Localized Patterns in Diffusive and Reaction-Diffusion Systems

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Overview: Localized Patterns in Diffusive Systems

Examples:

- Narrow escape and capture problems involving a particle undergoing Brownian motion to get absorbed by a trap set of small measure. (Berg-Purcell problem (Lecture 2)).
- Persistence threshold for a biological species in an environment with highly patchy food resources. Effect of fragmentation? (Lecture 2).
- Models inspired by bacterial communication involving the coupling of small dynamically active "cells" through a 2-D bulk diffusion field (Lecture 3).
- Existence, linear stabilty, and dynamics of localized spot patterns for activator-inhibitor reaction-diffusion systems in the limit of large diffusivity ratio (Lecture 4).

Ref: M. J. Ward, Spots, Traps, and Patches: Asymptotic Analysis of Localized Solutions to some Linear and Nonlinear Diffusive Processes, Nonlinearity, **31**(8), (2018), R189 (53 pages). (invited review article)

Strong Localized Perturbation Theory

Common Themes

- All are singular perturbation problems that require different spatial scales to resolve the localized features.
- Strong localized perturbation theory (SLPT) is a singular perturbation method that is tailored specifically for resolving small spatial features. Localized regions are replaced in the limit $\varepsilon \to 0$ by certain singularity structures for the problem on the macroscale.
- On the macroscale, the solution is represented by a Green's functions, and Green's matrices arise to characterize the interactions between localized regions.
- For 2-D problems, the expansion parameter is $\nu = -1/\log \varepsilon$ arising from the $\log r$ behavior of the Green's function for the Laplacian.
- To achieve high accuracy, need a methodology to "sum" the effect of logarithmic interactions $\sum a_j \nu^j$, rather than a finite series truncation.

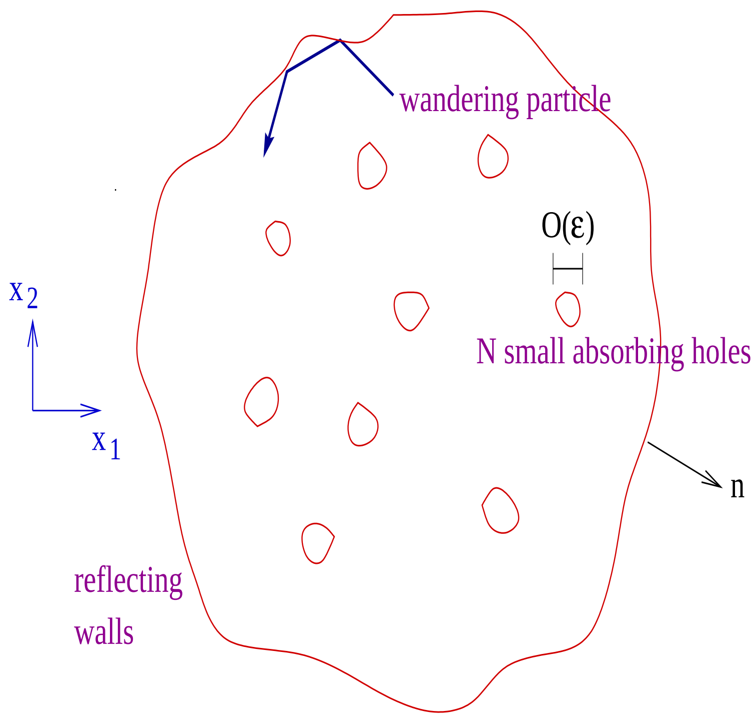
Ref: M. J. Ward, Asymptotics for Strong Localized Perturbation Theory: Theory and Applications, (lecture Notes for 4th winter school in Applied Mathematics, 2010, City U. Hong Kong), (101 pages).

https://www.cityu.edu.hk/ma/ws2010/doc/ward_notes.pdf

MFPT in a Bounded 3-D Domain (SLPT): I

The MFPT $T(\mathbf{x})$ for a Brownian particle starting at $\mathbf{x}$ with diffusivity D satisfies

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



Here Ω_a is the multiply-connected absorbing set. The average MFPT (uniform distribution for $\mathbf{x}$) is

$$\bar{T} \equiv \frac{1}{|\Omega_p|} \int_{\Omega_p} T(\mathbf{x})\, d\mathbf{x}\,, \quad |\Omega_p| \equiv |\Omega \backslash \Omega_a|\,.$$

- The average MFPT $\bar{T}$ is given asymptotically for $\varepsilon \to 0$ in terms of the principal eigenvalue λ_0 of the Laplacian by

$$\bar{T} \sim \frac{1}{D\lambda_0} + \mathcal{O}(\varepsilon)\,.$$

- For $\varepsilon \to 0$, we estimate $\bar{T} = \mathcal{O}(\varepsilon^{-1})$ and $\lambda_0 = \mathcal{O}(\varepsilon)$.

MFPT in a Bounded 3-D Domain (SLPT): II

Using a SLPT asymptotic analysis our main result is as follows:

Principal Result *In the limit $\varepsilon \to 0$ of small trap radius, the average MFPT $\bar{T}$, based on a uniform distribution of starting points for the Brownian motion, is*

$$\bar{T} \sim \frac{|\Omega|}{4\pi N \bar{C} D \varepsilon} \left[1 + \frac{4\pi\varepsilon}{N\bar{C}} p_c(\mathbf{x}_1, \ldots, \mathbf{x}_N) + \mathcal{O}(\varepsilon^2) \right] ,$$

where $\bar{C} = N^{-1} \sum_j C_j$ and C_j is the capacitance of the j-th trap. Here $p_c(\mathbf{x}_1, \ldots, \mathbf{x}_N) = \mathbf{c}^T \mathcal{G} \mathbf{c}$, where $\mathbf{c} \equiv (C_1, \ldots, C_N)^T$ and $\mathcal{G}$ is the Neumann Green's matrix. For N identical traps with a common capacitance C, we get

$$\bar{T} \sim \frac{|\Omega|}{4\pi N C D \varepsilon} \left[1 + \frac{4\pi\varepsilon C}{N} p(\mathbf{x}_1, \ldots, \mathbf{x}_N) + \mathcal{O}(\varepsilon^2) \right] ,$$

$$p(\mathbf{x}_1, \ldots, \mathbf{x}_N) = \mathbf{e}^T \mathcal{G} \mathbf{e} \equiv \sum_{i=1}^{N} \sum_{j=1}^{N} \mathcal{G}_{i,j} \, , \quad \mathbf{e} \equiv (1, \ldots, 1)^T \, .$$

Remark: $\mathcal{G}$ is the Green's interaction matrix and represents the effect of trap-trap interactions.

MFPT in a Bounded 3-D Domain (SLPT): III

We will derive this (for simplicity) when there are N small spherical traps, of radius εr_j. In the outer region, we expand

$$T = \varepsilon^{-1} T_0 + T_1 + \epsilon T_2 + \cdots \,,$$

where T_0 is an unknown constant to be determined.

The problem for T_1 is

$$\begin{cases} \Delta T_1 = -1/D & \text{for } \mathbf{x} \in \Omega \backslash \{\mathbf{x}_1, \ldots, \mathbf{x}_N\} \\ \partial_n T_1 = 0 & \text{for } \mathbf{x} \in \partial\Omega \\ T_1 \text{ singular} & \text{as } \mathbf{x} \to \mathbf{x}_j \,, \quad j = 1, \ldots, N \,, \end{cases}$$

while T_2 satisfies

$$\begin{cases} \Delta T_2 = 0 & \text{for } x \in \Omega \backslash \{\mathbf{x}_1, \ldots, \mathbf{x}_N\} \\ \partial_n T_2 = 0 & \text{for } \mathbf{x} \in \partial\Omega \\ T_2 \text{ singular} & \text{as } \mathbf{x} \to \mathbf{x}_j \,, \quad j = 1, \ldots, N \,. \end{cases}$$

Remark: In the outer region the traps shrink to points. The effect of the traps is replaced by a singularity condition (to be derived) at each order.

