to finding the minimal discrete energy of "electrons" confined to the boundary of a sphere. (Discovery of Carbon-60 molecules. Long list of references; Thompson, E. Saff, N. Sloane, A. Kuijlaars etc..) For narrow escape from a sphere, we show that a specific generalization of this discrete energy is central.

# Eigenvalues and Fekete Points: II

**Specific Question in 2-D:**

- **Elliptic Fekete points:** correspond to the minimum point of the logarithmic energy $\mathcal{H}_L$ on the unit sphere

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

(Long list of references; Smale and Schub, Saff, Sloane, Kuijlaars,...)
Is there a connection between these points and perturbed eigenvalue problems with traps? Yes, for diffusion on the surface of a sphere with traps.

# Eigenvalues in 2-D Perforated Domains: I

**Eigenvalue Optimization in 2-D:** T. Kolokolnikov, M. Titcombe, MJW, "Optimizing the Fundamental Neumann Eigenvalue for the Laplacian in a Domain with Small Traps", EJAM Vol. 16, No. 2, (2005), pp. 161-200.

**Key Quantity:** Neumann G-function $G_m(x;x_0)$, and regular part $R_m(x;x_0)$:

$$\Delta G_m = \frac{1}{|\Omega|} - \delta(x-x_0)\,, \quad x \in \Omega\,,$$

$$\partial_n G_m = 0\,, \quad x \in \partial\Omega\,; \qquad \int_\Omega G_m\,dx = 0\,,$$

$$G_m(x,x_0) = -\frac{1}{2\pi}\log|x-x_0| + R_m(x,x_0)\,.$$

The Green's matrix $\mathcal{G}$ is defined in terms of the interaction term $G_m(x_i;x_j) \equiv G_{mij}$, and the self-interaction $R_m(x_i;x_i) \equiv R_{mii}$ by

$$\mathcal{G} \equiv \begin{pmatrix} R_{m11} & G_{m12} & \cdots & \cdots & G_{m1N} \\ G_{m21} & R_{m22} & G_{m23} & \cdots & \cdots \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ G_{mN1} & \cdots & \cdots & G_{mNN-1} & R_{mNN} \end{pmatrix}.$$

# Eigenvalues in 2-D Perforated Domains: II

**Principal Result (KTW):** *For $N$ small holes centered at $x_1, \ldots, x_N$ with logarithmic capacitances $d_1, \ldots, d_N$, then*

$$\lambda_1(\varepsilon) \sim \frac{2\pi}{|\Omega|} \sum_{j=1}^{N} \nu_j - \frac{4\pi^2}{|\Omega|} \sum_{j=1}^{N} \sum_{k=1}^{N} \nu_j \nu_k \left(\mathcal{G}\right)_{jk} + O(\nu^3) \,.$$

*Here $\nu_j \equiv = -1/\log(\varepsilon d_j)$ and $(\mathcal{G})_{jk}$ are the entries of G-matrix $\mathcal{G}$. For $N$ circular holes of a common radius $\varepsilon$, then $d_j = 1$, $\nu = -1/\log \varepsilon$, and*

$$\lambda_1(\varepsilon) \sim \frac{2\pi N \nu}{|\Omega|} - \frac{4\pi^2 \nu^2}{|\Omega|} p(x_1, \ldots, x_N) + O(\nu^3) \,,$$

- Note: the logarithmic capacitance $d_j$ of the $j^{\text{th}}$ hole is defined by

$$\begin{aligned} \Delta_y v &= 0 \,, \quad y \notin \Omega_j \equiv \varepsilon^{-1} \Omega_{\varepsilon_j} \,, \\ v &= 0 \,, \quad y \in \partial \Omega_j \,, \\ v &\sim \log|y| - \log d_j + o(1) \,, \quad |y| \to \infty \,. \end{aligned}$$

It can be calculated analytically for ellipses, two closely spaced circular disks, etc.

# Eigenvalues in 2-D Perforated Domains: III

**Discrete Sum:** The discrete sum $p(x_1, \ldots, x_N)$ is defined by

$$p(x_1, \ldots, x_N) \equiv \sum_{j=1}^{N} \sum_{k=1}^{N} (\mathcal{G})_{jk} \; .$$

**Key Point:** For $N$ circular holes of radius $\varepsilon \ll 1$, $\lambda_1$ has a local maximum at a local minimum point of the "Energy-like" function $p(x_1, \ldots, x_N)$.

**Specific Questions Adressed in [KTW]:**

- For $N = 1$ (one hole), then $p = R_m(x_1, x_1)$. Can we find domains $\Omega$ where there are there several points $x_1$ that locally maximize $\lambda_1$. Multiplicity of critical points of $R_m$? (Yes, for a class of dumbell-shaped domains).
- For the unit disk $\Omega = |x| \leq 1$, determine ring-type configurations of holes $x_1, ..., x_N$ that maximize $\lambda_1$.

# Eigenvalues in 2-D Perforated Domains: IV

**Multiple Holes in the Unit Disk:** Let $\Omega$ be the unit disk with $|\Omega| = \pi$. Then, $G_m$ and $R_m$ are

$$G_m(x;\xi) = -\frac{1}{2\pi}\log|x-\xi| + R_m(x;\xi)$$
$$R_m(x;\xi) = -\frac{1}{2\pi}\log\left|x|\xi| - \frac{\xi}{|\xi|}\right| + \frac{(|x|^2+|\xi|^2)}{2} - \frac{3}{4}\,.$$

For the unit disk, minimizing $p(x_1,\ldots,x_N)$ is equivalent to the minimizing $\mathcal{F}(x_1,\ldots,x_N)$ for $|x_j|<1$ where

$$\mathcal{F}(x_1,\ldots,x_N) = -\sum_{j=1}^{N}\sum_{\substack{k=1\\k\neq j}}^{N}\log|x_j-x_k| - \sum_{j=1}^{N}\sum_{k=1}^{N}\log|1-x_j\bar{x}_k| + N\sum_{j=1}^{N}|x_j|^2\,.$$

- For the GL model of superconductivity in the unit disk, equilibrium vortices at $x_1,\ldots,x_N$ with $|x_j|<1$ and a common winding number are located at critical points of $\mathcal{F}$ without confining potential term.

# Eigenvalues in 2-D Perforated Domains: V

**Restricted Optimization:** Optimize $\mathcal{F}$ over certain ring-type configurations of holes. We then compare the results with those computed with optimization software from MATLAB.

- Two Patterns: I (one ring), II (ring with a center hole). Specifically,

$$x_j = re^{2\pi ij/N}, \quad j = 1, \ldots, N, \quad (\text{P I}),$$

$$x_j = re^{2\pi ij/(N-1)}, \quad j = 1, \ldots, N-1, \; x_N = 0, \quad (\text{P II}).$$

- More generally, construct $m$ ring patterns with equidistantly spaced traps on each ring. Paramaters are the ring radii $r_1, \ldots, r_m$, the number of traps on each ring, and the phase angle relative to each ring.
- For each pattern we can calculate $p(x_1, \ldots, x_N)$ explicitly and then optimize over the ring radii.

