Photoacoustic Scanning Tomography (PHAST) with Coded Optical Excitation: Theory and Experiment

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Photoacoustic Tomography: Objectives and Methods

**Imaging Objectives:**

1. Positions and dimensions of photoacoustic (PA) sources.
2. Characteristics of PA sources: absorption coefficient, chemical composition, blood flow rate etc.

**Standard PA Methods:**

1. Short (nanosecond) laser irradiation and broadband detection.
2. Photoacoustic microscopy with high frequency (> 30 MHz) sources.
3. Photoacoustic spectroscopy with narrow band tunable sources.
Photoacoustics: Historical Developments

Original Patent of “Photophone”

My invention consists in a method of utilizing radiant energy and of applying it by suitable apparatus to produce audible signals and to produce electric signals.

*Alexander G. Bell*

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Laser 1960

Pulsed Time-domain PA Imaging

\( f_m \)

\(<10\text{ns}\)

PA spectroscopy with tunable sources

Coded Optical Excitation

FD-PA Radar/Sonar

Laser Photoacoustics
Pulsed Laser Photoacoustics

\[ \nabla^2 p(\vec{r},t) - \frac{1}{c^2} \frac{\partial^2 p(\vec{r},t)}{\partial t^2} = \frac{-\beta}{C_p} \frac{\partial q(\vec{r},t)}{\partial t} \]

Confinement conditions:
\[ \sqrt{D_T t_L} < \mu_a^{-1} ; t_L < \frac{1}{c \mu_a} \]
\[ q(\vec{r},t) \approx \mu_a \Phi_0(\vec{r}) \delta(t) \]
\[ p_0(z) = \Gamma \mu_a \Phi_0 \exp(-\mu_a z) \]

Key Characteristics:
- High magnitude acoustic transients
- Signal profile carries information on light absorption and chromophore dimensions
- Depth information obtained from “time-of-flight” measurements
- Relatively expensive laser source, especially with tunable wavelength and high repetition rate options
- Broadband ultrasound detection – excessive level of noise and interference
Photoacoustic Imaging with Intensity Modulated CW Laser Source (Frequency Domain PA)

\[ \nabla^2 \tilde{p}(\vec{r}, \omega) + k^2 \tilde{p}(\vec{r}, \omega) = \frac{-i \omega \beta}{C_p} \tilde{q}(\vec{r}, \omega) \]

\[ \tilde{q}(\vec{r}, \omega) = \mu_a(\vec{r})I(\vec{r}) \tilde{F}(\omega) \]

Confinement conditions in FD:

\[ L_T = \left( \frac{D_I}{\omega} \right)^{1/2} \ll \mu_A^{-1} \]

\[ \omega < \omega_a = \mu_a c_a \]

Difficulties of FD photoacoustics:

1. Low optical power (0.1 – 1 W) → Low SNR
2. Long pulse duration (> 1 ms) → Poor spatial resolution
Spatially-Resolved PA Imaging with Chirped Waveforms – Photoacoustic Radar

Train of frequency-modulated pulses

\[ B(\tau) = \int_{-\infty}^{\infty} r(t+\tau)s(t)dt = \frac{1}{2\pi} \int_{-\infty}^{\infty} \tilde{R}^*(\omega)\tilde{S}(\omega)e^{i\omega\tau}d\omega \]

Correlation Processor

Transducer signal

\[ B(\tau) = \frac{A^2 T_{ch}}{2} \sin\left(\frac{\pi m \tau}{T_{ch}}\right) \left(1 - \frac{\tau}{T_{ch}}\right) \]

Peak Amplitude

Side lobes

Harmonic carrier

Time-Bandwidth product

\[ m = T_{ch}Af \]

Correlation amplitude of a linear chirp 1 – 5 MHz

Spectral windowed (Hamming) correlation
Analytical Model of PA Generation

1-D Model with Acoustic Impedance Discontinuity

\[ I(z) = I_0 e^{-w_0 z} \]

\[ \tilde{p}_{zz}(z, \omega) + k^2 \tilde{p}(z, \omega) = -\frac{i \omega \beta}{C_p} \tilde{q}(z, \omega) \]

\[ \tilde{q}(z, \omega) = \mu_a I_0 e^{-w_0 z} \tilde{F}(\omega), \quad \tilde{F}(\omega) \] - Spectrum of the laser modulation waveform

Method of transfer functions:

\[ \tilde{p}(\tilde{r}, \omega) = \tilde{H}_{PA}(\omega) \cdot I_0 \cdot \tilde{F}(\omega) \cdot \Phi(\tilde{r}) \]

