Mathematical Methods for Photoacoustical Imaging

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Coupled Physics Imaging: Sunlights Laughter

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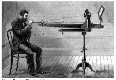
The Economist

Photoacoustic imaging

The sound of light

Biomedical technology: A novel scanning technique that combines optics with ultrasound could provide detailed images at greater depths

Jun 4th 2009 | from PRINT EDITION



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IF LIGHT passed through objects, rather than bouncing off them, people might now talk to each other on "photophones". Alexander Graham Bell demonstrated such a device in 1880, transmitting a conversation on a beam of light. Bell's invention stemmed from his discovery that exposing certain materials to focused, flickering beams of light caused them to emit sound—a phenomenon now known as the photoacoustic effect.

It was the world's first wireless audio transmission, and Bell regarded the photophone as his most important invention. Sadly its use was impractical before the development of optical fibres, so Bell concentrated instead on his more successful idea, the telephone. But more than a century later the photoacoustic effect is making a comeback, this time transforming the field of biomedical imaging.

A new technique called photoacoustic (or optoacoustic) tomography, which marries optics with ultrasonic imaging, should in theory be able to provide detailed scans comparable to those produced by magnetic-resonance imaging (MRI) or X-ray computerised tomography (CT), but with the cost and convenience of a hand-held scanner. Since the technology can operate at depths of several centimetres, its champions hope that within a few years it will be able to help guide biopsy needles deep within tissue, assist with gastrointestinal endoscopies and measure oxygen levels in vascular and lymph nodes, thereby helping to determine whether tumours are malignant or not. There is even scope to use photoacoustic imaging to monitor brain activity and gene expression within cells.

To create a photoacoustic image, pulses of laser light are shone onto the tissue being scanned. This heats the tissue by a tiny amount—just a few thousandths of a degree—that is perfectly safe, but is enough to cause the cells to expand and contract in response. As they do so, they emit sound waves in the ultrasonic range. An array of sensors placed on the skin picks up these waves, and a computer then uses a process of triangulation to turn the ultrasonic signals into a two- or three-dimensional image of what lies beneath.

The technique works at far greater depths (up to seven centimetres) than other optical-imaging techniques such as confocal microscopy or optical-coherence tomography, which penetrate to depths of only about a millimetre. And because the degree to which a particular wavelength of light is absorbed depends on the type of tissue and, in the case of blood, on whether it is oxygenated or deoxygenated, there is, in effect, a natural contrast agent. This makes the technique superior to ultrasound alone when it comes to picking out detailed features such as veins.

MRI and CT scans are also capable of delivering this kind of detail. But they usually require contrast dyes to be injected into the bloodstream, says Lihong Wang, a photoacoustic researcher at Washington University in St Louis, Missouri. CT scans also involve potentially harmful ionising radiation. And MRI and CT scans are very expensive, using machines that cost millions of dollars

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Figure: Photophone: Graham Bell, as early as 1880: Conversion of light into sound waves. Bell's main interest was in wireless telecommunication.

Photoacoustic Imaging – "Lightning and Thunder" (L.H. Wang)

- Specimen is uniformly illuminated by a short/pulsed electromagnetic pulse (visible or near infrared light - **Photoacoustics**, microwaves - **Thermoacoustics**).
- Two-step conversion process: Absorbed EM energy is converted into heat $\Rightarrow$ Material reacts with expansion $\Rightarrow$ Expansion produces pressure waves.
- **Imaging:** Pressure waves are detected at the boundary of the object (over time) and are used for reconstruction of conversion parameter (EM energy into expansion/ waves).

(Potential) Applications

1. Breast Screening [Kruger 1995], [Manohar 2005, The Twente Photoacoustic Mammoscope]
2. Brain Imaging (small animals) [L.H. Wang], [P. Beard]
3. Prostate Imaging: EU Project ADONIS, [M. Frenz et al]
4. Gen-Research: Different penetration depth than fluorescence imaging [Razansky et al]
5. ...