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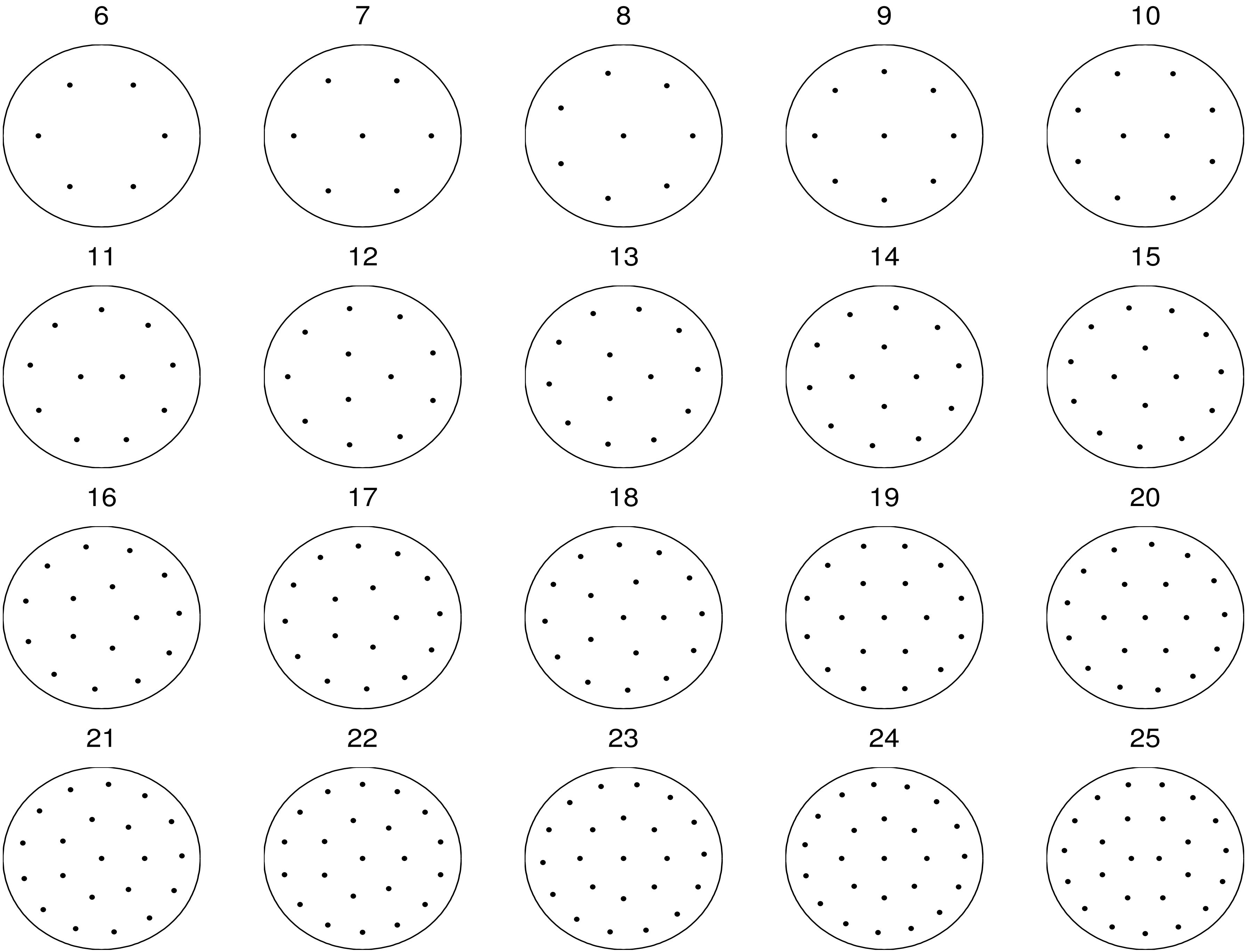
# Eigenvalues in 2-D Perforated Domains: VI



# Eigenvalues in 3-D Perforated Domains: I

In a 3-D bounded domain $\Omega$ consider

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

Here $\Omega_p = \cup_{i=1}^{N} \Omega_{\varepsilon_i}$, with $\Omega_{\varepsilon_i} \to x_i$ as $\varepsilon \to 0$ and non-overlapping.

**Principal Result (Cheviakov, MJW):** *For $N$ small traps centered at $x_1, \ldots, x_N$ with capacitances $C_1, \ldots, C_N$, then*

$$\lambda_1 \sim \frac{4\pi\varepsilon}{|\Omega|} \sum_{j=1}^{N} C_j - \frac{16\pi^2\varepsilon^2}{|\Omega|} \sum_{j=1}^{N} \sum_{k=1}^{N} C_j C_k \left(\mathcal{G}\right)_{jk} + O(\varepsilon^3) \,.$$

Here $\left(\mathcal{G}\right)_{jk} \equiv G_m(x_j; x_k)$ for $j \neq k$ and $\left(\mathcal{G}\right)_{jj} \equiv R_m(x_j; x_j)$ where $G_m(x;\xi)$ and $R_m(x;\xi)$ are now the 3-D Neumann G-function for the Laplacian.

# Eigenvalues in 3-D Perforated Domains: II

The matrix $\mathcal{G}$ can be found explicitly when $\Omega$ is the unit sphere. By summing series related to Legendre polynomials

$$G_m(x;\xi) = \frac{1}{4\pi|x-\xi|} + \frac{1}{4\pi|x|r'} + \frac{1}{4\pi}\ln\left[\frac{2}{1-|x||\xi|\cos\theta + |x|r'}\right] + \frac{1}{8\pi}\left(|x|^2+|\xi|^2\right) - \frac{7}{10\pi}\,.$$

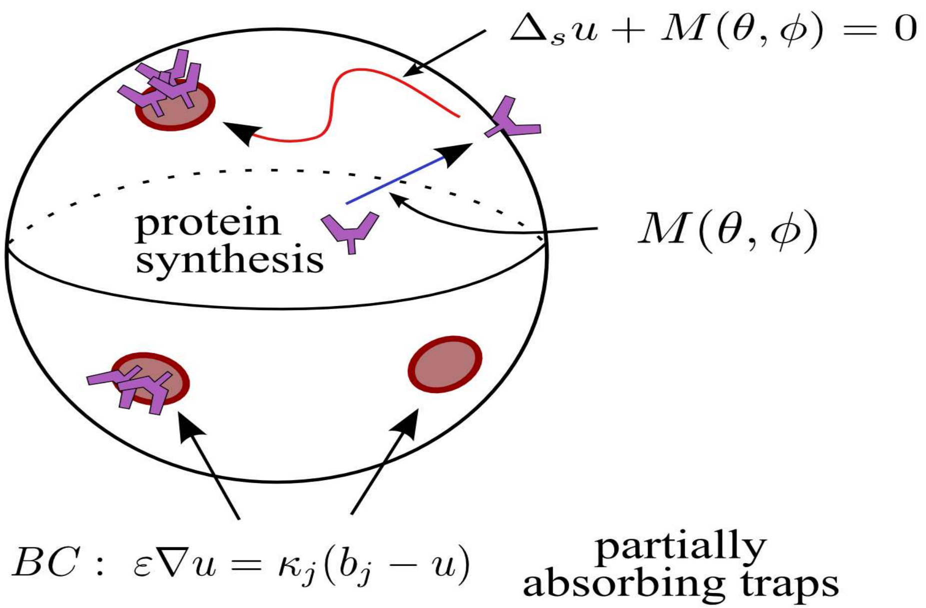
Here $r' = |x'-\xi|$, where $x' = x/|x|^2$ is the image point and $\theta$ is the angle between $x$ and $\xi$. The regular part $R_m(\xi,\xi)$ is

$$R_m(\xi,\xi) = \frac{1}{4\pi\left(1-|\xi|^2\right)} - \frac{1}{4\pi}\log\left(1-|\xi|^2\right) + \frac{|\xi|^2}{4\pi} - \frac{7}{10\pi}\,.$$

