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

Michael J. Ward (UBC)

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Collaborators:, W. Chen (UBC, Oxford); A. Cheviakov and R. Spiteri (U. Saskatchewan); D. Coombs (UBC); D. Iron (Dalhousie); T. Kolokolnikov (Dalhousie); A. Lindsay (UBC, Arizona); Y. Nec (Technion, UBC); A. Peirce (UBC); S. Pillay (UBC, JP Morgan), R. Straube (Max-Planck, Magdeburg); J. Wei (Chinese U. Hong Kong)

Outline of the Talk

THREE SPECIFIC (SEEMINGLY UNRELATED) TOPICS:

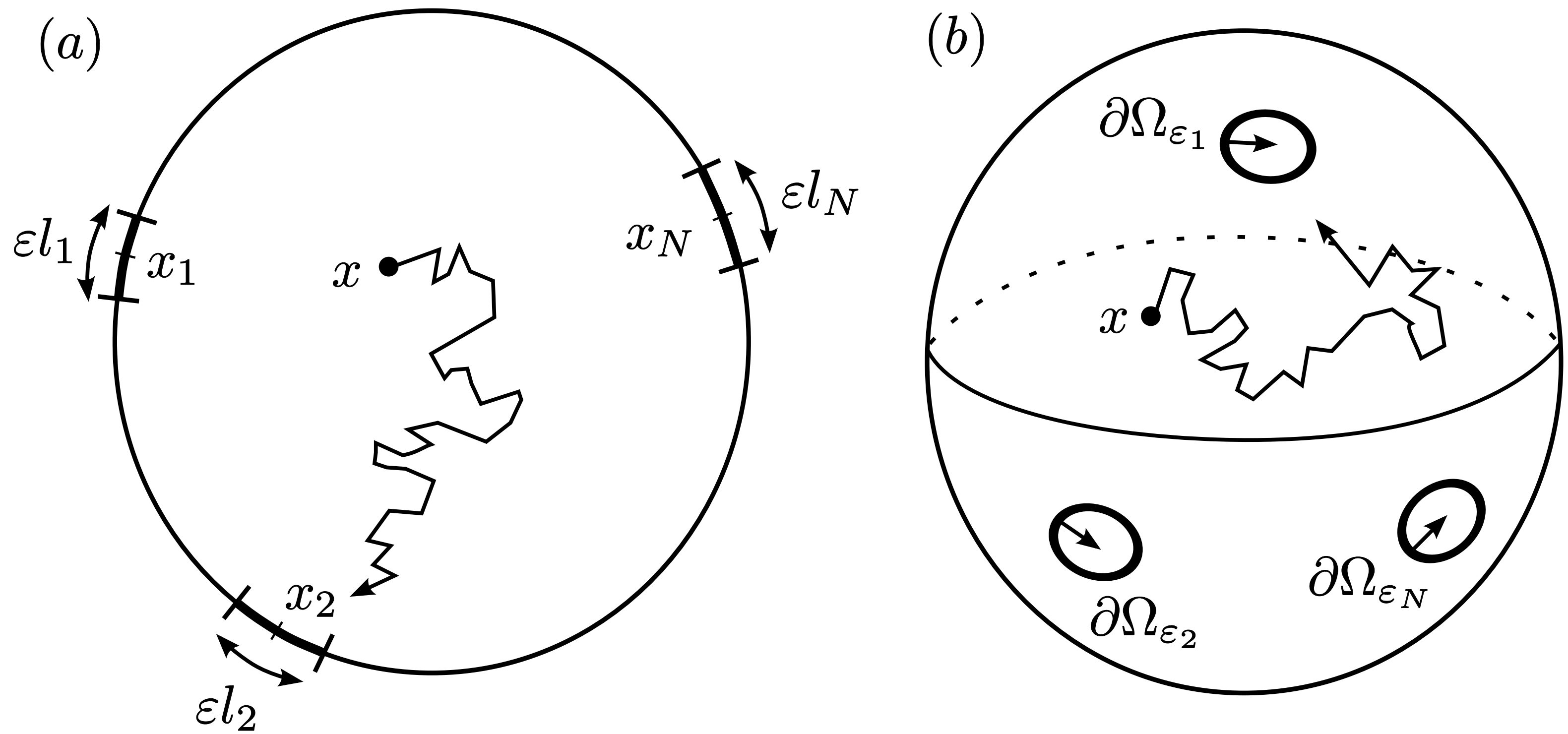
1. **Part I:** The Mean First Passage Time (MFPT) for Diffusive Escape from a Sphere Through a Narrow Window on its Boundary. The MFPT for Diffusion on the Surface of a Sphere with Localized Traps.
2. **Part II:** Calculation of the Persistence or Extinction Threshold for the Diffusive Logistic Model in Highly Patchy Spatial Environments (Alan Lindsay's lecture)
3. **Part III:** The Dynamics, Stability, and Self-Replication of Spots for RD Systems in Chemical Physics (Wan Chen'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 Ω with $\partial\Omega$ insulated except for an (multi-connected) absorbing patch $\partial\Omega_a$ of measure $O(\varepsilon)$. Let $\partial\Omega_a \to x_j$ as $\varepsilon \to 0$ and $X(0) = x \in \Omega$ be initial point for Brownian motion.



Left: 2-D Domain **Right: The Sphere**

Part I: Mathematical Formulation

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

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

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

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

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

Here λ_1 is the principal eigenvalue of

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

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

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:

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

RELEVANCE OF NARROW ESCAPE TIME PROBLEM IN BIOLOGY:

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

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

$$\Delta_y w = 0\,, \quad y_3 \geq 0\,, \; -\infty < y_1, y_2 < \infty\,; \quad w \sim C_j/|y|\,, \quad |y| \to \infty\,,$$
$$w = 1\,, \quad y_3 = 0\,, \, (y_1, y_2) \in \partial\Omega_j\,; \; \partial_{y_3} w = 0\,, \quad y_3 = 0\,, \, (y_1, y_2) \notin \partial\Omega_j\,.$$

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

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

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

- For arbitrary Ω 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 $\{x_1, \cdots, x_N\}$ of traps.
- What is the effect on $\bar{v}$ of fragmentation of the trap set?

