The Narrow Escape Potential, Optimal Arrangements of $N$ Traps on the Unit Sphere, and the Dilute Trap Limit for $N \gg 1$

Alexei F. Cheviakov $^1$

$^1$University of Saskatchewan, Saskatoon, Canada

May 27, 2014
Collaborators

- **Michael Ward**, UBC, Vancouver, Canada
- **Ashton Reimer**, U. Saskatchewan, Canada
- **Daniel Zawada**, U. Saskatchewan, Canada
Outline

1. Narrow Escape Problems, Mean First Passage Time (MFPT)
2. Asymptotic Results for Small Traps; Higher-Order MFPT for the Sphere
3. $N$ Traps on the Sphere: the Optimization Problem
4. Computation of Locally Optimal Arrangements
5. The $N^2$ Conjecture
6. Two Families of Traps
7. Homogenization Theory Approximation for $N \gg 1$ Small Equal Traps
8. Some Highlights and Open Problems
Outline

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

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

3 $N$ Traps on the Sphere: the Optimization Problem

4 Computation of Locally Optimal Arrangements

5 The $N^2$ Conjecture

6 Two Families of Traps

7 Homogenization Theory Approximation for $N \gg 1$ Small Equal Traps

8 Some Highlights and Open Problems
A Brownian particle escapes from a bounded domain through small windows.
Narrow Escape Problems

- A Brownian particle escapes from a bounded domain through small windows.

Examples of applications:

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

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

Figure 1: A Schematic of the Narrow Escape Problem in a 2-D and a 3-D domain.

Problem for the MFPT $v = v(x)$ \cite{Holcman, Schuss (2004)}:

$$
\begin{align*}
\Delta v &= -\frac{1}{D}, \quad x \in \Omega, \\
v &= 0, \quad x \in \partial\Omega_a; \quad \partial_n v = 0, \quad x \in \partial\Omega_r.
\end{align*}
$$

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

**Boundary Value Problem:**
- Linear;
- Strongly heterogeneous Dirichlet/Neumann BCs;
- Singularly perturbed:
  - \( \varepsilon \to 0^+ \Rightarrow v \to +\infty \) a.e.

**Problem for the MFPT:**
\[
\begin{align*}
\Delta v &= -\frac{1}{D}, \quad x \in \Omega, \\
v &= 0, \quad x \in \partial \Omega_a = \bigcup_{j=1}^N \partial \Omega_{\varepsilon_j}, \\
\partial_n v &= 0, \quad x \in \partial \Omega_r.
\end{align*}
\]
1 Narrow Escape Problems, Mean First Passage Time (MFPT)

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

3 $N$ Traps on the Sphere: the Optimization Problem

4 Computation of Locally Optimal Arrangements

5 The $N^2$ Conjecture

6 Two Families of Traps

7 Homogenization Theory Approximation for $N \gg 1$ Small Equal Traps

8 Some Highlights and Open Problems
Some Previously Known Results

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

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

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

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

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

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

\(H\): mean curvature at the center of the trap.
**Inner expansion** of solution near trap centered at \( x_j \) uses scaled coordinates:

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

**Outer expansion** (defined at \( O(1) \) distances from traps):

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

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

\[
v_{in} \sim v_{out}.
\]
Higher-Order Asymptotic MFPT for the Sphere

**Given:**
- Sphere with $N$ traps.
- Trap radii: $r_j = a_j \varepsilon$, $j = 1, \ldots, N$; capacitances: $c_j = 2a_j/\pi$.

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

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

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

- $G_s(x; x_j)$: spherical Neumann Green’s function (known);
- $\bar{c}$: average capacitance; $\kappa_j = \text{const}$;
- $p_c(x_1, \ldots, x_N)$: trap interaction term.
MFPT for the Sphere with \( N \) Equal Traps

\( N \) equal traps of radius \( \varepsilon \):

- **Average MFPT:**

\[
\bar{\nu} \sim \frac{\lvert \Omega \rvert}{4\varepsilon DN} \left[ 1 + \frac{\varepsilon}{\pi} \log \left( \frac{2}{\varepsilon} \right) + \frac{\varepsilon}{\pi} \left( -\frac{9N}{5} + 2(N - 2) \log 2 + \frac{3}{2} + \frac{4}{N} \mathcal{H}(x_1, \ldots, x_N) \right) \right].
\]

- **Interaction energy:**

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

Optimal arrangements minimizing \( \bar{\nu} \) for \( N \leq 200 \): LGO software.

