Narrow Escape and Narrow Capture problems in 3D, asymptotic solutions, optimal trap configurations

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Outline

Outline

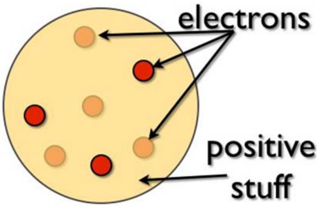
The Global Optimization Problem

Problem:

- Global optimization of some objective function that depends on positions of small "particles", or "pores", or "traps", on the surface of a 3D domain:

$$\min \mathcal{H}(x_1, \ldots, x_N), \qquad x_i \in \partial V, \qquad V \subset \mathbb{R}^3.$$

Example: the Thomson problem



- Total Coulombic interaction energy:

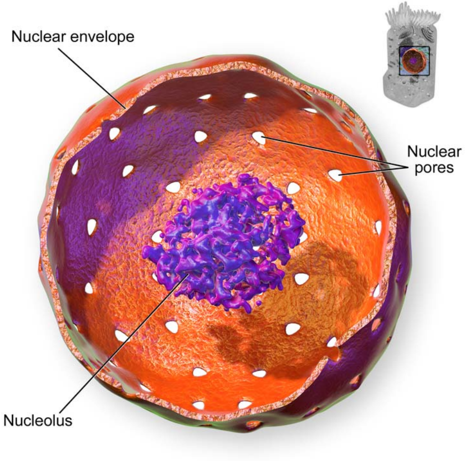
$$\mathcal{H}_C(x_1, \ldots, x_N) = \sum_{i=1}^{N} \sum_{j=i+1}^{N} h(x_i, x_j)$$

- Pairwise energy function: $h(x_i, x_j) = \dfrac{1}{|x_i - x_j|}$

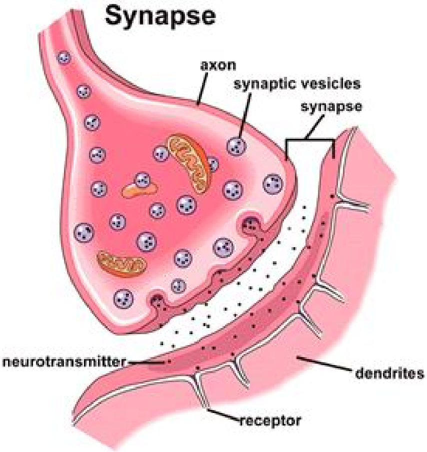
- **In this talk:** global optimization problems arising from Narrow Escape and Narrow Capture problems.

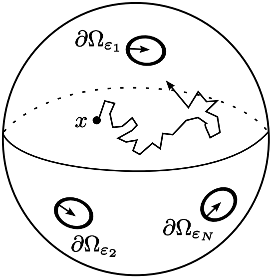
Chemical exchange through nuclear pores:

- mRNA, protein, smaller molecule transfer.
- ~ 1000 translocations per complex per second.
- Typical nucleus size: $\sim 6 \times 10^{-6}$ m.
- ~ 2000 nuclear pore complexes in a typical nucleus.
- Pore size $\sim 10^{-8}$ m.
- Pore separation $\sim 5 \times 10^{-7}$ m.



Synaptic receptors on dendrites:

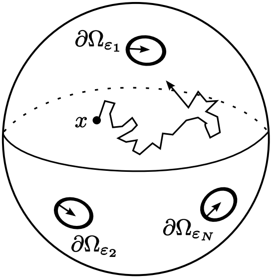




The setup:

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

Narrow Escape problem: the Math setup

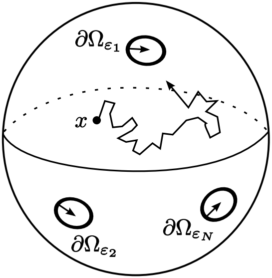


Problem for the MFPT $v = v(x)$ [*Holcman, Schuss (2004)*]:

$$\begin{cases} \triangle v = -\dfrac{1}{D}, & x \in \Omega, \\ v = 0, \quad x \in \partial\Omega_a; & \partial_n v = 0, \quad x \in \partial\Omega_r. \end{cases}$$

