Geometric Reconstruction in Bioluminescence Tomography (BLT)

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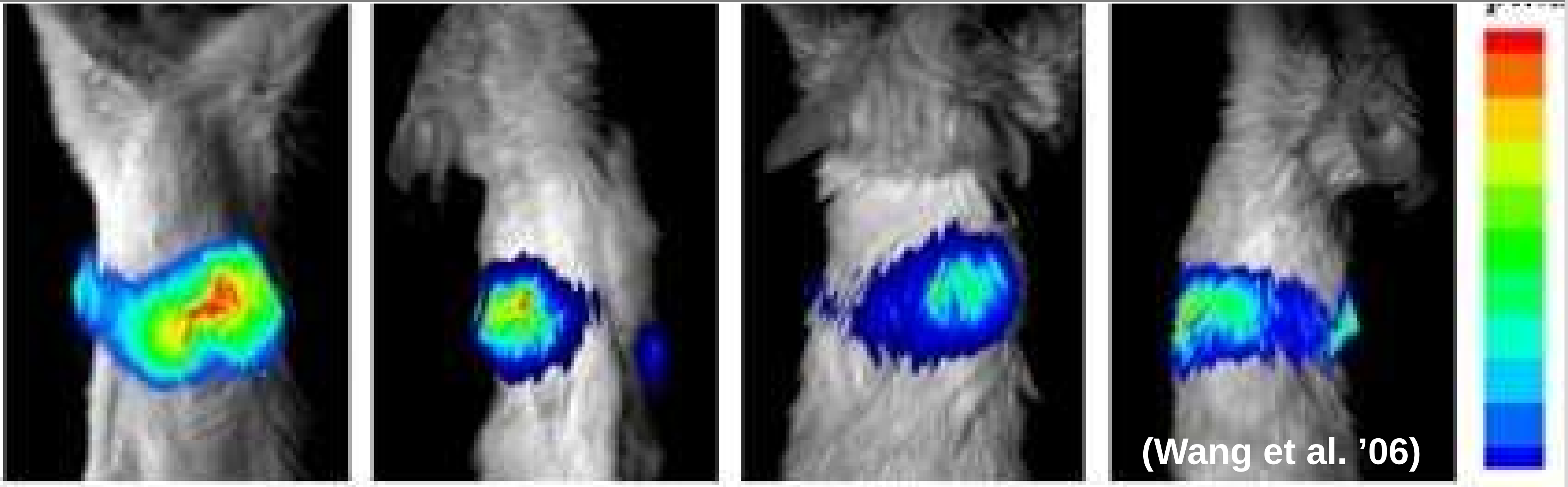

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Gradient of the minimization functional

Numerical experiments in 2D

Summary

Mathematical model

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The (stationary) radiative transfer equation (RTE)
(Boltzmann transport equation)

Let $u(x,\theta)$ be the photon flux (radiance) in direction $\theta \in S^2$ about $x \in \Omega \subset \mathbb{R}^3$. Then,

$$\theta \cdot \nabla u(x,\theta) + \mu(x) u(x,\theta) = \mu_{\mathrm{s}}(x) \int_{S^2} \eta(\theta \cdot \theta') u(x,\theta') \mathrm{d}\theta' + q(x,\theta)$$

$$u(x,\theta) = g^-(x,\theta), \quad x \in \partial\Omega, \ \mathbf{n}(x) \cdot \theta \le 0$$

$$g(x) = \frac{1}{4\pi} \int_{S^2} \mathbf{n}(x) \cdot \theta u(x,\theta) \mathrm{d}\theta, \quad x \in \partial\Omega$$

where $\mu = \mu_{\mathrm{s}} + \mu_{\mathrm{a}}$ and

μ_{s} / μ_{a}	scattering/absorption coefficients
η	scattering kernel ($\int_{S^2} \eta(\theta \cdot \theta') \mathrm{d}\theta' = 1$)
q	source term

$\mu_{\mathrm{s}} = 0$: RTE yields integral eqs. of transmission and emission tomography

(F. Natterer & F. Wübbeling, Math. Methods in Image Reconstr., SIAM, '01)

Diffusion approximation: setting

Assume that

$$u(x,\theta) = u_0(x) + 3\theta \cdot u_1(x)$$

where

$$u_0(x) = \frac{1}{4\pi}\int_{S^2} u(x,\theta)\mathrm{d}\theta \in \mathbb{R} \quad \text{and} \quad u_1(x) = \frac{1}{4\pi}\int_{S^2} \theta u(x,\theta)\mathrm{d}\theta \in \mathbb{R}^3.$$

By the Funk-Hecke theorem,

$$\int_{S^2} \theta\eta(\theta\cdot\theta')\mathrm{d}\theta = \overline{\eta}\,\theta'$$

where $\overline{\eta} = \int_{S^2} \theta' \cdot \theta\,\eta(\theta\cdot\theta')\mathrm{d}\theta$ is the scattering anisotropy.