Math: Connections to Approximation Theory: Let Ω 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

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

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

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

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

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

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

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

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 εa_j centered at x_j, $j = 1, \ldots, N$, a 3-term expansion for averaged MFPT $\bar{v}$ is*

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

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

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

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

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

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

Part I: Main Result for $\bar{v}$

Corollary: [CWS]: *For N circular traps of a common radius ε (for which $c_j = 2/\pi$ and $a_j = 1$ for $j = 1, \ldots, N$), then a three-term expansion is*

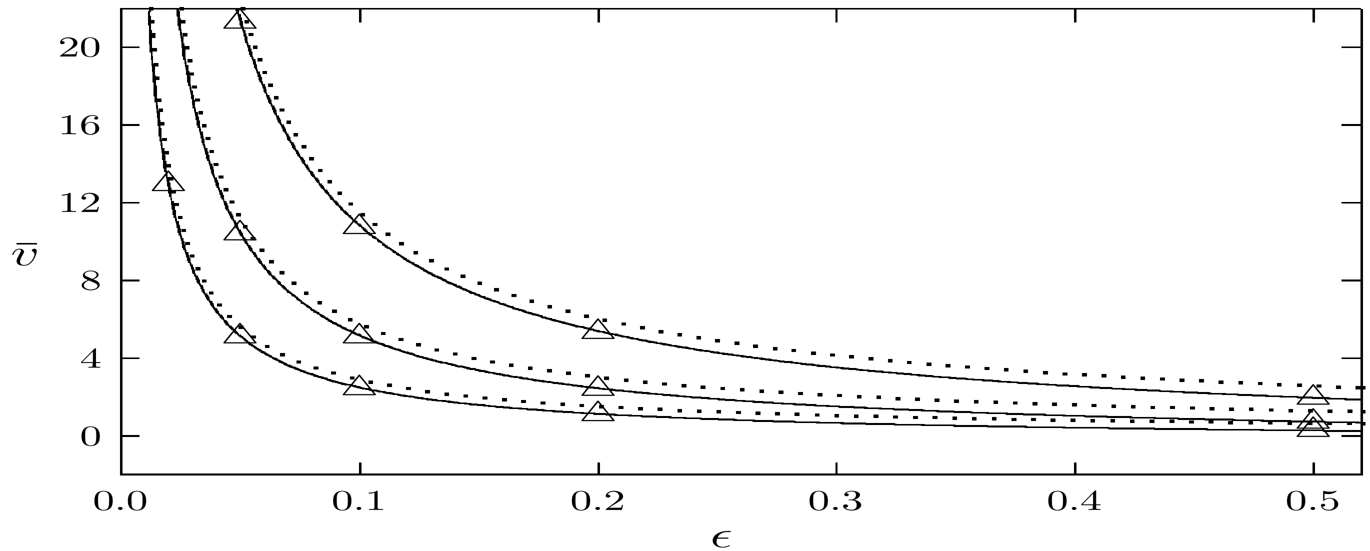
$$\bar{v} = \frac{|\Omega|}{4\varepsilon D N}\left[1 + \frac{\varepsilon}{\pi}\log\left(\frac{2}{\varepsilon}\right) + \frac{\varepsilon}{\pi}\left(\mathcal{H}(x_1, \ldots, x_N) - \frac{9N}{5} + \frac{3}{2} + (N-2)\log 4\right) + \mathcal{O}(\varepsilon^2 \log \varepsilon)\right],$$

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

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

- **Key point:** Minimizing $\bar{v}$ corresponds to minimizing $\mathcal{H}$. This discrete energy is a generalization of the purely Coulombic energy associated with Fekete points. Extra term in $\mathcal{H}$ involves surface diffusion effects.
- **Ref: [CWS]:** *A. Cheviakov, M.J. Ward, R. Straube, An Asymptotic Analysis of the Mean First Passage Time for Narrow Escape Problems: SIAM J. Multiscale Modeling and Simulation: Part II The Sphere,* **8**, *(2010), pp. 836–870.*

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

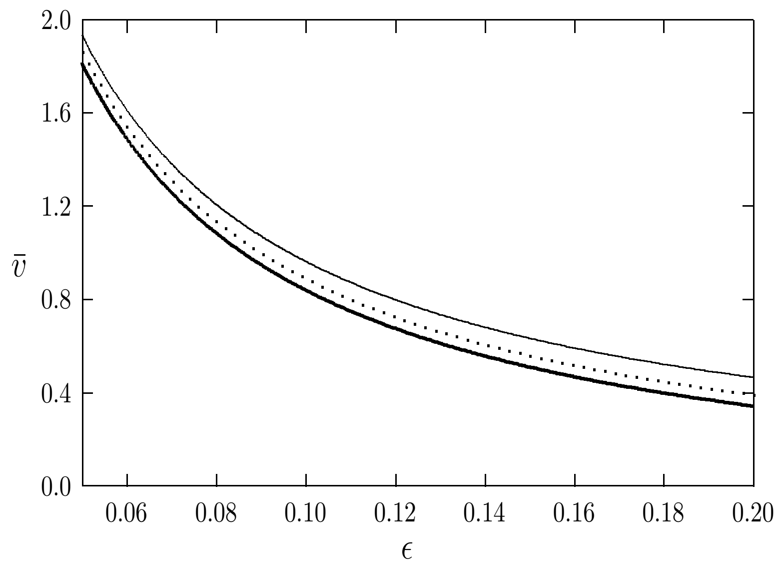


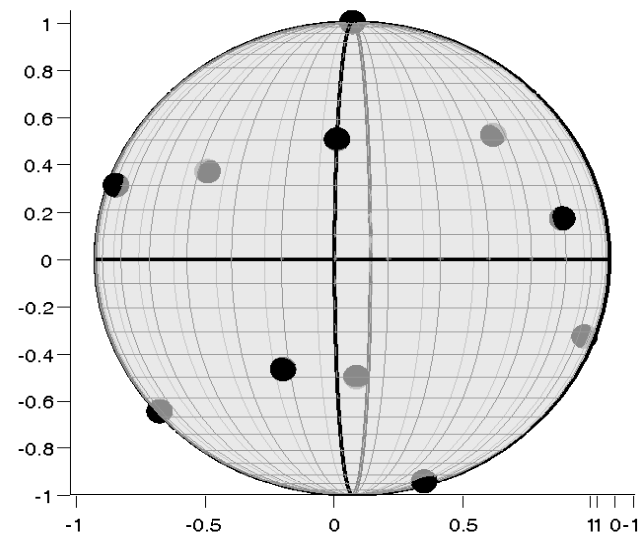
Plot: $\bar{v}$ vs. ε with $D = 1$ and either $N = 1, 2, 4$ equidistantly spaced circular windows of radius ε. **Solid:** 3-term expansion. **Dotted:** 2-term expansion. **Discrete:** COMSOL. **Top:** $N = 1$. **Middle:** $N = 2$. **Bottom:** $N = 4$.