Average MFPT: $\bar{v} = \dfrac{1}{|\Omega|} \displaystyle\int_\Omega v(x)\, dx = \text{const}.$

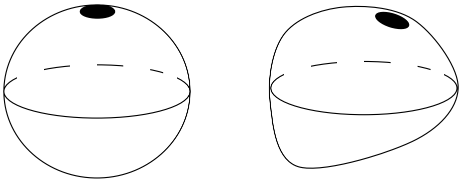
Narrow Escape problem: the Math setup



Problem for the MFPT $v = v(x)$ [*Holcman, Schuss (2004)*]:

$$\begin{cases} \triangle v = -\dfrac{1}{D}, \quad x \in \Omega, \\ v = 0, \quad x \in \partial\Omega_a; \quad \partial_n v = 0, \quad x \in \partial\Omega_r. \end{cases}$$

- Linear
- Strongly Heterogeneous Dirichlet/Neumann BCs
- Singularly perturbed: $\varepsilon \to 0^+ \quad \Rightarrow \quad v \to +\infty$ a.e.



Unit sphere; one trap of radius $\varepsilon \ll 1$ [*Singer et al (2006)*]

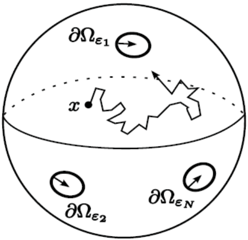
$$\bar{v} \sim \frac{|\Omega|}{4\varepsilon D}\left[1 - \frac{\varepsilon}{\pi}\log\varepsilon + \mathcal{O}(\varepsilon)\right]$$

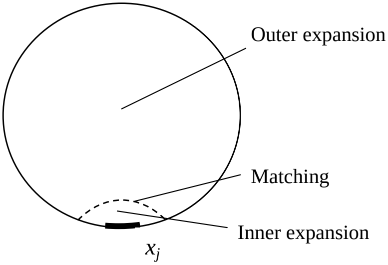
Arbitrary 3D domain with smooth boundary; one small trap [*Singer et al (2009)*]

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

H: mean curvature at the center of the trap.

Matched Asymptotic Expansions (Illustration for the Unit Sphere)





- Outer expansion, defined at $\mathcal{O}(1)$ distances from traps:

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

- Inner expansion of solution near trap centered at x_j uses scaled coordinates y:

$$v_{in} \sim \varepsilon^{-1} w_0(y) + \log\left(\frac{\varepsilon}{2}\right) w_1(y) + w_2(y) + \cdots .$$

- Matching condition: when $x \to x_j$ and $y = \varepsilon^{-1}(x - x_j) \to \infty$,

$$v_{in} \sim v_{out}.$$

A higher-order asymptotic MFPT formula for the unit sphere

Setup:

- A unit sphere with N traps located at $\{x_j\}$.
- Traps of different radii: $r_j = a_j\varepsilon,\ \ j = 1, \ldots, N;$ capacitances (disk): $c_j = 2a_j/\pi$.
- Traps are small $(\varepsilon \ll 1)$, well-separated.

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

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

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

- $G_s(x; x_j)$: spherical Neumann Green's function (known).
- $\bar{c}$: average capacitance; $\kappa_j = \mathrm{const}$.
- $p_c(x_1, \ldots, x_N)$: trap interaction term involving $G_s(x_i; x_j)$.

Narrow Escape Problem for the sphere: N equal traps

Asymptotic assumptions:

- Domain: a unit sphere
- $D = \text{const}$
- N equal traps of radius $\varepsilon \ll 1$

- The asymptotic average MFPT including trap position/interaction terms:

$$\bar{v} \sim \frac{|\Omega|}{4\varepsilon DN}\left[1 + \frac{\varepsilon}{\pi}\log\left(\frac{2}{\varepsilon}\right) + \frac{\varepsilon}{\pi}\left(-\frac{9N}{5} + 2(N-2)\log 2 + \frac{3}{2} + \frac{4}{N}\mathcal{H}_{MFPT}\right)\right];$$

$$\boxed{\mathcal{H}_{MFPT}(x_1, \ldots, x_N) = \sum_{i=1}^{N}\sum_{j=i+1}^{N} h(x_i, x_j),}$$

$$h(x_i, x_j) = \frac{1}{|x_i - x_j|} - \frac{1}{2}\log|x_i - x_j| - \frac{1}{2}\log(2 + |x_i - x_j|)$$