**Open Problems:**

- Where are the optimal trap locations $x_j$ for $j=1,\ldots,N$ inside the unit sphere that maximize the first eigenvalue? For identical traps we need to minimize the explicitly known function $p(x_1,\ldots,x_N) = \sum\sum \mathcal{G}_{jk}$.
- What about more general domains, such as a cube? Here we need Ewald summation techniques to build the matrix $\mathcal{G}$.

# Diffusion on the Surface of a Sphere: I




The surface diffusion problem is formulated as

$$\triangle_s u = -M\,, \quad x \in S_\varepsilon \equiv S \setminus \cup_{j=1}^{N} \Omega_{\varepsilon_j}\,,$$

$$\varepsilon \nabla_s u \cdot \hat{n} + \kappa_j (u - b_j) = 0\,, \quad x \in \partial\Omega_{\varepsilon_j}\,.$$

- $S$ is the unit sphere, $\Omega_{\varepsilon_j}$ are localized circular traps of radius $O(\varepsilon)$ on $S$ centered at $x_j$ with $|x_j| = 1$ for $j = 1, \ldots, N$.
- Traps are non-overlapping; $\Delta_s$ is surface Laplacian.

# Diffusion on the Surface of a Sphere: II

**Problem 1:** When $M = -1/D$, $u$ is the Mean First Passage Time (MFPT) for diffusion on $S$ with diffusivity $D$ (Z. Schuss).

**Problem 2:** $u$ is concentration and $M(\theta, \phi)$ arises from processes inside $S$.

**Goal:** Construct the asymptotic solution for $u$ in the limit of small trap radii $\varepsilon \to 0$ for both problems. We focus on Problem 1.

**Eigenvalue Problem:** The corresponding eigenvalue problem on $S$ is

$$\triangle_s \psi + \sigma \psi = 0 \,, \quad x \in S_\varepsilon \equiv S \backslash \cup_{j=1}^{N} \Omega_{\varepsilon_j} \,,$$
$$\varepsilon \nabla_s \psi \cdot \hat{n} + \kappa_j \psi = 0 \,, \quad x \in \partial \Omega_{\varepsilon_j} \,,$$
$$\int_S \psi^2 \, ds = 1 \,.$$

- **Goal:** Calculate the principal eigenvalue $\sigma_1$ in the limit $\varepsilon \to 0$. This determines the rate of approach to the steady-state.
- **Reference:** D. Coombs, R. Straube, MJW, *"Diffusion on a Sphere with Traps..."*, to appear, SIAM (2009).

# Diffusion on the Surface of a Sphere: III

**Previous Results for MFPT:** For one perfectly absorbing trap at the north pole with $M = 1/D$, we get an ODE problem for $u(\theta)$:

$$\frac{1}{\sin\theta}\frac{\partial}{\partial\theta}(\sin\theta\,\partial_\theta u) = -\frac{1}{D}\,, \quad \theta_c < \theta < \pi\,; \;\; u(\theta_c) = 0\,, \;\; u'(\pi) = 0\,.$$

The solution with $\theta_c = \varepsilon \ll 1$ is

$$u \sim \frac{1}{D}\left[-2\log\left(\frac{\varepsilon}{2}\right) + \log(1-\cos\theta)\right]\,, \quad \bar{u} \sim \frac{1}{D}\left[-2\log\left(\frac{\varepsilon}{2}\right) - 1\right]\,.$$

**Ref:** Lindeman, Laufenberger, Biophys. (1986); Singer et al. J. Stat. Phys. (2006).

**Previous Results for Principal Eigenvalue:** For one perfectly absorbing trap near the south pole, i.e. $\theta_c = \pi - \varepsilon$,

$$\partial_{\theta\theta}\psi + \cot(\theta)\partial_\theta\psi + \sigma\psi = 0\,, \quad 0 < \theta < \theta_c\,; \quad \psi(\theta_c) = 0\,, \;\; \psi'(0) = 0\,.$$

An explicit solution (Weaver (1983), Chao et. al. (1981), Biophys. J.) gives

$$\sigma \sim \frac{\mu}{2} + \mu^2\left(-\frac{\log 2}{2} + \frac{1}{4}\right)\,; \quad \mu = -\frac{1}{\log\varepsilon}$$

# Diffusion on the Surface of a Sphere: IV

**Problem 1 (MFPT):** Let $M$ be constant and $b_j = 0$. A matched asymptotic analysis yields

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

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

*where $A_j$ for $j = 1, \ldots, N$ has the asymptotics with logarithmic gauge $\mu_j$*

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

*The averaged MFPT $\bar{u} = \chi$ is given asymptotically by*

$$\bar{u} = \chi = \frac{2M}{N\bar{\mu}} + M \left[ (2\log 2 - 1) - \frac{4}{N^2 \bar{\mu}^2} p_w(x_1, \ldots, x_N) \right] + O(|\mu|) \,.$$

# Diffusion on the Surface of a Sphere: V

*Here* $\mu_j$, $\bar{\mu}$, *and the weighted discrete energy* $p_w(x_1, \ldots, x_N)$, *are*

$$\mu_j \equiv -\frac{1}{\log(\varepsilon \beta_j)}, \quad \beta_j \equiv a_j \exp\left(-1/a_j \kappa_j\right); \quad \bar{\mu} \equiv \frac{1}{N} \sum_{j=1}^{N} \mu_j ;$$

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

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

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

$G$ is $2\pi$ periodic in $\phi$ and smooth at $\theta = 0, \pi$ .

It is given analytically by

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

**Remark:** $G$ appears in various studies of the motion of fluid vortices on $S$ (P. Newton, S. Boatto, etc..).

# Diffusion on the Surface of a Sphere: VI

**Principal Result**: *For $N$ identical perfectly absorbing traps of a common radius $\varepsilon a$ centered at $x_j$, for $j = 1, \ldots, N$, on $S$, the principal eigenvalue has asymptotics*

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

*where $p(x_1, \ldots, x_N)$ is the discrete logarithmic energy and $\mu$ is*

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

- For $N = 1$, we get (in agreement with old results)

$$\sigma(\varepsilon) \sim \frac{\mu}{2} + \frac{\mu^2}{4} (1 - 2\log 2) \,.$$

- **Key Point:** $\sigma(\varepsilon)$ is maximized at the elliptic Fekete points.
- **Remark:** Can formulate a problem involving the Helmholtz Green's function on the sphere that sums the infinite logarithmic expansion for $\sigma(\varepsilon)$. Result above has error of $O(\mu^3)$.