Diffusion approximation: derivation

- Integrate RTE over S^2,
- multiply RTE by θ, integrate again, and
- assume $g^-(x,\theta) = g^-(x)$.

Then,

$$-\nabla \cdot (D\nabla u_0) + \mu_\mathrm{a} u_0 = q_0 := \frac{1}{4\pi}\int\limits_{S^2} q(\cdot,\theta)\mathrm{d}\theta,$$

$$u_0 + 2D\partial_\mathbf{n} u_0 = g^- \text{ on } \partial\Omega,$$

$$D\partial_\mathbf{n} u_0 = -g \text{ on } \partial\Omega,$$

where

$$D = \frac{1}{3(\mu - \overline{\eta}\mu_\mathrm{s})}$$

is the diffusion coefficient (reduced scattering coefficient).

Diffusion approximation: final equation

- Change of notation: $u = u_0$, $q = q_0$, $\mu = \mu_\mathrm{a}$, and $g = -g$.
- The photon density u obeys the BVP

$$\begin{aligned} -\nabla \cdot (D\nabla u) + \mu u &= q \quad \text{in } \Omega, \\ u + 2D\partial_{\mathbf{n}} u &= g^- \quad \text{on } \partial\Omega. \end{aligned}$$

- The measurements are given by

$$D\partial_{\mathbf{n}} u = g \quad \text{on } \partial\Omega.$$

- Assume $g^- = 0$ (no photons penetrate the object from outside).

Inverse problem: formulation & uniqueness

Inverse problem of BLT (in the diffusive regime)

Define the (linear) forward operator

$$
\begin{aligned}
A\colon L^2(\Omega) &\to H^{-\frac{1}{2}}(\partial\Omega),\\
q &\mapsto D\partial_{\mathbf{n}} u\,,
\end{aligned}
$$

where u solves the BVP with $g^- = 0$:

$$
\begin{aligned}
-\nabla\cdot(D\nabla u) + \mu u = q \quad &\text{in } \Omega,\\
u + 2D\partial_{\mathbf{n}} u = 0 \quad &\text{on } \partial\Omega.
\end{aligned}
$$

BLT Problem: Given $g \in \mathcal{R}(A)$, find a source $q \in L^2(\Omega)$ satisfying

$$Aq = g.$$

Null Space of A

Lemma (Wang, Li & Jiang '04, Kreutzmann '13):
There is an isomorphism $\Phi\colon H^1(\Omega) \to H^1(\Omega)'$ such that