"Thomson problem": optimal arrangements for the Coulomb potential.
MFPT for the Sphere with \( N \) Equal Traps

\( N \) equal traps of radius \( \varepsilon \):

- **Average MFPT**:
  \[
  \bar{v} \sim \frac{|\Omega|}{4\varepsilon DN} \left[ 1 + \frac{\varepsilon}{\pi} \log \left( \frac{2}{\varepsilon} \right) + \frac{\varepsilon}{\pi} \left( -\frac{9N}{5} + 2(N - 2) \log 2 + \frac{3}{2} + \frac{4}{N} \mathcal{H}(x_1, \ldots, x_N) \right) \right].
  \]

- **Interaction energy**:
  \[
  \mathcal{H}(x_1, \ldots, x_N) = \sum_{i=1}^{N} \sum_{j=i+1}^{N} \left[ \frac{1}{|x_i - x_j|} - \frac{1}{2} \log |x_i - x_j| - \frac{1}{2} \log (2 + |x_i - x_j|) \right].
  \]

**Optimal arrangements**

- \( \min \bar{v} \Leftrightarrow \min \mathcal{H}(x_1, \ldots, x_N) \), a global optimization problem.
- “Thomson problem”: optimal arrangements for the Coulomb potential.
- Optimal arrangements minimizing \( \bar{v} \) for \( N \leq 200 \): LGO software.
1. Narrow Escape Problems, Mean First Passage Time (MFPT)
2. Asymptotic Results for Small Traps; Higher-Order MFPT for the Sphere
3. $N$ Traps on the Sphere: the Optimization Problem
4. Computation of Locally Optimal Arrangements
5. The $N^2$ Conjecture
6. Two Families of Traps
7. Homogenization Theory Approximation for $N \gg 1$ Small Equal Traps
8. Some Highlights and Open Problems
$N \rightarrow N + 1$ Traps: Trap Insertion

- **Example:** optimal configuration for $N = 17$

**Topological derivative:**

Rate of change of $\bar{v}$ with respect to the size of the $(N + 1)$st trap of radius $\alpha \varepsilon$ at the point $x^*$ on the unit sphere, computed at $\alpha = 0$.

$$
\mathcal{T}(x^*) = \lim_{\alpha \to 0} \frac{\bar{v}(x_1, \ldots, x_N, x^*) - \bar{v}(x_1, \ldots, x_N)}{\alpha} \sim M(x^*),
$$

$$
M(x^*) = \sum_{i=1}^{N} \left[ \frac{1}{|x_i - x^*|} - \frac{1}{2} \log |x_i - x^*| - \frac{1}{2} \log (2 + |x_i - x^*|) \right].
$$
**N → N + 1 Traps: Trap Insertion**

- **Example:** optimal configuration for \( N = 17 \).
Example: optimal configuration for $N = 17$. 

Introduction of a trap of an arbitrary radius $\alpha \varepsilon$ at the point $x^*$. 

Change of the asymptotic average MFPT: 

$$\Delta \bar{v} \equiv \bar{v}_{N+1}(x_1, \ldots, x_N, x^*) - \bar{v}_N(x_1, \ldots, x_N) \sim f(\alpha, N) \mathcal{M}(x^*),$$

$$\mathcal{M}(x^*) = \sum_{i=1}^{N} \left[ \frac{1}{|x_i - x^*|} - \frac{1}{2} \log |x_i - x^*| - \frac{1}{2} \log (2 + |x_i - x^*|) \right].$$
A heuristic algorithm

(a) Start from a given $N$-trap arrangement.
(b) Compute triangle vertices.
(c) Compute the adjacent local minima of $\mathcal{M}(x^*)$ by solving $\nabla \mathcal{M}(x^*) = 0$.
(d) Introduce additional $k$ traps at $k$ lowest local minima of $\mathcal{M}$. Run a local optimization routine.

160 $\rightarrow$ 436 traps.
Outline

1 Narrow Escape Problems, Mean First Passage Time (MFPT)
2 Asymptotic Results for Small Traps; Higher-Order MFPT for the Sphere
3 $N$ Traps on the Sphere: the Optimization Problem
4 Computation of Locally Optimal Arrangements
5 The $N^2$ Conjecture
6 Two Families of Traps
7 Homogenization Theory Approximation for $N \gg 1$ Small Equal Traps
8 Some Highlights and Open Problems
The $N^2$ conjecture

For an optimal arrangement of $N \geq 2$ traps corresponding that minimizes the interaction energy $\mathcal{H}$ and the asymptotic average MFPT $\bar{v}$, the sum of squares of pairwise distances between traps is equal to $N^2$:

$$Q(x_1, \ldots, x_N) \equiv \sum_{i=1}^{N} \sum_{j=i+1}^{N} |x_i - x_j|^2 = N^2.$$

Evidence

- Can be shown to hold for small $N$ exactly.
- For known global minima $5 \leq N \leq 200$, holds numerically up to 10 significant digits.
- Supported by an asymptotic scaling law estimate of $Q(x_1, \ldots, x_N)$ as $N \to \infty$ [See A.C. & D. Zawada (2013)].
- *Not tested* for all local minima for each $N$...
### Table I. Values of the interaction energy