# Diffusion on the Surface of a Sphere: VII

Summing the infinite logarithmic series for $\sigma(\varepsilon)$ yields:

**Principal Result**: *Consider $N$ partially absorbing traps of radii $\varepsilon a_j$ for $j = 1, \ldots, N$. Let $\nu(\varepsilon)$ be the smallest root of the transcendental equation*

$$\text{Det}\left(I + 2\pi R_h \mathcal{U} + 2\pi \mathcal{G}_h \mathcal{U}\right) = 0\,.$$

*Here $\mathcal{U}$ is the diagonal matrix with $\mathcal{U}_{jj} = \mu_j$ for $j = 1, \ldots, N$, and $\mathcal{G}_h$ is the Helmholtz Green's function matrix with matrix entries*

$$\mathcal{G}_{hjj} = 0\,; \qquad \mathcal{G}_{hij} = -\frac{1}{4\sin(\pi\nu)} P_\nu\left(\frac{|x_j - x_i|^2}{2} - 1\right)\,, \quad i \neq j\,,$$

*Then, with an error of order $O(\varepsilon)$, $\sigma(\varepsilon) \sim \nu(\nu + 1)$.*

- $P_\nu(z)$ is the Legendre function of the first kind, with regular part

$$R_h(\nu) \equiv -\frac{1}{4\pi}\left[-2\log 2 + 2\gamma + 2\psi(\nu + 1) + \pi\cot(\pi\nu)\right]\,.$$

- $\gamma$ is Euler's constant, $\psi$ is Di-gamma function, and recall

$$\mu_j \equiv -\frac{1}{\log(\varepsilon\beta_j)}\,, \quad \beta_j \equiv a_j \exp\left(-1/a_j\kappa_j\right)\,;$$

# Diffusion on the Surface of a Sphere: VIII

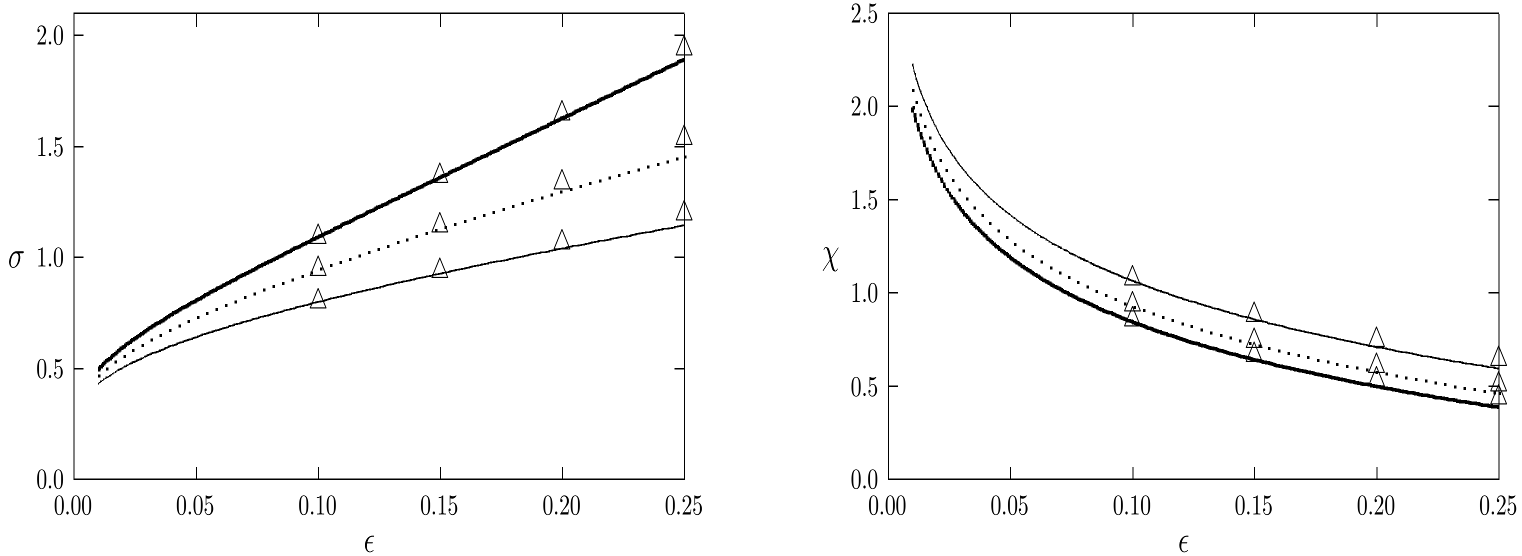
Table 1: Smallest eigenvalue $\sigma(\varepsilon)$ for the 2- and 5-trap configurations. For the 2-trap case the traps are at $(\theta_1, \phi_1) = (\pi/4, 0)$ and $(\theta_2, \phi_2) = (3\pi/4, 0)$. Here, $\sigma$ is the numerical solution found by COMSOL; $\sigma^*$ corresponds to summing the log expansion; $\sigma_2$ is calculated from the two-term expansion.

| | 5 traps | | | 2 traps | | |
|---|---|---|---|---|---|---|
| $\varepsilon$ | $\sigma$ | $\sigma^*$ | $\sigma_2$ | $\sigma$ | $\sigma^*$ | $\sigma_2$ |
| $0.02$ | $0.7918$ | $0.7894$ | $0.7701$ | $0.2458$ | $0.2451$ | $0.2530$ |
| $0.05$ | $1.1003$ | $1.0991$ | $1.0581$ | $0.3124$ | $0.3121$ | $0.3294$ |
| $0.1$ | $1.5501$ | $1.5452$ | $1.4641$ | $0.3913$ | $0.3903$ | $0.4268$ |
| $0.2$ | $2.5380$ | $2.4779$ | $2.3278$ | $0.5177$ | $0.5110$ | $0.6060$ |

**Note:** For $\varepsilon = 0.2$ and $N = 5$, we get $5\%$ trap surface area fraction. The agreement is very good.

# Diffusion on the Surface of a Sphere: IX

**Effect of Spatial Arrangement of 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 $\varepsilon$. **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: X

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

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

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

**Reference:** E. A. Rakhmanov, E. B. Saff, Y. M. Zhou, *"Electrons on the Sphere", in: Computational Methods and Function Theory 1994 (Penang), 293–309* and B. Bergersen, D. Boal, P. Palffy-Muhoray, *"Equilibrium Configurations of Particles on the Sphere: The Case of Logarithmic Interactions"*, J. Phys. A: Math Gen., **27**, No. 7, (1994), pp. 2579–2586.