MFPT in a Bounded 3-D Domain (SLPT): IV

In the j-th inner region we let $\mathbf{y} = \epsilon^{-1}(\mathbf{x} - \mathbf{x}_j)$ and $w(\mathbf{y}) \equiv T(\mathbf{x}_j + \epsilon \mathbf{y})$, and we expand

$$w = \frac{w_0}{\epsilon} + w_1 + \cdots .$$

We obtain, upon using the matching condition $w_0 \to T_0$ as $|\mathbf{y}| \to \infty$, that

$$\begin{cases} \Delta_{\mathbf{y}} w_0 = 0 & \text{for } |\mathbf{y}| \geq r_j \\ w_0 = 0 & \text{for } |\mathbf{y}| = r_j \\ w_0 \to T_0 & \text{as } |\mathbf{y}| \to \infty . \end{cases}$$

The explicit solution is $w_0 = T_0(1 - w_c)$, where $w_c = C_j/|\mathbf{y}|$ and $C_j = r_j$. The matching condition for $\mathbf{x} \to \mathbf{x}_j$ becomes

$$\underbrace{\frac{T_0}{\epsilon} + T_1 + \epsilon T_2 + \cdots}_{\mathbf{x} \to \mathbf{x}_j} \sim \underbrace{\frac{w_0}{\epsilon} + w_1 + \cdots}_{\mathbf{y} \to \infty} = \frac{T_0}{\epsilon}\left(1 - \frac{C_j}{|\mathbf{x} - \mathbf{x}_j|}\epsilon\right) + w_1 + \cdots .$$

Therefore, we obtain the singularity behavior

$$T_1 \to -\frac{T_0 C_j}{|\mathbf{x} - \mathbf{x}_j|}, \quad \text{as} \quad \mathbf{x} \to \mathbf{x}_j .$$

MFPT in a Bounded 3-D Domain (SLPT): V

The problem for T_1 is simply

$$\begin{cases} \Delta T_1 = -1/D & \text{for } \mathbf{x} \in \Omega \backslash \{\mathbf{x}_1, \ldots, \mathbf{x}_N\} \\ \partial_n T_1 = 0 & \text{for } \mathbf{x} \in \partial\Omega \\ T_1 \sim -\frac{T_0 C_j}{|\mathbf{x}-\mathbf{x}_j|} & \text{as } \mathbf{x} \to \mathbf{x}_j\,, \; j = 1, \ldots, N\,, \end{cases}$$

which is equivalent to

$$\begin{cases} \Delta T_1 = -1/D + 4\pi T_0 \sum_{j=1}^{N} C_j \delta(\mathbf{x} - \mathbf{x}_j) & \text{for } \mathbf{x} \in \Omega \\ \partial_n T_1 = 0 & \text{for } \mathbf{x} \in \partial\Omega\,. \end{cases}$$

Upon using the divergence theorem, we obtain that

$$-\frac{|\Omega|}{D} + 4\pi T_0 \sum_{j=1}^{N} C_j = 0\,.$$

This yields the leading-order outer solution as

$$T \sim \frac{T_0}{\epsilon}\,, \qquad \text{where} \qquad T_0 = \frac{|\Omega|}{4\pi D \sum_{j=1}^{N} C_j}\,, \qquad C_j = r_j\,.$$

MFPT in a Bounded 3-D Domain (SLPT): VI

To solve for T_1, we define the Neumann Green's function $G(\mathbf{x};\mathbf{x}_j)$ by

$$\Delta G = \frac{1}{|\Omega|} - \delta(\mathbf{x}-\mathbf{x}_j)\,, \quad \mathbf{x}\in\Omega\,; \quad \partial_n G = 0\,, \quad \mathbf{x}\in\partial\Omega\,; \quad \int_\Omega G\, d\mathbf{x} = 0\,,$$

$$G(\mathbf{x};\mathbf{x}_j) \sim \frac{1}{4\pi|\mathbf{x}-\mathbf{x}_j|} + R_j + o(1)\,, \quad \text{as} \quad \mathbf{x}\to\mathbf{x}_j\,,$$

where R_j, which depends on $\mathbf{x}_j$ and Ω, is called the regular part of G.
The solution for T_1 is simply

$$T_1 = -4\pi T_0 \sum_{i=1}^{N} C_i G(\mathbf{x};\mathbf{x}_i) + \bar{T}_1\,,$$

where $\bar{T}_1$ to be found. Now as $\mathbf{x}\to\mathbf{x}_j$ we obtain

$$T_1 \sim B_j + \bar{T}_1 - \frac{C_j}{|\mathbf{x}-\mathbf{x}_j|}\,, \quad \text{as} \quad \mathbf{x}\to\mathbf{x}_j\,,$$

where B_j is defined by

$$B_j = -4\pi T_0 \left(C_j R_j + \sum_{i\neq j}^{N} C_i G(\mathbf{x}_j;\mathbf{x}_i) \right).$$

MFPT in a Bounded 3-D Domain (SLPT): VII

We return to the matching condition

$$\frac{T_0}{\epsilon} + T_1 + \epsilon T_2 + \cdots \sim \frac{w_0}{\epsilon} + w_1 + \cdots \,,$$

which becomes

$$\frac{T_0}{\epsilon} + B_j + \bar{T}_1 - \frac{T_0 C_j}{|\mathbf{x} - \mathbf{x}_j|} + \epsilon T_2 \sim \frac{T_0}{\epsilon}\left(1 - \frac{C_j \epsilon}{|\mathbf{x} - \mathbf{x}_j|}\right) + w_1 \,.$$

This implies that for each $j = 1, \ldots, N$, w_1 must satisfy

$$\begin{cases} \Delta_y w_1 = 0 & \text{for } |\mathbf{y}| \geq r_j \\ w_1 = 0 & \text{for } |\mathbf{y}| = r_j \\ w_1 \sim B_j + \bar{T}_1 & \text{as } |\mathbf{y}| \to \infty \,. \end{cases}$$

The solution is given explicitly by

$$w_1 = (B_j + \bar{T}_1)\left(1 - \frac{C_j}{|\mathbf{y}|}\right) \,,$$

where $C_j = r_j$ is the capacitance of the j-th trap.

MFPT in a Bounded 3-D Domain (SLPT): VIII

Substituting this back into the matching condition we get that T_2 satisfies

$$\begin{cases} \Delta T_2 = 0 & \text{for } \mathbf{x} \in \Omega \backslash \{\mathbf{x}_1, \ldots, \mathbf{x}_N\} \\ \partial_n T_2 = 0 & \text{for } \mathbf{x} \in \partial\Omega \\ T_2 \sim -\left(B_j + \bar{T}_1\right) \frac{C_j}{|\mathbf{x}-\mathbf{x}_j|} & \text{as } \mathbf{x} \to \mathbf{x}_j \quad j = 1, \ldots, N\,. \end{cases}$$

This problem is equivalent to

$$\Delta T_2 = 4\pi \sum_{j=1}^{N} (B_j + \bar{T}_1) C_j \delta(\mathbf{x} - \mathbf{x}_j) \qquad \mathbf{x} \in \Omega\,; \quad \partial_n T_2 = 0\,, \quad \text{on} \quad \partial\Omega\,.$$

Finally, we determine $\bar{T}_1$ by the divergence theorem as

$$\sum_{j=1}^{N} (B_j + \bar{T}_1) C_j = 0\,, \qquad \to \qquad \bar{T}_1 = -\frac{\sum_{j=1}^{N} B_j C_j}{\sum_{j=1}^{N} C_j}\,.$$

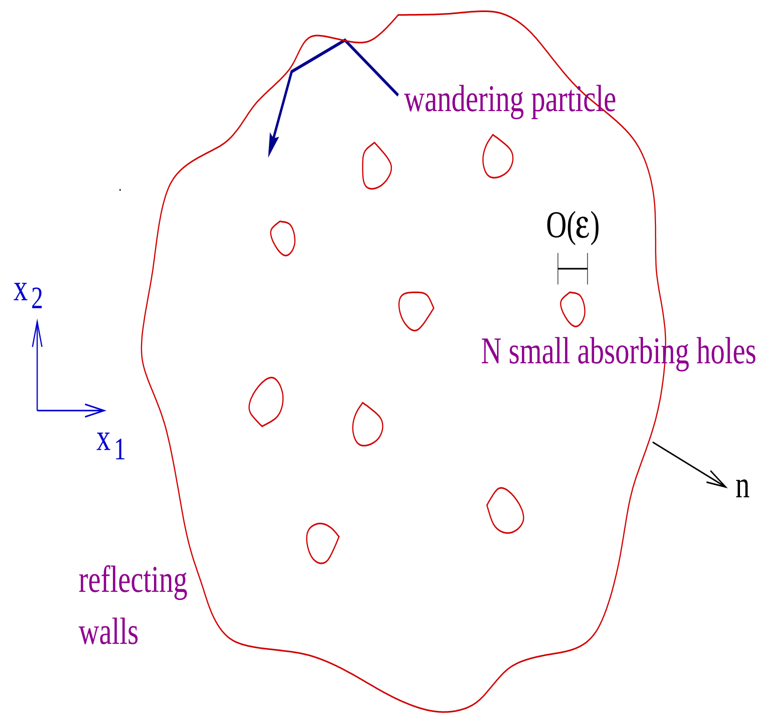
By using our result for B_j, we can write the average MFPT $\bar{T} = \varepsilon^{-1} T_0 + \bar{T}_1 + \cdots$ as the quadratic form (as stated earlier)

$$\bar{T} \sim \varepsilon^{-1} T_0 + \bar{T}_1 + \cdots\,, \qquad T_0 = \frac{|\Omega|}{4\pi D N \bar{C}}\,, \qquad \bar{T}_1 = \frac{4\pi T_0}{N \bar{C}} \mathbf{c} \mathcal{G} \mathbf{c}\,,$$

MFPT in a Bounded 2-D Domain (SLPT): I

The MFPT $T(\mathbf{x})$ for a Brownian particle starting at $\mathbf{x}$ with diffusivity D satisfies

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



Here Ω_a is the multiply-connected absorbing set. The average MFPT (uniform distribution for $\mathbf{x}$) is

$$\bar{T} \equiv \frac{1}{|\Omega_p|} \int_{\Omega_p} T(\mathbf{x})\, d\mathbf{x}\,, \quad |\Omega_p| \equiv |\Omega \backslash \Omega_a|\,.$$

- The key difference in this 2-D case is that the small parameters are $\nu_j = -1/\log[\varepsilon d_j]$, where d_j is the logarithmic capacitance of the j-th trap.
- We want an approximation for $\bar{T}$ that has an error smaller than any power of $(\max_j \nu_j)^m$ for any $m > 0$.