<table>
<thead>
<tr>
<th>N</th>
<th>H</th>
<th>Q</th>
<th>N</th>
<th>H</th>
<th>Q</th>
<th>N</th>
<th>H</th>
<th>Q</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>-0.53972077</td>
<td>4.0000000000</td>
<td>33</td>
<td>54.295972</td>
<td>1089.0000000</td>
<td>64</td>
<td>324.08963</td>
<td>4096.0000000</td>
</tr>
<tr>
<td>3</td>
<td>-1.0673453</td>
<td>9.0000000000</td>
<td>34</td>
<td>59.379488</td>
<td>1156.0000000</td>
<td>65</td>
<td>336.76971</td>
<td>4225.0000000</td>
</tr>
<tr>
<td>4</td>
<td>-1.6671799</td>
<td>16.0000000000</td>
<td>35</td>
<td>64.736711</td>
<td>1225.0000000</td>
<td>70</td>
<td>403.83089</td>
<td>4900.0000000</td>
</tr>
<tr>
<td>5</td>
<td>-2.0879876</td>
<td>25.0000000000</td>
<td>36</td>
<td>70.276097</td>
<td>1296.0000000</td>
<td>75</td>
<td>477.36359</td>
<td>5625.0000000</td>
</tr>
<tr>
<td>6</td>
<td>-2.5810055</td>
<td>36.0000000000</td>
<td>37</td>
<td>76.066237</td>
<td>1369.0000000</td>
<td>80</td>
<td>557.23154</td>
<td>6400.0000000</td>
</tr>
<tr>
<td>7</td>
<td>-2.7636584</td>
<td>49.0000000000</td>
<td>38</td>
<td>82.080300</td>
<td>1444.0000000</td>
<td>85</td>
<td>643.77234</td>
<td>7225.0000000</td>
</tr>
<tr>
<td>8</td>
<td>-2.9495765</td>
<td>64.0000000000</td>
<td>39</td>
<td>88.329560</td>
<td>1521.0000000</td>
<td>90</td>
<td>736.65320</td>
<td>8100.0000000</td>
</tr>
<tr>
<td>9</td>
<td>-2.9764336</td>
<td>81.0000000000</td>
<td>40</td>
<td>94.817831</td>
<td>1600.0000000</td>
<td>95</td>
<td>836.12537</td>
<td>9025.0000000</td>
</tr>
<tr>
<td>10</td>
<td>-2.8357352</td>
<td>100.00000000</td>
<td>41</td>
<td>101.56854</td>
<td>1681.0000000</td>
<td>100</td>
<td>942.12865</td>
<td>10000.00000</td>
</tr>
<tr>
<td>11</td>
<td>-2.4567341</td>
<td>120.9999505</td>
<td>42</td>
<td>108.54028</td>
<td>1764.0000000</td>
<td>105</td>
<td>1054.8688</td>
<td>11025.00000</td>
</tr>
<tr>
<td>12</td>
<td>-2.1612842</td>
<td>144.00000000</td>
<td>43</td>
<td>115.77028</td>
<td>1849.0000000</td>
<td>110</td>
<td>1174.1103</td>
<td>12100.00000</td>
</tr>
<tr>
<td>13</td>
<td>-1.3678269</td>
<td>168.9999763</td>
<td>44</td>
<td>123.16343</td>
<td>1936.0000000</td>
<td>115</td>
<td>1300.1081</td>
<td>13225.00000</td>
</tr>
<tr>
<td>14</td>
<td>-0.55259278</td>
<td>196.00000000</td>
<td>45</td>
<td>130.90532</td>
<td>2025.0000000</td>
<td>120</td>
<td>1432.6666</td>
<td>14400.00000</td>
</tr>
<tr>
<td>15</td>
<td>0.47743760</td>
<td>225.00000000</td>
<td>46</td>
<td>138.92047</td>
<td>2116.0000000</td>
<td>125</td>
<td>1572.0271</td>
<td>15625.00000</td>
</tr>
<tr>
<td>16</td>
<td>1.6784049</td>
<td>256.00000000</td>
<td>47</td>
<td>147.15035</td>
<td>2209.0000000</td>
<td>130</td>
<td>1718.0039</td>
<td>16900.00000</td>
</tr>
<tr>
<td>17</td>