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

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

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

# Diffusion on the Surface of a Sphere: XI

**Application:** Estimate, with physical parameters, the minimum time taken 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 $\approx 0.25\mu$m$^2$/s and consider $N = 100$ signaling regions (traps) of radius $10$nm on a cell of radius $5\mu$m. With these parameters,

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

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

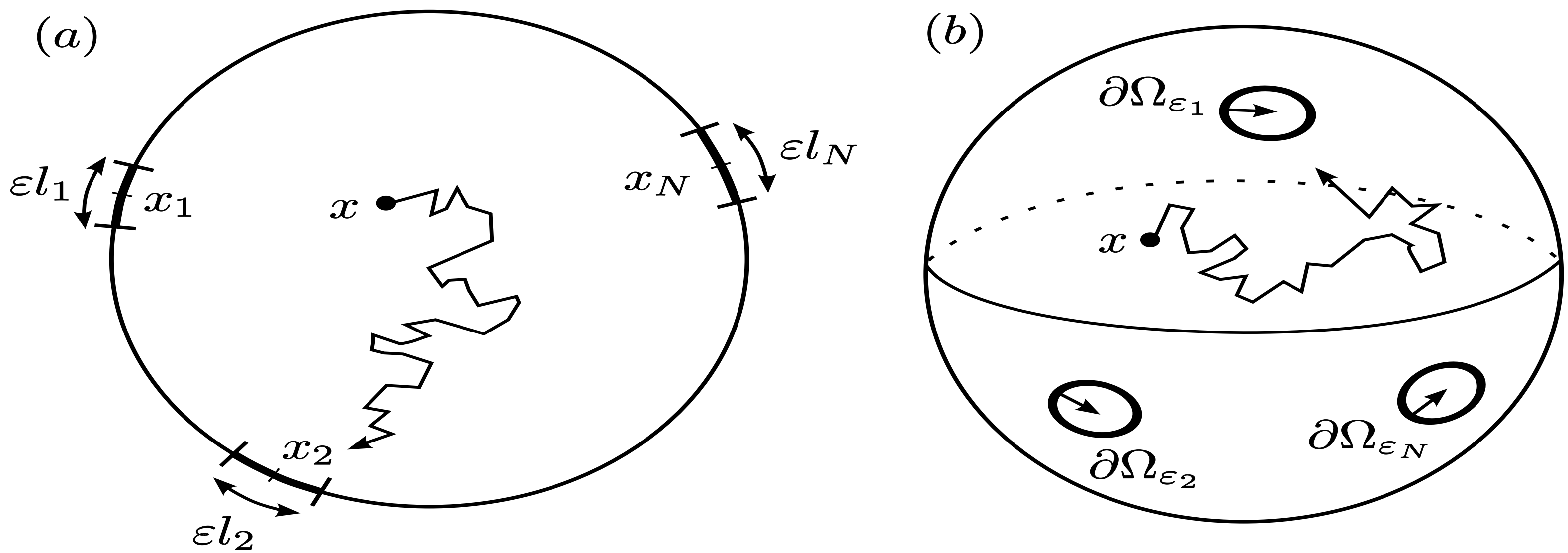
**One Big Trap:** As a comparison, for one big trap of the same area the averaged MFPT is 360s, which is very different.

Conclusion: Both the Spatial Distribution and Fragmentation Effect of Localized Traps are Rather Signficant at Moderately Small Values of $\varepsilon$.

# Narrow Escape Problem Revisited

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

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




**Key Question:** What is effect of spatial arrangement of traps on the boundary in 2-D and 3-D? Need a higher order asymptotic theory.

**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).

# Narrow Escape From a Sphere: I

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

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

<u>**Lemma**</u>: *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:

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

# Narrow Escape From a Sphere: II

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

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

*Here $c_j = 2a_j/\pi$ is the capacitance of the $j^{th}$ circular absorbing window of radius $\varepsilon a_j$, $\bar{c} \equiv N^{-1}(c_1 + \ldots + c_N)$, $|\Omega| = 4\pi/3$, and $\kappa_j$ 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 $\varepsilon$ arises from the subdominant singularity in $G_s$.

# Narrow Escape From a Sphere: III

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

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

- **N Identical Circular Traps:** of common radius $\varepsilon$:

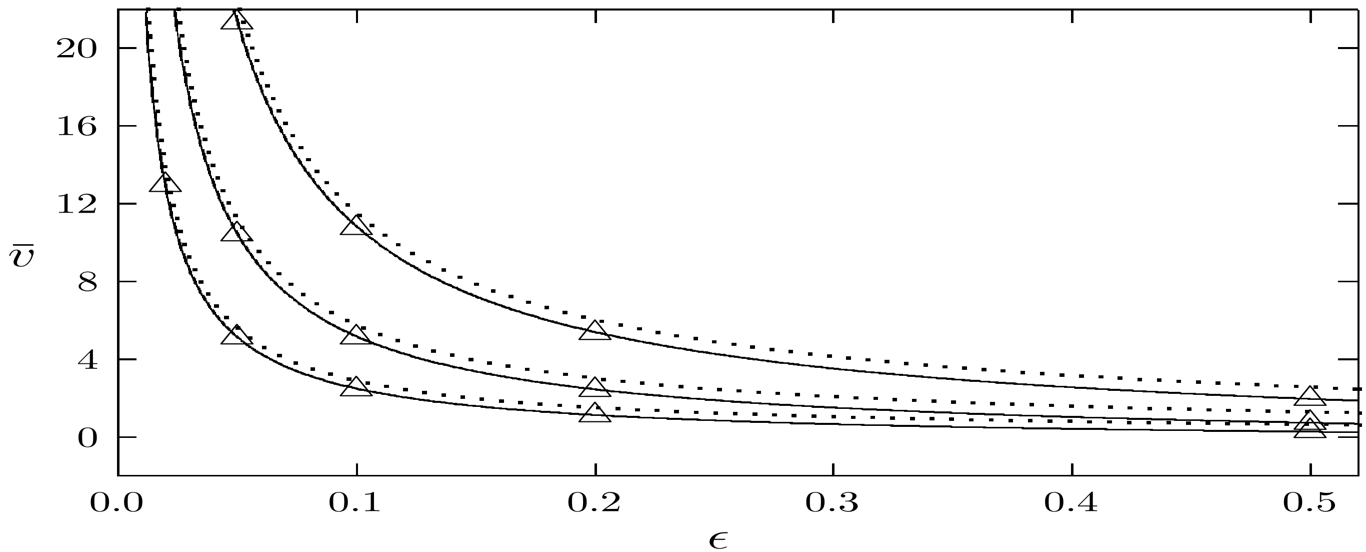
$$\bar{v} = \frac{|\Omega|}{4\varepsilon DN}\left[1 + \frac{\varepsilon}{\pi}\log\left(\frac{2}{\varepsilon}\right) + \frac{\varepsilon}{\pi}\left(-\frac{9N}{5} + 2(N-2)\log 2 + \frac{3}{2} + \frac{4}{N}\mathcal{H}(x_1,\ldots,x_N)\right) + \mathcal{O}(\varepsilon^2 \log\varepsilon)\right],$$