$$\mathcal{N}(A) = \Phi\big(H_0^1(\Omega)\big) \cap L^2(\Omega).$$

If $D \in W^{1,\infty}$ then

$$\mathcal{N}(A) = \Phi\big(H_0^1(\Omega) \cap H^2(\Omega)\big).$$

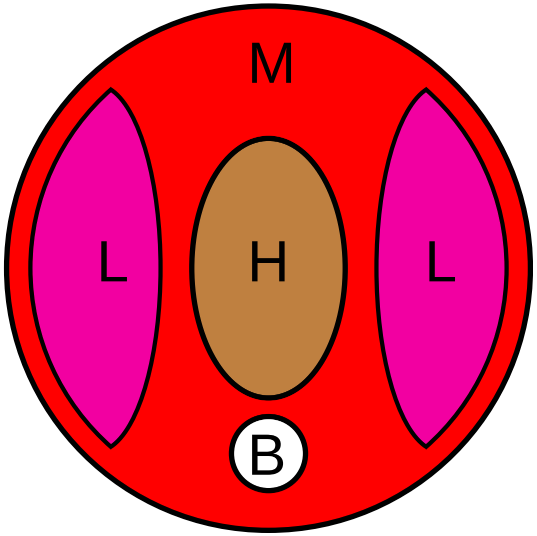
Proof: Define

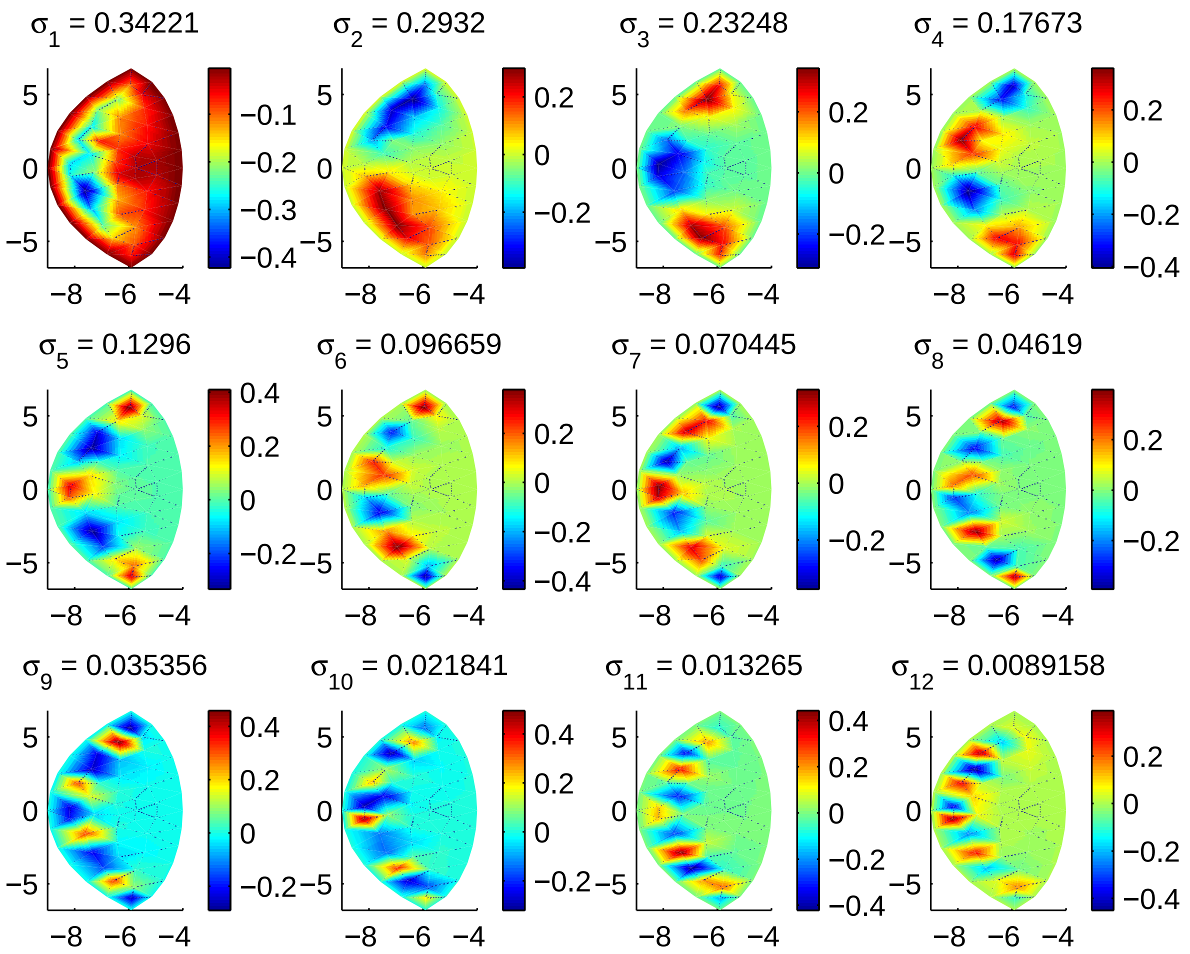
$$\Phi\colon H^1(\Omega) \to H^1(\Omega)', \quad u \mapsto (\Phi u)(v) = a(u,v)$$

where

$$a(u,v) = \int_\Omega \big(D\nabla u \cdot \nabla v + \mu u v\big)\mathrm{d}x + \frac{1}{2}\int_{\partial\Omega} uv\,\mathrm{d}s.$$

Singular Functions of $A\colon L^2(\Omega_0) \to L^2(\partial\Omega)$





Can we restore uniqueness by *a priori* information?

Consider, for instance,

$$q = \lambda \chi_S \quad \text{where } \lambda \geq 0 \text{ is a constant and } S \subset \Omega.$$

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Lemma (Wang, Li & Jiang '04):

There exist $z \in \Omega$, $\lambda_1 \neq \lambda_2$ and $r_1 \neq r_2$ such that

$$A(\lambda_1 \chi_{B_1}) = A(\lambda_2 \chi_{B_2})$$

with $B_k = B_{r_k}(z)$.

Inverse problem: reformulation & stabilization

Reformulation

Ansatz: $q = \sum_{i=1}^{I} \lambda_i \chi_{S_i}$ where $S_i \subset \Omega$, $\lambda_i \in [\underline{\lambda}_i, \overline{\lambda}_i] = \Lambda_i$, and $I \in \mathbb{N}$.

For the ease of presentation: $I = 1$.

Define the nonlinear operator

$$\begin{aligned} F\colon \Lambda \times \mathfrak{L} &\to L^2(\partial\Omega), \\ (\lambda, S) &\mapsto D\partial_{\mathbf{n}} u|_{\partial\Omega} \end{aligned}$$

where $\mathfrak{L}$ is the set of all measurable subsets of Ω.

