Traps, Patches, and Spots: Asymptotic Analysis of Localized Solutions to Some Diffusive and Reaction-Diffusion Systems

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Outline of the Talk

THREE SPECIFIC (SEEMINGLY UNRELATED) TOPICS:

1. **Part I**: The Mean First Passage Time (MFPT) for Diffusive Escape from a Sphere Through a Narrow Window on its Boundary. The MFPT for Diffusion on the Surface of a Sphere with Localized Traps.

2. **Part II**: Calculation of the Persistence or Extinction Threshold for the Diffusive Logistic Model in Highly Patchy Spatial Environments (Alan Lindsay’s lecture)


KEY THEME: THESE STUDIES SERVE A DUAL ROLE

1) **Links to mathematics**: develop new theoretical approaches in applied math that serve to formulate, resolve, or inform, various problems relating to PDE theory, approximation theory, etc..

2) **Links to applications**: make specific predictions and provide useful approximate formulae for users in the area of application.
Part I: Narrow Escape Problem

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.
Part I: Mathematical Formulation

The mean first passage time (MFPT) \( v(x) = E[\tau|X(0) = x] \) for the narrow escape problem satisfies a Poisson problem with Dirichlet/Neumann boundary conditions (Z. Schuss (1980))

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

An eigenfunction expansion shows that the average MFPT \( \bar{v} \) satisfies

\[
\bar{v} = \frac{1}{|\Omega|} \int_{\Omega} v \, dx \sim \frac{1}{D\lambda_1}, \quad \text{as} \quad \varepsilon \to 0.
\]

Here \( \lambda_1 \) is the principal eigenvalue of

\[
\Delta u + \lambda u = 0, \quad x \in \Omega; \quad \int_{\Omega} u^2 \, dx = 1,
\partial_n u = 0 \quad x \in \partial\Omega_r, \quad u = 0, \quad x \in \partial\Omega_a = \bigcup_{j=1}^{N} \partial\Omega_{\varepsilon_j}.
\]

Since \( |\partial\Omega_a| = O(\varepsilon) \), then \( \bar{v} \to \infty \) and \( \lambda_1 \to 0 \) as \( \varepsilon \to 0 \).
Part I: Relevance to Biophysics

KEY GENERAL REFERENCES:


RELEVANCE OF NARROW ESCAPE TIME PROBLEM IN BIOLOGY:

- time needed for a reactive particle released from a specific site to activate a given protein on the cell membrane

- biochemical reactions in cellular microdomains (dendritic spines, synapses, microvesicles), consisting of a small number of particles that must exit the domain to initiate a biological function.

- determines reaction rate in Markov model of chemical reactions
Part I: Some Previous Results

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

\[ \lambda_1 \sim \frac{2\pi \varepsilon}{|\Omega|} \sum_{j=1}^{N} C_j. \]

Here \( C_j \) is the capacitance of the electrified disk problem

\[ \Delta_y w = 0, \quad y_3 \geq 0, \quad -\infty < y_1, y_2 < \infty; \quad w \sim C_j/|y|, \quad |y| \to \infty, \]

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

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

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


For arbitrary \( \Omega \) with smooth \( \partial \Omega \) and one circular trap at \( x_0 \in \partial \Omega \)

\[ \bar{v} \sim \frac{|\Omega|}{4\varepsilon D} \left[ 1 - \frac{\varepsilon}{\pi} H(x_0) \log \varepsilon + O(\varepsilon) \right]. \]

Here \( H(x_0) \) is the mean curvature of \( \partial \Omega \) at \( x_0 \in \partial \Omega \). Ref: D. Holcman, A. Singer, et al. Phys. Rev. E., 78, No. 5, 051111, (2009).
Part I: Main Goals

Applications: Specific Scientific Questions:

- Calculate an explicit and useful higher-order asymptotic formula for $v(x)$ and $\bar{v}$ as $\varepsilon \to 0$.
- Determine whether there is a significant effect on $\bar{v}$ of the spatial configuration $\{x_1, \ldots, x_N\}$ of traps.
- What is the effect on $\bar{v}$ of fragmentation of the trap set?

