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5aBAb6. Dynamic time reversal acoustic focusing of ultrasound for biomedical applications

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Time Reversal Acoustic (TRA) system provides effective focusing in inhomogeneous media that can be used in various biomedical applications including high intensity ultrasound treatment, ultrasound-assisted drug delivery, ultrasonic battery charging of implants, etc. In many cases the temporal variation of propagating media properties leads to a degradation of the focusing. The in situ adjustment of radiated TRA signal is required in order to restore focusing. We present the feedback algorithm with Tikhonov regularization that enables the refocusing of acoustic field based on the changes in the focused signal received by a beacon. Temporal and spatial quality of the feedback refocusing was characterized experimentally using hydrophone and compared with standard TRA focusing. Algorithm is applicable for power delivery to implantable wireless cardiac pacemakers, percutaneous devices and neuro-stimulators.

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INTRODUCTION

Time Reversal Acoustic (TRA) systems are used to focus ultrasound in inhomogeneous media. TRA principles are applicable in various biomedical applications including high intensity ultrasound treatment, ultrasound-assisted drug delivery, ultrasonic battery charging of implants, etc. In many cases the temporal variation of propagating media properties degrades the TRA focusing. An in situ adjustment of radiated TRA signal is necessary to maintain the good focusing. We present an algorithm based on the Tikhonov Inverse Filter (TIF) that enables the refocusing of acoustic field based on the changes in the focused signal received by a beacon. Temporal and spatial quality of the TIF refocusing is characterized experimentally using hydrophone and compared with the TRA focusing. Algorithm is applicable for power delivery to implantable wireless cardiac pacemakers, percutaneous devices and neuro-stimulators.

Focusing energy in space and time received considerable interest in the studies of electromagnetic and acoustic wave propagation. Focusing with lenses and phased arrays becomes deficient in media with random phase inhomogeneities. Atmosphere, ocean, Earth’s interior and biological tissues are few examples. The first method of focusing through inhomogeneous media was developed in optics (Zeldovich et al. 1985). Later, methods exploring the principle of time-reversal invariance and wave phase conjugation were introduced in acoustics (Fink 1997, Brysev 2004). The TRA focusing methods were investigated in application for diagnostic imaging and therapy, such as kidney stone removal (Montaldo et al. 2002), therapeutic ultrasound for breast cancer treatment (Huang et al. 2006), atrial fibrillation treatment (Sinelnikov et al. 2008), detection of flaws in solids (Prada et al. 2002) etc.

Focusing ultrasound inside human bodies is a subject of body part movement, breathing, heart beating, temperature changes etc. The TRA principle provides a method of acoustic compensation for all these changes. It was realized in the first TRA system for kidney stone disintegration (Montaldo et al. 2002). In this work we consider an alternative TIF method that restores TRA focusing at the receiver location. The TIF and TRA filter are two commonly known filter design that are applicable to the linear time invariant systems (Dumuid et al. 2005). The TIF filter enables to compensate for the temporal changes in propagating media and to minimize the variation of the focused signal amplitude. This method can be used for convection enhanced drug delivery methods (Pitt et al. 2004), treatment of focal neurological disorders and spinal cord degeneration. The dynamic refocusing can be applicable for power delivery to implantable wireless cardiac pacemakers, percutaneous devices and neuro-stimulators (Seip et al. 1994). The TIF method opens a perspective to overcome the variability in tissue and anatomy in a broad range of new minimally invasive medical applications.

The paper is structured in two sections. In the first section the mathematical description of the standard time reversal and Tikhonov inverse filter refocusing are outlined. The second section demonstrates experimental results of TRA focusing and compares it with TIF refocusing. At the end of the paper we considered the use of the proposed method for implantable and percutaneous devices tracking and motion compensation.

MATHEMATICAL DESCRIPTION

Considers a stationary linear causal system comprised of a single ultrasonic transducer and a receiver hydrophone and fully characterized by its impulse responses. The output signal, \( s(t) \), received by the hydrophone is a convolution of the input signal \( e(t) \), applied to an emitting transducer, and impulse response \( h(t) \). In case of multiple transducers, the output signal from all transducers is a superposition of individual output signals. For sake of simplicity we consider single transducer receiver pair. The output signal from the single transducer is:

\[
s(t) = e(t) \otimes h(t)
\]  \hspace{1cm} (1)