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

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

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

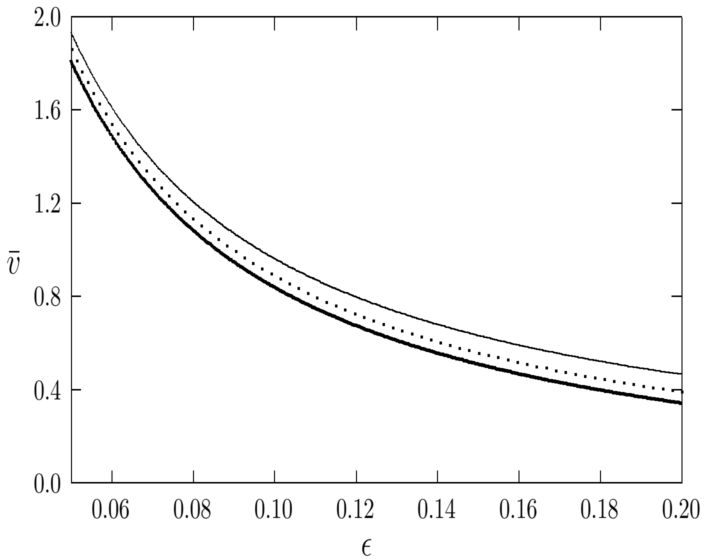
# Narrow Escape From a Sphere: IV

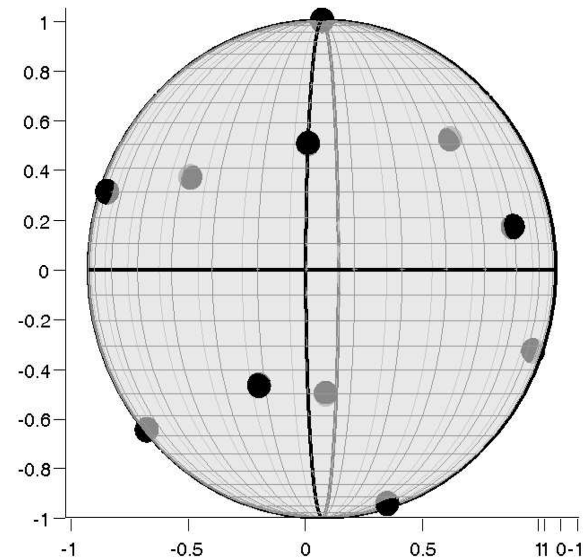



**Plot:** $\bar{v}$ vs. $\varepsilon$ with $D = 1$ and either $N = 1, 2, 4$ equidistantly spaced circular windows of radius $\varepsilon$. **Solid:** $3$-term expansion. **Dotted:** $2$-term expansion. **Discrete:** COMSOL. **Top:** $N = 1$. **Middle:** $N = 2$. **Bottom:** $N = 4$.

| | $N=1$ | | | $N=2$ | | | $N=4$ | | |
|---|---|---|---|---|---|---|---|---|---|
| $\varepsilon$ | $\bar{v}_2$ | $\bar{v}_3$ | $\bar{v}_n$ | $\bar{v}_2$ | $\bar{v}_3$ | $\bar{v}_n$ | $\bar{v}_2$ | $\bar{v}_3$ | $\bar{v}_n$ |
| 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 |

# Narrow Escape From a Sphere: V




**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 $\approx 10\%$.
- 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.

# Narrow Escape From a Sphere: VI

**Conclusion:** spatial arrangement and fragmentation of traps on the sphere is a very significant factor for $\bar{v}$

**Key Ingredients 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 $\varepsilon$ 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 $\kappa_j$.
- Asymptotic matching and solvability conditions (Divergence theorem) determine $v$ and $\bar{v}$

# Narrow Escape From a Sphere: VII

**Numerical Computations:** to compare optimal points of $\mathcal{H}$ with those of classic energies

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

(preliminary work with A. Cheviakov, MJW).

**Numerical Methods:**

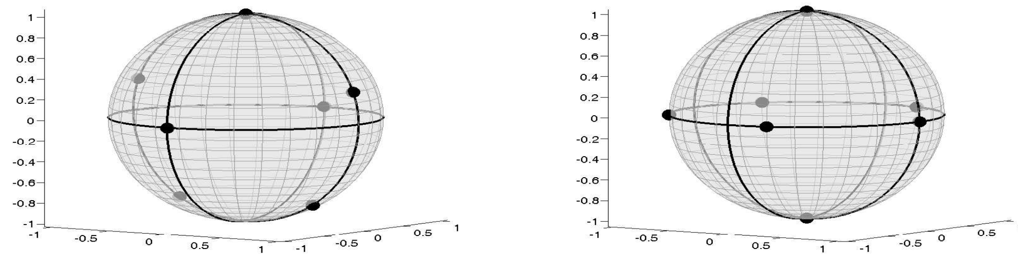
- **Extended Cutting Angle method (ECAM).** (cf. G. Beliakov, Optimization Methods and Software, **19** (2), (2004), pp. 137-151).
- **Dynamical systems – based optimization (DSO).** (cf. M.A. Mammadov, A. Rubinov, and J. Yearwood, (2005)).

**Results:**

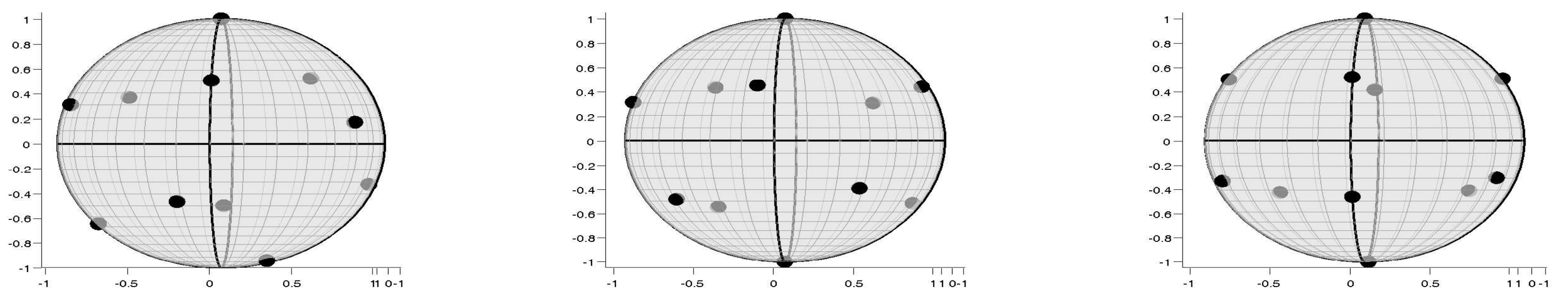
- For $N = 5, 6, 8, 9, 10$ and $12$, optimal point arrangments coincide
- Some differences for $N = 7, 11, 16$.

# Narrow Escape From a Sphere: VIII

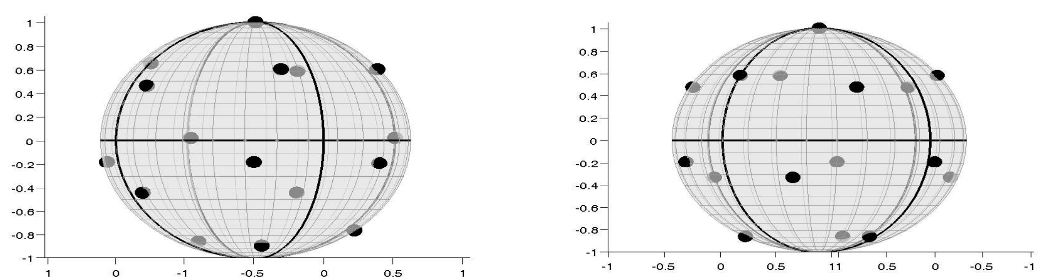
**N=7:** Left: $\mathcal{H}$. Right: $\mathcal{H}_c$ and $\mathcal{H}_{log}$.