1-D solution for exponential source:

\[ \tilde{H}_{PA}(\omega) = \frac{-i \mu_a c_r}{C_p (\xi c_r / \omega)^2 + \omega^2} \left( \xi k_f + i \mu_a c_r / \omega \right) \cos(k_f L) + \left( i k_f - \xi c_r / \omega \right) \sin(k_f L) \]

\[ \tilde{p}(z, \omega) = \tilde{H}_{PA}(\omega) \cdot I_0 \cdot \tilde{F}(\omega) \cdot e^{-ik_f z}, \quad k_f = \omega / c_f \]
Correlation Processing of Chirped PA Signals

**Simulation Results for a 1-D layer:**

Layer thickness: 5 mm  
$\rho_s c_s = 1.54$ MRyals  
$\rho_f c_f = 1.48$ MRyals  
Absorption: 4 cm$^{-1}$

Optical Modulation:  
Sine chirp: 1 – 5 MHz  
Chirp duration: 1 ms

Zero-mean Gaussian noise:  
Input SNR = -40 dB  
Coherent averaging of 1000 chirps  
Axial Resolution: $c / \Delta f < 1$ mm

**SNR Improvement** $\sim 56$ dB

Estimated SNR of the pulsed PA under the same conditions exceeds that of CW by $\sim 10$ dB
Correlation Processing for a Distributed Source

PA Source:

\[ q(z, t) = \mu z I_0 e^{-\mu z} f(t) \]

\[ f(t) \] - linear chirp

1. Uniform distribution (weak absorption)

2. Exponential distribution

\[ \mu_a = 4 \text{ cm}^{-1} \]

Discontinuities of source function produce correlation peaks
Signal-to-Noise of Frequency Domain PA Measurements

Matched Filter (Correlation):
\[
B(\tau) = \frac{1}{2\pi} \int \hat{R}(\omega) \hat{S}(\omega) e^{i\omega \tau} d\omega
\]
\[
|B(\tau)| = \sqrt{R^2 B(\tau) + S^2 B(\tau)}
\]

Gaussian noise PSD:
\[
N_0 = \frac{\langle P_N \rangle}{f_s/2} = \frac{2\sigma^2}{f_s}
\]

Noise of matched filter (Rayleigh distribution):
\[
PDF = \frac{A}{\sigma_A^2} \exp\left(-A^2/2\sigma_A^2\right)
\]
\[
E[A] = \sqrt{\frac{\pi}{2} \sigma_A^2} = \frac{E_s \sigma^2}{f_s}
\]
\[
Var = 0.43 \sigma_A^2
\]

SNR of Matched Filter (Single Chirp):
\[
SNR_{MF} = \frac{B^2(0)}{\langle P_{NB} \rangle} = \frac{E_s f_s}{0.43 \sigma^2}
\]

Multiple Chirps: Coherent vs Incoherent Averaging of \(N_p\) Chirps

1) Coherent Averaging (Phase retained):
\[
\langle P_N \rangle = \frac{\sigma^2}{N_p}; \quad E[B_N] = \sqrt{\frac{\pi E_s}{2 f_s N_p}} \sigma \quad \text{- Noise Background}
\]
\[
Var[B_N] = 0.43 \frac{E_s \sigma^2}{f_s N_p} \quad \text{- Noise Variance}
\]
\[
SNR = \frac{(E_s - E[B_N])^2 f_s N_p}{0.43 \sigma^2 E_s}
\]

2) Incoherent Averaging (Post processing):
\[
B_{av}(\tau) = B(\tau) + \frac{1}{N_p} \sum_{i=1}^{N_p} B_N(\tau) = B(\tau) + n_B
\]
\[
E[n_B] = \sqrt{\frac{\pi E_s}{2 f_s}} \sigma \quad \text{- Independent on } N_p
\]
\[
SNR = \frac{(E_s - \sqrt{\frac{\pi E_s}{2 f_s}} \sigma)^2}{0.43 \sigma^2 E_s} f_s N_p
\]
SNR of Coherent vs Incoherent Averaging

Two methods of signal detection with different level of the input noise (zero-mean Gaussian noise with std deviation $\sigma$)

- Coherent Averaging of 100 chirps
  - $\sigma = 100$
  - SNR = -23 dB

- Incoherent Averaging of 100 chirps
  - $\sigma = 150$
  - SNR = -25 dB
SNR and Laser Safety Limit

Maximum Permissible Exposure (1064nm, 10-7 – 10s):

\[ E_{MPE} = 5.5 \cdot T^{1/4} \ [J/cm^2] \]

SNR of Matched Filter Processing:

\[ SNR_{MF} \sim E_s \sim A_s^2 T_{ch} \]

Signal Amplitude:

\[ A_s \sim I_L \] - Laser Irradiance [W/cm²]

Assuming: \[ I_L = I_{MPE} = 5.5 \cdot T_{ch}^{-3/4} \]

Then: \[ SNR \sim I_{MPE}^2 \cdot T_{ch} \sim T_{ch}^{-1/2} \]