	$N=1$			$N=4$		
ε	$\bar{v}_2$	$\bar{v}_3$	$\bar{v}_n$	$\bar{v}_2$	$\bar{v}_3$	$\bar{v}_n$
0.02	53.89	53.33	52.81	13.47	13.11	12.99
0.05	22.17	21.61	21.35	5.54	5.18	5.12
0.10	11.47	10.91	10.78	2.87	2.51	2.47
0.20	6.00	5.44	5.36	1.50	1.14	1.13
0.50	2.56	1.99	1.96	0.64	0.28	0.30

Part I: Fragmentation and Location of Traps

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





Plot: $\bar{v}$ vs. ε 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 $\varepsilon = 0.1907$, $N = 11$ 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.

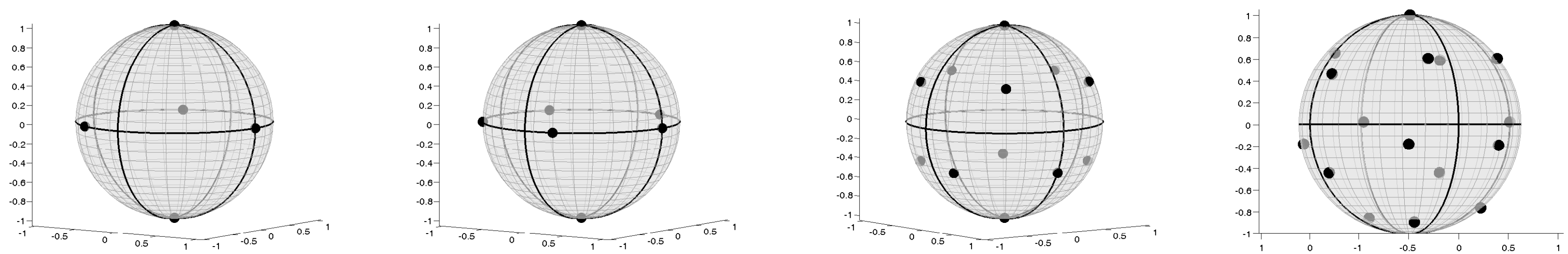
Part I: The Discrete Variational Problem

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

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

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

N=5 **N=7** **N=12** **N=16**



- Optimal $\mathcal{H}$ grows more slowly with N than for other discrete energies.
- For $N = 2, \ldots, 20$ optimal point arrangments 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 $\mathcal{H}(x_1, \ldots, x_N)$ has the form (formal derivation)

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

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

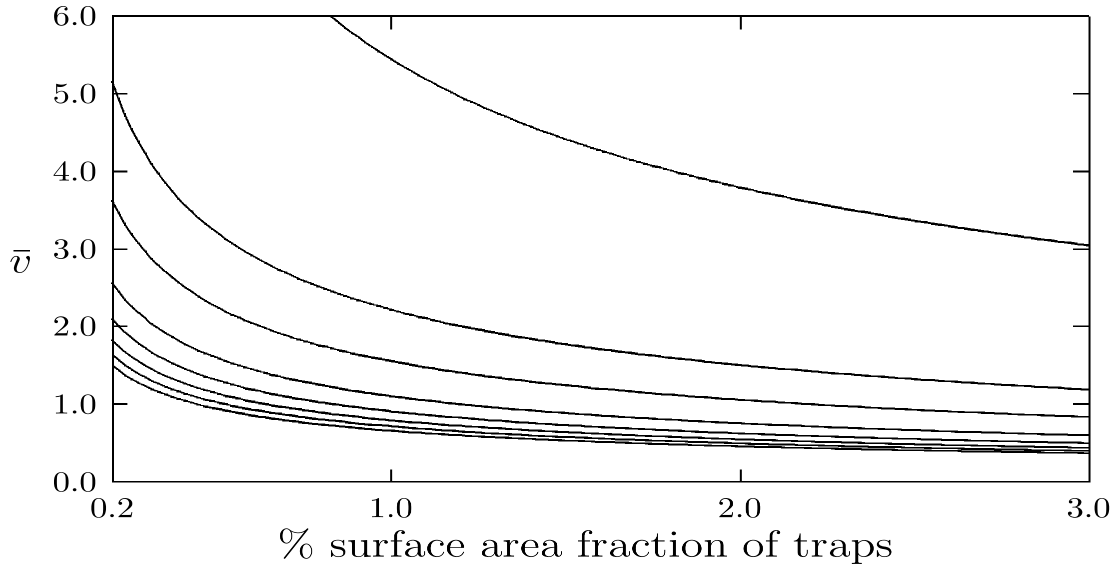
$$b_1 \approx -0.5668\,, \qquad b_2 \approx 0.0628\,, \qquad b_3 \approx -0.8420\,,$$
$$b_4 \approx 3.8894\,, \qquad b_5 \approx -1.3512\,, \qquad b_6 \approx -2.4523\,.$$

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

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

Similar analysis for the 2-D narrow escape problem: **Ref: [PWPK]:** S. Pillay, MJW, A. Peirce, T. Kolokolnikov, Part I: Two-Dimensional Domains, SIAM J. Multiscale Modeling, **8**, (2010), pp. 808–836.

Principal Result: [PWPK]: *When a smooth 2-D boundary $\partial\Omega$ has exactly one absorbing boundary trap of length ε 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,

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

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

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 κ? In other words, will a boundary trap centered at the maximum of κ minimize the heat loss from the domain? (i.e. yield the smallest λ_1, and thus largest $\bar{v}$)

Part I: The 2-D Narrow Escape Problem

- **Note:** Related to conjecture of J. Denzler, *Windows of a Given Area with Minimal Heat Diffusion*, Trans. Amer. Math. Soc., **351**, (1999).
- **3-D Case:** The conjecture is true in $3-D$ since for $\varepsilon \to 0$

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

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 κ of the boundary of a smooth perturbation of the unit disk. Consequently, for $\varepsilon \to 0$, λ_1 does not necessarily have a local minimum at the location of a local maximum of the curvature of a smooth boundary.*

Proof: counterxample 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 Ω with traps satisfies

$$\triangle_s v = -\frac{1}{D}\,, \qquad x \in \Omega_\varepsilon \equiv \Omega \backslash \cup_{j=1}^{N} \Omega_{\varepsilon_j}\,,$$

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

The corresponding eigenvalue problem on the surface Ω_ε is

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

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

Remarks:

- Ω_{ε_j} are non-overlapping circular traps of radius $O(\varepsilon)$ on Ω centered at x_j with $|x_j| = 1$ for $j = 1, \ldots, N$.
- **Key Relationship:** $\bar{v} \sim 1/(D\lambda_1)$ as $\varepsilon \to 0$.