**N=11:** Left: $\mathcal{H}$. Middle: $\mathcal{H}_c$. Right: $\mathcal{H}_{log}$.



**N=16:** Left: $\mathcal{H}$ and $\mathcal{H}_{log}$. Right: $\mathcal{H}_c$.



# Narrow Escape From a Sphere: IX

**Main Result:** holds for arbitrary-shaped traps with two changes. Let $\Omega_j$ be the trap magnified by $O(\varepsilon^{-1})$. (possibly multi-connected to allow for receptor clustering).

**Capacitance:** $c_j$ is now determined from

$$\mathcal{L} w_c = 0 \,, \quad \eta \geq 0 \,, \quad -\infty < s_1, s_2 < \infty \,,$$
$$\partial_\eta w_c = 0 \,, \quad \text{on} \quad \eta = 0 \,, \; (s_1, s_2) \notin \Omega_j \,; \quad w_c = 1 \,, \quad \text{on} \quad \eta = 0 \,, \; (s_1, s_2) \in \Omega_j \,,$$
$$w_c \sim c_j / \rho \,, \quad \text{as} \quad \rho \to \infty \,.$$

**Correction to Tangent Plane:** $\kappa_j$ now determined from

$$w_{2h\eta\eta} + w_{2h s_1 s_1} + w_{2h s_2 s_2} = 0 \,, \qquad \eta \geq 0 \,, \quad -\infty < s_1, s_2 < \infty \,,$$
$$\partial_\eta w_{2h} = 0 \,, \quad \eta = 0 \,, \; (s_1, s_2) \notin \Omega_j \,; \quad w_{2h} = -\mathcal{K}(s_1, s_2) \,, \quad \eta = 0 \,, \; (s_1, s_2) \in \Omega_j \,,$$
$$w_{2h} \sim -\kappa_j c_j / \rho \,, \quad \text{as} \quad \rho = (\eta^2 + s_1^2 + s_2^2)^{1/2} \to \infty \,,$$

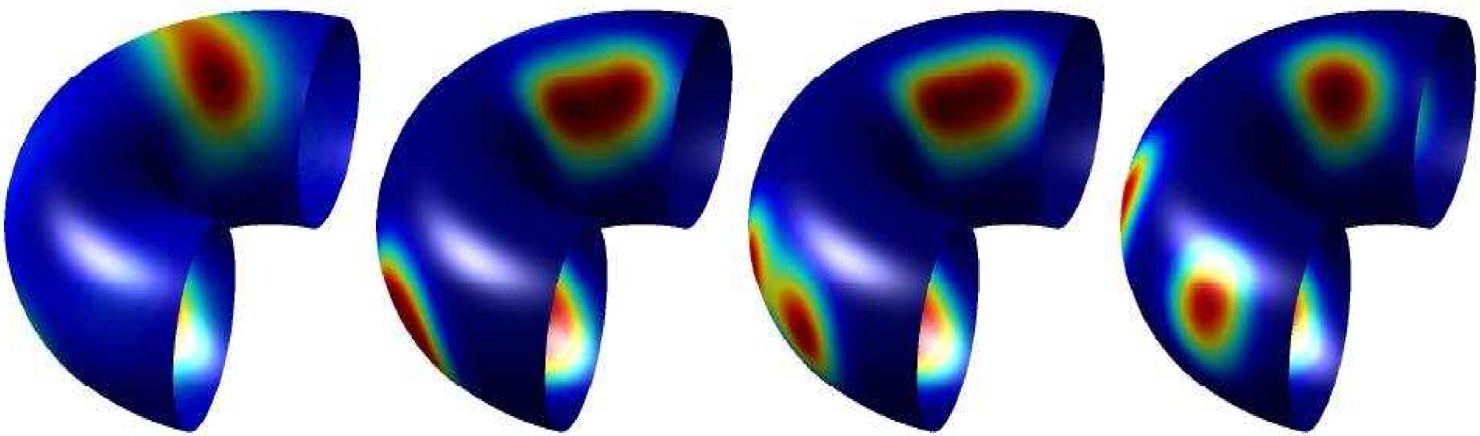
where $\mathcal{K}(s_1, s_2)$ is defined from

$$\mathcal{K}(s_1, s_2) = -\frac{1}{4\pi} \int_{\Omega_j} \log |\tilde{s} - s| \, w_{c\eta}|_{\eta=0} \, ds \,.$$

# Further Directions

- Narrow escape problems in arbitrary 3-d domains: require Neumann G-functions with boundary singularity
- Surface diffusion on arbitrary 2-d surfaces: require Neumann G-function and regular part.
- Include chemical reactions occurring within each trap, with detailed mechanism of escape from trap through 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? Formulation leads to a **Steklov-type eigenvalue problem.**
- Pattern formation for reaction-diffusion systems with localized spots on curved and evolving surfaces.

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



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


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# Narrow Escape in 2-D: I

Consider the narrow escape problem from a 2-D domain. The surface Neumann G-function, $G$, with $\int_\Omega G\,dx = 0$ is key:

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

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

Then define the Green's function matrix

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

The local or inner problem near the $j^{\text{th}}$ arc determines a constant $d_j$

$$w_{0\eta\eta} + w_{0ss} = 0\,, \quad 0 < \eta < \infty\,, \quad -\infty < s < \infty\,,$$

$$\partial_\eta w_0 = 0\,, \quad \text{on } |s| > l_j/2\,, \quad \eta = 0\,; \quad w_0 = 0\,, \quad \text{on } |s| < l_j/2\,, \quad \eta = 0\,.$$

$$w_0 \sim [\log|y| - \log d_j + o(1)]\,, \quad \text{as } |y| \to \infty\,, \quad d_j = l_j/4\,.$$

# Narrow Escape in 2-D: II

**Principal Result**: *Consider $N$ well-separated absorbing arcs of length $\varepsilon l_j$ for $j = 1, \ldots, N$ centered at $x_j \in \partial\Omega$. Then, in the outer region $|x - x_j| \gg \mathcal{O}(\varepsilon)$ for $j = 1, \ldots, N$ the MFPT is*

$$v \sim -\pi \sum_{i=1}^{N} A_i G(x; x_i) + \chi \,, \quad \chi = \bar{v} = \frac{1}{|\Omega|} \int_\Omega v \, dx \,,$$

*where a two-term expansion for $A_j$ and $\chi$ are*

$$A_j \sim \frac{|\Omega| \mu_j}{N D \pi \bar{\mu}} \left( 1 - \pi \sum_{i=1}^{N} \mu_i \mathcal{G}_{ij} + \frac{\pi}{N \bar{\mu}} p_w(x_1, \ldots, x_N) \right) + \mathcal{O}(|\mu|^2) \,,$$

$$\bar{v} \equiv \chi \sim \frac{|\Omega|}{N D \pi \bar{\mu}} + \frac{|\Omega|}{N^2 D \bar{\mu}^2} p_w(x_1, \ldots, x_N) + \mathcal{O}(|\mu|) \,.$$

