The Method of Small Volume Expansions for Emerging Medical Imaging

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Motivation and Principles of the MSVE

- Inverse problems in medical imaging: ill-posed, they literally have no solution! (Steven Pinker, *How the Minds Work*)

(a) MRI Image of breast cancer  
(b) X-ray image of breast cancer
Motivation and Principles of the MSVE

- Multi-physics Imaging Methods.

- Multi-scale Imaging Methods: Add structural information or supply missing information (kind of regularization) to determine specific features with satisfactory resolution. One such knowledge: find unknown small anomalies (potential tumors at early stage)

- MSVE key role

- Emerging Medical applications: electrical impedance tomography (EIT), radiation force imaging, impedigraphy (EIT by Ultrasound Focusing), magnetic resonance elastography, and photo-acoustic imaging.
Emerging Medical Applications

- EIT: impose boundary voltages, measure the induced boundary currents to estimate the electrical conductivity.

- Radiation force imaging: generate vibrations inside the organ, acquire a spatio-temporal sequence of the propagation of the induced transient wave inside the organ to estimate its viscoelastic parameters.

- Impediography: use an EIT system, perturb the medium during the electric measurements, by focusing ultrasonic waves on regions of small diameter inside the organ → the pointwise value of the electrical energy density at the center of the perturbed zone. Find the conductivity distribution. (Patent WO 2008/037929 A2).
Emerging Medical Applications

- Magnetic resonance elastography: reconstruct the shear modulus from measurements of the displacement field in the whole organ.

- Photo-acoustic imaging: generation of acoustic waves by the absorption of optical energy. Reconstruct absorbing regions inside the organ from boundary measurements of the induced acoustic signal.
Principles of the Imaging Techniques

- Boundary and Scattering Measurements: EIT
  - anomaly detection

- Internal Measurements: Radiation force imaging, MRE
  - distribution of physical parameters

- Boundary Measurements from Internal Perturbations of the Medium: Impediography, photo-acoustic imaging.
  - distribution of physical parameters
Motivation and Principles of the MSVE

Small volume asymptotic expansions:

- **Boundary Measurements**: outer expansions in terms of the characteristic size of the anomaly
  - anomaly detection
- **Internal Measurements**: inner expansions
  - distribution of physical parameters
Reference

Conductivity Problem

Notation: \( \Omega \in \mathbb{R}^d (d \geq 2) \): smooth bounded domain.

\( N(x, z) \): Neumann function for \(-\Delta\) in \( \Omega \) corresponding to a Dirac mass at \( z \in \Omega \):

\[
\begin{align*}
-\Delta_x N(x, z) &= \delta_z \quad \text{in } \Omega, \\
\frac{\partial N}{\partial \nu_x}|_{\partial \Omega} &= -\frac{1}{|\partial \Omega|}, \\
\int_{\partial \Omega} N(x, z) \, d\sigma(x) &= 0.
\end{align*}
\]

\( B \): smooth bounded domain. \( \hat{v} \): corrector the solution to

\[
\begin{align*}
\Delta \hat{v} &= 0 \quad \text{in } \mathbb{R}^d \setminus \overline{B}, \\
\Delta \hat{v} &= 0 \quad \text{in } B, \\
\hat{v}|_- - \hat{v}|_+ &= 0 \quad \text{on } \partial B, \\
k \frac{\partial \hat{v}}{\partial \nu}|_- - \frac{\partial \hat{v}}{\partial \nu}|_+ &= 0 \quad \text{on } \partial B, \\
\hat{v}(\xi) - \xi &\to 0 \quad \text{as } |\xi| \to +\infty.
\end{align*}
\]
Conductivity Problem

\[ D = \delta B + z : \text{anomaly } \subset \Omega; \delta: \text{characteristic size of the anomaly}; \]
\text{conductivity } 0 < k \neq 1 < +\infty. \]

The voltage potential \( u \):

\[
\begin{align*}
\nabla \cdot \left( \chi(\Omega \setminus \overline{D}) + k\chi(D) \right) \nabla u &= 0 \quad \text{in } \Omega, \\
\left. \frac{\partial u}{\partial \nu} \right|_{\partial \Omega} &= g \quad \left( g \in L^2(\partial \Omega), \int_{\partial \Omega} g \, d\sigma = 0 \right), \\
\int_{\partial \Omega} u \, d\sigma &= 0.
\end{align*}
\]

\( U \): the background solution.
Outer Expansion

- A. Friedman, M. Vogelius, J.K. Seo, H. Kang, . . .
- Dipole-type approximation of the conductivity anomaly.
- The following boundary asymptotic (outer) expansion on $\partial \Omega$ holds for $d = 2, 3$:

$$ (u - U)(x) \approx -\delta^d \nabla U(z) M(k, B) \nabla z N(x, z). $$

- $M(k, B) := (k - 1) \int_B \nabla \hat{v}(\xi) \, d\xi$: the polarization tensor (PT)
- The location $z$ and the matrix $M(k, B)$: reconstructed.
- $M(k, B)$: characterizes all the information about the anomaly that can be learned from boundary measurements.
- $M(k, B)$: mixture of $k$ and low-frequency geometric information.
Polarization Tensor

- Properties of the polarization tensor:
  
  (i) $M$ is symmetric.
  