Math: Connections to Approximation Theory: Let $\Omega$ be the unit sphere with $N$-circular holes on $\partial \Omega$ of a common radius. Is minimizing $\bar{v}$ equivalent to minimizing the discrete Coulomb energy $\mathcal{H}_c$, where

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

Such Fekete points give the minimal energy configuration of “electrons” on a sphere (Ref: J.J. Thomson, E. Saff, N. Sloane, A. Kuijlaars, etc..)
Part I: The Surface Neumann $G$-function

A key player is the surface Neumann G-function, $G_s$, satisfying

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

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

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

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

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

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

$$G_s(x; x_j) \sim \frac{1}{2\pi|x - x_j|} - \frac{1}{4\pi} \log |x - x_j| + R + o(1).$$
Part I: Main Result for $\bar{v}$

Principal Result: [CWS]: For $\varepsilon \to 0$, and for $N$ circular traps of radii $\varepsilon a_j$ centered at $x_j$, $j = 1, \ldots, N$, a 3-term expansion for averaged MFPT $\bar{v}$ is

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

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

$$
\kappa_j = \frac{c_j}{4\pi} \left[ 2 \log 2 - \frac{3}{2} + \log a_j \right].
$$

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

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

Remarks: 1) A similar result holds for non-circular traps. 2) The logarithmic term in $\varepsilon$ arises from the subdominant singularity in $G_s$. 
Corollary: [CWS]: For $N$ circular traps of a common radius $\varepsilon$ (for which $c_j = 2/\pi$ and $a_j = 1$ for $j = 1, \ldots, N$), then a three-term expansion is

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

where the discrete energy $\mathcal{H}(x_1, \ldots, x_N)$ is

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

Key point: Minimizing $\bar{v}$ corresponds to minimizing $\mathcal{H}$. This discrete energy is a generalization of the purely Coulombic energy associated with Fekete points. Extra term in $\mathcal{H}$ involves surface diffusion effects.

Part I: Numerical Validation of $\bar{v}$

![Graph](image)

**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**: $N = 4$.

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Part I: Fragmentation and Location of Traps

Table: \( \bar{v}_3 \) agrees well with COMSOL even at \( \epsilon = 0.5 \). For \( \epsilon = 0.5 \) and \( N = 4 \), traps occupy \( \approx 20\% \) of the surface, but 3-term asymptotics for \( \bar{v} \) differs from COMSOL by only \( \approx 7.5\% \).

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Plot: \( \bar{v} \) vs. \( \epsilon \) for \( D = 1 \), \( N = 11 \), and three configurations of traps. Bottom: global minimum of \( \mathcal{H} \) (right figure shows optimal point configuration). Top: equidistant points on equator. Middle: random.

For \( \epsilon = 0.1907 \), \( N = 11 \) 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.
Part I: The Discrete Variational Problem

Compare optimal energies and point arrangements of $\mathcal{H}$ with those of classic Coulomb or Logarithmic energies

$$
\mathcal{H}_C = \sum_{i=1}^{N} \sum_{j>i}^{N} \frac{1}{|x_i - x_j|}, \quad \mathcal{H}_L = -\sum_{i=1}^{N} \sum_{j>i}^{N} \log |x_i - x_j|.
$$

Numerics: Extended Cutting Angle Method: Implemented for $N \leq 65$ in open software library GANSO by R. Spiteri, S. Richards, A. Cheviakov.

Optimal $\mathcal{H}$ grows more slowly with $N$ than for other discrete energies.

For $N = 2, \ldots, 20$ optimal point arrangements coincide for the three energies (Proof?). Does agreement persist for large values of $N$?
Part I: Scaling Law for Optimal Energy

For \( N \gg 1 \), the optimal \( H(x_1, \ldots, x_N) \) has the form (formal derivation)

\[
H \approx \frac{N^2}{2} \log \left( \frac{e}{2} \right) + b_1 N^{3/2} + N (b_2 \log N + b_3) + b_4 N^{1/2} + b_5 \log N + b_6,
\]

where the least-squares fit of coefficients to GANSO numerical data is

\[
\begin{align*}
    b_1 &\approx -0.5668, & b_2 &\approx 0.0628, & b_3 &\approx -0.8420, \\
    b_4 &\approx 3.8894, & b_5 &\approx -1.3512, & b_6 &\approx -2.4523.
\end{align*}
\]

By using this result for the optimal \( H \) in our result for \( \bar{v} \) we obtain:

**Scaling Law:** For \( 1 \ll N \ll 1/\epsilon \), the optimal average MFPT \( \bar{v} \), in terms of the trap surface area fraction \( f = N \epsilon^2/4 \), satisfies

\[
\bar{v} \sim \frac{|\Omega|}{8D \sqrt{fN}} \left[ 1 - \frac{\sqrt{f/N}}{\pi} \log \left( \frac{4f}{N} \right) + \frac{2 \sqrt{fN}}{\pi} \left( \frac{1}{5} + \frac{4b_1}{\sqrt{N}} \right) \right].
\]
Part I: Effect of Fragmentation of Trap Set

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

Qualitative Remarks and Open Issues:

- **Fragmentation** effect of trap set is a significant factor when $N$ small.
- **Only marginal benefit** by increasing $N$ when $N$ is already large. Does $\bar{v}$ approach a limiting curve obtainable also by taking dilute fraction limit of homogenization theory?
- **Mathematical Challenge:** derive rigorously the form of optimum $\mathcal{H}$ using techniques in approximation theory.
Part I: The 2-D Narrow Escape Problem


Principal Result: [PWPK]: When a smooth 2-D boundary $\partial \Omega$ has exactly one absorbing boundary trap of length $\varepsilon$ centered at $x_1 \in \partial \Omega$, then

$$\bar{v} \sim \frac{1}{D\lambda_1}, \quad \lambda_1 \sim \frac{\pi \mu}{|\Omega|} - \frac{\pi^2 \mu^2}{|\Omega|} R_s(x_1, x_1) + o(\mu^2) ; \quad \mu \equiv \frac{-1}{\log(\varepsilon/4)},$$

where $R_s(x_1; x_1)$ is the regular part of the surface Neumann $G$-function,

$$\Delta G_s = \frac{1}{|\Omega|}, \quad x \in \Omega; \quad \partial_n G_s = 0, \quad x \in \partial \Omega \setminus \{x_1\}; \quad \int_\Omega G_s \, dx = 0,$$

$$G_s(x; x_1) \sim -\frac{1}{\pi} \log |x - x_1| + R_s(x_1; x_1), \quad \text{as } x \to x_1 \in \partial \Omega.$$

Question: For $\partial \Omega$ smooth, is the global maximum of $R_s(x_1; x_1)$ attained at the global maximum of the boundary curvature $\kappa$? In other words, will a boundary trap centered at the maximum of $\kappa$ minimize the heat loss from the domain? (i.e. yield the smallest $\lambda_1$, and thus largest $\bar{v}$)
Part I: The 2-D Narrow Escape Problem


3-D Case: The conjecture is true in $3-D$ since for $\varepsilon \to 0$

$$\bar{v} \sim \frac{|\Omega|}{4\varepsilon D} \left[ 1 - \frac{\varepsilon}{\pi} H(x_0) \log \varepsilon + O(\varepsilon) \right], \quad \lambda_1 \sim \frac{1}{D \bar{v}}$$

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

Principal Result: [PWPK]: Local maxima of $R_s(x_1, x_1)$ do not necessarily coincide with the local maxima of the curvature $\kappa$ of the boundary of a smooth perturbation of the unit disk. Consequently, for $\varepsilon \to 0$, $\lambda_1$ does not necessarily have a local minimum at the location of a local maximum of the curvature of a smooth boundary.

Proof: counterexample constructed based on explicit perturbation formula for $R_s(x_1, x_1)$ for arbitrary smooth perturbations of the unit disk derived by T. Kolokolnikov.
Part I: The MFPT on the Surface of a Sphere

The MFPT on the surface of the unit sphere $\Omega$ with traps satisfies

$$\Delta_s v = -\frac{1}{D}, \quad x \in \Omega_\varepsilon \equiv \Omega \setminus \bigcup_{j=1}^N \Omega_{\varepsilon_j},$$

$$v = 0, \quad x \in \partial \Omega_{\varepsilon_j}; \quad \bar{v} \sim \frac{1}{|\Omega_\varepsilon|} \int_{\Omega_\varepsilon} v \, ds.$$  

The corresponding eigenvalue problem on the surface $\Omega_\varepsilon$ is

$$\Delta_s \psi + \lambda \psi = 0, \quad x \in \Omega_\varepsilon,$$

$$\psi = 0, \quad x \in \partial \Omega_{\varepsilon_j}; \quad \int_{\Omega_\varepsilon} \psi^2 \, ds = 1.$$  

Remarks:

- $\Omega_{\varepsilon_j}$ are non-overlapping circular traps of radius $O(\varepsilon)$ on $\Omega$ centered at $x_j$ with $|x_j| = 1$ for $j = 1, \ldots, N$.

- **Key Relationship:** $\bar{v} \sim 1/(D\lambda_1)$ as $\varepsilon \to 0$.  

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Part I: Main Goals: MFPT on the Sphere

Applications: Specific Scientific Questions:
- Calculate an explicit higher-order asymptotic formula for $\bar{v}$ as $\varepsilon \to 0$.
- Investigate effect on $\bar{v}$ of spatial configuration $\{x_1, \cdots, x_N\}$ of traps.
- What is effect of fragmentation of the trap set?

Math: Connections to Approximation Theory: Is minimizing $\bar{v}$ equivalent to minimizing the discrete logarithmic energy?