MFPT in a Bounded 2-D Domain (SLPT): II

In the outer region we expand

$$T \sim T_0(\mathbf{x};\boldsymbol{\nu}) + \sigma T_1(\mathbf{x};\boldsymbol{\nu}) + \cdots .$$

where $\boldsymbol{\nu} \equiv (\nu_1, \ldots, \nu_N)$ with $\nu_j \equiv -1/\log(\varepsilon d_j)$ for $j = 1, \ldots, N$. Here d_j is the logarithmic capacitance of the j-th trap. The correction term σ is assumed to satisfy $\sigma \ll \nu_j^m$ for each $j = 1, \ldots, N$ and $\forall m > 0$.

Remark: This (negligible) correction term is said to be beyond-all-orders or transcendentally small wrt all of the logarithmic terms captured by T_0.

We obtain that T_0 satisifes

$$\begin{cases} \Delta T_0 = -1/D & \text{for } \mathbf{x} \in \Omega \backslash \{\mathbf{x}_1, \ldots, \mathbf{x}_N\} \\ \partial_n T_0 = 0 & \text{for } \mathbf{x} \in \partial\Omega \\ T_0 \text{ singular} & \text{as } \mathbf{x} \to \mathbf{x}_j \,, \quad j = 1, \ldots, N \,, \end{cases}$$

Remark: In the outer region the traps shrink to points. The effect of the traps is replaced by a singularity structure (to be derived) at each order.

MFPT in a Bounded 2-D Domain (SLPT): III

In the j-th inner region, we let $\mathbf{y} = \varepsilon^{-1}(\mathbf{x} - \mathbf{x}_j)$ and define Ω_j by $\Omega_j = \varepsilon^{-1}\Omega_{\varepsilon j}$. We write $w_j(\mathbf{y}) = T(\mathbf{x}_j + \varepsilon \mathbf{y})$, and we expand

$$w_j \sim \nu_j \gamma_j(\boldsymbol{\nu}) w_{cj}(\mathbf{y}) + \alpha(\varepsilon, \boldsymbol{\nu}) w_{1j}(\mathbf{y}) + \cdots .$$

Here γ_j is an unknown constant to be determined. The gauge function α is assumed to be beyond-all-orders and satisfies $\alpha \ll \nu_j^m \; \forall m > 0$.

The leading term $w_{cj}(y)$ satisfies the canonical problem for the j-th trap:

$$\Delta_{\mathbf{y}} w_{cj} = 0 \,, \quad \mathbf{y} \notin \Omega_j \,; \qquad w_{cj} = 0 \,, \quad \mathbf{y} \in \partial\Omega_j \,,$$
$$w_{cj} \sim \log|\mathbf{y}| - \log d_j + o(1) \quad \text{as} \quad |\mathbf{y}| \to \infty \,.$$

The constant d_j is known as the logarithmic capacitance of Ω_j.

<u>**Remark:**</u> The logarithmic capacitance is known explicitly for various trap shapes (disk, ellipse, square, etc..). It is invariant under rotation.

MFPT in a Bounded 2-D Domain (SLPT): IV

Upon using the far-field behavior of w_{cj} as $|\mathbf{y}| \to \infty$, we obtain the following matching condition for T_0 for each $j = 1, \ldots, N$:

$$T_0(x, \boldsymbol{\nu}) \sim \nu_j \gamma_j \log |\mathbf{x} - \mathbf{x}_j| + \gamma_j + o(1)\,, \quad \text{as} \quad \mathbf{x} \to \mathbf{x}_j\,.$$

Key Observation: For each $j = 1, \ldots, N$, in the singularity structure for T_0 we are specifying both the strength of the singularity and the regular part of the singularity. For each j, the specification of the precise form of the regular part introduces one constraint for the determination of the γ_j.

The problem for T_0 is equivalent to

$$\Delta T_0 = -\frac{1}{D} + 2\pi \sum_{i=1}^{N} \nu_i \gamma_i \delta(\mathbf{x} - \mathbf{x}_i)\,, \quad \mathbf{x} \in \Omega\,; \quad \partial_n T_0 = 0\,, \quad \mathbf{x} \in \partial\Omega\,,$$

where T_0 must satisfy the singularity structure given above.

By applying the divergence theorem, we obtain the constraint that

$$\sum_{i=1}^{N} \nu_i \gamma_i = \frac{|\Omega|}{2\pi D}\,.$$

MFPT in a Bounded 2-D Domain (SLPT): V

Next, we write T_0 in terms of the Neumann Green's function G as

$$T_0 = -2\pi \sum_{i=1}^{N} \nu_i \gamma_i G(\mathbf{x}; \mathbf{x}_i) + \bar{T}_0 \,,$$

where $\bar{T}_0$ is the unknown average MFPT.

To determine the linear algebraic system, we expand T_0 as $\mathbf{x} \to \mathbf{x}_j$ and equate the resulting expression with the required singular behavior. This leads, for each $j = 1, \ldots, N$, to

$$-2\pi \sum_{i \neq j}^{N} \nu_i \gamma_i G(\mathbf{x}_j, \mathbf{x}_i) + \nu_j \gamma_j \log|\mathbf{x} - \mathbf{x}_j| - 2\pi \gamma_j \nu_j R_j + \bar{T}_0 \sim \nu_j \gamma_j \log|\mathbf{x} - \mathbf{x}_j| + \gamma_j \,.$$

From the nonsingular terms in this expression, together with the constraint from the divergence theorem, we obtain a linear algebraic system of dimension $N+1$ for $\bar{T}_0$ and for γ_j, for $j = 1, \ldots, N$.

MFPT in a Bounded 2-D Domain (SLPT): VI

Principal Result *For $\varepsilon \ll 1$, and for N arbitrarily shaped-traps of logarithmic capacitance d_j that concentrate to $\mathbf{x}_j$, for $j = 1, \ldots, N$, as $\varepsilon \to 0$, the asymptotic solution for the MFPT in the outer region is given by*

$$T_0 \sim -2\pi \sum_{j=1}^{N} \nu_j \gamma_j G(x; x_j) + \bar{T}_0 \,, \qquad \nu_j = -1/\log(\varepsilon d_j) \,.$$

Here the γ_j for $j = 1, \ldots, N$, and the constant $\bar{T}_0$ are the solution to the $N+1$ dimensional linear algebraic system

$$\gamma_j + 2\pi \gamma_j \nu_j R_j + 2\pi \sum_{i \neq j}^{N} \nu_i \gamma_i G(\mathbf{x}_j; \mathbf{x}_i) = \bar{T}_0 \,, \quad j = 1, \ldots, N \,,$$

$$\sum_{j=1}^{N} \nu_j \gamma_j = \frac{|\Omega|}{2\pi D} \,.$$

Remark: This linear algebraic system has the effect of summing all of the logarithmic corrections for $\bar{T}_0$.

MFPT in a Bounded 2-D Domain (SLPT): VII

Consider identical traps, where $d_j = d$ for all j, so that $\nu_j = \nu = -1/\log(\varepsilon d)$ for $j = 1, \ldots, N$.

Then, the linear system in matrix form is

$$\gamma + 2\pi\nu\mathcal{G}\gamma = \bar{T}_0\mathbf{e}\,, \qquad \mathbf{e}^T\gamma = \frac{|\Omega|}{2\pi D\nu}\,.$$

Here $\gamma = (\gamma_1, \ldots, \gamma_N)^T$, $\mathbf{e} = (1, \ldots, 1)^T$, and $\mathcal{G}$ is the Neumann Green's matrix with diagonal entries $R(\mathbf{x}_j)$ and off-diagonal entries $G(\mathbf{x}_i; \mathbf{x}_j)$.