<td>3.0751594</td>
<td>289.00000000</td>
<td>48</td>
<td>155.41742</td>
<td>2304.0000000</td>
<td>135</td>
<td>1870.6706</td>
<td>18225.00000</td>
</tr>
<tr>
<td>18</td>
<td>4.6651247</td>
<td>324.00000000</td>
<td>49</td>
<td>164.21746</td>
<td>2401.0000000</td>
<td>140</td>
<td>2030.3338</td>
<td>19600.00000</td>
</tr>
<tr>
<td>19</td>
<td>6.5461714</td>
<td>361.00000000</td>
<td>50</td>
<td>173.07868</td>
<td>2500.0000000</td>
<td>145</td>
<td>2196.5017</td>
<td>21025.00000</td>
</tr>
<tr>
<td>20</td>
<td>8.4817896</td>
<td>400.00000000</td>
<td>51</td>
<td>182.26664</td>
<td>2601.0000000</td>
<td>150</td>
<td>2369.6548</td>
<td>22500.00000</td>
</tr>
<tr>
<td>21</td>
<td>10.701320</td>
<td>441.00000000</td>
<td>52</td>
<td>191.72428</td>
<td>2704.0000000</td>
<td>155</td>
<td>2549.6182</td>
<td>24025.00000</td>
</tr>
<tr>
<td>22</td>
<td>13.101742</td>
<td>484.00000000</td>
<td>53</td>
<td>201.38475</td>
<td>2809.0000000</td>
<td>160</td>
<td>2736.2180</td>
<td>25600.00000</td>
</tr>
<tr>
<td>23</td>
<td>15.821282</td>
<td>529.00000000</td>
<td>54</td>
<td>211.28349</td>
<td>2916.0000000</td>
<td>165</td>
<td>2929.8023</td>
<td>27225.00000</td>
</tr>
<tr>
<td>24</td>
<td>18.581981</td>
<td>576.00000000</td>
<td>55</td>
<td>221.46381</td>
<td>3025.0000000</td>
<td>170</td>
<td>3130.1596</td>
<td>28900.00000</td>
</tr>
<tr>
<td>25</td>
<td>21.724913</td>
<td>625.00000000</td>
<td>56</td>
<td>231.85497</td>
<td>3136.0000000</td>
<td>175</td>
<td>3337.4168</td>
<td>30625.00000</td>
</tr>
<tr>
<td>26</td>
<td>25.010031</td>
<td>676.00000000</td>
<td>57</td>
<td>242.51803</td>
<td>3249.0000000</td>
<td>180</td>
<td>3551.5021</td>
<td>32400.00000</td>
</tr>
<tr>
<td>27</td>
<td>28.429699</td>
<td>729.00000000</td>
<td>58</td>
<td>253.43460</td>
<td>3364.0000000</td>
<td>185</td>
<td>3772.5761</td>
<td>34225.00000</td>
</tr>
<tr>
<td>28</td>
<td>32.192933</td>
<td>784.00000000</td>
<td>59</td>
<td>264.57186</td>
<td>3481.0000000</td>
<td>190</td>
<td>4000.3892</td>
<td>36100.00000</td>
</tr>
<tr>
<td>29</td>
<td>36.219783</td>
<td>841.00000000</td>
<td>60</td>
<td>275.90942</td>
<td>3600.0000000</td>
<td>195</td>
<td>4235.2645</td>
<td>38025.00000</td>
</tr>
<tr>
<td>30</td>
<td>40.354439</td>
<td>900.00000000</td>
<td>61</td>
<td>287.62114</td>
<td>3721.0000000</td>
<td>200</td>
<td>4477.0669</td>
<td>40000.00000</td>
</tr>
<tr>
<td>31</td>
<td>44.757617</td>
<td>961.00000000</td>
<td>62</td>
<td>299.48031</td>
<td>3844.0000000</td>
<td>205</td>
<td>4733.0669</td>
<td>42025.00000</td>
</tr>
<tr>
<td>32</td>
<td>49.240949</td>
<td>1024.0000000</td>
<td>63</td>
<td>311.65585</td>
<td>3969.0000000</td>
<td>210</td>
<td>5000.0000</td>
<td>44025.00000</td>
</tr>
</tbody>
</table>