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?

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

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

Ref: [CSW]: D. Coombs, R. Straube, MJW, *"Diffusion on a Sphere with Traps..."*, SIAM J. Appl. Math., **70**, (2009), pp. 302–332.

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:** λ_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 2π periodic in ϕ and smooth at $\theta = 0, \pi$,

Explicitly: $\quad G(x; x_0) = -\frac{1}{2\pi} \log |x - x_0| + \frac{1}{4\pi} [2\log 2 - 1] \,.$

Part I: Scaling Law for Optimum MFPT

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

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

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

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

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

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

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

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:

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

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

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

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

Key: Fragmentation effect of trap set is very significant even at small ε

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 $x \in \Omega \in \mathbb{R}^2$

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

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

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

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

Key Previous Result I: Assume that $\int_\Omega m_\varepsilon \, dx < 0$, but that $m_\varepsilon > 0$ on a set of positive measure. Then, there exists a positive principal eigenvalue λ_1, with corresponding positive eigenfunction ϕ (Brown and Lin, (1980))

Key Previous Result II: The optimal growth rate $m_\varepsilon(x)$ that minimizes λ_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 λ_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

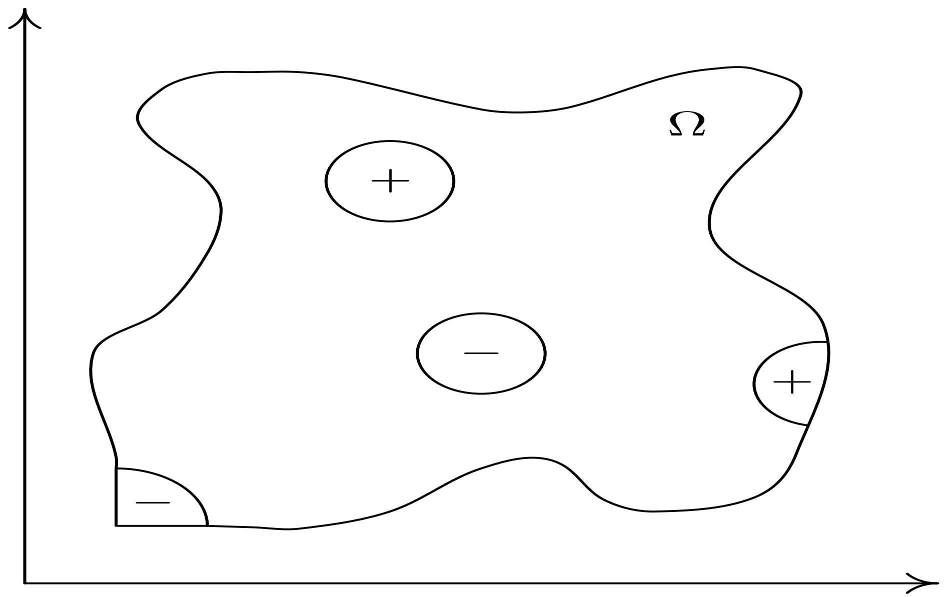
$$\Delta\phi + \lambda\, m_\varepsilon(x)\phi = 0\,, \quad x \in \Omega; \quad \partial_n \phi = 0\,, \quad x \in \partial\Omega\,; \quad \int_\Omega \phi^2 \, dx = 1\,,$$

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

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

- **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 λ_1.

Part II: Formulation of Patch Model

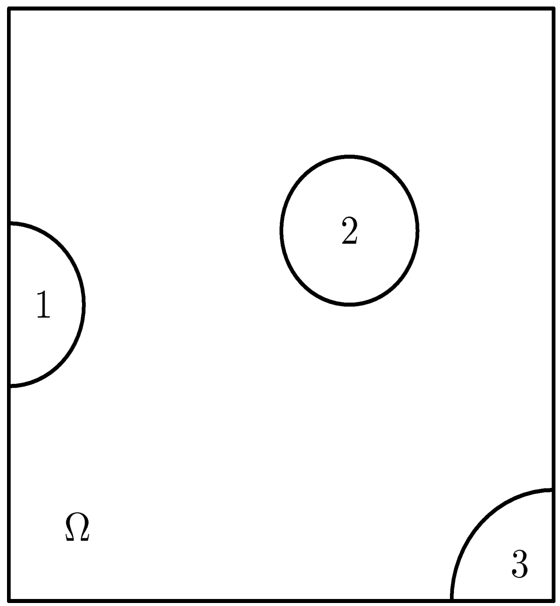


Remarks and Terminology:

- Patches Ω_{ε_j} of radius $O(\varepsilon)$ are portions of small circular disks strictly inside Ω. Circular patches are locally optimal (Hamel, Roques (2007)).
- The constant m_j is the local growth rate of the j^{th} patch, with $m_j > 0$ for a favorable habitat and $m_j < 0$ for a non-favorable habitat.
- The constant m_b 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 Ω;



Patch	Angle	Radius
1	$\alpha_1 = \pi$	$\epsilon\rho_1$
2	$\alpha_2 = 2\pi$	$\epsilon\rho_2$
3	$\alpha_3 = \pi/2$	$\epsilon\rho_3$