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

Such points are Elliptic Fekete points. (Ref: Smale and Schub, Saff, Sloane, Kuijlaars, D. Boal, P. Palfy-Muhoray,...)

Part I: Main Result for MFPT on the Sphere

**Principal Result: [CSW]**: For \( N \) circular traps of a common radius \( \varepsilon \ll 1 \) centered at \( x_j \), for \( j = 1, \ldots, N \), the averaged MFPT \( \bar{v} \) satisfies

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

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

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

- **Key:** \( \lambda_1 \) is maximized and \( \bar{v} \) minimized at elliptic Fekete points.
- Analysis relies on Neumann \( G \)-function (known in fluid vortex studies):

\[
\triangle_s G = \frac{1}{4\pi} - \delta(x - x_0), \quad x \in \Omega; \quad \int_{\Omega} G \, ds = 0,
\]

\( G \) is \( 2\pi \) periodic in \( \phi \) and smooth at \( \theta = 0, \pi \),

Explicitly: \( G(x; x_0) = -\frac{1}{2\pi} \log |x - x_0| + \frac{1}{4\pi} [2 \log 2 - 1] \).
Part I: Scaling Law for Optimum MFPT

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

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

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


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

**Principal Result: [CSW]** For $N \gg 1$, and $N$ circular disks of common radius $\epsilon$, and with small trap area fraction $N\epsilon^2 \ll 1$ with $|\Omega| = 4\pi$, then

$$\min \bar{v} \sim \frac{1}{ND} \left[ -\log \left( \frac{\sum_{j=1}^{N} |\Omega \epsilon_j|}{|\Omega|} \right) - 4l_1 - \log 4 + O(N^{-1}) \right].$$
Part I: Specific Application of Scaling Law

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

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

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

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

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

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

**Key:** Fragmentation effect of trap set is very significant even at small $\varepsilon$. 

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Part I: New Directions and Open Issues

- **Rigorous Proof For $\bar{v}$ For Escape From Sphere**: recent preprint of X. Chen and A. Friedman, submitted to SIMA (2010).

- Narrow escape problems in arbitrary 3-d domains: require Neumann G-functions in 3-D with boundary singularity

- Surface diffusion on arbitrary 2-d surfaces with traps: require Neumann G-function and regular part on surface. Eigenvalue asymptotics on arbitrary surface with traps.

- **Improved Biological Models**: 1) Replace passive diffusion with subdiffusive behavior (with Y.Nec and D. Coombs); 2) Narrow escape in 3-D under sticky boundaries modeling binding/unbinding events on the surface; 3) Intermittent directed transport (motors) coupled to Brownian motion.

- **Spatial Aspects of Cell-Signalling (motivated by B. Kholodenko)**: Include chemical reactions occurring within each trap. **Can passive diffusive transport between traps induce temporal oscillations for localized reactions (ode’s) valid inside each trap (with Y. Nec and D. Coombs)?** Yields a new Steklov-type eigenvalue problem.
Part II: Persistence in Patchy Environments

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

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

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

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

 Threshold for species persistence is determined by the stability border to the extinct solution \( u = 0 \), with \( \lambda = 1/D \), and \( D \) the diffusivity.

 Growth rate \( m_\varepsilon \) changes sign \( \rightarrow \) indefinite weight eig. problem.

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**Key Previous Result I:** Assume that \( \int_\Omega m_\varepsilon \ dx < 0 \), but that \( m_\varepsilon > 0 \) on a set of positive measure. Then, there exists a positive principal eigenvalue \( \lambda_1 \), with corresponding positive eigenfunction \( \phi \) (Brown and Lin, (1980))

**Key Previous Result II:** The optimal growth rate \( m_\varepsilon(x) \) that minimizes \( \lambda_1 \) is of bang-bang type. (Theorem 1.1 of Lou and Yanagida, 2006)

**Key Previous Result III:** Transcritical Bifurcation: \( u \rightarrow u_\infty(x) \neq 0 \) as \( t \rightarrow \infty \) if \( \lambda > \lambda_1 \), while \( u \rightarrow 0 \) as \( t \rightarrow \infty \) if \( 0 < \lambda < \lambda_1 \). (many authors).
Part II: Formulation of Patch Model

Long-standing Open Problem: Minimize $\lambda_1$ wrt $m_\varepsilon(x)$, subject to a fixed $\int_\Omega m_\varepsilon \, dx < 0$: i.e. determine the largest $D$ that allows for persistence of the species. (Cantrell and Cosner 1990’s, Lou and Yanagida, (2006); Kao, Lou, and Yanagida, (2008); Hamel and Roques, (2007); Berestycki, Hamel, (2005)).