For $\nu \to 0$, we need to expand

$$\gamma = \nu^{-1}\gamma_{\mathbf{0}} + \gamma_{\mathbf{1}} + \cdots\,, \qquad \bar{T}_0 = \nu^{-1}\chi_0 + \chi_1 + \cdots\,.$$

From the $\mathcal{O}(\nu^{-1})$ terms we get

$$\gamma_{\mathbf{0}} = \chi_0\mathbf{e}\,, \qquad \mathbf{e}^T\gamma_{\mathbf{0}} = \frac{|\Omega|}{2\pi D}\,,$$

so that

$$\chi_0 = \frac{|\Omega|}{2\pi D N}\,, \qquad \gamma_{\mathbf{0}} = \chi_0\mathbf{e}\,.$$

MFPT in a Bounded 2-D Domain (SLPT): VIII

From the $\mathcal{O}(1)$ terms, we get

$$\gamma_{\mathbf{1}} + 2\pi \mathcal{G} \gamma_{\mathbf{0}} = \chi_1 \mathbf{e} \,, \qquad \mathbf{e}^T \gamma_{\mathbf{1}} = 0 \,.$$

By taking the dot product with $\mathbf{e}^T$ we get

$$\chi_1 = \frac{2\pi}{N} \mathbf{e}^T \mathcal{G} \gamma_{\mathbf{0}} = \frac{2\pi \chi_0}{N} \mathbf{e}^T \mathcal{G} \mathbf{e} \,.$$

This yields the two-term expansion for the average MFPT

$$\bar{T}_0 \sim \frac{|\Omega|}{2\pi D N \nu} \left(1 + \frac{2\pi}{N} \nu \mathbf{e}^T \mathcal{G} \mathbf{e} \right) \,.$$

Finally, we substitute this last expression into the eigenvalue estimate

$$\lambda_0 \sim 1/(D \bar{T}_0) \,.$$

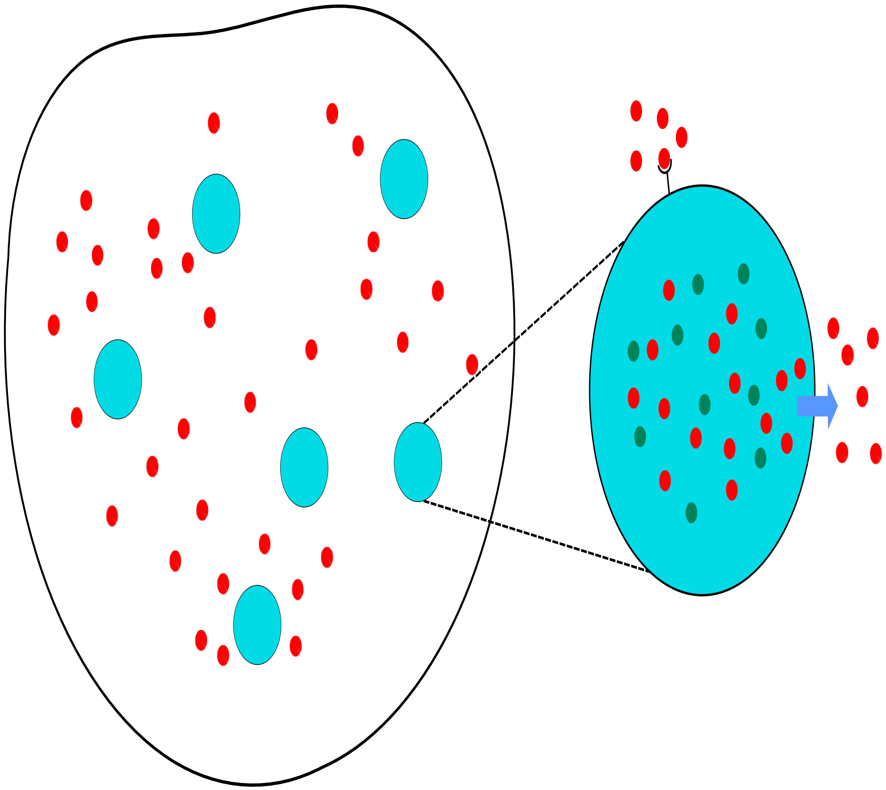
This yields the two-term estimate for the principal eigenvalue of the 2-D Laplacian in a domain with small traps:

$$\lambda_0 \sim \frac{2\pi N \nu}{|\Omega|} \left(1 - \frac{2\pi \nu}{N} p(\mathbf{x}_1, \ldots, \mathbf{x}_N) \right) \,, \qquad p(\mathbf{x}_1, \ldots, \mathbf{x}_N) \equiv \mathbf{e}^T \mathcal{G} \mathbf{e} \,.$$

Lecture 3: Active Cells Coupled by Bulk Diffusion

Formulate and analyze a model of (ODE) dynamically active small “cells”, with arbitrary intracellular kinetics, that are coupled spatially by a linear bulk-diffusion field (PDE) in a bounded 2-D domain.

Motivation: Inspired by problems of bacterial communication through an autoinducer: leads to collective dynamics and synchronization.



- m circular cells. Each contains n chemicals $\mu_j = (\mu_{1j}, \ldots, \mu_{nj})^T$. When isolated they interact via ODE's $\mathbf{d}\mu_j/dt = \mathbf{F}_j(\mu_{\mathbf{j}})$.
- A scalar bulk diffusion field (autoinducer) diffuses in the space between the cells:

$$\mathcal{U}_T = D_B \Delta_{\mathbf{X}} \mathcal{U} - k_B \mathcal{U} \,.$$

- There is an exchange across the cell membrane, regulated by permeability parameters, between the autoinducer and one intracellular species (Robin condition).

Formulation of the 2-D Model

- Our PDE-ODE coupled cell-bulk model in 2-D with m cells is

$$\mathcal{U}_T = D_B \Delta_{\boldsymbol{X}} \mathcal{U} - k_B \mathcal{U}\,, \quad \boldsymbol{X} \in \Omega \setminus \cup_{j=1}^{m} \Omega_j\,; \quad \partial_{n_{\boldsymbol{X}}} \mathcal{U} = 0\,, \quad \boldsymbol{X} \in \partial\Omega\,,$$

$$D_B \partial_{n_{\boldsymbol{X}}} \mathcal{U} = \beta_{1j} \mathcal{U} - \beta_{2j} \mu_j^1\,, \qquad \boldsymbol{X} \in \partial\Omega_j\,, \quad j = 1, \ldots, m\,.$$

  Each cell $\Omega_j \in \Omega$ is a disk of radius σ centered at some $\boldsymbol{X}_j \in \Omega$.

- Inside each cell there are n interacting species with mass vector $\boldsymbol{\mu}_j \equiv (\mu_j^1, \ldots, \mu_j^n)^T$ whose dynamics are governed by n-ODEs, with (rank-one) coupling via integration over the j-th "cell"-membrane $\partial\Omega_j$:

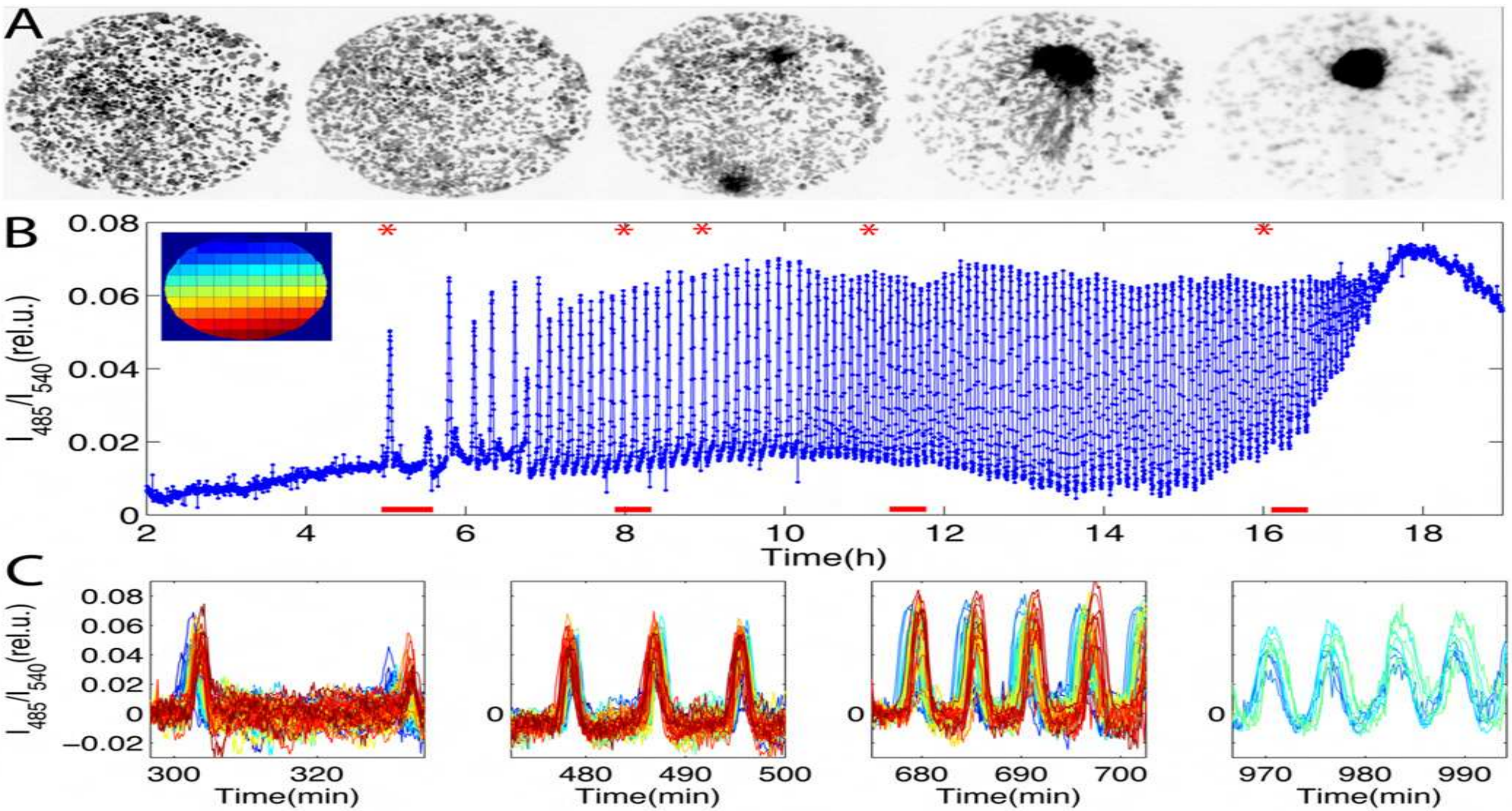
$$\frac{d\boldsymbol{\mu}_j}{dT} = k_R \mu_c \boldsymbol{F}_j \left(\boldsymbol{\mu}_j / \mu_c \right) + \boldsymbol{e}_1 \int_{\partial\Omega_j} \left(\beta_{1j} \mathcal{U} - \beta_{2j} \mu_j^1 \right) \, dS_j\,, \quad j = 1, \ldots, m\,,$$

  where $\boldsymbol{e}_1 \equiv (1, 0, \ldots, 0)^T$, and μ_c is typical mass.