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

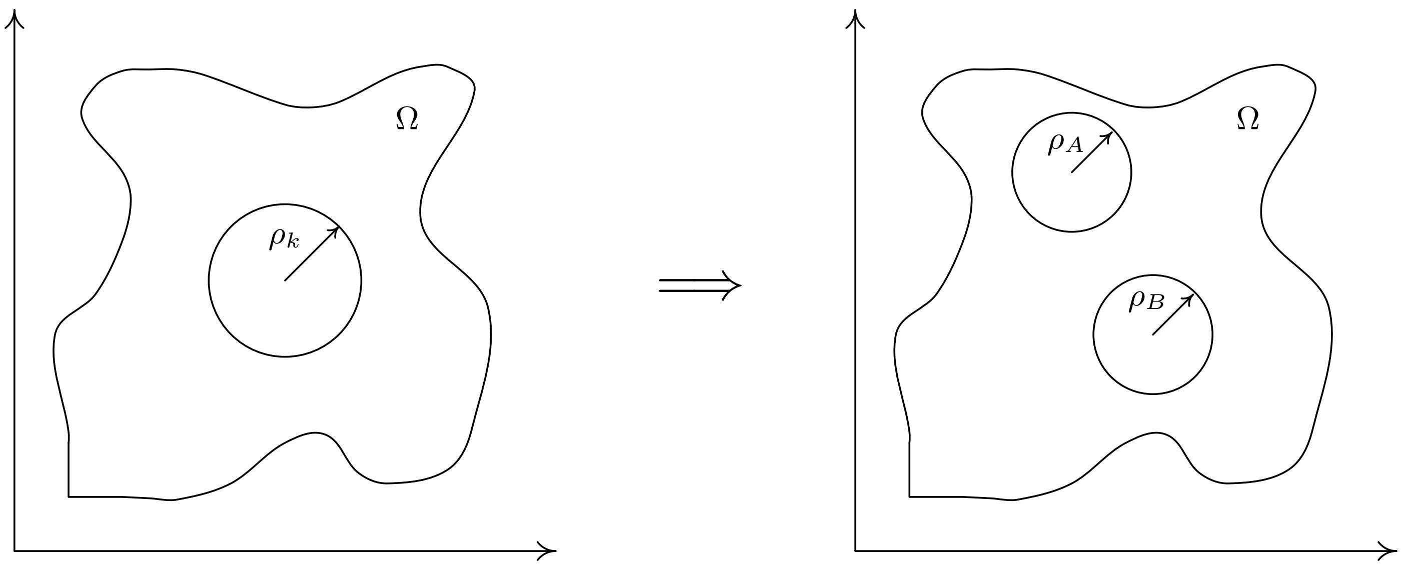
$$\int_\Omega m_\varepsilon \, dx = -m_b|\Omega| + \frac{\pi}{2}\sum_{j=1}^{n} \alpha_j m_j \rho_j^2 + \mathcal{O}(\varepsilon^2) < 0 \, .$$

Part II: Main Questions

Main Goal: Calculate λ_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 λ_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 $\int_\Omega m_\varepsilon \, \mathrm{d}x$, we need that $m_k\rho_k^2 = m_A\rho_A^2 + m_B\rho_B^2$.



Part II: Main Mathematical Result

Principal Result:[LW]: *In the limit $\varepsilon \to 0$, the positive principal eigenvalue λ_1 has the following two-term asymptotic expansion*

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

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

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

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 $\mathcal{B}(\mu_0) = 0$ on the range $0 < \mu_0 < \mu_{0u} \equiv 2/(m_J \rho_J^2)$, where $m_J \rho_J^2 = \max_{m_j > 0} \{ m_j \rho_j^2 \,|\, j = 1, \ldots, n \}$. The corresponding eigenfunction is positive.*

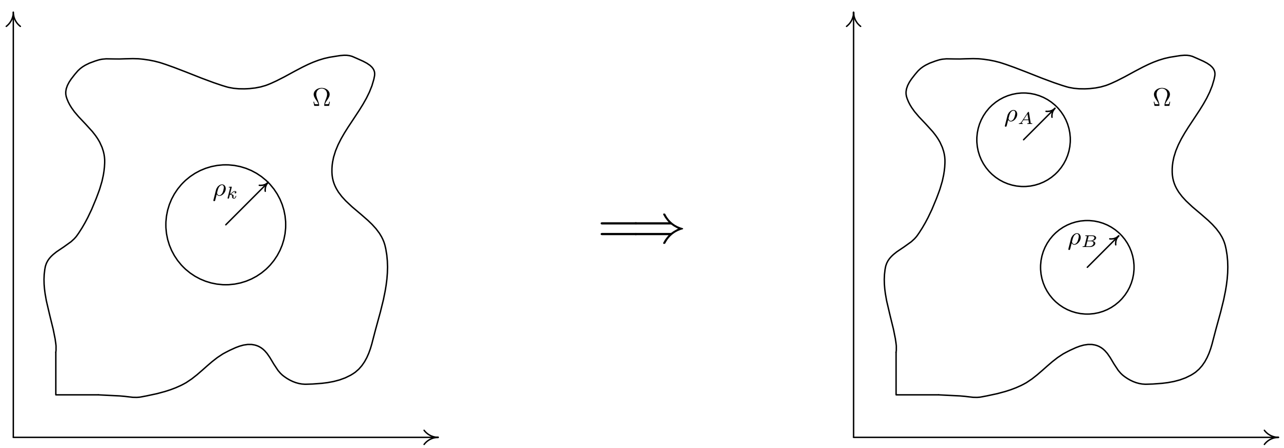
Ref: [LW]: A. Lindsay, MJW, *An Asymptotic Analysis of the Persistence Threshold for the Diffusive Logistic Model in Spatial Environments with Localized Patches*, to appear, DCDS-B, (2010), (41 pages)

Part II: Resource Location and Fragmentation

In **[LW]** we (rigorously) optimize μ_0 subject to $\int_\Omega m_\varepsilon dx < 0$ fixed.