- Fast and precise MFPT computations
- Global optimization problem

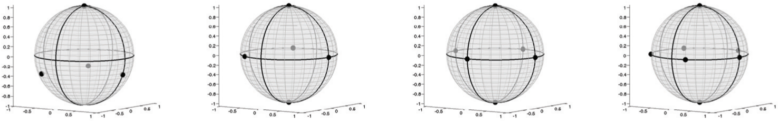
Global optimization

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

- A high-dimensional problem; $\sim 2N$ degrees of freedom in $\mathbb{R}^3$ ($2N - 3$ for S^2).
- May be hard to distinguish equivalent configurations.
- "Black box" software: standard approaches (genetic algorithms, simulated annealing, dynamical systems, etc.)
- Potential- and domain-specific software.
- In the literature, putative numerical global minima are presented; virtually no works discuss local minima [*Erber & Hockney (1996)*].

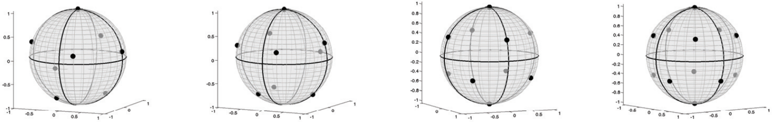
Low-N optimal MFPT for the unit sphere

- Globally optimal configurations for $N = 4 \ldots 12$ [*A.C., M.Ward, R.Straube (2010)*]:



(a) $N = 4$ (b) $N = 5$ (c) $N = 6$ (d) $N = 7$

FIG. 4.3. *Minimal energy trap configurations for* $N = 4, 5, 6, 7$ *traps, common for the three discrete energy functions.*



(a) $N = 8$ (b) $N = 9$ (c) $N = 10$ (d) $N = 12$

FIG. 4.4. *Minimal energy trap configurations for* $N = 8, 9, 10, 12$ *traps, common for the three discrete energy functions.*

- Some monotone repelling pairwise potentials:

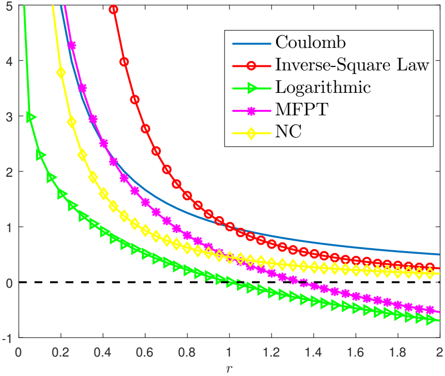
$$h_c(r) = \frac{1}{|r|}, \quad h_p(r) = \frac{1}{|r|^p},$$

$$h_{\log}(r) = -\log|r|, \quad h_{\mathrm{MFPT}}(r) = \frac{1}{|r|} - \frac{1}{2}\log|r| - \frac{1}{2}\log(2+|r|)$$

- Universally optimal configurations in $\mathbb{R}^3$:

- antipodal points ($N = 2$)
- an equilateral triangle ($N = 3$)
- a tetrahedron ($N = 4$)
- an octahedron ($N = 6$)
- an icosahedron ($N = 12$)

- Not much is known analytically in other situations...



Dilute trap fraction limit of homogenization theory

- $N \gg 1$ small boundary traps, distributed "homogeneously" over the sphere.
- Assumptions: $N \gg 1$, $\varepsilon \ll 1$, Total trap area fraction $\sigma = \pi\varepsilon^2 N/(4\pi) = N\varepsilon^2/4 \ll 1$.
- Approximate the mixed Dirichlet-Neumann Narrow Escape problem by a Robin problem: $v(x) \simeq_h v(x)$:

$$\begin{cases} \triangle v = -\dfrac{1}{D}, & x \in \Omega, \\ v = 0, \quad x \in \partial\Omega_a; & \partial_n v = 0, \quad x \in \partial\Omega_r \end{cases} \rightarrow \begin{cases} \triangle v_h = -\dfrac{1}{D}, & \rho = |x| < 1; \\ f(\varepsilon)\partial_r v_h + \kappa(\sigma) v_h = 0, & \rho = 1. \end{cases}$$