The $N^2$ conjecture
The $N^2$ conjecture

<table>
<thead>
<tr>
<th>$N$</th>
<th>$\mathcal{H}$</th>
<th>$Q$</th>
<th>$N$</th>
<th>$\mathcal{H}$</th>
<th>$Q$</th>
<th>$N$</th>
<th>$\mathcal{H}$</th>
<th>$Q$</th>
</tr>
</thead>
<tbody>
<tr>
<td>206</td>
<td>4776.8410</td>
<td>42436.0000</td>
<td>406</td>
<td>20535.947</td>
<td>164836.0000</td>
<td>650</td>
<td>55251.870</td>
<td>422500.0000</td>
</tr>
<tr>
<td>219</td>
<td>5459.4441</td>
<td>47961.0000</td>
<td>413</td>
<td>21292.863</td>
<td>170569.0000</td>
<td>697</td>
<td>63918.659</td>
<td>485809.0000</td>
</tr>
<tr>
<td>248</td>
<td>7151.7851</td>
<td>61504.0000</td>
<td>424</td>
<td>22511.130</td>
<td>179776.0000</td>
<td>704</td>
<td>65263.714</td>
<td>495616.0000</td>
</tr>
<tr>
<td>253</td>
<td>7466.6853</td>
<td>64009.0000</td>
<td>436</td>
<td>23879.932</td>
<td>190096.0000</td>
<td>764</td>
<td>77386.805</td>
<td>583696.0000</td>
</tr>
<tr>
<td>260</td>
<td>7920.1793</td>
<td>67600.0000</td>
<td>437</td>
<td>23996.280</td>
<td>190969.0000</td>
<td>778</td>
<td>80361.722</td>
<td>605284.0000</td>
</tr>
<tr>
<td>268</td>
<td>8455.6701</td>
<td>71824.0000</td>
<td>442</td>
<td>24579.608</td>
<td>195364.0000</td>
<td>781</td>
<td>81008.459</td>
<td>609961.0000</td>
</tr>
<tr>
<td>272</td>
<td>8729.6105</td>
<td>73984.0000</td>
<td>449</td>
<td>25409.395</td>
<td>201601.0000</td>
<td>802</td>
<td>85602.707</td>
<td>643204.0000</td>
</tr>
<tr>
<td>291</td>
<td>10094.183</td>
<td>84681.0000</td>
<td>462</td>
<td>26987.790</td>
<td>213444.0000</td>
<td>850</td>
<td>96587.973</td>
<td>722500.0000</td>
</tr>
<tr>
<td>308</td>
<td>11401.557</td>
<td>94864.0000</td>
<td>480</td>
<td>29251.492</td>
<td>230400.0000</td>
<td>868</td>
<td>100878.53</td>
<td>753424.0000</td>
</tr>
<tr>
<td>310</td>
<td>11560.554</td>
<td>96100.0000</td>
<td>529</td>
<td>35888.599</td>
<td>279841.0000</td>
<td>891</td>
<td>106503.70</td>
<td>793881.0000</td>
</tr>
<tr>
<td>333</td>
<td>13471.931</td>
<td>110889.0000</td>
<td>536</td>
<td>36896.959</td>
<td>287296.0000</td>
<td>922</td>
<td>114327.22</td>
<td>850084.0000</td>
</tr>
<tr>
<td>337</td>
<td>13819.916</td>
<td>113569.0000</td>
<td>546</td>
<td>38354.222</td>
<td>298116.0000</td>
<td>928</td>
<td>115873.47</td>
<td>861184.0000</td>
</tr>
<tr>
<td>368</td>
<td>16669.611</td>
<td>135424.0000</td>
<td>548</td>
<td>38648.578</td>
<td>300304.0000</td>
<td>992</td>
<td>133031.24</td>
<td>984064.0000</td>
</tr>
<tr>
<td>369</td>
<td>16766.235</td>
<td>136161.0000</td>
<td>577</td>
<td>43063.555</td>
<td>332929.0000</td>
<td>1004</td>
<td>136383.69</td>
<td>1008016.0000</td>
</tr>
<tr>
<td>380</td>
<td>17846.466</td>
<td>144400.0000</td>
<td>618</td>
<td>49718.287</td>
<td>381924.0000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>382</td>
<td>18045.887</td>
<td>145924.0000</td>
<td>636</td>
<td>52794.233</td>
<td>404496.0000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Outline

1. Narrow Escape Problems, Mean First Passage Time (MFPT)
2. Asymptotic Results for Small Traps; Higher-Order MFPT for the Sphere
3. $N$ Traps on the Sphere: the Optimization Problem
4. Computation of Locally Optimal Arrangements
5. The $N^2$ Conjecture
6. Two Families of Traps
7. Homogenization Theory Approximation for $N \gg 1$ Small Equal Traps
8. Some Highlights and Open Problems
Two Families of Traps

- **2N traps**: \( N \) having radius \( \varepsilon \); \( N \) having radius \( \alpha \varepsilon \), \( \alpha > 1 \).

Asymptotic MFPT \([\text{A.C., A.Reimer, M.Ward (2012)}]\):
\[
\bar{v} \sim |\Omega|^{4/\varepsilon} D(N) (1 + \alpha) \left[ 1 + \varepsilon \pi \log \left( \frac{2 \varepsilon}{1 + \alpha} \right) \left( 1 + \alpha \right)^2 \right] + \varepsilon \pi \left( S + 4N \sum_{i=1}^{N} h(x_i, x_j) \right),
\]
where the same pairwise energy function

\[
h(x_i, x_j) = \frac{1}{2} \left| x_i - x_j \right| - \frac{1}{2} \log \left| x_i - x_j \right| - \frac{1}{2} \log (2 + |x_i - x_j|).
\]
Two Families of Traps

- **2N traps**: $N$ having radius $\varepsilon$; $N$ having radius $\alpha \varepsilon$, $\alpha > 1$.