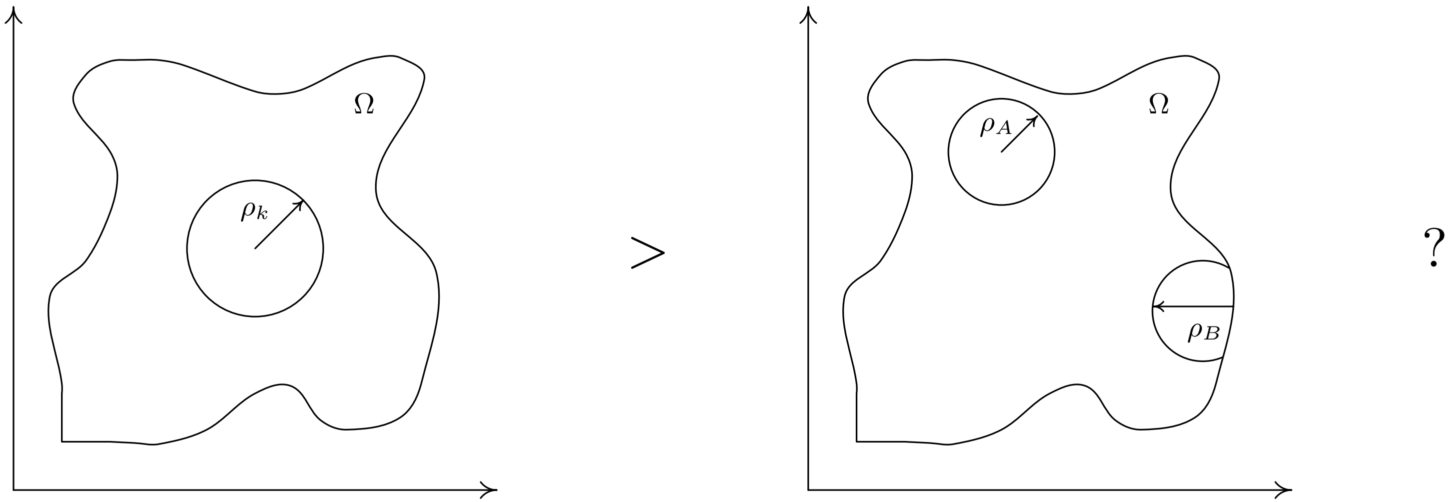
Main Result I: *Relocating a single favorable habitat to the boundary of the domain is advantageous for the persistence of the species.*

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 μ_0, which maximizes the chance for the persistence of the species.

Remark: If $\partial\Omega$ is smooth, then to minimize λ_1 we must minimize the second-order coefficient μ_1. Minimizing μ_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 $\partial\Omega$, μ_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*

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

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

Part II: Further Directions and Commonalities

- Determine effect of resource fragmentation for predator-prey systems

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

  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

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

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

Various Well-Known Kinetics With No Variational Structure:

$g(u,v) = -v + v^2/u\,, \quad f(u,v) = -u + v^2\,,$ GM; Gierer-Meinhardt (1972)

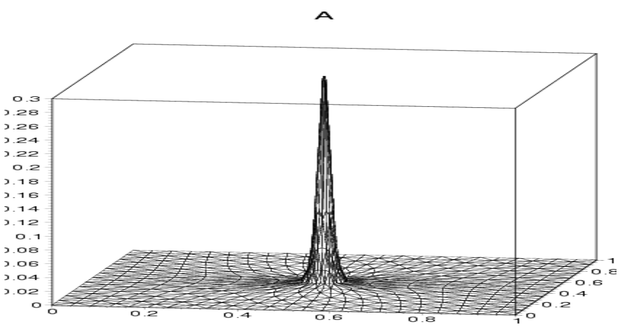
$g(u,v) = -v + Auv^2\,, \quad f(u,v) = (1-u) - uv^2\,.$ GS model; Pearson (1993)

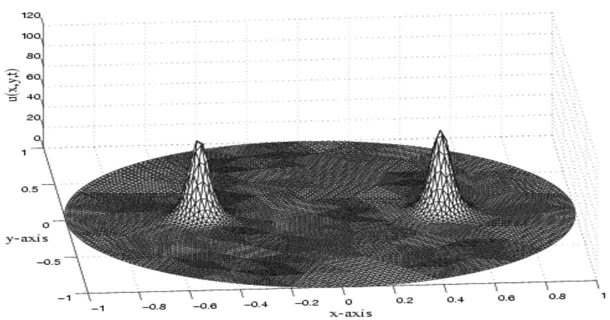
$g(u,v) = -v + uv^2\,, \quad f(u,v) = a - uv^2\,,$ Schnakenburg model .

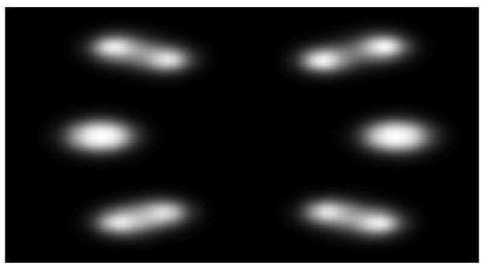
Overview: Localized Spot Solutions to RD systems

- Since $\varepsilon \ll 1$, v can be localized in space as a spot pattern, consisting of concentration at a discrete set of points in $\Omega \in R^2$.
- **Spot Instability Types:** Self-Replicating, Oscillatory, or Over-Crowding instabilities.
- **Theoretical Approaches ?**