- Functions $f(\varepsilon)$, $\kappa(\sigma)$ can be estimated using the asymptotic formulas:

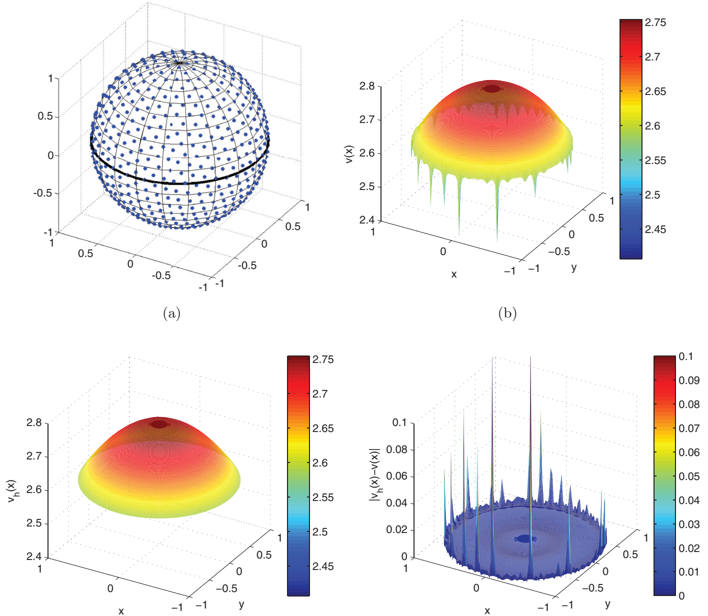
$$f(\varepsilon) = \varepsilon - \frac{\varepsilon^2}{\pi}\log\varepsilon + \frac{\varepsilon^2}{\pi}\log 2, \qquad \kappa(\sigma) = \frac{4\sigma}{\pi - 4\sqrt{\sigma}}.$$

- A simple formula for the homogeneous Robin solution:

$$v_h(\rho) = \frac{f(\varepsilon)}{3D\kappa(\sigma)} + \frac{1-\rho^2}{6D}, \qquad \bar{v}_h = \frac{f(\varepsilon)}{3D\kappa(\sigma)} + \frac{1}{15D}.$$

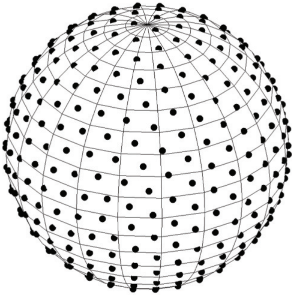
- Example: $N = 802$ traps of radius $\varepsilon = 0.0005$. Comparison of asymptotic and homogenization solution.

Dilute Trap Fraction Limit of Homogenization Theory



(a) (b)

Geometrical features



436 traps

- How to "uniformly mesh" a sphere (or another closed surface)?
- How does one distinguish between two similar/close configurations?

Geometrical features

488 *M.J. Bowick and L. Giomi*

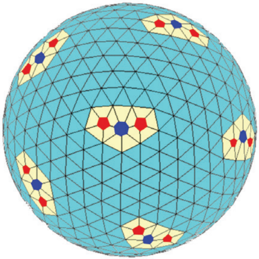


Figure 16. Results of a minimization of 500 particles interacting with a Coulomb potential, showing the appearance of scars.

- Coordination number c_i of a particle: number of neighbours (usually $c_i = 6$).
- Topological constraints: Euler's Theorem, $V - E + F = 2$; can show that

$$\sum_i (6 - c_i) = 12,$$

where $(6 - c_i)$ is the "topological charge" of a "defect".