### Asymptotic MFPT [A.C., A.Reimer, M.Ward (2012)]:

\[ \tilde{\nu} \sim \frac{|\Omega|}{4\varepsilon DN(1 + \alpha)} \left[ 1 + \frac{\varepsilon}{\pi} \log \left( \frac{2}{\varepsilon} \right) \left( \frac{1 + \alpha^2}{1 + \alpha} \right) + \frac{\varepsilon}{\pi} \left( S + \frac{4}{N(1 + \alpha)} \tilde{H}(x_1, \ldots, x_N) \right) \right], \]

where

- \( S = S(N, \alpha) \),

\[ \tilde{H}(x_1, \ldots, x_N) = \sum_{i=1}^{N} \sum_{j=i+1}^{N} h(x_i; x_j) + \alpha \sum_{i=1}^{N} \sum_{j=N+1}^{2N} h(x_i; x_j) + \alpha^2 \sum_{i=N+1}^{2N} \sum_{j=i+1}^{2N} h(x_i; x_j), \]

with the same pairwise energy function

\[ h(x_i; x_j) = \frac{1}{|x_i - x_j|} - \frac{1}{2} \log |x_i - x_j| - \frac{1}{2} \log (2 + |x_i - x_j|). \]
Two Families of Traps

- **Example:** three locally optimal configurations of $2N=10$ traps; $\alpha = 10$.
- **Global minimum:**
- **Nearby local minima:**

![Diagram](image-url)

Figure 18: Spherical trap configurations for $2N=10$ traps of two kinds with radius ratio $\alpha = 10$.

The larger traps are shown in red, the smaller traps in black.

(a) the configuration corresponding to the global minimum of the average MFPT $\bar{v}$.

(b), (c): configurations corresponding to nearby local minima of $\bar{v}$ with $\tilde{H} = (-198.36939, -197.76083)$.

Figure 19: Trap fragmentation effects. The average spherical MFPT $\bar{v}(2.22)$ versus $N$ (number of traps) for a fixed trap surface area percentage. Curves for $f = 0.1\%, 0.2\%, 0.3\%, 0.5\%, 1\%, 2\%, 4\%, 10\%$ (top to bottom).
Two Families of Traps

- **Example:** three locally optimal configurations of $2N=10$ traps; $\alpha = 10$.

- Global minimum (a): $\tilde{H} = -198.80759$.

- Nearby local minima (b,c): $\tilde{H} = (-198.36939, -197.76083)$.

![Diagram of spherical trap configurations for 2N=10 traps of two kinds with radius ratio $\alpha = 10$. The larger traps are shown in red, the smaller traps in black. (a) the configuration corresponding to the global minimum of the average MFPT $\bar{v}$. (b), (c): configurations corresponding to nearby local minima of $\bar{v}$ with $\tilde{H} = (-198.36939, -197.76083)$.

Figure 18:

![Figure 18: Spherical trap configurations for 2N=10 traps of two kinds with radius ratio $\alpha = 10$. The larger traps are shown in red, the smaller traps in black. (a) the configuration corresponding to the global minimum of the average MFPT $\bar{v}$. (b), (c): configurations corresponding to nearby local minima of $\bar{v}$ with $\tilde{H} = (-198.36939, -197.76083)$.

Figure 19: Trap fragmentation effects. The average spherical MFPT $\bar{v}(2.22)$ versus $N$ (number of traps) for a fixed trap surface area percentage. Curves for $f = 0.1\%, 0.2\%, 0.3\%, 0.5\%, 1\%, 2.2\%, 4\%, 10\%$ (top to bottom).
Outline

1. Narrow Escape Problems, Mean First Passage Time (MFPT)
2. Asymptotic Results for Small Traps; Higher-Order MFPT for the Sphere
3. $N$ Traps on the Sphere: the Optimization Problem
4. Computation of Locally Optimal Arrangements
5. The $N^2$ Conjecture
6. Two Families of Traps
7. Homogenization Theory Approximation for $N \gg 1$ Small Equal Traps
8. Some Highlights and Open Problems
Dilute Trap Fraction Limit of Homogenization Theory

- $N \gg 1$ small boundary traps, distributed “homogeneously” over the sphere.
- **Dilute trap limit** [Muratov & Shvartsman, 2008, unit disk]:
  - Approximate the mixed Dirichlet-Neumann problem for the MFPT $\nu(x)$ by a Robin problem for $\nu_h(x) \sim \nu(x)$.