Setups: Microscopic and Tomographic

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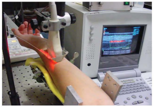
Real-Time Biomedical Optoacoustic Imaging



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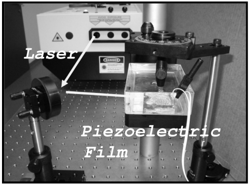

Figure: Microscopic - Tomographic.

Basic Equation of Forward Model

Wave equation for the pressure (Thunder)

$$\boxed{\frac{1}{v_s^2 = 1}\frac{\partial^2 p}{\partial t^2}(x,t) - \Delta p(x,t) = \frac{dj}{dt}(t)\underbrace{\frac{\mu_{\mathrm{abs}}(x)\beta(x)J(x)}{c_p(x)}}_{=:f(x)}}$$

Parameters and Functions:

- Material-parameters: c_p specific heat capacity, μ_{abs} absorption coefficient, β thermal expansion coefficient, J spatial density distribution, v_s speed of sound
- $j(t) \approx \delta$-impulse (Lightning)
- Alternative: Standard formulation as homogeneous wave equation with initial values $p(x,0) = f(x)$, $p_t(x,0) = 0$

Measurement Devices

- Small piezo crystals [Kruger, Wang,...]: Reconstruction from spherical means (small detectors are considered as points): [Agranovsky, Finch, Kuchment, Kunyansky, Quinto, Uhlmann, ...]
- Area detectors [Haltmeier et al]: Measure the averaged pressure over large areas
- Line detectors [Paltauf et al]: E.g. optical sensors, measure the averaged pressure over a long line

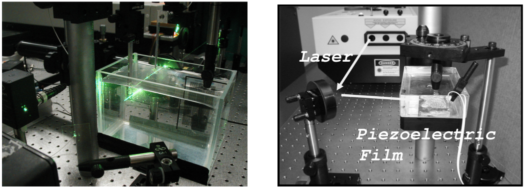

Figure: Tomograph with line and planar detectors

Inverse Problem of Photoacoustic Tomography

- Given: $p(x, t)$ for $x \in S$ (or averaged - Integrating Detectors), S measurement region on the boundary of the probe contained in Ω
- Reconstruction of $f(x)$

Equivalent Mathematical Reconstructions

- Reconstructions from spherical means in $\mathbb{R}^3$
- Reconstruction from circular means and inversion of Abel transform in $\mathbb{R}^2$
- Integrating detectors require additional inversion of planar or linear Radon transformation

A Unified Backprojection Formula for a Sphere

Wave equation and Helmholtz equation:

$$\boxed{\begin{array}{c} \dfrac{\partial^2 p}{\partial t^2}(x,t) - \Delta p(x,t) = 0\,, \quad \forall t \\ \Leftrightarrow \\ k^2 \hat{p}(x,k) + \Delta \hat{p}(x,k) = 0\,, \quad \forall k \end{array}}$$

Explicit Inversion Formulas Using Scattering Results [Kunyansky'07]

- Green's function of Helmholtz Equation (single-frequency case)

$$\Phi = \Phi_k(x,y) \;:=\; \begin{cases} \dfrac{\exp(ik|x-y|}{4\pi|x-y|} & \text{for } n = 3\,, \\[2ex] \dfrac{i}{4}\,H_0^{(1)}(k|x-y|) & \text{for } n = 2\,, \end{cases} \qquad x \neq y$$

- J Bessel function

Explicit Inversion Formulas Using Scattering Results [Kunyansky'07]

$S = \partial\Omega$ (ball)

$$J(k\,|y-x|) = \int_{\partial\Omega} J(k\,|z-x|)\frac{\partial}{\partial n_z}\Phi(x,y,k) - \Phi(x,y,k)\frac{\partial}{\partial n_z}J(k\,|z-x|)\,ds(z)$$

$$(2\pi)^{n/2} f(y) = \int_{\mathbb{R}^+}\int_{\Omega} f(x) J(k\,|y-x|) k^{n-1}\,dx\,dk$$

Idea: Using (1) in (2) gives a boundary integral, and after some calculations inversion formulas