- **Scaling Limit:** $\epsilon \equiv \sigma / L \ll 1$, where $L = \text{diam}(\Omega)$.
- Only one species μ_j^1 can cross the j-th cell membrane into the bulk.
- $k_R > 0$ is intracellular reaction rate; β_{1j}, β_{2j} are $\mathcal{O}(\varepsilon^{-1})$ permeabilities.
- The dimensionless function $\boldsymbol{F}_j(\boldsymbol{u}_j)$ models the intracellular dynamics.

Amoeba Colony (*Dictyostelium discoideum*)

- About 180 cells are confined into an area of 420 μm in diameter (2-D).
- When resources are scarce, each cell secretes cAMP into the medium.
- Main Question: Is the oscillation an intrinsic property of the cells or does it only occur at the population level?



Caption: The cells secrete cAMP into the medium which first initiates a coordinated collective response. On longer time-scale cells aggregate. **Ref:** The Onset of Collective Behavior in Social Amoebae, T. Gregor et al. Science 2010

Lecture 4: Spots for Singularly Perturbed RD Models

Spatially localized solutions can occur for singularly perturbed RD models

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

Assume semi-strong interactions: $\varepsilon \ll 1$ and $D = \mathcal{O}(1)$.

Key: Since $\varepsilon \ll 1$, v can be localized in space as a spot pattern, i.e. concentration at a discrete set of points.

Prototypical Kinetics: Brusselator, Gray-Scott, GM, Schnakenberg, etc..

Two Distinct Methodologies

- **Classical Approach**: stability of spatially uniform states, Turing and weakly nonlinear analysis of small amplitude patterns, leading to normal form amplitude equations.
- **Localized Patterns:** "Far-from equilibrium patterns" (Nishiura) consisting of "particles" interacting through a "diffusion field".
  - **Key:** $\nu = -1/\log \varepsilon$ is expansion parameter.
  - Spot interactions via Green's functions and Green's matrices
  - Optimization of stability thresholds yield new (discrete) variational problems.

RD Modeling with Localized Spots: I

- Biological morphogenesis (Meinhardt 1984–), gene expresssion time delays (Gaffney 2005–2010): (GM Model and its variants, delayed reaction-kinetics, etc) Analysis: Wei, Winter, MJW, Doelman, Kaper... 1998–.
- Chemical instabilities and self-replicating spot patterns in FIS reaction (Swinney 1994, Pearson 1994). (Gray Scott Model) Analysis: Doelman, Kaper, Gardner, Nishiura, Wei, Winter, Kolokolnikov, MJW, 2000–2012...
- Plant root-hair formation driven by auxin gradient (Payne, Grierson 2009): (Schnakenberg-type model with spatially heterogeneous nonlinearity). Analysis: Brena-Medina, Champneys, Avitabile, MJW, 2014–
- Spatial distribution of urban crime with or without police intervention (based on UCLA Group, Bertozzi, Short,..2009–); (3-component RD system with chemotaxis): Analysis of Crime Hotspots: Berestycki, Pitcher, Kolokolnikov, Ward, Wei, Winter, Tse,...
- Models of patchy patterns of vegetation in semi-arid environments (Doelman et al., Meron, etc.)

Example: Scaling Limit of Brusselator for Spots

Construct "Spot Patterns" for 2-D Brusselator (with no flux BC or on sphere):

$$V_\sigma = \epsilon_0^2 \Delta V + E_{\mathsf{f}} - (B+1)V + UV^2 \,, \quad U_\sigma = \mathcal{D}\Delta U + BV - UV^2 \,.$$

Asymptotic Limit: Assume large diffusivity ratio and small "fuel" E_{f}:

$$\epsilon_0 \ll 1 \,, \qquad D = \mathcal{O}(1) \,, \qquad E_{\mathsf{f}} = \epsilon_0 E_0 E(\mathbf{x}) \,.$$

Introduce: $V = E_0 v/\epsilon_0$, $U = \epsilon_0 B u / E_0$, and $\sigma = t/(B+1)$, to get:

<u>Non-Dimensional Brusselator</u>

$$v_t = \epsilon^2 \Delta v + \epsilon^2 E - v + f u^2 v \,, \quad \tau u_t = D\Delta u + \frac{1}{\epsilon^2}\left(v - uv^2\right)$$

where $E = E(\mathbf{x}) = \mathcal{O}(1)$. The non-dimensional parameters are

$$f \equiv \frac{B}{B+1} < 1 \,, \quad \tau \equiv \frac{(B+1)^2}{E_0^2} \,, \quad D \equiv \frac{\mathcal{D}(B+1)}{E_0^2} \,, \quad \epsilon \equiv \frac{\epsilon_0}{\sqrt{B+1}} \,.$$

Classical Theory: Turing-Type Analysis I

Classicial Turing Approach: The spatially uniform state is

$$v_e = \varepsilon^2 \mathrm{E}/(1-f)\,, \quad u_e = (1-f)/(\varepsilon^2 \mathrm{E})\,.$$

Turing-Type stability analysis: Introduce perturbation of the uniform state:

$$(u,v) = (u_e, v_e) + e^{\lambda t} Y_l^m(\theta,\phi)(\hat{u},\hat{v})\,, \qquad k^2 \equiv l(l+1)\,, \quad |m| \le l\,.$$

We obtain that λ satisfies $\tau\lambda^2 - T_k\lambda + d_k = 0$, where

$$T_k \equiv (2f-1)\tau - \tau\varepsilon^2 k^2 - \mathcal{D}k^2 - \frac{\varepsilon^2 \mathrm{E}^2}{(1-f)^2}\,,$$

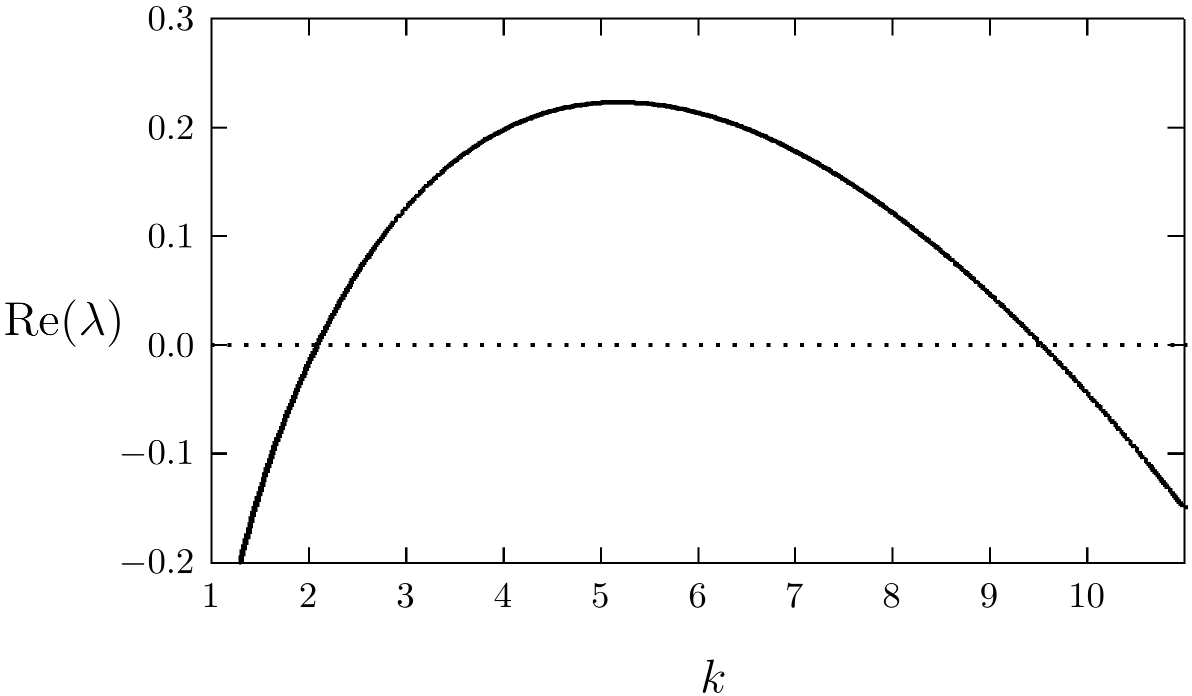
$$d_k \equiv \frac{\varepsilon^2 \mathrm{E}^2}{(1-f)} - (2f-1)\mathcal{D}k^2 + \mathcal{D}\varepsilon^2 k^4 + \frac{\varepsilon^4 \mathrm{E}^2 k^2}{(1-f)^2}\,,$$

with $k^2 \equiv l(l+1)$ and $|m| \le l$.