  (ii) If $k > 1$, then $M$ is positive definite, and it is negative definite if $0 < k < 1$.
  
  (iii) Hashin-Shtrikman bounds:
  
  \[
  \begin{align*}
  \frac{1}{k - 1} \text{trace}(M) &\leq (d - 1 + \frac{1}{k})|B|, \\
  (k - 1) \text{trace}(M^{-1}) &\leq \frac{d - 1 + k}{|B|}.
  \end{align*}
  \]

- Optimal size estimates; Thickness estimates; Pólya–Szegö conjecture.

Figure 1: When the two disks have the same radius and the conductivity of the one on the right-hand side is increasing, the equivalent ellipse is moving toward the right anomaly.
Figure 2: When the conductivities of the two disks is the same and the radius of the disk on the right-hand side is increasing, the equivalent ellipse is moving toward the right anomaly.
Polarization Tensor

EIT Anomaly Detection System

(with J.K. Seo, O. Kwon, and E.J. Woo, SIAP 05)

EIT system for anomaly detection: location of the anomaly and reconstruction of its polarization tensor.

Reconstruction depends on the boundary: inaccurate model of the boundary causes severe errors for the reconstructions.

Separate conductivity/size: Higher-order polarization tensors.

Separate conductivity/size: Requires very sensitive EIT system.
Inner Expansion

The following inner asymptotic formula holds:

\[ u(x) \approx U(z) + \delta \hat{\nu} \left( \frac{x - z}{\delta} \right) \cdot \nabla U(z) \quad \text{for } x \text{ near } z. \]

- Boundary independent reconstruction: no need of an exact knowledge of the boundary of the domain \( \Omega \)
- Local Reconstruction
- Separate conductivity/ Geometry
- Interface Approximation: high frequency information
Acoustic Radiation Force

(with P. Garapon, L. Guadarrama Bustos, and H. Kang, JDE 09)

Use of the acoustic radiation force of an ultrasonic focused beam to remotely generate mechanical vibrations in organs.

The radiation force acts as a dipolar source at the pushing ultrasonic beam focus.

Generate the Green function of the medium.

A spatio-temporal of the propagation of the induced transient wave can be acquired ⇒ Quantitative estimation of the viscoelastic parameters of the studied medium in a source-free region.
\[ U_y(x, t) \] retarded Green’s function generated at \( y \in \Omega \) and \( t = 0 \) without the anomaly.

The wave in the presence of the anomaly:

\[
\begin{aligned}
\frac{\partial^2}{\partial t^2} u - \nabla \cdot (\chi(\mathbb{R}^3 \setminus \overline{D}) + k \chi(D)) \nabla u &= \delta_{x=y} \delta_{t=0}, \mathbb{R}^3 \times [0, +\infty[,
\end{aligned}
\]
\[
\begin{aligned}
&\left\{ u(x, t) = 0 \quad \text{for} \quad x \in \mathbb{R}^3 \quad \text{and} \quad t \ll 0. \right.
\end{aligned}
\]

No (uniform) asymptotic formula for both high and low-frequencies.

Truncate the high-frequency component of the signal up to

\[
\rho = O(\delta^{-\alpha}), \alpha < \frac{1}{2},
\]

\[
P_\rho[u](x, t) = \int_{|\omega| \leq \rho} e^{-\sqrt{-1}\omega t} \hat{u}(x, \omega) d\omega.
\]
\[ T = |y - z| \] travel time between the source and the anomaly.

After truncation of the high frequency component, the perturbation due to the anomaly is (approximately) a wave emitted from the point \( z \) at \( t = T \).

Truncation parameter \( \rho \) up to \( O(\delta^{-\alpha}) \), \( \alpha < \frac{1}{2} \).