Our Patch Model: The eigenvalue problem for the persistence threshold is

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

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

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

Math: Assume that one $m_j > 0$ and $\int_\Omega m_\varepsilon \, dx < 0$. Then, there is a principal eigenvalue $\lambda_1 > 0$ with positive eigenfunction.

Biologically: On the whole, the environment is hostile, but at least one region can support growth. This gives an extinction threshold $\lambda_1$. 
Part II: Formulation of Patch Model

Remarks and Terminology:

- Patches $\Omega_{\varepsilon_j}$ of radius $O(\varepsilon)$ are portions of small circular disks strictly inside $\Omega$. Circular patches are locally optimal (Hamel, Roques (2007)).

- The constant $m_j$ is the local growth rate of the $j^{\text{th}}$ patch, with $m_j > 0$ for a favorable habitat and $m_j < 0$ for a non-favorable habitat.

- The constant $m_b$ the background bulk growth rate.

- The boundary $\partial \Omega$ is piecewise smooth, with possible corner points.
Part II: Formulation of Patch Model

Assign for each \( x_j \) an angle \( \pi \alpha_j \) denoting the angular fraction of a circular patch that is contained within \( \Omega \);

\[
\int_{\Omega} m_\varepsilon \, dx < 0 \quad \text{is equivalent for } \varepsilon \to 0 \text{ to}
\]

\[
\int_{\Omega} m_\varepsilon \, dx = -m_b |\Omega| + \frac{\pi}{2} \sum_{j=1}^{n} \alpha_j m_j \rho_j^2 + O(\varepsilon^2) < 0.
\]
Part II: Main Questions

Main Goal: Calculate $\lambda_1$ as $\varepsilon \to 0$, and minimize it for a fixed $\int_\Omega m \varepsilon \, dx < 0$. The parameter set is $\{m_1 \rho_1^2, \ldots, m_n \rho_n^2\}$, $\{x_1, \ldots, x_n\}$, and $\{\alpha_1, \ldots, \alpha_n\}$.

Q1: What is the effect of $\lambda_1$ of resource location? Are boundary habitats preferable to interior habitats with regards to the extinction threshold?

Q2: What is the effect of resource fragmentation? To maintain the value of $\int_\Omega m \varepsilon \, dx$, we need that $m_k \rho_k^2 = m_A \rho_A^2 + m_B \rho_B^2$. 

![Diagram showing resource location and fragmentation](image)
Part II: Main Mathematical Result

Principal Result: [LW]: In the limit $\varepsilon \to 0$, the positive principal eigenvalue $\lambda_1$ has the following two-term asymptotic expansion

$$
\lambda_1 = \mu_0 \nu + \mu_1 \nu^2 + O(\nu^3), \quad \nu = -\frac{1}{\log \varepsilon}.
$$

Here $\mu_0 > 0$ is the first positive root of $B(\mu_0) = 0$, where

$$
B(\mu_0) \equiv -m_b|\Omega| + \pi \sum_{j=1}^{n} \frac{\alpha_j m_j \rho_j^2}{2 - m_j \rho_j^2 \mu_0},
$$

and $\mu_1 = \mu_1(x_1, \ldots, x_n)$ is determined in terms of a quadratic form of a certain Green's function matrix, representing patch interaction effects.

Principal Result: [LW]: There is a unique root to $B(\mu_0) = 0$ on the range

$$
0 < \mu_0 < \mu_{0u} \equiv 2/(m_J \rho_J^2), \text{ where } m_J \rho_J^2 = \max_{m_j > 0 \{m_j \rho_j^2 | j = 1, \ldots, n\}}.
$$

The corresponding eigenfunction is positive.

Ref: [LW]: A. Lindsay, MJW, An Asymptotic Analysis of the Persistence Threshold for the Diffusive Logistic Model in Spatial Environments with Localized Patches, to appear, DCDS-B, (2010), (41 pages)
Part II: Resource Location and Fragmentation

In [LW] we (rigorously) optimize $\mu_0$ subject to $\int_\Omega m_\varepsilon dx < 0$ fixed.

**Main Result I**: Relocating a single favorable habitat to the boundary of the domain is advantageous for the persistence of the species.

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

**Main Result III**: The clumping of a favorable boundary habitat and an unfavorable interior habitat into one single interior habitat is not advantageous when the resulting interior habitat is still unfavorable.
Part II: Effect of Partial Fragmentation

Note: To preserve $\int_{\Omega} m_\varepsilon dx$ we need $m_k \rho_k^2 = m_A \rho_A^2 + (\alpha_B/2)m_B \rho_B^2$.