Note: $F(\lambda, S) = \lambda A \chi_S$

BLT Problem: Given measurements g, find an intensity $\lambda \in \Lambda$ and a domain $S \in \mathfrak{L}$ such that

$$F(\lambda, S) = g.$$

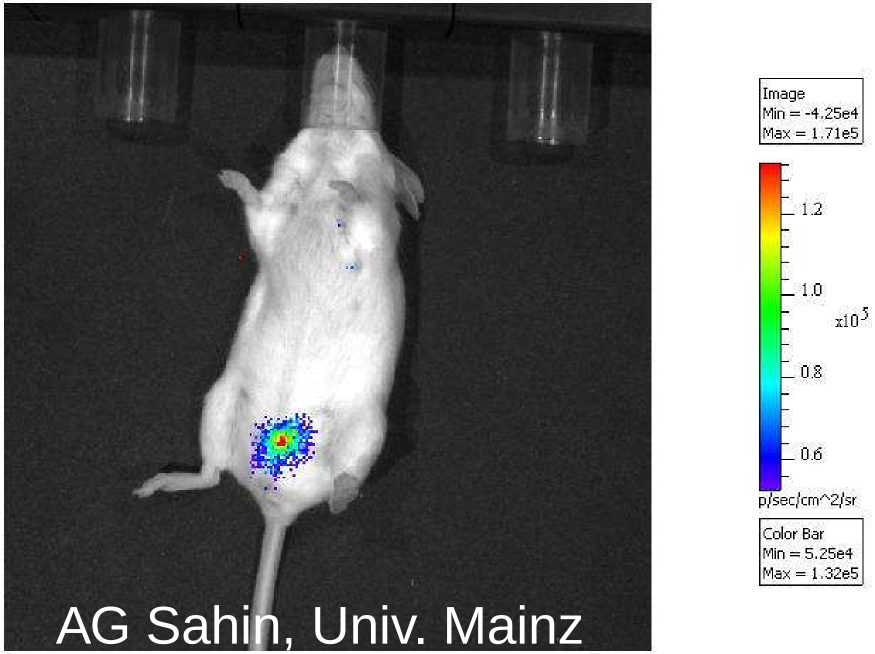
Tikhonov-like regularization

Minimize $J_\alpha(\lambda, S) = \frac{1}{2}\|F(\lambda, S) - g\|_{L^2}^2 + \alpha \mathrm{Per}(S)$ over $\Lambda \times \mathcal{L}$

where $\alpha > 0$ is the regularization parameter and $\mathrm{Per}(S)$ is the perimeter of S:

$$\mathrm{Per}(S) = |\mathrm{D}(\chi_S)|,$$

with $|\mathrm{D}(\cdot)|$ denoting the BV-semi-norm (Ramlau & Ring '07, '10).



Existence of a minimizer & stability

Theorem: For all $\alpha > 0$ and $g \in L^2(\partial\Omega)$ there exists a minimizer $(\lambda^*, S^*) \in \Lambda \times \mathfrak{L}$, that is,

$$J_\alpha(\lambda^*, S^*) \leq J_\alpha(\lambda, S) \qquad \text{for all } (\lambda, S) \in \Lambda \times \mathfrak{L}.$$

Theorem: Let $g_n \to g$ in L^2 as $n \to \infty$ and let (λ^n, S^n) minimize

$$J_\alpha^n(\lambda, S) = \tfrac{1}{2}\|F(\lambda, S) - g_n\|_{L^2}^2 + \alpha \mathrm{Per}(S) \text{ over } \Lambda \times \mathfrak{L}.$$

Then there exists a subsequence $\{(\lambda^{n_k}, S^{n_k})\}_k$ converging to a minimizer $(\lambda^*, S^*) \in \Lambda \times \mathfrak{L}$ of J_α in the sense that

$$\|\lambda^{n_k}\chi_{S^{n_k}} - \lambda^*\chi_{S^*}\|_{L^2} \to 0 \quad \text{as } k \to \infty.$$

Furthermore, every convergent subsequence of $\{(\lambda^n, S^n)\}_n$ converges to a minimizer of J_α.

Regularization property

Theorem: Let g be in $\mathrm{range}(F)$ and let $\delta \mapsto \alpha(\delta)$ where

$$\alpha(\delta) \to 0 \quad \text{and} \quad \frac{\delta^2}{\alpha(\delta)} \to 0 \quad \text{as } \delta \to 0.$$

In addition, let $\{\delta_n\}_n$ be a positive null sequence and $\{g_n\}_n$ such that

$$\|g_n - g\|_{L^2} \leq \delta_n.$$

Then, the sequence $\{(\lambda^n, S^n)\}$ of minimizers of $J^n_{\alpha(\delta_n)}$ possesses a subsequence converging to a solution (λ^+, S^+) where

$$S^+ = \arg\min\{\mathrm{Per}(S) : S \in \mathfrak{L} \text{ s.t. } \exists \lambda \in \Lambda \text{ with } F(\lambda, S) = g\}.$$

Furthermore, every convergent subsequence of $\{(\lambda^n, S^n)\}_n$ converges to a pair $(\lambda^\dagger, S^\dagger)$ with above property.