Far field expansion of \( P_{\rho}[u - U_y](x, t) \):

\[
= -\delta^3 \int_{\mathbb{R}} \nabla P_{\rho}[U_z](x, t - \tau) \cdot M(k, B) \nabla P_{\rho}[U_y](z, \tau) \, d\tau + O(\epsilon^{4(1 - \frac{3}{4} \alpha)}).
\]

The anomaly behaves then like a dipolar source.
To detect the anomaly from far-field measurements one can use a time-reversal technique.

One measures the perturbation on a closed surface surrounding the anomaly, truncates its high-frequency component, and retransmits it through the background medium in a time-reversed chronology.

The perturbation will travel back to the location of the anomaly.
The reversed wave (after high-frequency truncation)

\[ w_{tr}(x, t) = \int_{\mathbb{R}} ds \int_{S} \left[ U_x(x', t - s) \frac{\partial P_\rho[u - U_y]}{\partial \nu}(x', t_0 - s) \right. \\
\left. - \frac{\partial U_x}{\partial \nu}(x', t - s) P_\rho[u - U_y](x', t_0 - s) \right] d\sigma(x'). \]

\[ (p := M(k, B) \nabla P_\rho[U_y](z, T)) \]

\[ w_{tr}(x, t) \approx -\epsilon^3 p \cdot \nabla_z [P_\rho[U_z](x, t_0 - T - t) - P_\rho[U_z](x, t - t_0 + T)]. \]

The reversed wave is the sum of incoming and outgoing spherical waves.
Time-Reversal Imaging

- Frequency domain ($\Phi_\omega$ outgoing Green’s function):

$$\int_S \left[ \Phi_\omega(x - x') \frac{\partial \Phi_\omega}{\partial \nu}(z - x') - \overline{\Phi_\omega(z - x')} \frac{\partial \Phi_\omega}{\partial \nu}(x - x') \right] d\sigma(x')$$

$$= 2\sqrt{-1} \Im \Phi_\omega(z - x) \text{ (resolution limit in imaging)}.$$

- Inhomogeneous media: similar formula.

- Resolution limit in imaging: size of the focal spot of order half the wavelength.

- Sharper the behavior of $\Im \Phi_\omega$ at $z$, higher the resolution.

- Super-resolution: how the behavior of $\Im \Phi_\omega$ depends on the heterogeneity of the medium?
Near field expansion:

\[ P_\rho[u - U_y](x, t) = \delta \hat{v} \left( \frac{x - z}{\delta} \right) \cdot \nabla P_\rho[U_y](x, t) + O(\delta^{2(1-\alpha)}) \]

Local and accurate reconstruction from near field measurements.
Multi-Scale Approaches

- Far-field measurements: detection

\[(u - U)(x) \approx -(k - 1)\delta^d\nabla U(z) \left( \int_B \nabla \hat{v}(\xi) \, d\xi \right) \nabla_z N(x, z) \, . \]

- Near-field measurements: shape reconstruction and material parameter characterization

\[u(x) \approx U(z) + \delta \hat{v}\left(\frac{x - z}{\delta}\right) \cdot \nabla U(z) \, . \]
Multi-Physics Approaches

- Impediography
- Magnetic resonance elastography
- Photo-acoustic imaging
Impediography

(with E. Bonnetier, Y. Capdeboscq, M. Tanter, and M. Fink, SIAP 08)

To couple electric measurements to localized acoustic perturbations.

$u$ the voltage potential induced by a current $g$, in the absence of acoustic perturbations:

\[
\begin{cases}
\nabla_x \cdot (\gamma(x) \nabla_x u) = 0 \text{ in } \Omega, \\
\gamma(x) \frac{\partial u}{\partial \nu} = g \text{ on } \partial \Omega,
\end{cases}
\]
Impediography

$u_\delta$ induced by $g$, in the presence of acoustic perturbations localized in a disk-shaped domain $D := z + \delta B$:

$$\left\{\begin{array}{l}
\nabla_x \cdot \left( \gamma_\delta(x) \nabla_x u_\delta(x) \right) = 0 \text{ in } \Omega , \\
\gamma(x) \frac{\partial u_\delta}{\partial \nu} = g \text{ on } \partial \Omega ,
\end{array}\right.$$ 

$$\gamma_\delta(x) = \gamma(x) \left[1 + \chi(D)(x) (\nu(x) - 1) \right].$$

$$\mathcal{E}(z) = \left( \int_D \frac{(\nu(x) - 1)^2}{\nu(x) + 1} dx \right)^{-1} \int_{\partial \Omega} (u_\delta - u) g \, d\sigma$$

$$\approx \gamma(z) |\nabla u(z)|^2$$
Impediography

- Inverse problem: reconstruct $\gamma$ knowing $\mathcal{E} \approx \gamma |\nabla u|^2$ (electrical energy density).
- Substitute $\gamma$ by $\mathcal{E} / |\nabla u|^2$.
- Nonlinear PDE (the 0–Laplacian)

\[
\begin{align*}
\nabla_x \cdot \left( \frac{\mathcal{E}}{|\nabla u|^2} \nabla u \right) &= 0 \quad \text{in } \Omega , \\
\frac{\mathcal{E}}{|\nabla u|^2} \frac{\partial u}{\partial \nu} &= g \quad \text{on } \partial \Omega .
\end{align*}
\]