Key: For $\varepsilon \to 0$ and $f > 1/2$ (correspnding to $B > 1$) the (wide) instability band where Re$(\lambda) > 0$ is

$$0 < k_{\text{low}} < k < k_{\text{up}} \sim \sqrt{2f-1}/\varepsilon\,.$$

Classical Theory: Turing-Type Analysis II



Plot: Re(λ) versus k for $f = 0.8$, $\varepsilon = 0.075$, $\mathcal{D} = 0.2$, and $\mathrm{E} = 4$.

Key: For $\varepsilon \ll 1$, any $Y_l^m(\theta, \phi)$ with integers l and m satisfying $4.45 \leq l(l+1) \leq 91.6$ and $|m| \leq l$ is unstable. This gives $l = 2, \ldots, 9$.

Classical: Normal Form Theory

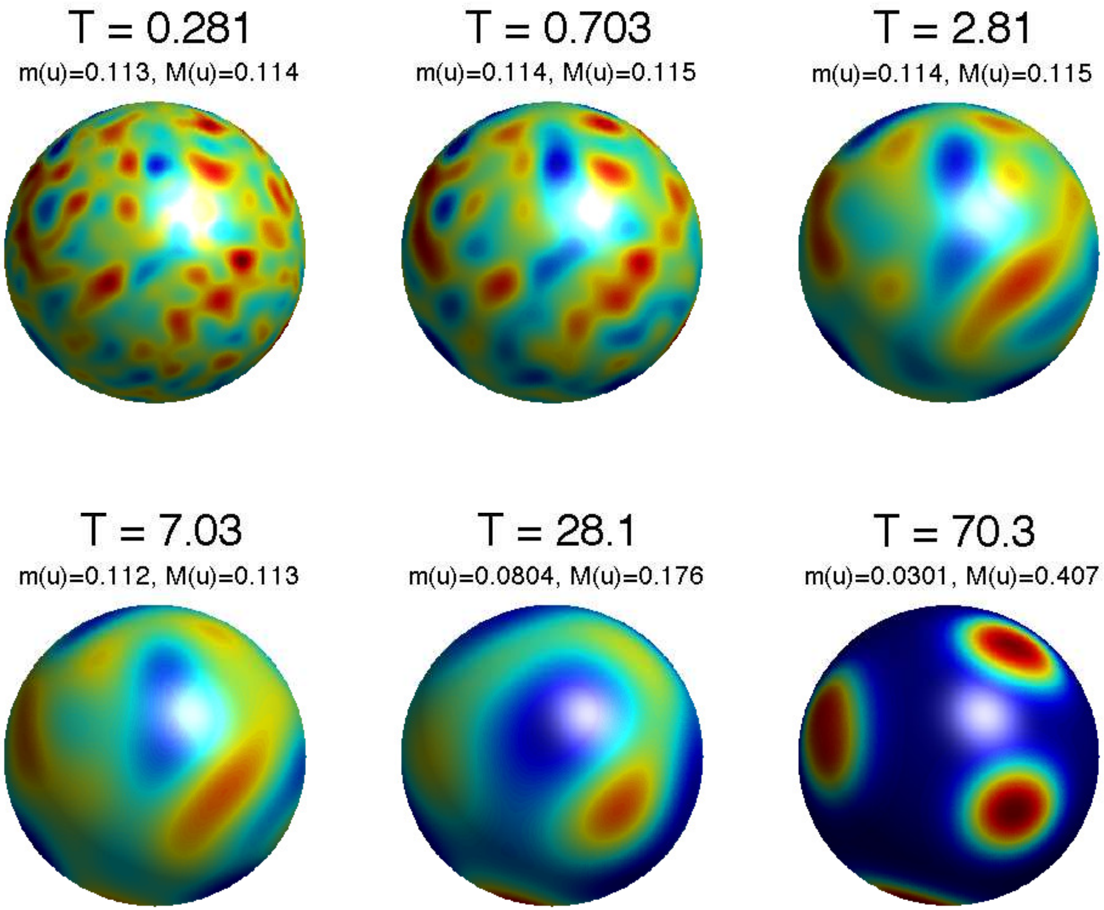
Fundamental Difficulty: The linear stability problem with $f > 1/2$ and $\varepsilon \ll 1$ is highly degenerate with many unstable modes of comparable growth rate. Pattern forms from weakly nonlinear interaction of many unstable modes with comparable growth rates.

Weakly Nonlinear Analysis: Non-Singular Limit

- Simultaneous zero-eigenvalue crossing due to degeneracy of spherical harmonics $Y_l^m(\theta, \phi)$.
- **Equivariant bifurcation theory** characterizes the form of coupled amplitude equations (Chossat, et al. ARMA 1990), which increase in size as l increases.
- However, quadratic terms predict instability, with possible re-stablization at cubic terms (through saddle-node).
- For $l = 1, \ldots, 6$ the coefficients in the normal form for the brusselator have been derived (Callaghan, Physica D 2003) in a tuning-limit where quadratic and cubic terms are of comparable order.

Brusselator Patterns: Numerics

Full Numerics: $f = 0.8$, $\varepsilon = 0.075$, $\mathcal{D} = 0.2$, **and** $\mathrm{E} = 4$. **The initial data is a** 2% **random perturbation from the spatially uniform state.**



Numerics: New PDE methodologies: “Closest Point Algorithms to Compute PDE’s on Surfaces”; S. Ruuth (SFU) , C. McDonald (Oxford, UBC).

Brusselator Patterns: Challenges

- Very complicated transient dynamics due to the weakly nonlinear interaction of many unstable spherical harmonics.
- A distinct localized pattern with 8 localized spots at $t \approx 70.3$.
- Due to mode degeneracy, linear and weakly nonlinear analysis is of only limited use in predicting pattern development.

Challenge: Develop a mathematical theory to analyze the existence, stability, and dynamics, of localized "far-from equilibrium" spot patterns.

- **Question 1:** Do such localized patterns undergo secondary instabilities on longer time-scales? (competition, self-replication, etc.)
- **Question 2:** Are spot dynamics similar to that of Eulerian point vortices?
- **Question 3:** Are steady-state spot patterns related to elliptic Fekete point distributions of point charges?

References:

- **[RRW] Rozada, Ruuth, Ward; The Stability of Localized Spot Patterns for the Brusselator on the Sphere**, SIADS **13**(1), (2014), pp. 564–627.
- **[TW] Trinh, Ward; Dynamics of Localized Spot Patterns for RD Systems on the Sphere**, Nonlinearity, **29**(3), (2016), pp. 766–806.

Brusselator on the Sphere: Quasi-Equilibria: I

$$v_t = \varepsilon^2 \Delta_s v + \varepsilon^2 \mathrm{E} - v + f v^2 u \,, \quad \tau u_t = D \Delta_s u + \frac{1}{\varepsilon^2}(v - v^2 u) \,.$$

Quasi-equilibrium patterns: Construct quasi-equilibrium localized spot patterns for $\varepsilon \to 0$ using SLPT.

Core Problem: Consider a collection of N spots centered at $\mathbf{x}_j \in \Omega$ for $j = 1, \ldots, N$. On the local-in-ε-tangent-plane at $\mathbf{x}_j$, we let

$$v \sim \sqrt{D} \left[V_j(\rho) + \cdots \right] \,, \qquad u \sim \frac{1}{\sqrt{D}} \left[U_j(\rho) + \cdots \right] \,,$$

where $\rho \equiv \varepsilon^{-1} |\mathbf{x} - \mathbf{x}_j|$. This leads to the BVP core problem:

$$\Delta_\rho V_{j0} - V_{j0} + f V_{j0}^2 U_{j0} = 0 \,, \qquad \Delta_\rho U_{j0} + V_{j0} - V_{j0}^2 U_{j0} = 0 \,,$$
$$V_{j0} \to 0 \,, \quad U_{j0} \sim S_j \log \rho + \chi + o(1) \quad \text{as } \rho \to \infty.$$

where $\Delta_\rho \equiv \partial^2_{\rho\rho} + \rho^{-1} \partial_\rho$. Here $\chi = \chi(S_j; f)$ must be computed numerically from a simple BVP solver.