For \( I = I_{MPE} \), shorter chirp duration is expected to give higher SNR

\[ E_{CW} = I_L t_L \]

- Red: P = 1.76 W
- Yellow: P = 0.8 W
  (diam = 5 mm)

Laser safety curve
Effect of the Chirp Duration

Numerical Simulation using 1D Model

Chirp: 1 – 5 MHz
$T_{ch1} = 1\text{ms}$
$T_{ch2} = 250\text{us}$

+ Gaussian Noise

Theoretical SNR increase:
$$\left(\frac{SNR_2}{SNR_1}\right) = \left(\frac{T_{ch1}}{T_{ch2}}\right)^{1/2} = 2$$

Predicted increase of SNR was observed in experiments with chromophores in liquid phantoms

Optical inclusion in scattering media

Correlation SNR ($B/B_0$)

MPE Laser Power (W)
Axial Resolution Measurements of Correlation PA

Plastic sample with 10 steps ~ 250 um height inside of a scattering substrate

Laser chirp: 1 – 12 MHz, 1 ms

Correlation peak FWHM: ~250 ns translates into axial resolution ~ 375 um
Measurements of Maximum Imaging Depth

1. Modulation chirp: 1 – 5 MHz

Chromophore: 12x8mm (cross section), $\mu_a = 4 \text{ cm}^{-1}$
Transducer: 3.5 MHz, $F = 2.54 \text{ cm}$, Laser spot diam = 1.5 mm

Intralipid solution (0.47%): $\mu_{eff} \approx 1.3 \text{ cm}^{-1}$

Depth, Power
3mm, 190 mW
6mm, 190 mW
8mm, 190 mW
8mm, 540 mW
10mm, 540 mW
12mm, 1W

2. Modulation chirp: 200 – 800 kHz

Transducer: 500 kHz, $F = 5 \text{ cm}$

Graph showing correlation peak versus chromophore depth (mm).
Scanning Chromophores in Tissue

Ex-vivo muscle tissue of small animal (rat)
(Three wires inserted in muscle tissue)

Imaging of blood vessels in human wrist in-vivo

3.5 MHz focused transducer

Surface

Skin surface

1 cm
 Imaging of Subcutaneous Cancer in-vivo

Tumour implanted subcutaneously in a thigh of immunodeficient rat

Conventional Ultrasound Image

PA Correlation Image
(Chirp: 1 – 5 MHz)
Phased Array Correlation Imaging

Correlation Phased Array – multichannel matched filter processing and beamforming in frequency domain

1) Array acquisition and FFT of signal matrix
\[ \tilde{B}_i(\omega) = \tilde{W}(\omega) \cdot \tilde{R}^*(\omega) \cdot \tilde{S}_i(\omega) \] - matrix \( N_x \times N_t \), \( N_t = 100k \)

2) Digital beamforming, i.e. spatial filtering by creating directional beams and beam steering
\[ \tilde{U}(\omega, \theta) = \sum_{n=1}^{N_t} w_n \cdot \tilde{B}_n(\omega) \cdot \exp(-i \omega t_n(\theta)) \]
\[ t_n(\theta) = \frac{y_n}{c_{\alpha}} \sin(\theta) + t_r \]
\[ k = \frac{\omega}{c_{\alpha}} = k_x^2 + k_y^2 \] \( \Rightarrow \) \( \tilde{U}(k, \theta) \) - Spatial spectrum

3) Backprojection:
\[ u(x, y) = \text{FFT}^{-1}[\tilde{U}] \]
Phased array PA Correlation Imaging

Transducer phased array: 64 elements, 3.5 MHz central frequency
Laser mean power: 1W, spot diam 2.8 mm, chirp f = 1 – 5 MHz, 1ms

System PSF, SNR = -34dB
Optical inclusion in scattering phantom
Discrete chromophores in Intralipid

Phased array probe for PA imaging
PA correlation image of wrist
Phased Array Correlation PA Imaging in vivo

Immunodeficient rats with FaDu (carcinoma cells) injected intramuscularly

Laser beam (1 W, 1.5 mm in diameter) is scanned along the array axis
Conclusions

Depth-resolved PA imaging with CW laser sources is feasible using coded optical excitation (linear chirps) and correlation signal processing.

Correlation processing of coded PA response provides significant increase of SNR (> 50 dB).

Axial resolution determined by the correlation peak width can be < 300 um for the chirp bandwidth > 10 MHz.

Imaging of tissue chromophores within 2 cm depth range is feasible with inexpensive laser sources and coded modulation waveforms.

To achieve maximum SNR performance multiple chirps must be averaged coherently in pre-processing and chirp duration should be set according to MPE.

Phased array PA correlation imaging was demonstrated using conventional ultrasound array and a frequency-domain reconstruction algorithm.

Other forms of coded optical excitation including phase-coded waveforms are possible.
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