Gradient of the minimization functional

Domain derivative: general definition

Let $\Gamma \in \mathcal{S} = \{\widetilde{\Gamma} \subset \Omega : \partial\widetilde{\Gamma} \in C^2\}$ and let $h \in C_0^2(\Omega, \mathbb{R}^d)$. Define

$$\Gamma_h = \{x + h(x) : x \in \Gamma\}.$$

If h is small enough, say if $\|h\|_{C^2} < 1/2$, then $\Gamma_h \in \mathcal{S}$.

By the domain derivative of $\Phi\colon \mathcal{S} \to Y$ about Γ we understand $\Phi'(\Gamma) \in \mathcal{L}(C^2, Y)$ satisfying

$$\|\Phi(\Gamma_h) - \Phi(\Gamma) - \Phi'(\Gamma)h\|_Y = \mathrm{o}(\|h\|_{C^2})$$

where Y is a normed space.

Domain derivative of $F(\lambda, \cdot)\colon \mathcal{S} \to L^2(\partial\Omega)$

Reminder: $F(\lambda, S) = \lambda A \chi_S$

Lemma: We have that

$$\partial_S F(\lambda, S)h = u'|_{\partial\Omega}$$

where $u' \in H^1(\Omega \backslash \partial S)$ solves the transmission bvp

$$\begin{aligned}
-\nabla \cdot (D\nabla u') + \mu u' &= 0 \quad \text{in } \Omega\backslash\partial S,\\
2D\partial_{\mathbf{n}} u' + u' &= 0 \quad \text{on } \partial\Omega,\\
[u']_{\pm} &= 0 \quad \text{on } \partial S,\\
\big[D\partial_{\mathbf{n}} u'\big]_{\pm} &= -\lambda h \cdot \mathbf{n} \quad \text{on } \partial S.
\end{aligned}$$

Proof: similar to Hettlich's habilitation thesis 1999.

Domain derivative of $\mathrm{Per}\colon \mathbb{S} \to \mathbb{R}$

Lemma (Simon 1980):

We have that

$$\partial_S \mathrm{Per}(S)h = \int_{\partial S} \mathrm{H}_{\partial S}(h \cdot \mathbf{n}) \, \mathrm{d}s$$

where $\mathrm{H}_{\partial S}$ denotes the mean curvature of ∂S.

Derivative of $J_\alpha \colon \Lambda \times \mathcal{S} \to \mathbb{R}$

$$J_\alpha(\lambda, S) = \frac{1}{2}\|F(\lambda, S) - g\|_{L^2}^2 + \alpha \mathrm{Per}(S)$$

$$\partial_\lambda F(\lambda, S)k = kA\chi_S = F(k, S)$$

Theorem: We have that

$$J'_\alpha(\lambda, S)(k, h) = \big\langle F(\lambda, S) - g, F(k, S) + u' \big\rangle_{L^2(\partial\Omega)} + \alpha \int_{\partial S} \mathrm{H}_{\partial S}(h \cdot \mathbf{n})\, \mathrm{d}s$$

for $k \in \mathbb{R}$, $h \in C_0^2(\Omega, \mathbb{R}^3)$.

Proof:

$$J'_\alpha(\lambda, S)(k, h) = \partial_\lambda J_\alpha(\lambda, S)k + \partial_S J_\alpha(\lambda, S)h$$

Approximate variational principle (Ekeland 1974)

There exist smooth almost critical points of J_α near to any of its minimizers.

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Theorem: Let (λ^*, S^*) be a minimizer of J_α where λ^* is an inner point of Λ. Then, for any $\varepsilon > 0$ sufficiently small there is a $(\lambda^\varepsilon, S^\varepsilon) \in \Lambda \times \mathcal{S}$ with

$$J_\alpha(\lambda^\varepsilon, S^\varepsilon) - J_\alpha(\lambda^*, S^*) \leq \varepsilon,$$

$$\|\lambda^\varepsilon \chi_{S^\varepsilon} - \lambda^* \chi_{S^*}\|_{L^1} \leq \varepsilon,$$

$$\|J'_\alpha(\lambda^\varepsilon, S^\varepsilon)\|_{\mathbb{R}\times C^2 \to \mathbb{R}} \leq \varepsilon.$$

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$$\|\lambda^\varepsilon \chi_{S^\varepsilon} - \lambda^* \chi_{S^*}\|_{L^1} \leq \varepsilon,$$

$$\|J'_\alpha(\lambda^\varepsilon, S^\varepsilon)\|_{\mathbb{R}\times C^2 \to \mathbb{R}} \leq \varepsilon.$$