Main Result IV: Fragmenting a favorable interior habitat into a smaller interior favorable habitat and a favorable boundary habitat is beneficial for persistence when the boundary habitat is strong enough in that

$$m_B \rho_B^2 > \frac{4}{2 - \alpha_B} m_A \rho_A^2 > 0.$$  

It is not advantageous when the new boundary habitat is too weak in that

$$0 < m_B \rho_B^2 < m_A \rho_A^2.$$
Part II: Optimal Strategy

Best Strategy: [LW]: Given a fixed amount of favorable resources to distribute, the optimal strategy is to clump them all together at a point on $\partial \Omega$, and specifically at the corner point of $\partial \Omega$ (if available) with the smallest angle $\leq 90^\circ$. This strategy minimizes $\mu_0$, which maximizes the chance for the persistence of the species.

Remark: If $\partial \Omega$ is smooth, then to minimize $\lambda_1$ we must minimize the second-order coefficient $\mu_1$. Minimizing $\mu_1$ is also often needed when we are adding an additional resource to a pre-existing patch distribution.

Principal Result: [LW]: For a single boundary patch centered at $x_1$ on a smooth boundary $\partial \Omega$, $\mu_1$ is minimized at the global maximum of the regular part $R_s(x_1; x_1)$ of the surface Neumann Green’s function defined by

$$\triangle G_s = \frac{1}{|\Omega|}, \quad x \in \Omega; \quad \partial_n G_s = 0, \quad x \in \partial \Omega \setminus \{x_1\}; \quad \int_\Omega G_s \, dx = 0,$$

$$G_s(x; x_1) \sim -\frac{1}{\pi} \log |x - x_1| + R_s(x_1; x_1), \quad \text{as } x \to x_1 \in \partial \Omega.$$
Part II: Further Directions and Commonalities

Determine effect of resource fragmentation for predator-prey systems

\[ u_t = D \Delta u + m_\varepsilon(x)u(1 - u) - \beta uv, \quad v_t = \Delta v - \sigma v + \mu + \beta uv \]

If prey is concentrated, predator has an advantage. Perhaps a partial fragmentation is optimal strategy for prey. Other models include: 1) a chemotactic predator drift term directed towards prey maxima. 2) Allee effect in prey so that persistence threshold results from saddle-node bifurcation point.

Common Features for Parts I and II

- resolution of localized traps by singular perturbation methodology
- central role of Neumann G-functions
- the eigenvalue optimization problem is reduced to finding optimum points of limiting discrete variational problems derived by asymptotics
- some clear mathematical connections: either PDE or approximation theory
Part III: Spot Patterns in RD Systems

Spatially localized solutions can occur for singularly perturbed RD models

\[ v_t = \varepsilon^2 \Delta v + g(u,v); \quad \partial_n v = 0, \quad x \in \Omega \in \mathbb{R}^2, \]
\[ \tau u_t = D \Delta u + f(u,v); \quad \partial_n u = 0, \quad x \in \partial \Omega. \]

Semi-strong interaction: \( D = O(1), \varepsilon \to 0. \)

Various Well-Known Kinetics With No Variational Structure:

\( g(u,v) = -v + v^2 / u, \quad f(u,v) = -u + v^2, \quad \text{GM; Gierer-Meinhardt (1972)} \)
\( g(u,v) = -v + Auv^2, \quad f(u,v) = (1 - u) - uv^2. \quad \text{GS model; Pearson (1993)} \)
\( g(u,v) = -v + uv^2, \quad f(u,v) = a - uv^2, \quad \text{Schnakenburg model}. \)

Overview: Localized Spot Solutions to RD systems

- Since \( \varepsilon \ll 1, v \) can be localized in space as a spot pattern, consisting of concentration at a discrete set of points in \( \Omega \in \mathbb{R}^2. \)

- **Spot Instability Types:** Self-Replicating, Oscillatory, or Over-Crowding instabilities.

- **Theoretical Approaches?**
Part III: Visual on Types of Spot Instabilities

For GM model, the local profile for \( v \) is to leading-order approximated locally by a radially symmetric ground-state solution of \( \Delta w - w + w^2 = 0 \). Particle-like solution to GM model.

GM Over-Crowding and Oscillatory Instabilities: Slowly drifting spots can undergo sudden (fast) instabilities due to dynamic bifurcations, such as over-crowding, or competition, instability (movie), or oscillatory instabilities in the spot amplitude (movie).

Self-Replicating Spot Patterns: An initial collection of spots for the Schnakenburg model can undergo self-replication events (movie).
Part III: Experimental Evidence of Spot Splitting


Part III: Numerical Evidence of Spot-Splitting

- Pearson, *Complex Patterns in a Simple System*, Science, **216**.