488 *M.J. Bowick and L. Giomi*

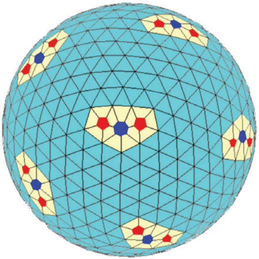
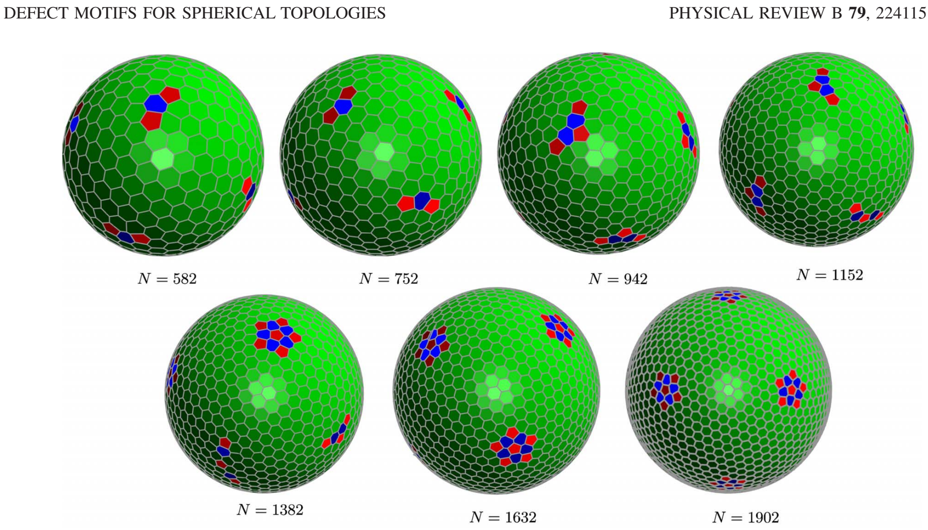


Figure 16. Results of a minimization of 500 particles interacting with a Coulomb potential, showing the appearance of scars.

- At least 12 particles with five-fold coordination (soccer ball!)
- A scar: a cluster of particles where $c_i \neq 6$.
- For the same N, different configurations may or may not have different scar pictures.
- Applications: 2D matter; crystalline particle packings.

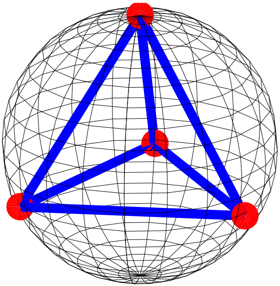
Geometrical features



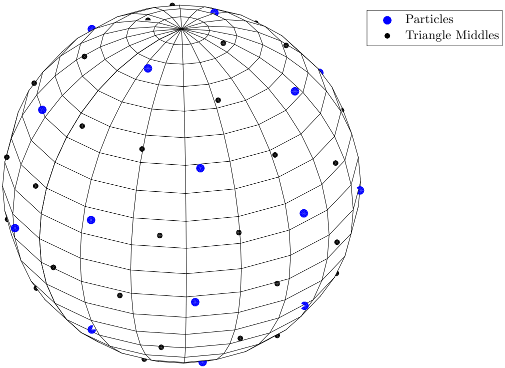
From *Wales et al (2009)*.

- Optimization in literature: random starting positions; global minima are usually sought.

, *2019* : based on trap insertions, dynamical system flow, exclusion of redundant configurations.



- Implemented mainly in Matlab.
- Start from $N = 4$: tetrahedron.



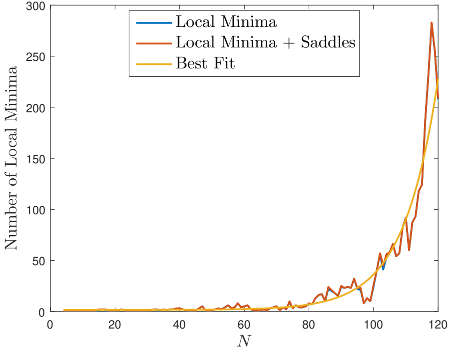
- Starting configurations: Introduce, one by one, triangle middles. Remove redundant configurations.