Proof: Key ingredient is
To any bounded measurable $\Gamma \subset \mathbb{R}^d$ with finite perimeter exists a sequence $\{\Gamma^n\}_n$ of C^∞-domains such that

$$\int_{\mathbb{R}^d} |\chi_{\Gamma^n} - \chi_\Gamma| \mathrm{d}x \to 0 \quad \textit{and} \quad \mathrm{Per}(\Gamma^n) \to \mathrm{Per}(\Gamma) \quad \textit{as } n \to \infty.$$

Numerical experiments in 2D

Star-shaped domains

- For the numerical experiments we consider a star-shaped domain only:

$$S = \{x \in \mathbb{R}^2 : x = m + t\,\theta(\vartheta)r(\vartheta),\ 0 \le t \le 1,\ 0 \le \vartheta \le 2\pi\}$$

  where m is the center (assumed to be known) and $r\colon [0,2\pi] \to [0,\infty[$ parameterizes the boundary of S.

- All previous results hold in this setting as well if we work in a space of smooth parameterizations, say, $r \in H^3_{\mathrm{p}}(0,2\pi) \subset C^2_{\mathrm{p}}(0,2\pi)$.
- $(\lambda, S) \rightsquigarrow (\lambda, r) \in \Lambda \times \mathcal{R}_{ad}$ where $\mathcal{R}_{ad} = \left\{r \in H^3_{\mathrm{p}}(0,2\pi) : r \ge 0\right\}$.
- Gradient equation: $\left\langle \mathrm{grad} J_\alpha(\lambda, r), (k, h)\right\rangle_{\mathbb{R}\times H^3} = J'_\alpha(\lambda, r)(k, h)$.
- We have implemented star-shaped domains using trigonometric polynomials.

Algorithm: *Projected Gradient Method*

(S0) Choose $(\lambda^0, r^0) \in \mathcal{C} := \Lambda \times \mathcal{R}_{ad}$, $k := 0$

(S1) Iterate (S2)-(S4) until 

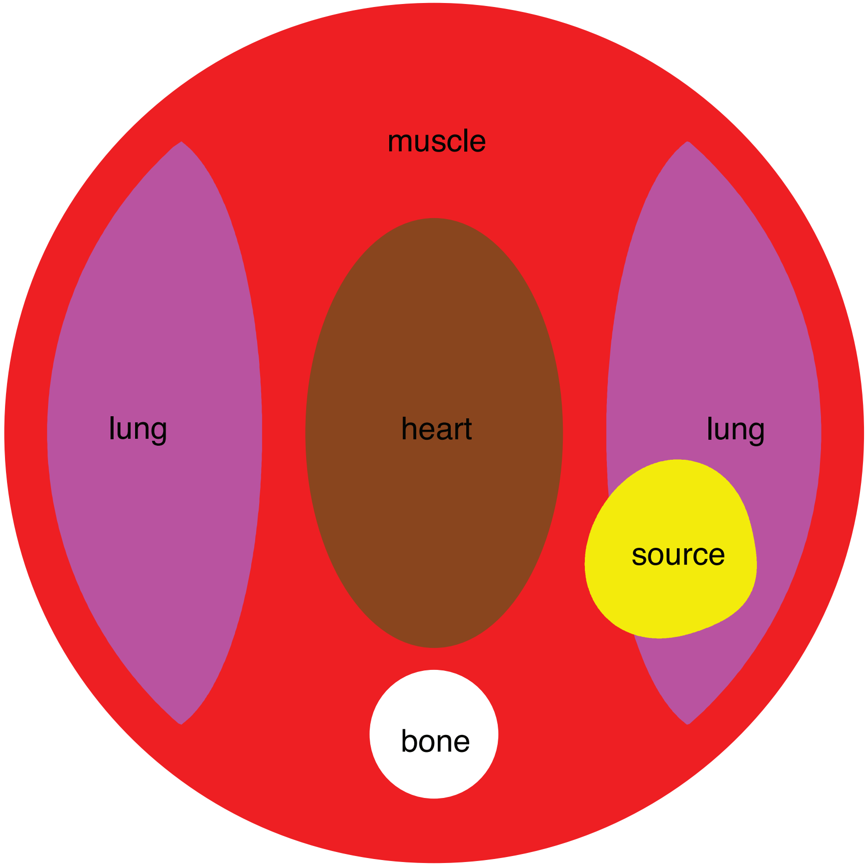
(S2) Set $\nabla_k := -\mathrm{grad} J_\alpha(\lambda^k, r^k)$.