Quasi-Equilibrium Patterns II

In the outer region we have

$$v \sim \varepsilon^2 \mathrm{E}\,, \qquad \varepsilon^{-2}\left(v - v^2 u\right) \to \mathrm{E} - 2\pi\sqrt{D}\sum_{j=1}^{N} S_j \delta(\mathbf{x}-\mathbf{x}_j)\,.$$

Outer Approximation: The leading-order inhibitor field satisfies

$$\Delta_s u = -\frac{\mathrm{E}}{D} + \frac{2\pi}{\sqrt{D}}\sum_{i=1}^{N} S_i \delta(\mathbf{x}-\mathbf{x}_i)\,, \qquad \sum_{i=1}^{N} S_i = \frac{\mathrm{E}|\Omega|}{2\pi\sqrt{D}}\,,$$

$$u \sim \frac{1}{\sqrt{D}}\left[S_j \log|\mathbf{x}-\mathbf{x}_j| - S_j \log\varepsilon + \chi(S_j)\right]\,, \quad \text{as} \quad \mathbf{x}\to\mathbf{x}_j\,, \quad j=1,\ldots,N\,.$$

In terms of the well-known source-neutral Green's function G, we have

$$u = -\frac{2\pi}{\sqrt{D}}\sum_{i=1}^{N} S_i G(\mathbf{x};\mathbf{x}_i) + \bar{u}\,,$$

where $G(\mathbf{x};\mathbf{x}_i) = -\frac{1}{2\pi}\log|\mathbf{x}-\mathbf{x}_i| + R$, with $R \equiv \frac{1}{4\pi}(\log 4 - 1)$, satisfies

$$\Delta_s G = \frac{1}{|\Omega|} - \delta(\mathbf{x}-\mathbf{x}_i)\,; \qquad \int_\Omega G\, ds = 0\,; \qquad G \sim -\frac{1}{2\pi}\log|\mathbf{x}-\mathbf{x}_i| + R \text{ as } \quad \mathbf{x}\to\mathbf{x}_j\,.$$

Quasi-Equilibrium Patterns III

Asymptotic Matching: to account for the regular part of the singularity structure gives for each $j = 1, \ldots, N$:

$$-\frac{2\pi}{\sqrt{D}} \left[-\frac{S_j}{2\pi} \log|\mathbf{x} - \mathbf{x}_j| + S_j R + \sum_{i \neq j} S_i G_{ji} \right] + \bar{u} \sim$$

$$\frac{1}{\sqrt{D}} \left[S_j \log|\mathbf{x} - \mathbf{x}_j| - S_j \log \varepsilon + \chi(S_j) \right] .$$

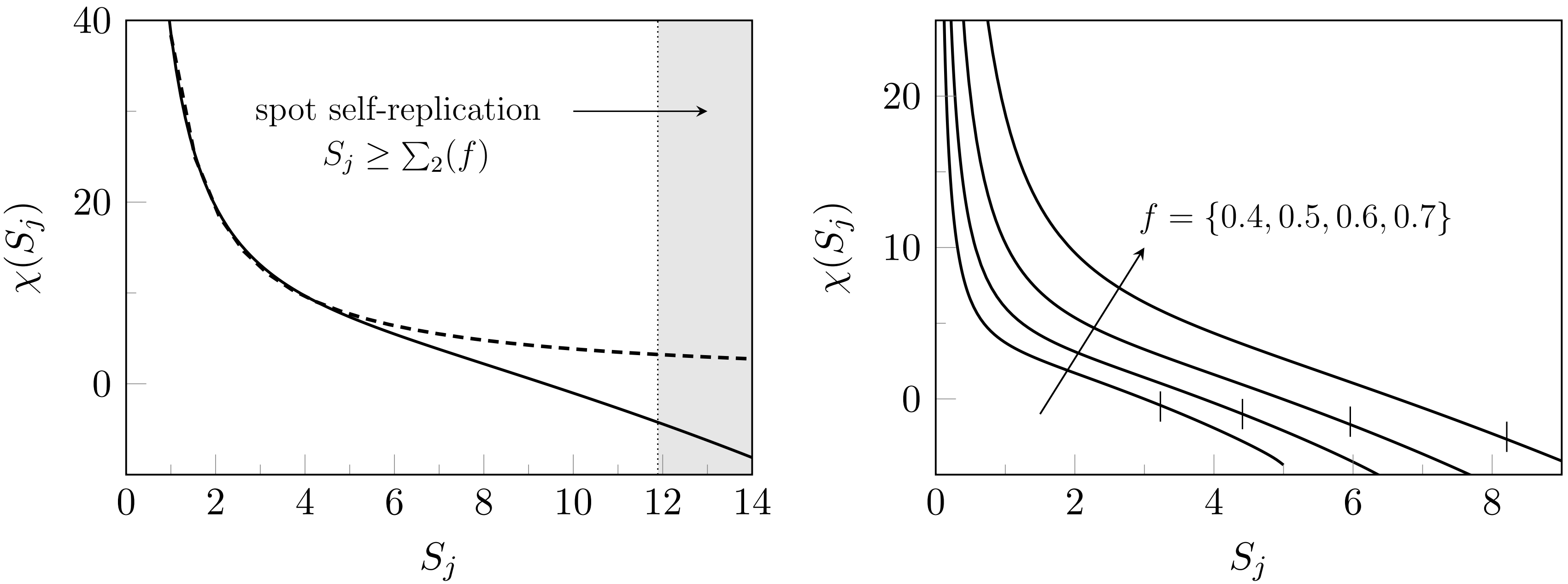
Upon using G, R and $|\Omega| = 4\pi$, we get for the sphere a nonlinear algebraic system (NAS) for the source strengths S_j:

$$S_j + \nu \chi(S_j; f) - \nu \sum_{\substack{i=1 \\ i \neq j}}^{N} S_i L_{ij} = \bar{u}_c \,, \quad j = 1, \ldots, N \,; \qquad \sum_{i=1}^{N} S_i = \frac{2\mathrm{E}}{\sqrt{D}} \,,$$

where ν, L_{ij}, and $\bar{u}_c$ are defined by

$$\nu \equiv -1/\log \varepsilon \,, \qquad L_{ij} = \log|\mathbf{x}_i - \mathbf{x}_j| \,, \qquad \bar{u} \equiv \frac{\bar{u}_c}{\nu} + (2\log 2 - 1)\mathrm{E} \,.$$

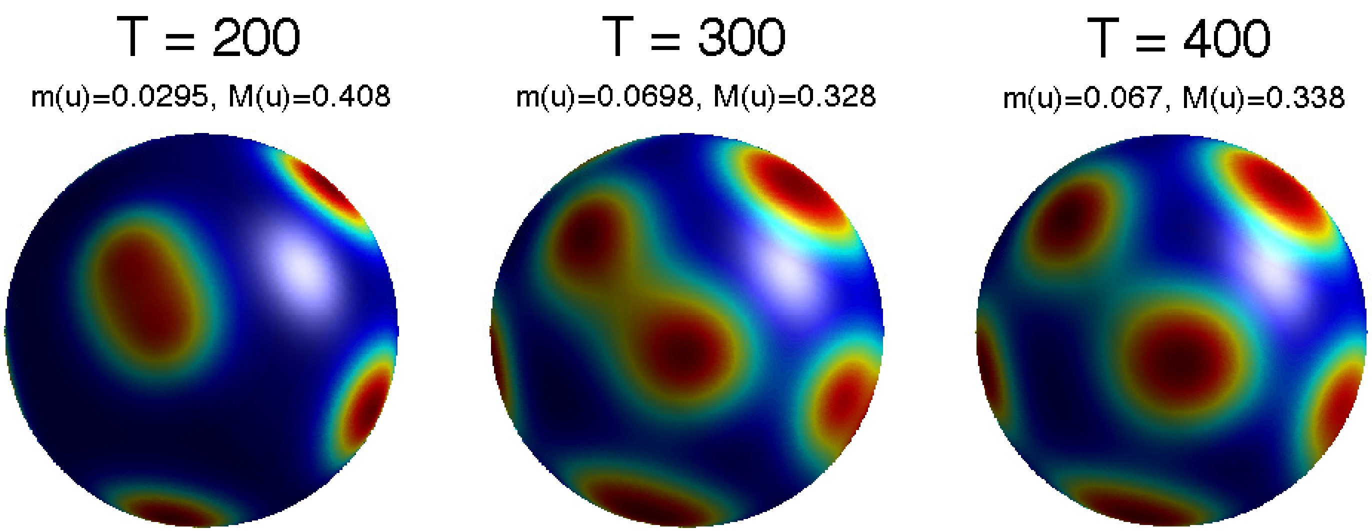
Quasi-Equilibrium Patterns IV



Caption: Left: χ versus S_j for $f = 0.3$ (heavy solid), compared with asymptotics. Right: χ versus S_j for $f = 0.4$, $f = 0.5$, $f = 0.6$, and $f = 0.7$, showing spot self-replication threshold $S_j = \Sigma_2(f)$ as thin vertical line.

Peanut-Splitting Instability: Numerical computations of a 1-D eigenvalue problem show that for $S_j > \Sigma_2(f)$, the j-th spot is linearly unstable on an $\mathcal{O}(1)$ time-scale to peanut-splitting. This is the trigger of a nonlinear spot self-replication event.