- Choose two currents $g_1$ and $g_2$ s.t. $\nabla u_1 \times \nabla u_2 \neq 0$ for all $x \in \Omega$.
- The reconstruction algorithm is based on an approximation of a linearized version of the nonlinear 0–Laplacian problem.
Start from an initial guess for the conductivity $\gamma$, and solve the corresponding Dirichlet conductivity problem

$$\begin{cases}
\nabla \cdot (\gamma \nabla u_0) = 0 \quad \text{in } \Omega , \\
u_0 = \psi \quad \text{on } \partial \Omega .
\end{cases}$$

$\psi$: the Dirichlet data measured as a response to the current $g$ (say $g = g_1$) in absence of elastic deformation.

The discrepancy between the data and the guessed solution:

$$\epsilon_0 := \frac{\mathcal{E}}{|\nabla u_0|^2} - \gamma .$$
Introduce a corrector:

\[
\nabla \cdot (\gamma \nabla \delta u) = -\nabla \cdot (\varepsilon_0 \nabla u_0) \quad \text{in } \Omega ,
\]

\[
\delta u = 0 \quad \text{on } \partial \Omega ,
\]

Update the conductivity

\[
\gamma := \frac{\varepsilon - 2\gamma \nabla \delta u \cdot \nabla u_0}{|\nabla u_0|^2}.
\]

Iteratively update the conductivity, alternating directions (with \( g = g_2 \)).
Impediography

(a) True conductivity  
(b) Initial guess  
(c) Measurements  
(d) Reconstructed map
Vibration Potential Tomography: Physical Background

- (with Y. Capdebsocq, H. Kang, and A. Kozhemyak, EJAP 09)
- Ultrasonic waves are focused on regions of small diameter inside a charged body placed on a static magnetic field.
- Compared to Impediography: Instead of creating a perturbation in the conductivity, create a source term using Lorenz force density which is proportional to the local electrical conductivity.
Replace the conductivity problem by a Nonlinear PDE:

\[
\begin{cases}
\nabla \cdot \left( \frac{\mathcal{E}}{u} \nabla u \right) = 0 \quad \text{in } \Omega , \\
u = f \quad \text{on } \partial \Omega .
\end{cases}
\]

Reconstruct \( \gamma \) from

\[\mathcal{E}(z)/u(z) = \gamma(z), \quad z \in \Omega.\]

\( \mathcal{E} \) computed from the boundary measurements.
Vibration Potential Tomography: Reconstruction

A simple minded solution: put $w = \ln u$, then $w$ is the solution to

$$\begin{cases}
\nabla \cdot \mathcal{E} \nabla w = 0 \quad \text{in } \Omega, \\
w = \ln f \quad \text{on } \partial \Omega,
\end{cases}$$

Then $\gamma(z) = \frac{\mathcal{E}(z)}{\exp w(z)}$. (Error may be amplified.)
Vibration Potential Tomography: Numerical Example

Linearization Procedure:

Figure 3: Left: actual conductivity distribution; middle: conductivity projected onto pixels; right: reconstructed conductivity
Vibration Potential Tomography: Numerical Example

Optimal Control Approach:

Figure 4: Perturbed reconstruction test with incomplete data.
Magnetic Resonance Elastography

(with P. Garapon, H. Kang, and H. Lee, Quart. Appl. Math. 08)

Initial idea: the shear elasticity can be correlated with the pathological state of tissues.

Detect the shape, the location, and the shear modulus of an elastic anomaly from internal measurements of the displacement field generated by an external vibration.

Compressional modulus is 4 orders of magnitude larger than the shear modulus in biological tissues (quasi-incompressibility).
Magnetic Resonance Elastography

- Formula $\mu = -\omega^2 \rho u / \Delta u$ is not a right approximation.
- Assumption of incompressibility ($\nabla \cdot u = 0$) is not correct.
- Taking derivatives amplifies the error (in particular across the boundary of the anomaly).
Magnetic Resonance Elastography

- The elasticity system should be replaced by a modified Stokes system.
- The elastic moment tensor $M(B, \lambda, \mu, \tilde{\lambda}, \tilde{\mu})$ ($B$ scaled domain) characterizes all the information about an elastic anomaly that can be learned from boundary measurements.
- $P$: orthogonal projection from the space of symmetric matrices onto the space of symmetric matrices with trace zero

$$PM(B, \lambda, \mu, \tilde{\lambda}, \tilde{\mu})P$$ has a limit as $\lambda, \tilde{\lambda} \to +\infty$.