Part III: Visual on Types of Spot Instabilities



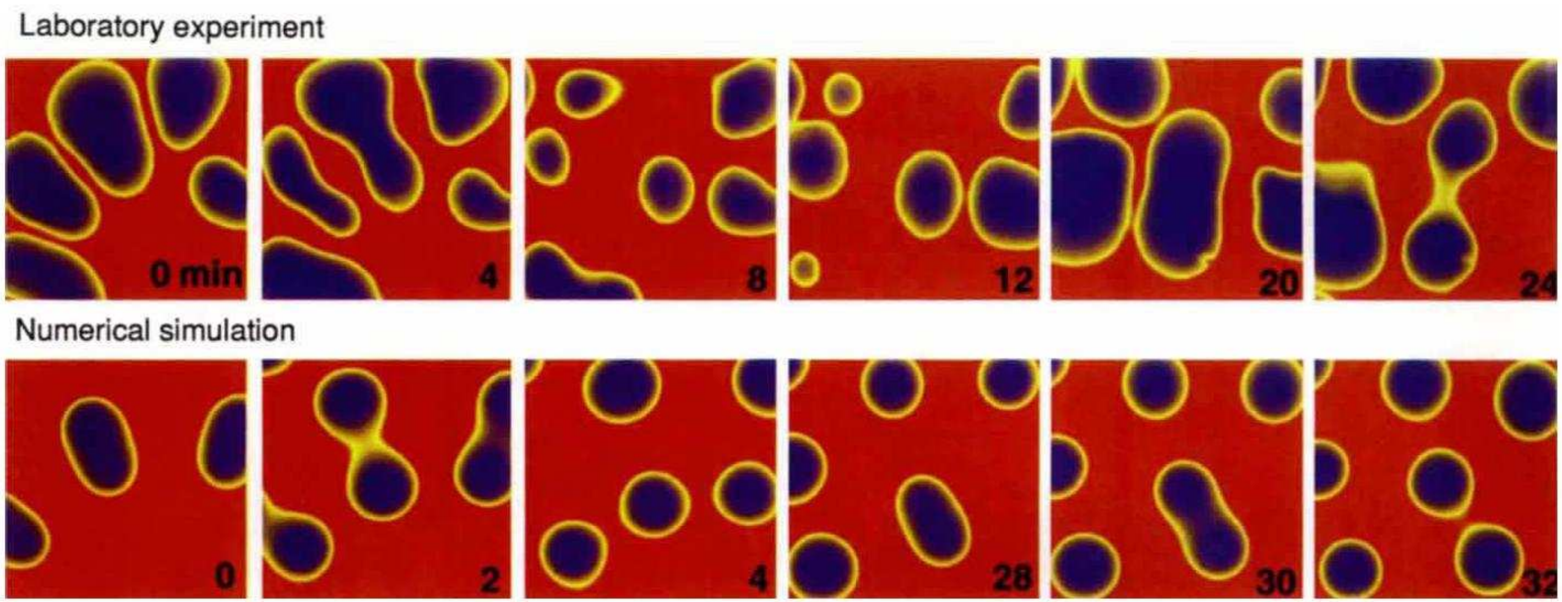




- For GM model, the local profile for v is to leading-order approximated locally by a radially symmetric ground-state solution of $\Delta w - w + w^2 = 0$. Particle-like solution to GM model.
- **GM Over-Crowding and Oscillatory Instabilities:** Slowly drifting spots can undergo sudden (fast) instabilities 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

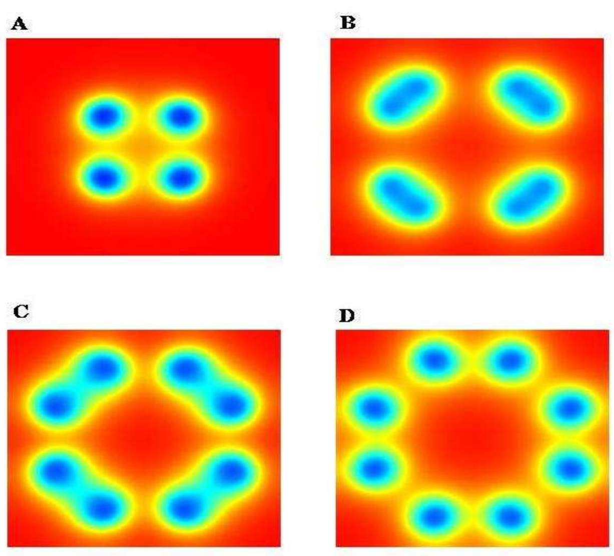
- The Ferrocyanide-iodate-sulphite reaction. (Swinney et al., Nature, V. 369, (1994), pp. 215-218). The numerical simulations are for GS model by Pearson (Science, 1993).



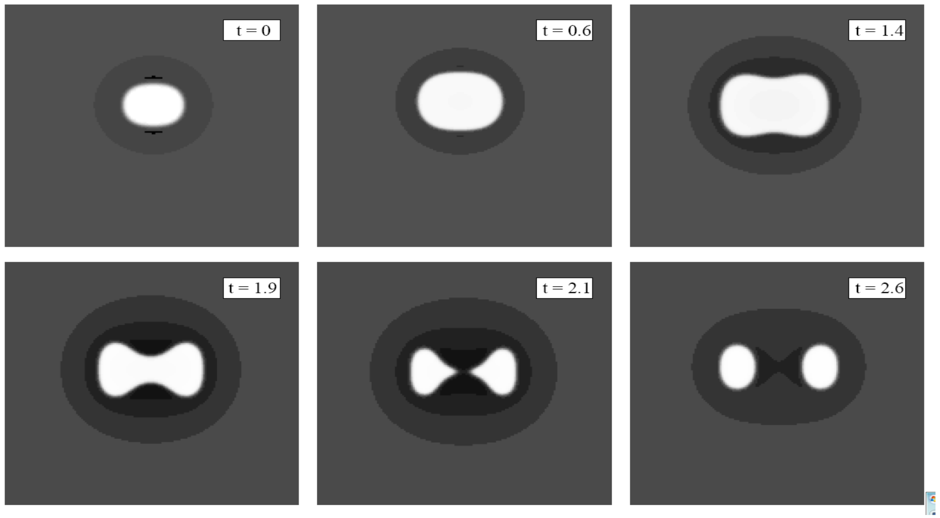
- A planar gas discharge system. (Astrov & Purwins, Phys. Lett. A, V. 283, (2001), pp. 349-354. Such systems often modeled by 3-component RD systems.

Part III: Numerical Evidence of Spot-Splitting

- Pearson, *Complex Patterns in a Simple System*, Science, **216**.
- Nishiura & Ueyama, *Spatial-Temporal Chaos in the Gray-Scott model*, Physica D, **150**, (3-4), (2001), pp. 137–152.
- Muratov & Osipov, *Scenarios of Domain Pattern Formation in Reaction-Diffusion Systems*, Phys. Rev. E, **54**, (1996), pp. 4860–4879.
- Self-replication of spots for the Schnakenburg model in a 2-D domain (**Ref:** J. Zhu, J. Zhang, S. Newman, M. Alber, J. Sci. Comput., (2009). Also **Ref:** A. Madvamuse, P. Maini, JCP, **225**, (2007), pp. 100-119.



Left: Pearson (1993).



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, represeting 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, Promisolow, 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 ε.
  - 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 Ω under Neumann BC, consider

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

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.

Ref: [KWW]: Kolokolnikov, MJW, Wei, *Spot Self-Replication and Dynamics for the Schnakenburg Model...* J. Nonl. Sci., 19, (2009), pp. 1–56.

Ref: [CW]: Wan Chen, MJW, *Localized Spot Patterns for the Gray Scott Model*, Parts I, II; under review for SIADS (2010).