Right: Muratov and Osipov (1996).
Part III: Theoretical Framework

- **Turing Stability Analysis**: linearize RD around a spatially homogeneous steady state. Look for diffusion-driven instabilities (Turing 1952, and ubiquitous first step in RD models of math biology.

- **Weakly Nonlinear Theory**: capture nonlinear terms in multi-scale perturbative way and derive normal form GL and CGL amplitude equations (Cross and Hohenberg, Knobloch, .....).

- **Singular Perturbation Theory for Localized Spot Patterns**:
  - Use singular perturbation techniques to construct quasi-steady pattern consisting of localized spots.
  - Dynamics of spots in terms of “collective” coordinates. Derive by asymptotics a reduced dynamical system for spot locations, representing essentially moving 2-D coulomic singularities.
  - For stability, analyze singularly perturbed eigenvalue problems. For $D = O(1)$, $\varepsilon \to 0$, the leading order in $-1/ \log \varepsilon$ theory often lead to Nonlocal Eigenvalue Problems (NLEP).
  - Key point is that RD systems have no variational structure (unlike the study of vortices in superconductivity).
Part III: Some Previous Work

1-D Theory: Spike Solutions to RD System
- Stability and dynamics of pulses for the GM and GS models in the regime $D = O(1)$ (Doelman, Kaper, Promislov, Muratov, Osipov, Iron, MJW, Kolokolnikov, Chen, Wei),
- Pulse-splitting mechanism for the GS model for $D = O(\varepsilon^2)$ based on global bifurcation scenario (Nishiura, Ei, Ueyama).

2-D Theory: Spot Solutions to RD Systems
- Weakly interacting (repulsive) spots (Mimura, Ei, Ohta...)
- NLEP stability theory for spot stability for GM and GS in for $D = O(1)$ (Wei-Winter, series of papers). NLEP problems arise from leading-order terms in infinite logarithmic expansion in $\varepsilon$.
- One-Spot dynamics for GM (Chen, Kowalczyk, Kolokolnikov, MJW). Equilibria at critical points of regular part of various $G$-functions

Largely Open: Give an analytical theory for self-replication of spots, dynamics of spots, and other instabilities (oscillatory and annihilation).
Part III: Schnakenburg Model Outline

Schnakenburg Model: in a 2-D domain $\Omega$ under Neumann BC, consider

$$v_t = \varepsilon^2 \Delta v - v + uv^2, \quad \varepsilon^2 u_t = D \Delta u + a - \varepsilon^{-2} uv^2,$$

Here $0 < \varepsilon \ll 1$, and the parameters are $D > 0$, and $a > 0$.

Example 1: (Collection of Initial Spots): $\Omega = [0, 1]^2$, $\varepsilon = 0.02$, $a = 51$, $D = 0.1$. (movie 1). Dynamics? Criteria for Spot Splitting? Why do only some split?

Example 2: (Splitting is Orthogonal to Motion): Let $\Omega = [0, 1]^2$, $\varepsilon = 0.02$, $a = 10$, and $D = 0.1$. (movie 2). Is splitting direction perpendicular to the motion?

Main Results from Asymptotics

- **Quasi-Equilibria**: Asymptotic construction (summing log expansion).
- **Slow Dynamics**: DAE system for the evolution of $K$ spots.
- **Criteria and Direction of Spot-Splitting**: A specific criteria in terms of the “strength” of the logarithmic singularity for the outer approximation.


Part III: The Quasi-Equilibrium Solution

**Inner Region:** near a spot location \( x_j \in \Omega \) define \( V_j \) and \( U_j \) by
\[
u = \frac{1}{\sqrt{D}} U_j(y), \quad v = \sqrt{D} V_j(y), \quad y = \varepsilon^{-1}(x - x_j), \quad x_j = x_j(\varepsilon^2 t).
\]

To leading order, \( U_j \) and \( V_j \) are radially symmetric and
\[
V_j + \frac{1}{\rho} V_j - V_j + U_j V_j^2 = 0, \quad U_j + \frac{1}{\rho} U_j - U_j V_j^2 = 0, \quad 0 < \rho < \infty,
\]
\[
V_j \to 0, \quad U_j \sim S_j \log \rho + \chi(S_j) + o(1), \quad \text{as} \quad \rho = |y| \to \infty.
\]

Here \( S_j > 0 \) is the “source strength” to be determined and \( \chi(S_j) \) must be computed numerically.