- Notion of a Viscous Moment Tensor as the limit of $PM^2 P$, $M$: the elastic moment tensor.
Magnetic Resonance Elastography

- Similar inner and outer expansions as the ones for the scalar problem hold.

- Local algorithm for reconstructing the shape and the shear modulus of the anomaly from the inner expansion is developed.

- (with P. Gapaon and F. Jouve, JCM 09) Satisfactory results obtained from minimizing the discrepancy functional in the near-field of the anomaly.

- Minimization of the discrepancy functional: trade off between resolution and stability.

- Quantify the window size.
Magnetic Resonance Elastography

Figure 5: Internal displacement field
Magnetic Resonance Elastography

Figure 6: Reconstruction from internal elastic measurements
Figure 7: Achievable resolutions
Photo-Acoustic Imaging

(with E. Bossy, V. Jugnon, and H. Kang, SIAM Rev. 09)

Photo-acoustic imaging: generation of acoustic waves by the absorption of optical energy. Reconstruct absorbing regions inside the organ from boundary measurements of the induced acoustic signal.

\[ D_l: \text{absorbing regions inside the organ} \]

\[ A_l: \text{absorbed optical energy density in } D_l. \]

\[ A_l = \mu_l \Phi, \quad \mu_l: \text{optical absorption coefficient, } \Phi: \text{light fluence.} \]
Photo-Acoustic Imaging

\[ \frac{\partial^2 p}{\partial t^2} (x, t) - c_s^2 \Delta p(x, t) = 0, \quad x \in \Omega, \quad t \in ]0, T[, \]

\( c_s \): acoustic speed in \( \Omega \).

Initial conditions

\[ p|_{t=0} = \sum_{l=1}^{m} \chi_{D_l}(x) A_l(x) \quad \text{and} \quad \frac{\partial p}{\partial t} \bigg|_{t=0} = 0 \quad \text{in} \ \Omega. \]

Boundary conditions:

\[ p = 0 \quad \text{or} \quad \frac{\partial p}{\partial \nu} = 0 \quad \text{on} \ \partial \Omega \times ]0, T[. \]
Photo-Acoustic Imaging

- Without boundary conditions: Spherical Radon transform

\[ p(x, t) = \frac{c_s}{4\pi} \frac{d}{dt} \left[ t \sum_{l=1}^{m} \int_{|x'|=1} \chi_{D_l}(x + c_s tx') A_l(x + c_s tx') \ dS(x') \right]. \]

- P. Kuchment, O. Scherzer

- With boundary conditions, spherical Radon transform does not apply.
For $y \in \mathbb{R}^3 \setminus \overline{\Omega}$,

\[
\nu_y(x, t; \tau) := \delta \left( t + \tau - \frac{|x-y|}{c_s} \right) \frac{4\pi|x-y|}{4\pi|x-y|} \quad \text{in } \Omega \times ]0, T[,
\]

$\tau > \frac{\text{dist}(y, \partial \Omega)}{c_s}$: a parameter.

Use $\tau \mapsto \int_0^T \int_{\partial \Omega} \frac{\partial p}{\partial \nu} (x, t) \nu_y(x, t; \tau) \, d\sigma(x) \, dt$: probe the medium as a function of $\tau$. 
The probe is nonzero only on the interval $]\tau_a, \tau_e[$, $\tau_a$: arrival-time, $\tau_e$: exit-time of the sphere of center $y$ and radius $\tau$ hits $D$.

Convolution of the data with an incoming wave $\Rightarrow$ strong connection with time-reversal techniques.

Reconstruct the optical absorption coefficient $\mu$ inside the small absorbing region from the absorbed optical energy density. ($A = \mu \Phi$, $\Phi$ solution to the diffusion Eq.).
Figure 8: Real and reconstructed configurations of the medium.
Photo-Acoustic Imaging: Selective Imaging

Figure 9: MUSIC simulation with 7 inclusions, contrast=2.

Figure 10: Multi-frequency approach results.
Conclusion

Promising:
- Multi-Scale + Multi-Physics imaging approaches

Important:
- Develop Boundary independent imaging/Multi-frequency imaging
- Control the trade-off between Resolution/Stability