Part III: The Quasi-Equilibrium Solution

Inner Region: near a spot location $x_j \in \Omega$ define $\mathcal{V}_j$ and $\mathcal{U}_j$ by

$$u = \frac{1}{\sqrt{D}} \mathcal{U}_j(\boldsymbol{y}) \,, \quad v = \sqrt{D} \mathcal{V}_j(\boldsymbol{y}) \,, \quad \boldsymbol{y} = \varepsilon^{-1}(\boldsymbol{x} - x_j) \,, \quad x_j = x_j(\varepsilon^2 t) \,.$$

To leading order, $\mathcal{U}_j$ and $\mathcal{V}_j$ are radially symmetric and

$$V_{j\rho\rho} + \frac{1}{\rho} V_{j\rho} - V_j + U_j V_j^2 = 0 \,, \quad U_{j\rho\rho} + \frac{1}{\rho} U_{j\rho} - U_j V_j^2 = 0 \,, \quad 0 < \rho < \infty \,,$$
$$V_j \to 0 \,, \qquad U_j \sim S_j \log \rho + \chi(S_j) + o(1) \,, \quad \text{as} \quad \rho = |\boldsymbol{y}| \to \infty \,.$$

- 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

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

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

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

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

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*

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

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

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

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

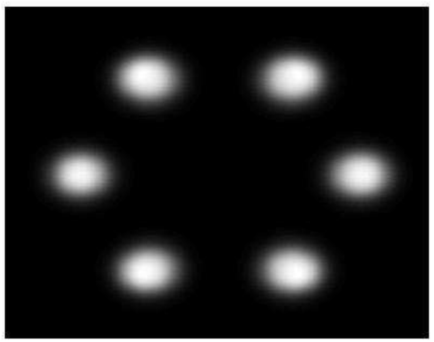
Here $G_{j,i} \equiv G(x_j; x_i)$ and $R_{j,j} \equiv R(x_j; x_j)$ (Neumann G-function).

Part III: An Example

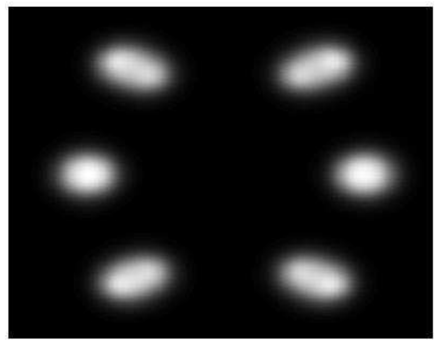
Let $\Omega = [0,1]^2$, $\varepsilon = 0.02$, $a = 51$, $D = 0.1$ and let

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

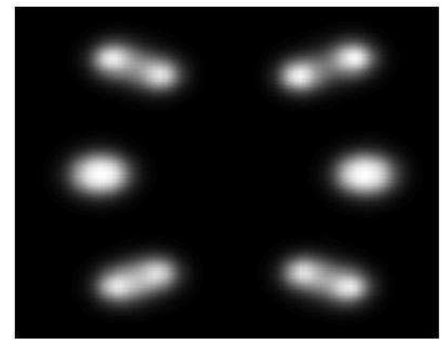
The DAE system gives $S_1 = S_4 \approx 4.01$, and $S_2 = S_3 = S_5 = S_6 \approx 4.44$. Thus, since $\Sigma_2 \approx 4.3$, we predict that four spots split (movie). The DAE system closely tracks the spots after the splitting.



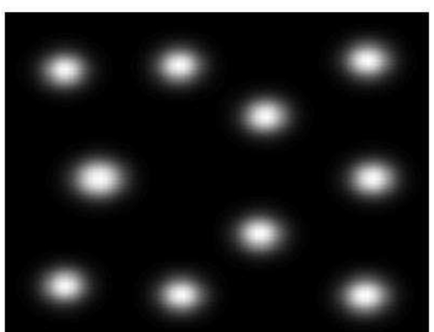
$t = 4.0$



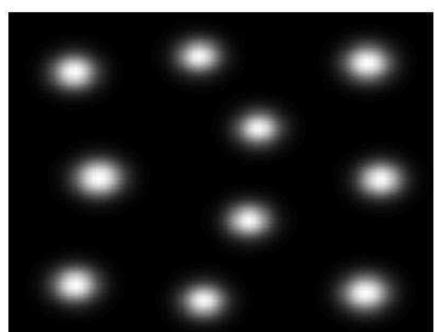
$t = 25.5$



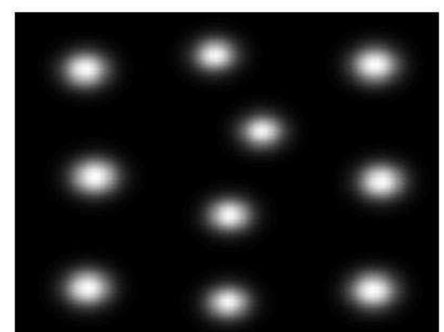
$t = 40.3$.



$t = 280.3$



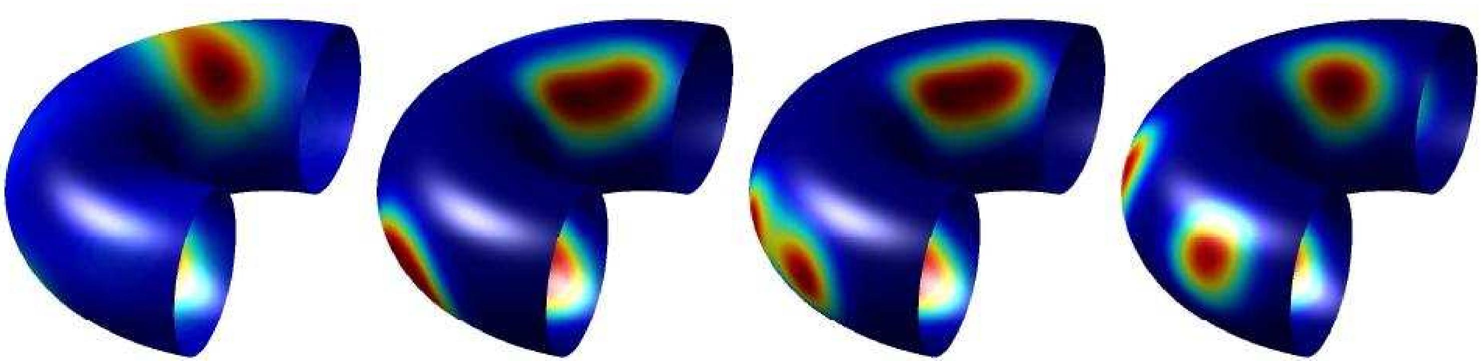
$t = 460.3$



$t = 940.3$.

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 occuring in the interior Note: Schnakenburg model on a Manifold: S. Ruuth (JCP, 2008), C. McDonald



A Little Philosophy

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...).

(Hong Kong 1, April 2010).
(Hong Kong 2, April 2010).

Many Thanks

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