**Assumptions:**

- $N \gg 1$, $\varepsilon \ll 1$,
- Total trap area fraction $\sigma = \pi \varepsilon^2 N / (4\pi) = N \varepsilon^2 / 4 \ll 1$.
- $\nu(x) \sim \nu_h(\rho)$, where the latter satisfies the Robin problem

\[
\nabla^2 \nu_h = -\frac{1}{D}, \quad \rho = |x| < 1;
\]

\[
f(\varepsilon) \partial_r \nu_h + \kappa(\sigma) \nu_h = 0, \quad \rho = 1.
\]

- Functions $f(\varepsilon), \kappa(\sigma)$ can be estimated using the asymptotic formula for $\nu(x)$ derived earlier.
Dilute Trap Fraction Limit of Homogenization Theory

- $N \gg 1$ small boundary traps, distributed “homogeneously” over the sphere.
- **Dilute trap limit** [Muratov & Shvartsman, 2008, unit disk]:
  - Approximate the mixed Dirichlet-Neumann problem for the MFPT $\nu(x)$ by a **Robin problem** for $\nu_h(x) \simeq \nu(x)$.

**Assumptions:**

- $N \gg 1$, $\varepsilon \ll 1$,
- Total trap area fraction $\sigma = \pi \varepsilon^2 N / (4\pi) = N \varepsilon^2 / 4 \ll 1$.
- $\nu(x) \sim \nu_h(\rho)$, where the latter satisfies the **Robin problem**

\[
\triangle \nu_h = -\frac{1}{D}, \quad \rho = |x| < 1;
\]

\[
f(\varepsilon) \partial_r \nu_h + \kappa(\sigma) \nu_h = 0, \quad \rho = 1.
\]

- The solution is given by a simple formula

\[
\nu_h(\rho) = \frac{f(\varepsilon)}{3D \kappa(\sigma)} + \frac{1 - \rho^2}{6D}, \quad \bar{\nu}_h = \frac{f(\varepsilon)}{3D \kappa(\sigma)} + \frac{1}{15D}.
\]
Principal result [A.C. & D. Zawada, 2013]:

In an asymptotic limit $\varepsilon \to 0$, $N \ll \mathcal{O}(\log \varepsilon)$, the asymptotic expression for $v(x)$ and the average MFPT $\bar{v}$ can be approximated, within the four leading terms, by a solution $v_h(\rho)$ of the Robin problem with parameters

$$f(\varepsilon) = \varepsilon - \frac{\varepsilon^2}{\pi} \log \varepsilon + \frac{\varepsilon^2}{\pi} \log 2, \quad \kappa(\sigma) = \frac{4\sigma}{\pi - 4\sqrt{\sigma}}.$$
Dilute Trap Fraction Limit of Homogenization Theory

**Principal result [A.C. & D. Zawada, 2013]:**

In an asymptotic limit $\varepsilon \to 0$, $N \ll \mathcal{O}(\log \varepsilon)$, the asymptotic expression for $v(x)$ and the average MFPT $\bar{v}$ can be approximated, within the four leading terms, by a solution $v_h(\rho)$ of the Robin problem with parameters

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

- The values of $v(x)$ and $\bar{v}$ can be approximately computed without the computation of trap coordinates of the actual globally optimal trap arrangement.

$$v_h(\rho) = \frac{f(\varepsilon)}{3D\kappa(\sigma)} + \frac{1 - \rho^2}{6D}, \quad \bar{v}_h = \frac{f(\varepsilon)}{3D\kappa(\sigma)} + \frac{1}{15D}.$$
Principal result [A.C. & D. Zawada, 2013]:

In an asymptotic limit $\varepsilon \to 0$, $N \ll O(\log \varepsilon)$, the asymptotic expression for $v(x)$ and the average MFPT $\bar{v}$ can be approximated, within the four leading terms, by a solution $v_h(\rho)$ of the Robin problem with parameters

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

- The values of $v(x)$ and $\bar{v}$ can be approximately computed without the computation of trap coordinates of the actual globally optimal trap arrangement.

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

- Example: $N = 802$ traps of radius $\varepsilon = 0.0005$. Comparison of asymptotic and homogenization solution.
Dilute Trap Fraction Limit of Homogenization Theory

In order to match additional terms of (5.7), one can consider the coefficients $f(\varepsilon)$ and $\kappa(\sigma)$ of the extended form

$$ f(\varepsilon) = \varepsilon + \alpha \varepsilon^2 \log \varepsilon + \beta \varepsilon^2, \quad \kappa(\sigma) = \frac{4}{\pi} \sigma + \gamma \sqrt{\sigma}. $$

(5.10)