A numerical method for local and global optimization

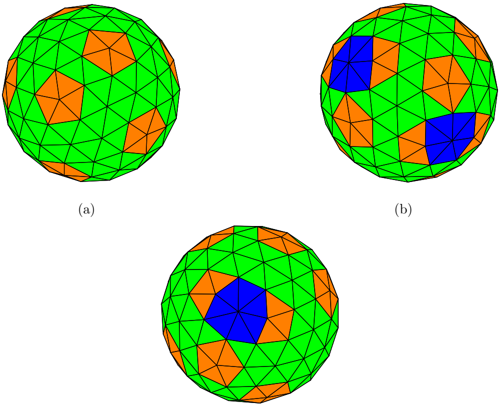
- For each starting configuration, perform local optimization (C++).
- Remove redundant configurations (using pairwise distances).
- Remove saddle points (Maple).
- Repeat $N \rightarrow N+1$.
- Applied to various potentials [*W.Ridgway and A.C. 2018, 2019*].

New results:

- Improvements of global minima for some N.
- Numbers of local minima, energy values, particle configurations of local minima:

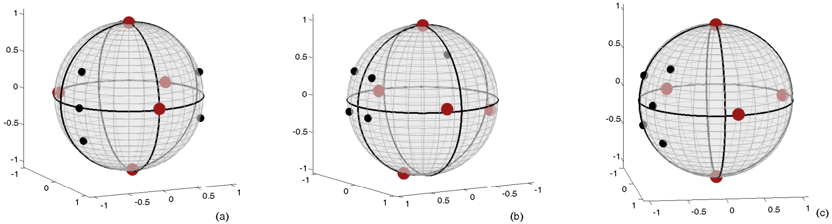


- $N = 60$: five local minima.
- $N = 117$: 265 local minima.
  Three lowest: $\mathcal{H} = 1352.341$, 1352.513, and 1352.514.



(a) (b) (c)

- For traps of different sizes, numerical computations are generally more complex.
- For example, two families of traps: for example,
  N having radius ε; N having radius $\alpha\varepsilon$, $\alpha > 1$ [*A.C., A.Reimer, M.Ward (2012)*].
- $N = 5$, $\alpha = 10$.
  Global minimum (a): $\mathcal{H} = -198.80759$.
  Nearby local minima (b,c): $\mathcal{H} = -198.36939, \; -197.76083$.



Some results for Narrow Escape problems in non-spherical domains

Non-spherical domains [*D. Gomez and A.C., 2015*]

- For surfaces that are a part of an orthogonal coordinate triple.
- Average MFPT for the unit sphere:

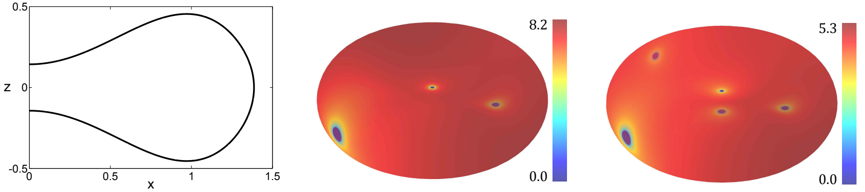
$$\bar{v} = \frac{|\Omega|}{2\pi\varepsilon D N\bar{c}} \left[1 - \varepsilon \log\left(\frac{\varepsilon}{2}\right) \frac{\sum_{j=1}^{N} c_j^2}{2N\bar{c}} + \frac{2\pi\varepsilon}{N\bar{c}} p_c(x_1, \ldots, x_N) - \frac{\varepsilon}{N\bar{c}} \sum_{j=1}^{N} c_j \kappa_j + \mathcal{O}(\varepsilon^2 \log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

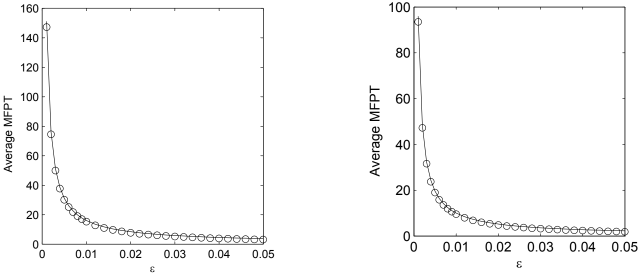
- Average MFPT for in a non-spherical domain:

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

- $H(x_i)$: the mean curvature of the boundary at x_i.