Exact Reconstruction Formulae

Measurement Geometry is a

- Sphere, Cylinder, Plane [Xu, Wang, 2002]
- Circle [Finch, Haltmeier, Rakesh, 2007]
- Universal Backprojection [Wang et al, 2005] in $\mathbb{R}^3$. Natterer'12 shows that it is exact for ellipsoids

Modeling Aspects

Standard Photoacoustics does not model variable sound speed, attenuation, **variable illumination** and does not recover physical parameters

- Quantitative Photoacoustics (components of f) [Bal, Scotland, Arridge,...]
- Sound speed variations [Hristova, Kuchment, Stefanov, Uhlmann,...]
- Attenuation [Anastasio, Patch, Riviere, Burgholzer, Kowar, S, Ammari, Wahab, ...]
- Dispersion
- Measurements have a finite band-width [Haltmeier, Zangerl, S.]
-

Hybrid, Quantitative Imaging - Terminology

- Can be used as synonyms for coupled physics imaging (conversion).
- Hybrid is also a term for fusion and alignment of images from different modalities. Not, what is meant here $\Rightarrow$ Computer Vision
- Hybrid itself is a phrase for quantitative imaging, where information on common physical/diagnostical parameters are reconstructed from the conversion parameters. Common diagnostic parameters of interest are diffusion or scattering parameters [Ammari, Bal, Kuchment, Uhlmann...]
- Quantitative imaging: Synonym for inverse problems with internal measurements

Quantitative Photoacoustic Imaging

- Requires modeling of illumination (optical, near infrared, microwave,...)
- With Photoacoustics disposed energy ($f = \kappa|\nabla u|^2$ and/or $f = \mu|u|$) are recorded
- Inverse Problem: Recover κ and/or μ in

$$\boxed{-\nabla \cdot (\kappa \nabla u) + \mu u = 0}$$

[Ammari, Kang, Bal, Capdebosque, Uhlmann, Wang, ...]

Mathematical Problems in Quantitative Photoacoustic Imaging

- Uniqueness, typically requires at least two experiments: $\kappa\,|\nabla p_i|^2$, $i = 1, 2$, to recover κ [Bal et al, Kuchment, Steinhauer]
- Alternative investigations [Ammari, Capdebosque,..] $\kappa < \nabla p_i, \nabla p_j >$ measured
- With a single measurement. Edges can be rediscovered [Naetar, S'14]. Numerical solution by edge detection
- Older/Sophisticated Techniques with MRI

Photoacoustic Sectional Imaging

- No uniform illumination
- Illumination is controlled to a plane (ideally)
- It is less harmless to the body because the experiment requires less laser energy
- Disadvantage: Out-of-Focus blur

Sectional Imaging (Elbau, S., Schulze)

Illumination is focused to slices/planes:

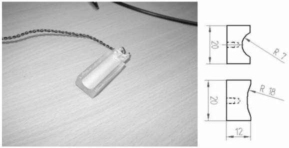

Figure: Focusing Line Detectors

- Realization with (acoustic) lenses for recording (ultrasound transducers) and focused illumination
- Physical experiments: [Razansky et al, Gratt et al]

Illustration

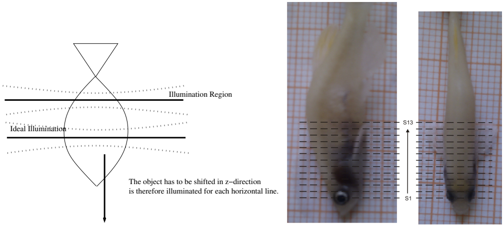

Figure: Out-of-Blur Illustration and the probe

Results With an Heuristic Method

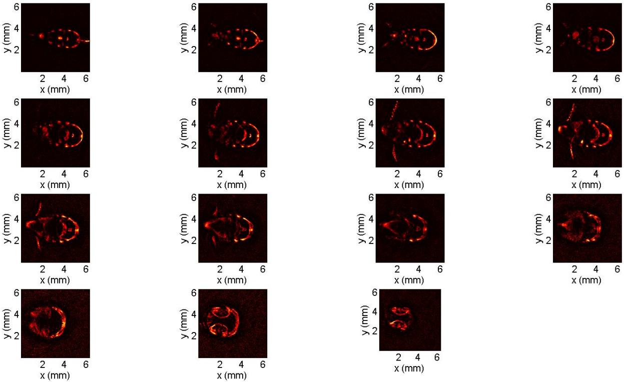

Figure: Results with horizontal integrating line detectors. Data courtesy of S. Gratt, R. Nuster and G. Paltauf (University Graz)