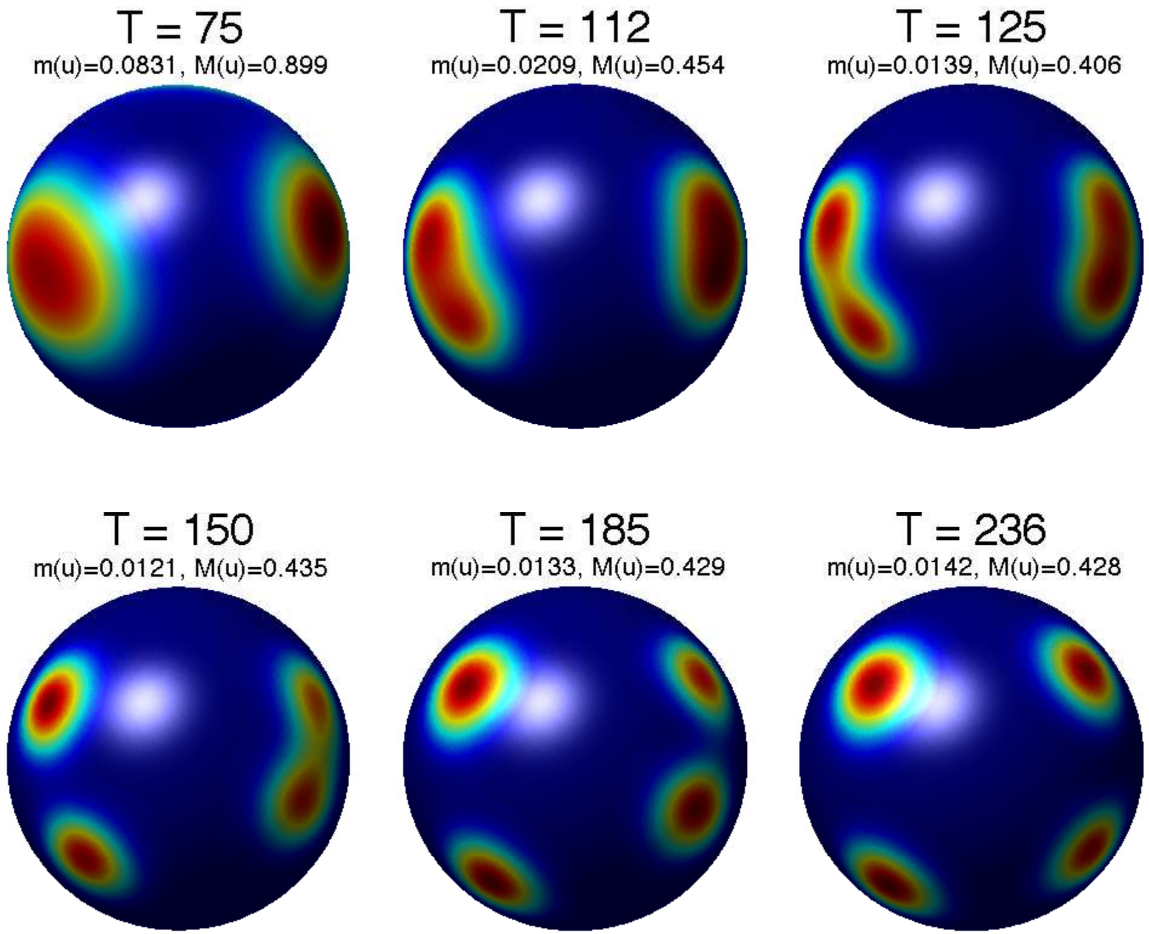
Spot Self-Replication



Plot: Solution at later times for $f = 0.8$, $\varepsilon = 0.075$, and $D = 0.2$. For $t \leq 70$ we take $\mathrm{E} = 4$. and then slowly increase E as $\mathrm{E} = \min(4 + 0.05(t - 70), 6)$.
Key: Spot self-replication occurs over a rather long time-scale due to dynamically-triggered bifurcation.

Spot self-replication (Another Example): Take $f = 0.7$, $\varepsilon = 0.06$, $D = 0.7$, and $\mathrm{E} = 2.5$ for $0 < t < 50$. Increase the fuel E as $\mathrm{E} = 2.5 + \sigma(t - 50)$ with $\sigma = 0.05$ for $t \geq 50$. Roughly simultaneous spot splitting occurs. (Movie)

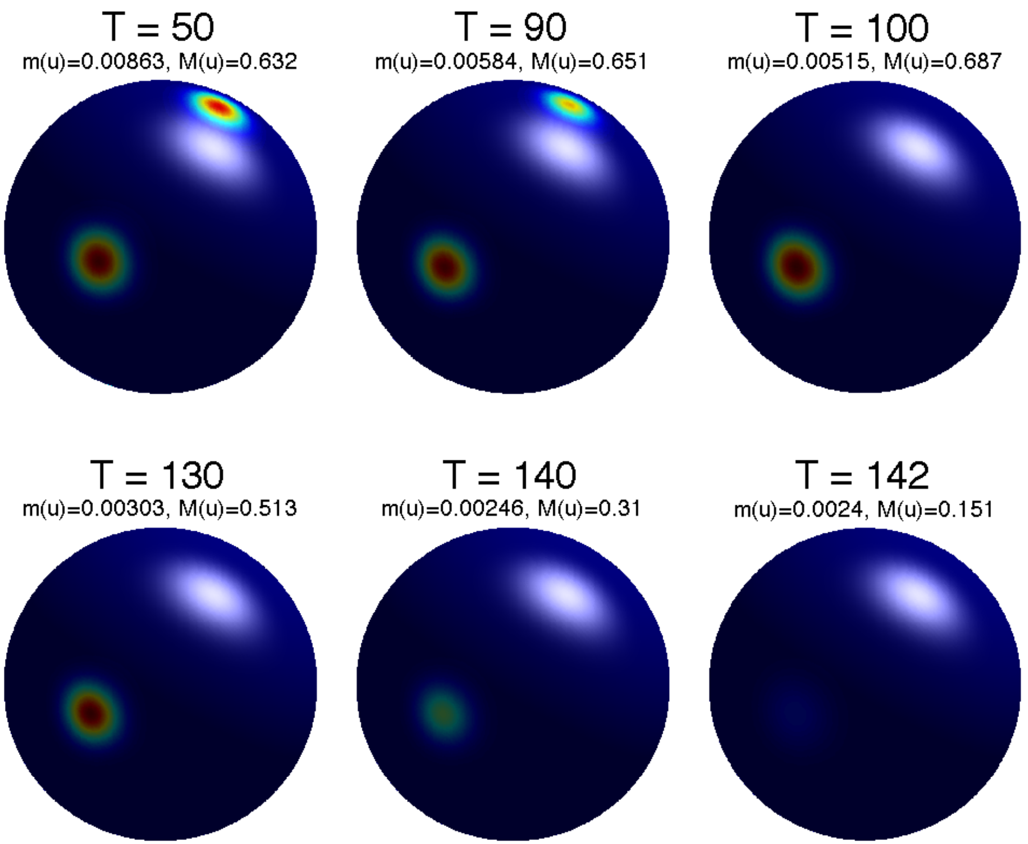
Self-Replication: Growing Domain



Plot: Solution at later times for $f = 0.8$, $\varepsilon = 0.12$, and $D = 1.0$. For $t \leq 70$ we take $\mathrm{E} = 4$. For $t \geq 75$ we take $\varepsilon = 0.12/L$ and $D = 1/L^2$, where $L = \min(1.0 + 0.02(t - 75), 2.0)$, for sphere of radius L.

Key: Four spots undergo (roughly) simultaneous spot self-replication.

Competitition Instabilities



Plot: Solution for $f = 0.7$, $\varepsilon = 0.06$, $D = 0.7$, and $\mathrm{E} = 2.5$. For $0 < t < 50$, we take $\mathrm{E} = 2.5$ for $0 \leq t \leq 50$, and then slowly decrease E as $\mathrm{E} = 2.5 - \sigma(t - 50)$ with $\sigma = 0.02$ for $t \geq 50$. The four-spot pattern that exists at the end of the transient dynamics undergoes a competition instability destroying two spots.

Three Main $\mathcal{O}(1)$-Time Scale Instabilities

Competition Instability: instability from a positive real eigenvalue with sign fluctuating eigenfunction. Triggers monotonic collapse of spots.

Oscillatory Instability: An instability due to a Hopf bifurcation with in-phase eigenfunction that triggers a synchronous oscillatory collapse of spots (subcritical?)

Self-Replication Instability: An instability of the shape of the spot profile to locally non-radially symmetric perturbations. This linear instability triggers a nonlinear spot-splitting event.

All Can Be Dynamically triggered: i.e. each $\mathcal{O}(1)$ time-scale instability can be triggered only at some later time through the collective slow dynamics of the spot locations. Bifurcations induced by intrinsic spot motion, not necessarily by externally varying control parameter.

Mathematical Challenge: Classify instability types and determine instability thresholds in a phase diagram in parameter space for certain equilibrium and quasi-equilibrium spot patterns. Characterize the slow dynamics of quasi-equilibria before/after fast instabilities.

Thanks For Your Attention!