- Example: Biconvace disk – "blood cell" shape, $N = 3$ ad $N = 5$ traps of different sizes.





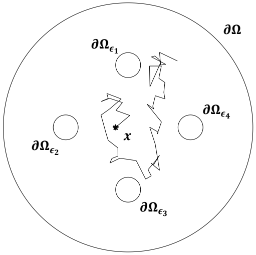
Outline

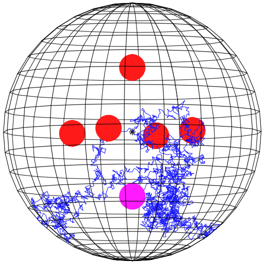
Trapping reactions: whenever a diffusing particle hits a trap, it is immediately and permanently trapped.

- exiton trapping
- fluorescence quenching
- spin relaxation processes
- mean first-passage time: $v(x)$
- narrow capture: small trap size

$$\begin{cases} \Delta v(x) = -\dfrac{1}{D}\ , \quad x \in \Omega \backslash \Omega_a, \\ \partial_n v = 0\ , \quad x \in \partial\Omega, \\ \quad v = 0\ , \quad x \in \partial\Omega_a = \cup_{j=1}^{N} \partial\Omega_{\varepsilon_j} \end{cases}$$

$$\bar{v} = \frac{1}{|\Omega|} \int_\Omega v(x)\, d^n x$$





- Exact solution when a single trap (radius$=\varepsilon$) is at the origin:

$$v_e(r) = \frac{1}{6D}\left[\frac{\varepsilon^3+2}{\varepsilon} - \frac{r^3+2}{r}\right], \quad \bar{v}_e = \frac{1}{6D}\left[\frac{\varepsilon^3+2}{\varepsilon} - \frac{18}{5}\right]$$

- Multiple traps: repel from each other and their own "reflections" in the boundary

- Asymptotic solutions: small, well-separated traps, far from the boundary; include an interaction term [*A.C., M. Ward, 2011*]

$$v_A(x) = \frac{|\Omega|}{4\pi N\bar{c}D\varepsilon}\left[1 - 4\pi\varepsilon\sum_{j=1}^{N} c_j G(x;x_j) + \frac{4\pi\varepsilon}{N\bar{c}} p_c(\xi_1,\ldots,\xi_N) + \mathcal{O}(\varepsilon^2)\right]$$

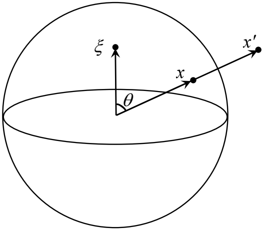
$$\bar{v}_A = \frac{|\Omega|}{4\pi N\bar{c}D\varepsilon}\left[1 + \frac{4\pi\varepsilon}{N\bar{c}} p_c(x_1,\ldots,x_N) + \mathcal{O}(\varepsilon^2)\right]$$

- Expressed in terms of the Green's functions $G(x,\xi)$ computed on trap pairs, and their regular parts $R(\xi)$, and trap capacitances c_j.

- Capacitance depends on trap shape and size.
- Green's function:

$$\Gamma(x;\xi) = G(x,\xi) = \frac{1}{4\pi|x-\xi|} + \frac{1}{4\pi|x||x'-\xi|}$$
$$+\frac{1}{4\pi}\log\left(\frac{2}{1-|x||\xi|\cos\theta+|x||x'-\xi|}\right)+\frac{1}{8\pi}(|x|^2+|\xi|^2)-\frac{7}{10\pi}$$

- Every trap (ξ) interacts with other traps (x) and their images (x'): $xx' = r^2 = 1$.