**Key:** For the trap problem in Part I the inner problem is linear and in 2-D we must solve
\[
\Delta_y U_j = 0, \quad y \notin \Omega_j; \quad U_j = 0, \quad y \in \partial \Omega_j,
\]
\[
U_j \sim \log |y| - \log d_j, \quad |y| \to \infty,
\]

where \( d \) is the logarithmic capacitance. Our inner nonlinear core problem yields \( U_j \sim S_j \log |y| + \chi(S_j) \) as \( |y| \to \infty \).
Part III: Self-Replication Threshold

The outer approximation for $u$ is the superposition

$$u(x) = -\frac{2\pi}{\sqrt{D}} \sum_{j=1}^{K} S_j G(x; x_j) + u_c,$$

where $G(x; x_j)$ is the Neumann G-function with regular part $R(x_j; x_j)$.

**Stability analysis:** Set $u = u_e + e^{\lambda t} \eta$ and $v = v_e + e^{\lambda t} \phi$, and in the inner region introduce the local angular modes $m = 0, 2, 3, \ldots$ by

$$\eta = \frac{1}{D} e^{im\theta} N(\rho), \quad \phi = e^{im\theta} \Phi(\rho), \quad \rho = |y|, \quad y = \varepsilon^{-1}(x - x_j).$$

From a study of the eigenvalue problem:

**Spot-Splitting Criterion:** The quasi-equilibrium solution is stable wrt the local angular modes $m \geq 2$ iff $S_j < \Sigma_2 \approx 4.303$ for all $j = 1, \ldots, K$. The $J^{th}$ spot is unstable to the $m = 2$ peanut-splitting mode when $S_J > \Sigma_2$, which triggers a nonlinear spot self-replication process.
Part III: Reduced DAE Dynamics

Collective Slow Variables $S_j, x_j$, for $j = 1, \ldots, K$ satisfy a DAE system:

**Principal Result: [KWW]:** For “frozen” spot locations $x_j$, the source strengths $S_j$ and $u_c$ satisfy the nonlinear algebraic system

$$S_j + 2\pi \nu \left( S_j R_{j,j} + \sum_{\substack{i=1 \atop j \neq i}}^{N} S_i G_{j,i} \right) + \nu \chi(S_j) = -2\pi \nu u_c, \quad j = 1, \ldots, K,$$

$$\sum_{j=1}^{K} S_j = a |\Omega| \frac{1}{2\pi \sqrt{D}}, \quad \nu \equiv -\frac{1}{\log \varepsilon}.$$

The spot locations $x_j$, with speed $O(\varepsilon^2)$, satisfy

$$x'_j \sim -2\pi \varepsilon^2 \gamma(S_j) \left( S_j \nabla R(x_j; x_j) + \sum_{\substack{i=1 \atop j \neq i}}^{N} S_i \nabla G(x_j; x_i) \right), \quad j = 1, \ldots, K.$$

Here $G_{j,i} \equiv G(x_j; x_i)$ and $R_{j,j} \equiv R(x_j; x_j)$ (Neumann G-function).
Part III: An Example

Let $\Omega = [0, 1]^2$, $\varepsilon = 0.02$, $a = 51$, $D = 0.1$ and let

$$x_j = x_c + 0.33 e^{i\pi(j-1)/3}, \quad j = 1, \ldots, 6;$$

The DAE system gives $S_1 = S_4 \approx 4.01$, and $S_2 = S_3 = S_5 = S_6 \approx 4.44$. Thus, since $\Sigma_2 \approx 4.3$, we predict that four spots split [(movie)]. The DAE system closely tracks the spots after the splitting.
Part III: Open Issues and Further Directions

- **Green’s Function (PDE):** Rigorous results needed for critical points of regular part of Neumann and Reduced-wave Green’s functions.

- **Universality:** Apply framework to RD systems with classes of kinetics, to derive general principles for dynamics, stability, replication.

- **Annihilation-Creation Attractor:** construct a “chaotic” attractor or “loop” for GS model composed of spot-replication events, leading to spot creation, followed by an over-crowding instability (spot-annihilation. (Wan Chen’s lecture)

- **Localized Patterns on Surfaces:** Dynamics and instabilities of localized RD patterns on closed surfaces, with possible coupling to diffusion processes occurring in the interior. Note: Schnakenburg model on a Manifold: S. Ruuth (JCP, 2008), C. McDonald
A Final (Opinionated) Message:

Applied Mathematics should not be viewed solely as an endeavor consisting of modeling on a case-by-case basis trying to explain some experimental results etc... Equally worthy is Applied Mathematics that advances theory, develops new methodologies, and algorithms, etc.. that can be applied to a range of diverse applications, and that succeeds in making some connections with contemporary topics, directions, and conjectures related to purer aspects of mathematical research (such as PDE theory, etc...).

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