(S3) Choose σ_k by a projected step size rule such that

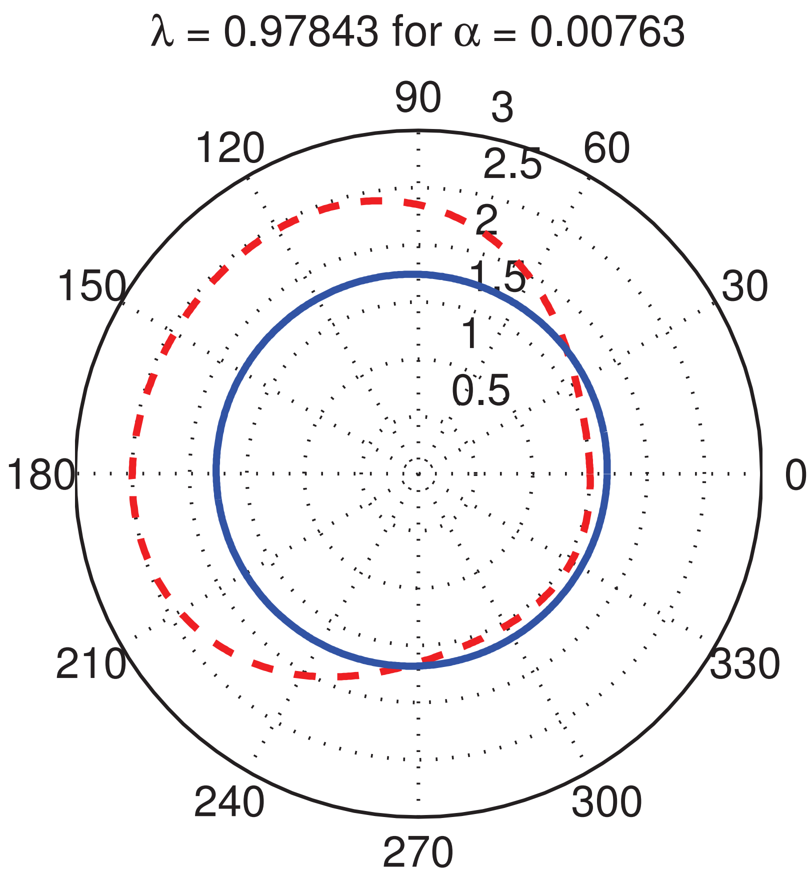
$$J_\alpha\Big(P_{\mathcal{C}}\big((\lambda^k, r^k) + \sigma_k \nabla_k\big)\Big) < J_\alpha(\lambda^k, r^k).$$

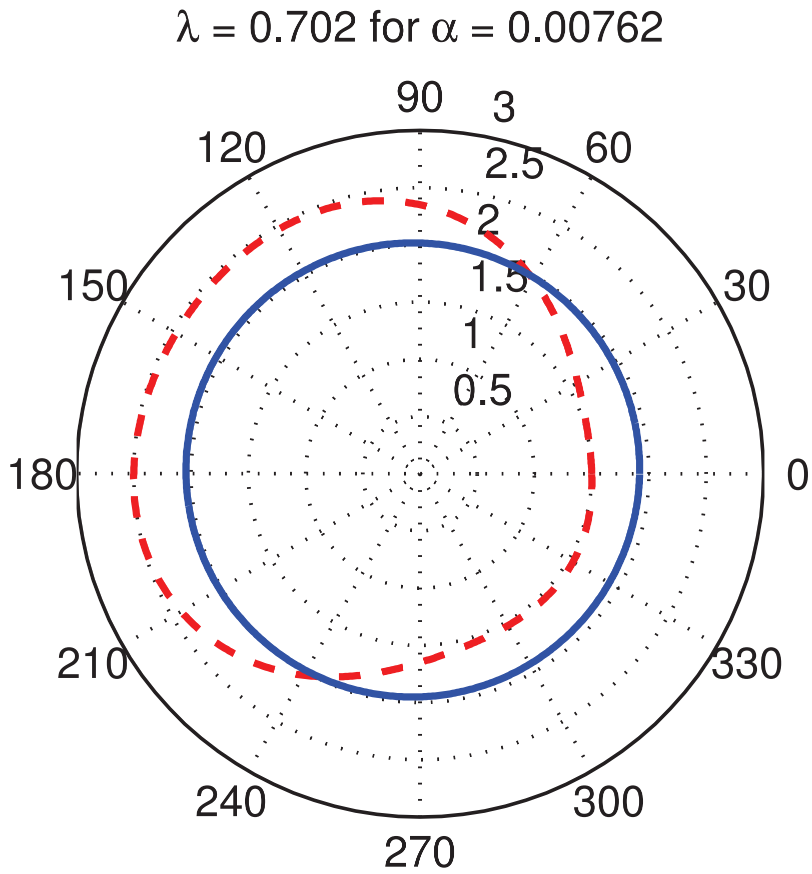
(S4) Set $(\lambda^{k+1}, r^{k+1}) := P_{\mathcal{C}}\big((\lambda^k, r^k) + \sigma_k \nabla_k\big)$.