*Here $p_w$ is a weighted discrete sum in terms of $\mathcal{G}_{ij}$:*

$$p_w(x_1, \ldots, x_N) \equiv \sum_{i=1}^{N} \sum_{j=1}^{N} \mu_i \mu_j \mathcal{G}_{ij} \,, \qquad \mu_j = -\frac{1}{\log(\varepsilon d_j)} \,, \quad d_j = \frac{l_j}{4} \,.$$

**Remark:** there is an analogous result that sums all logarithmic terms for $\bar{v}$.

# Narrow Escape in 2-D: III

- **For $N = 1$ arc** of length $|\partial\Omega_{\varepsilon_1}| = 2\varepsilon$ (i.e. $d = 1/2$), then

$$v(x) \sim \frac{|\Omega|}{D\pi}\left[-\log\left(\frac{\varepsilon}{2}\right) + \pi\left(R(x_1;x_1) - G(x;x_1)\right)\right],$$

$$\bar{v} = \chi \sim \frac{|\Omega|}{D\pi}\left[-\log\left(\frac{\varepsilon}{2}\right) + \pi R(x_1;x_1)\right].$$

  Extension of work of Singer et al. to arbitrary $\Omega$ with smooth $\partial\Omega$.

- For the unit disk, $G$ and $R$ are

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

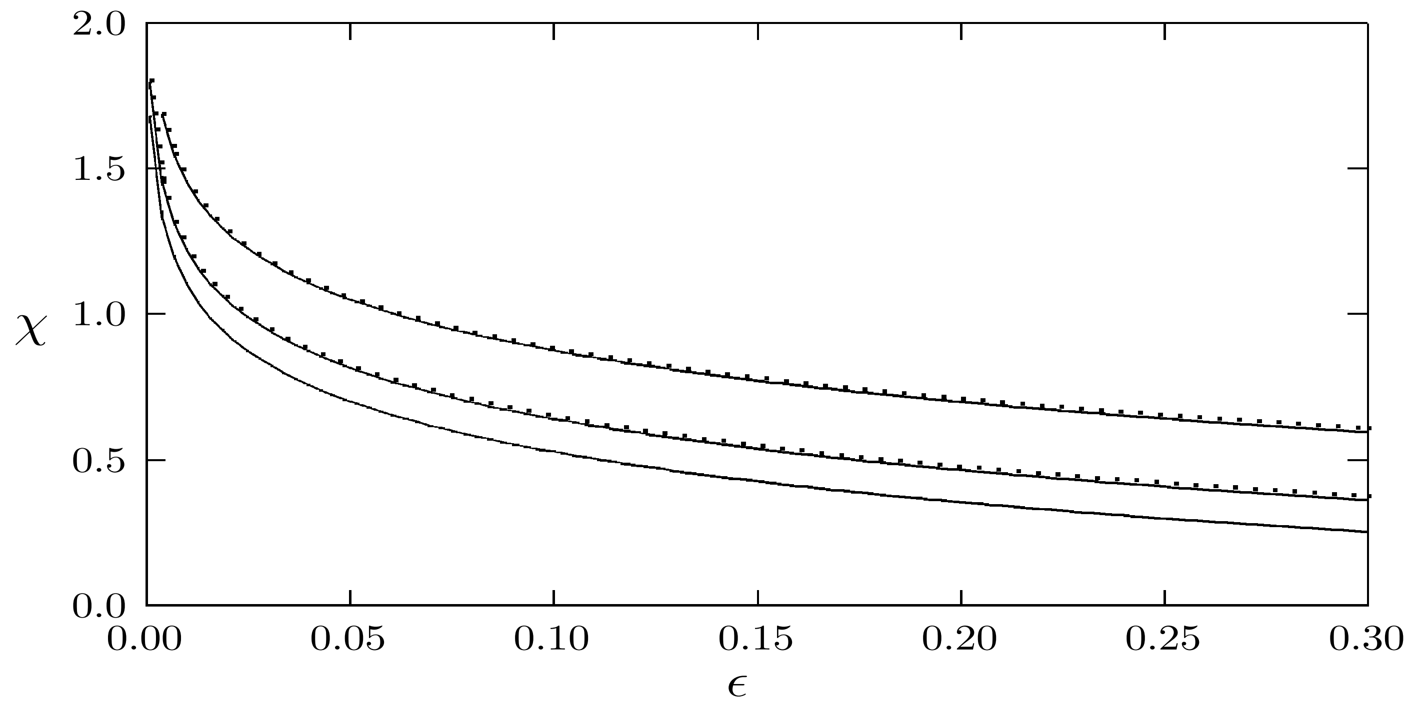
- For $N$ equidistant arcs on unit disk, i.e. $x_j = e^{2\pi i j/N}$ for $j = 1, \ldots, N$,

$$v(x) \sim \frac{1}{DN}\left[-\log\left(\frac{\varepsilon N}{2}\right) + \frac{N}{8} - \pi\sum_{j=1}^{N} G(x;x_j)\right],$$

$$\chi \sim \frac{1}{DN}\left[-\log\left(\frac{\varepsilon N}{2}\right) + \frac{N}{8}\right],$$

# Narrow Escape in 2-D: IV

Key Point: Spatial Arrangement of Arcs is Very Significant




**Plot:** Comparison of the two-term result for $\chi$ (dotted curves) with the log-summed result (solid curves) vs.$\varepsilon$ for $D = 1$ and for four traps on the boundary of the unit disk. Trap locations at $x_1 = e^{\pi i/6}$, $x_2 = e^{\pi i/3}$, $x_3 = e^{2\pi i/3}$, $x_4 = e^{5\pi i/6}$ (**top curves**); $x_1 = (1, 0)$, $x_2 = e^{\pi i/3}$, $x_3 = e^{2\pi i/3}$, $x_4 = (-1, 0)$ (**middle curves**); $x_1 = e^{\pi i/4}$, $x_2 = e^{3\pi i/4}$, $x_3 = e^{5\pi i/4}$, $x_4 = e^{7\pi i/4}$ (**bottom curves**).

# Narrow Escape in 2-D: V

**Optimization:** For one absorbing arc of length $2\varepsilon$ on a smooth boundary,

$$\bar{v} = \chi \sim \frac{|\Omega|}{D\pi} \left[ -\log\left(\frac{\varepsilon}{2}\right) + \pi R(x_1; x_1) \right] .$$

$$\lambda(\varepsilon) \sim \lambda^* \sim \frac{\pi\mu_1}{|\Omega|} - \frac{\pi^2\mu_1^2}{|\Omega|} R(x_1; x_1) + \mathcal{O}(\mu_1^3) , \quad \mu_1 \equiv -\frac{1}{\log[\varepsilon/2]}$$

**Principal Result**: *The maxima (minima) of $R(x_0, x_0)$ do not necessarily coincide with the maxima (minima) of the curvature $\kappa(\theta)$ of the boundary of a smooth perturbation of the unit disk. Consequently, for $\varepsilon \to 0$, $\lambda(\varepsilon)$ does not necessarily have a local minimum (maximum) at the location of a local maximum (minimum) of the curvature of a smooth boundary.*

**Proof:** based on explicit perturbation formula for $R(x_0, x_0)$ for arbitrary smooth perturbations of the unit disk.