Sectional Imaging - Mathematical Model

Absorption density is of the

$$f(\xi, z) = \tilde{f}(\xi)\delta(z) \text{ for all } \xi \in \mathbb{R}^2, z \in \mathbb{R}$$

Wave equation with initial conditions

$$\boxed{\begin{gathered} \partial_{tt} p(\xi, z; t) - \Delta_{\xi, z} p(\xi, z; t) = 0\,, \\ p(\xi, z; 0) = f(\xi, z) = \tilde{f}(\xi)\delta(z)\,, \quad \partial_t p(\xi, z; 0) = 0 \end{gathered}}$$

2D Imaging Problem: Recover f from certain measurements.
However: Data in 3D

Sectional Imaging - A Technical Slide

- $S^1 \subseteq \mathbb{R}^2$ denotes the unit circle.
- $\Omega \subset \mathbb{R}^2$ is convex and smooth. $\partial\Omega$ is parameterized:
  - $0 \in \Omega$ and
  - for every $\theta \in S^1$, $\zeta(\theta) \in \partial\Omega$ is the *point of tangency*:

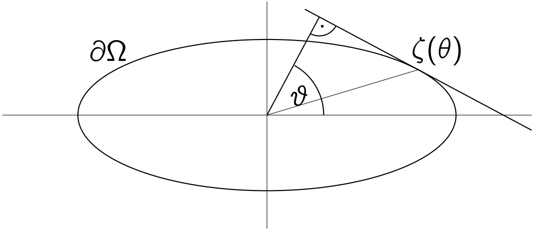

Figure: Definition of the point $\zeta(\theta)$, $\theta = (\cos\vartheta, \sin\vartheta)$.

- Tangent in the point $\zeta(\theta)$ $T(\theta)$, tangential plane $P(\theta)$ of the cylinder $\Omega \times \{z\}$ at $(\zeta(\theta), 0)$

Sectional Imaging - Measurements

Vertical Line Detectors: $m_1(\theta; t) := \int_{\mathbb{R}} p(\zeta(\theta), z; t) dz$ measure the overall pressure along a line orthogonal to the illumination plane.

Vertical Plane Detectors: $m_2(\theta; t) := \int_{P(\theta)} p(x; t) ds(x)$. *Planar detectors*, which are moved tangentially around the object.

Point Detectors: $m_3(\theta; t) := p(\zeta(\theta), 0; t)$. Measure the pressure on the boundary of $\partial\Omega$ over time. [Razansky et al]

Horizontal Line Detectors: $m_4(\theta; t) := \int_{T(\theta)} p(\xi, 0; t) ds(\xi)$. [Gratt et al]

Measurements with Vertical Line Detectors I

$$\tilde{p}(\xi;t) = \int_{-\infty}^{\infty} p(\xi,z;t)dz, \quad \xi \in \mathbb{R}^2,\ t > 0$$

satisfies the two-dimensional wave equation

$$\partial_{tt}\tilde{p}(\xi;t) = \Delta_\xi \tilde{p}(\xi;t) \quad \text{for all} \quad \xi \in \mathbb{R}^2,\ t > 0$$

with the initial conditions

$$\tilde{p}(\xi;0) = \tilde{f}(\xi)\,, \quad \partial_t \tilde{p}(\xi;0) = 0$$

2D Imaging Problem: Recover $\tilde{f}(\xi)$ from

$$m_1(\theta;t) = \tilde{p}(\zeta(\theta);t), \quad \theta \in S^1,\ t > 0$$

Measurements with Vertical Line Detectors II

Analytical reconstruction formulas for 2D problem for special geometries:

- Halfspace
- Circle
- Ellipsis [Palmadov, Elbau]