The model



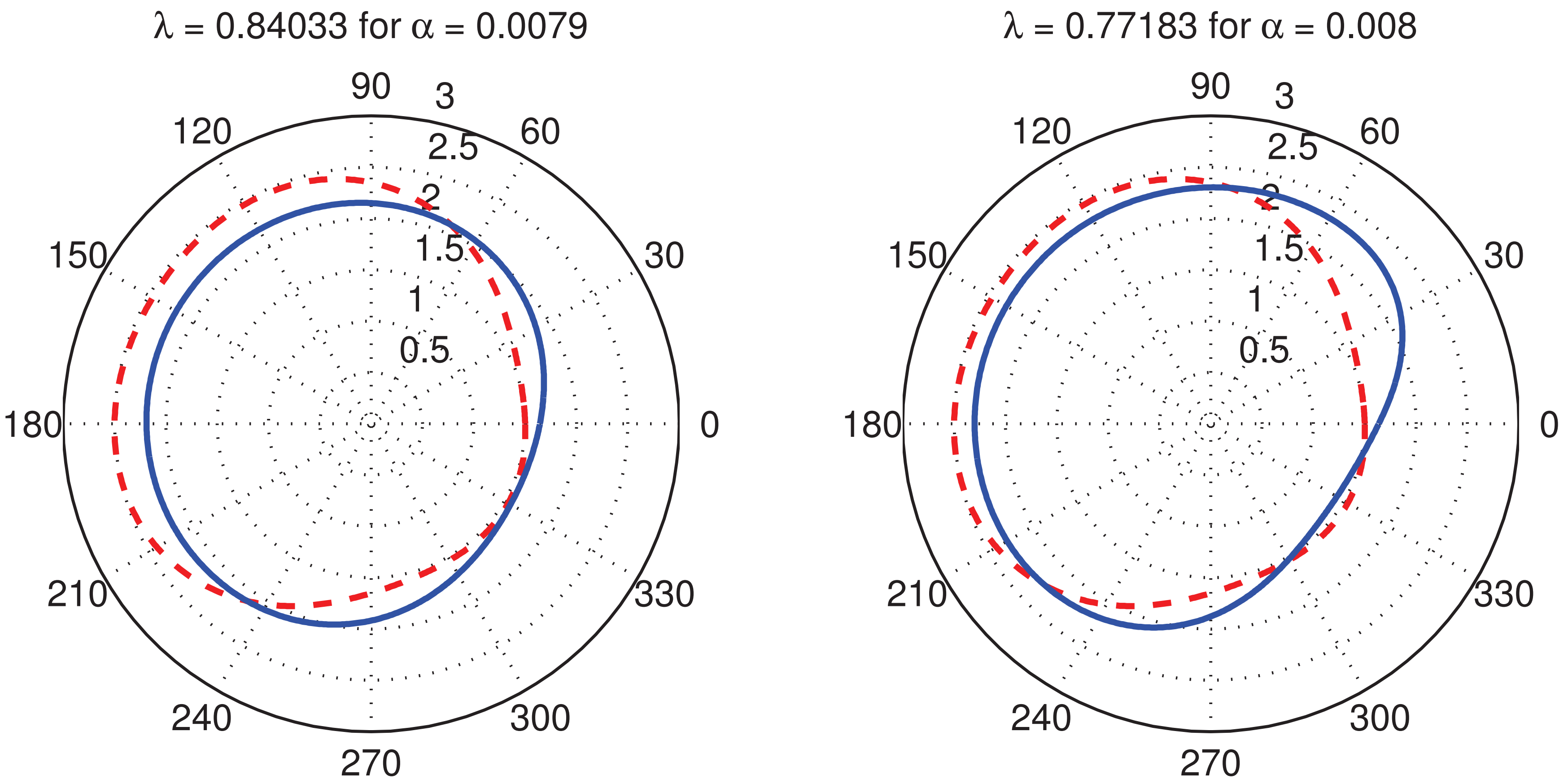
H^3-Reconstructions





Reconstructions (blue) and source (red).
Left: 69 iterations, right: $k = 17$ iterations

L^2-Reconstructions



Reconstructions (blue) and source (red).

Left: 37 iterations, right: noisy data (rel. 3%), 24 iterations

L^2-Reconstruction with variable center

Summary

What to remember from this talk

- Bioluminescence tomography images cells *in vivo*. From a mathematical point of view it is an inverse source problem which suffers from non-uniqueness (diffusion approximation) and ill-posedness.
- To overcome these difficulties the sources are modeled as ”hot spots” leading to a nonlinear problem which is stabilized by a Tikhonov-like regularization penalizing the perimeter of the hot spots.
- The approximate variational principle justifies the restriction to hot spots with smooth boundaries.
- For star-shaped domains in 2D a projected steepest decent solver has been implemented and tested.