The homogenization MFPT (5.5) consequently becomes

$$ \bar{v}_h = \frac{\pi \varepsilon}{12} D \sigma + \frac{\pi \varepsilon^2}{12} D \sigma (\beta + \alpha \log \varepsilon) + \frac{1}{15} D + \gamma \sqrt{\frac{\varepsilon}{D}} + Q(\varepsilon, \sigma), $$

(5.11)

where

$$ Q(\varepsilon, \sigma) = \gamma \varepsilon \sqrt{\frac{\varepsilon}{D}} (\beta + \alpha \log \varepsilon). $$

(5.12)

The form (5.11) of the homogenization MFPT can be used to match the first four leading terms of (5.7) upon choosing $\alpha = -\frac{1}{\pi}, \beta = -\frac{1}{\pi} \log 2, \gamma = \frac{8}{b_1}$. (5.13)

A direct computation shows that under the choice of parameters (5.13), the additional term $Q(\varepsilon, \sigma)$ (5.12) is small compared to both of the higher-order terms $A(\varepsilon, \sigma)$ and $B(\varepsilon, \sigma)$ in the limit $\varepsilon \to 0, N \ll O(\log \varepsilon)$. We have thus arrived at the following result.

Principal result 2. Consider an arrangement of $N \gg 1$ equal small traps on a unit sphere. Suppose that this arrangement is optimal, i.e., it minimizes the interaction energy (2.8). Then, in an asymptotic limit $\varepsilon \to 0, N \ll O(\log \varepsilon)$, the asymptotic expression for the MFPT $v(x)$ (2.1) and the average

$$ -0.5 -1 0 0.5 1$$

$$ 2.4 2.5 2.6 2.7 2.8$$

(a) The putative optimal trap arrangement. (b) The equatorial cross section ($z = 0$) of the asymptotic MFPT $v(x)$ (2.1). (c) The equatorial cross section of the homogenization MFPT $v_h(\rho)$ (5.4). (d) The absolute difference $|v_h(\rho) - v(x)|$. 

FIG. 7. (Color online) MFPT comparison plots for $N = 802$ traps with $\varepsilon = 0.0005$. (a) The putative optimal trap arrangement. (b) The equatorial cross section ($z = 0$) of the asymptotic MFPT $v(x)$ (2.1). (c) The equatorial cross section of the homogenization MFPT $v_h(\rho)$ (5.4). (d) The absolute difference $|v_h(\rho) - v(x)|$. 

042118-10
Compare Average Asymptotic and Homogenization MFPT

Homogenization MFPT:

\[
\bar{v}_h = \frac{f(\varepsilon)}{3D\kappa(\sigma)} + \frac{1}{15D}, \quad f(\varepsilon) = \varepsilon - \frac{\varepsilon^2}{\pi} \log \varepsilon + \frac{\varepsilon^2}{\pi} \log 2, \quad \kappa(\sigma) = \frac{4\sigma}{\pi - 4\sqrt{\sigma}}.
\]

Asymptotic MFPT Scaling Law:

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

\[
\mathcal{H} \sim \frac{N^2}{2} \left(1 - \log 2\right) + b_1 N^{3/2} + b_2 N \log N + b_3 N + b_4 \sqrt{N} + b_5 \log N + b_6 + o(1).
\]
Comparison:

- $\bar{v}, \bar{v}_h$ are formally simultaneously valid when
  \[ \varepsilon \ll 1, \quad N \gg 1, \quad N \ll O(\log \varepsilon). \]

- The difference:
Outline

1. Narrow Escape Problems, Mean First Passage Time (MFPT)
2. Asymptotic Results for Small Traps; Higher-Order MFPT for the Sphere
3. \( N \) Traps on the Sphere: the Optimization Problem
4. Computation of Locally Optimal Arrangements
5. The \( N^2 \) Conjecture
6. Two Families of Traps
7. Homogenization Theory Approximation for \( N \gg 1 \) Small Equal Traps
8. Some Highlights and Open Problems
Some Highlights and Open Problems

Results

- An asymptotic formula for spherical MFPT taking into account mutual locations of $N$ different traps is available.
- An algorithm for putative optimal arrangements for higher $N$ is suggested.
- The $N^2$ conjecture.
- For $N \gg 1$ small equal traps: a simple homogenization theory-based formula for the approximate average MFPT is in close agreement with asymptotic results.

Open problems

- How to describe local minima for a fixed $N$?
- Extend results to non-spherical domains: spheroidal, red blood cell-shaped, etc.
- Applications: consider more realistic, variable diffusion coefficients; time-dependent models.
Some References

D. P. Hardin and E. B. Saff,

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

C. B. Muratov and S. Y. Shvartsman,

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

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

A. F. Cheviakov and D. Zawada,
Some References

D. P. Hardin and E. B. Saff,  

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

C. B. Muratov and S. Y. Shvartsman,  

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

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

A. F. Cheviakov and D. Zawada,  

Thank you for attention!