Measurements with Vertical Planar Detectors

$$\tilde{p}_\theta(r;t) = \int_{P(r,\theta)} p(x;t)ds(x)\,,$$

where $P(r,\theta)$ denotes the plane *surrounding* the object, solves

$$\boxed{\partial_{rr}\tilde{p}_\theta(r;t) = \partial_{tt}\tilde{p}_\theta(r;t)}$$

with the initial conditions

$$\tilde{p}_\theta(0;t) = m_2(\theta;t),, \qquad \partial_t\tilde{p}_\theta(r;0) = 0$$

Reconstruction in 2 steps:

- d'Alembert's formula $(m_2 \to \tilde{p}_\theta)$

$$\boxed{\tilde{p}_\theta(r;t) = m_2(\theta;-t-r) + m_2(\theta;t-r)}$$

- and Inverse Radon transform $\mathcal{R}$ $(\tilde{p}_\theta \to \tilde{f})$

$$\boxed{\tilde{p}_\theta(r;0) = \mathcal{R}[\tilde{f}](r + \langle\zeta(\theta),\theta\rangle\,,\theta)}$$

2 step algorithm is exact for every convex 2D measurement geometry

Parallel Estimation (Variable Sound Speed) with A. Kirsch (Karlsruhe)

Sectional Imaging with focusing to all planar slices

$$\boxed{\begin{array}{c} \frac{1}{c^2(x)}\partial_{tt}p - \Delta p = 0\,, \\ p(x,0) = f(x)\delta_{r,\theta}(x)\,, \quad \partial_t p(x,0) = 0 \end{array}}$$

Problem: Reconstruct c and f from measurements of p on S

Born Approximation

$$\boxed{p \approx u + v \text{ and } q := 1/c^2 - 1 \text{ (Contrast function)}}$$

$u = u^{r,\theta}$ is the solution of the wave equation

$$\boxed{\begin{aligned} \partial_{tt} u - \Delta u = 0\,, \\ u(x,0) = f(x)\,\delta_{r,\theta}(x)\,, \quad \partial_t u(x,0) = 0 \end{aligned}}$$

and $v = v^{r,\theta}$ solves

$$\boxed{\begin{aligned} \partial_{tt} v - \Delta v = -q(x)\,\partial_{tt} u\,, \\ v(x,0) = 0\,, \qquad \partial_t v(x,0) = 0 \end{aligned}}$$

Modified goal: Reconstruct q and f from measurements of

$$\boxed{m^{r,\theta}(x,t) = m(x,t) = u(x,t) + v(x,t)\,, \quad (x,t) \in S \times (0,T)}$$

Reconstruction Formula

After some calculations:

$$\hat{m}^{(r,\theta)}(x,k) = -ik \int_{z\in E(r,\theta)} f(z)$$

$$\left[k^2 \int_{\mathbb{R}^n} q(y)\Phi_k(y,z)\Phi_k(x,y)\,dy + (q(z)+1)\Phi_k(x,z)\right] ds(z)$$

Thus

$$\boxed{\hat{m}^{(r,\theta)}(x,k) = \mathcal{R}\big[(f(\cdot)\,L(x,\cdot,k))\big](r,\theta)}$$

where

- $R[f](r,\theta)$ is the $(n-1)$-dimensional Radon transform of f in direction (r,θ)
- L Volterra Integral operator

Reconstruction Procedure

1. Invert Radon transform to get the product $f(z)L(x, z, k)$ for all $x \in S$, $z \in \Omega$, $k \in \mathbb{R}$
2. Take into account the structure of L. Inversion of an ellipsoidal mean operator.

Some Curious Things

- The problem of reconstruction of f and c is unstable in any scale of Sobolev spaces [Stefanov and Uhlmann'13]
- Sectional Imaging seems to stabilize the problem

Open Questions

1. Actually the Born approximation does not hold and model assumption results in blurring. How much?
2. Reconstructions without Born. Nonlinear inverse problem
3. Taking into account semi cylindrical detectors
4. How much data is really needed? Cylindrical sampling would be great, but is unlikely
5. My favorite model: Spiral tomography approach

Thank you for your attention