Exact and asymptotic solutions

- Capacitance depends on trap shape and size.
- Green's function:

$$\Gamma(x;\xi) = G(x,\xi) = \frac{1}{4\pi|x-\xi|} + \frac{1}{4\pi|x||x'-\xi|} + \frac{1}{4\pi}\log\left(\frac{2}{1-|x||\xi|\cos\theta + |x||x'-\xi|}\right) + \frac{1}{8\pi}(|x|^2+|\xi|^2) - \frac{7}{10\pi}$$

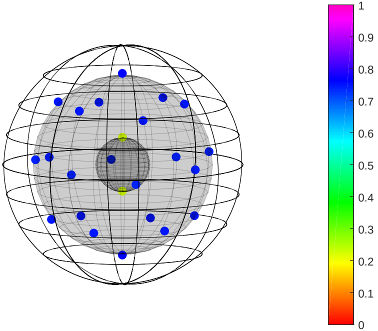
- Every trap (ξ) interacts with other traps (x) and their images (x'): $xx' = r^2 = 1$.
- Green's function regular part:

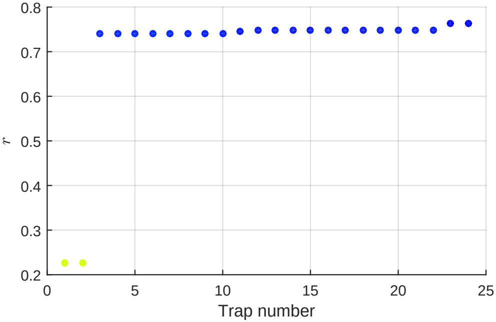
$$\Gamma(\xi;\xi) = R(\xi) = \frac{1}{4\pi(1-|\xi|^2)} + \frac{1}{4\pi}\log\left(\frac{1}{1-|\xi|^2}\right) + \frac{|\xi|^2}{4\pi} - \frac{7}{10\pi}$$

- Trap interaction term:

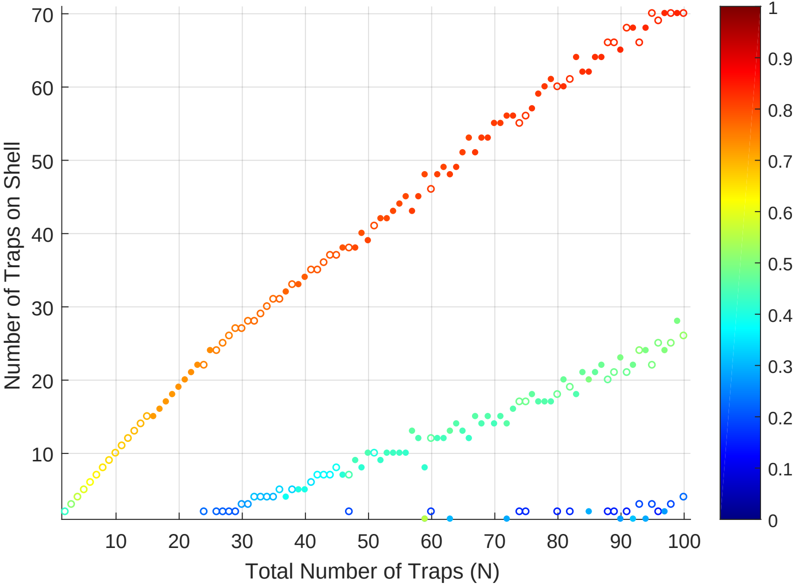
$$p_c(\xi_1, ..., \xi_N) = \sum_{i=1}^{N}\sum_{j=1}^{N} c_i c_j \Gamma(\xi_i, \xi_j)$$

- Asymptotic MFPT formulas tested vs. exact/numerical: work far beyond limits [*J. Gilbert and A.C., 2019*].
- Putative locally optimal configurations for $1 \leq N \leq 100$ computed.
- Traps often lie close to spherical shells.
- There may or may not be a trap at the center.
- Example: $N = 24$





Global optimization: traps (approximately) on shells



Some highlights and open problems

Narrow escape problems:

- Asymptotic solutions for spherical and non-spherical domains, dilute trap limits, scaling laws.
- 'Good' asymptotic formulas work beyond applicability limits.
- Global and local optimization – "scars", interesting geometry.

Narrow capture problems:

- Brownian motion simulation.
- Asymptotic solutions for the sphere.
- Global optimization – "shell" structure.

Open problems:

- Variable diffusivity?
- Moving traps?
- More complex domains?

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