The impulse response \( h(t) \) is a convolution of transducer, receiver and media impulse responses. In frequency domain equation (1) takes the form:

\[
S(\omega) = E(\omega)H(\omega)
\]  \hspace{1cm} (2)
Where capitalized letters stand for the respective Fourier transforms. As time reversed signal \( s_n(-t) \) is applied to the input transducer, TRA focusing occurs at receiver. The frequency transform of the focused signal is:

\[
F'_n(\omega) = E^*(\omega)H^*(\omega)H(\omega)
\]  

(3)

The knowledge of the impulse response is sufficient to construct any desired output signal in stationary linear system. From equation (2) the inverse filtering technique yields the frequency transform of the impulse response:

\[
H(\omega) = S(\omega)/E(\omega)
\]  

(4)

which becomes unstable as the magnitude of \( E(\omega) \) approaches zero. Impulse response derived from (4) enables to reconstruct the output signal in the focus. In case of TRA focusing the goal is to achieve maximum focusing amplitude. The solution is given by the Tikhonov inverse filtering:

\[
H(\omega) = S(\omega)E^*(\omega)/(E(\omega)E^*(\omega) + \zeta)
\]  

(5)

where \( \zeta \) is a regularization factor (Tikhonov, 1963). Equations (2) and (5) provide a way to construct a transform of the input signal \( S^*(\omega) \), such that when it is transmitted through the media, the maximum amplitude focused TRA signal is reproduced at the receiver location.

**EXPERIMENT**

Acoustic measurements were conducted in the experimental setup schematically shown in Figure 1. The TRA reverberator was fabricated from an aluminum tapered cone with random planar cuts for enhanced reverberations. The PZT disk transducer with 25 mm diameter and resonance frequency around 1 MHz was attached to one of the planar surfaces of the cone. The tapered side of the cone was submerged into water tank by few millimeters. The ultrasound signal in the tank was recorded using two different hydrophone: the needle-type HNA series hydrophone from Onda Corporation with aperture size of 400 microns and the cylindrical transducer with 2 mm diameter and wall thickness resonance around 1 MHz. The hydrophones were rigidly attached to a computer controlled 3-D positioning system integrated with the TRA signal generation and processing module. The acoustic reverberator cone faced downward into acoustic tank with its tapered tip submerged by few millimeters into water. The Matlab graphical user interface provided an arbitrary waveform signal generation, signal processing and acquisition functions.

The snap shot of the signals in the process of the TRA focusing is presented in Figure 2. The left panel demonstrate the initial step of TRA focusing: a short burst of 1 MHz and was applied to the cone transducer and corresponding long reverberation signal was recorded by the hydrophone inside the water tank. The multiple reflections predominantly originated from within aluminum cone and its internal boundaries. The right panel of the Figure 2 demonstrates the second step of TRA focusing: the time reversed signal is applied to a transducer and corresponding TRA focused signal is recorded by hydrophone.

**FIGURE 1.** Experimental setup is shown schematically. Signals are generated by the TRA system and applied to a single transducer (1) mounted on solid aluminum reverberating cone (2). The acoustic waves reverberate in the cone and propagate into a water tank. The needle hydrophone (3) picks up the acoustic signal that is amplified and fed into the TRA system.
The signals in the process of the TIF refocusing to a point shifted by a few mm from the original TRA focus location are shown in Figure 3. The left panel shows the input time reversed signal and respective received hydrophone signal that is no longer focused and has much lower peak amplitude than the original TRA focused in previous figure, shown to scale. The right panel illustrates the TIF refocusing: the input signal is obtained by applying the equations (2) and (5) to a pair of input – received signals shown on the left panel. New input signal is applied to the transducer and respective refocused signal is shown on the right panel of Figure 3. The TIF refocused signal is characterized by good time recompression and peak amplitude significantly higher than on the left panel and comparable to the original TRA focused signal.

The regularization coefficient was chosen empirically from the preliminary experiments. From the above formalism it is evident that the impulse response transform $H(\omega)$ depends on the Tikhonov regularization factor $\zeta$. The equation (5) is ill posed for $\zeta \to 0$, while its solution deviates from original problem for sufficiently large $\zeta$. The optimal regularization factor depends on the signals, setup geometry, noise conditions. A series of the TIF refocusing experiments were performed at a distance 2 mm away from the original location for a set of regularization factors $\zeta$ (Figure 4). The experimental amplitudes achieved by the TIF refocusing were smaller than those attained by TRA focusing for small $\zeta$ and the TIF refocusing outperformed TRA focusing by about 10% for values of $\zeta > 10^4$. The increase in TIF refocusing performance correlated with the maximum of the waveform amplitude.
FIGURE 4. Experimental results demonstrating the efficiency of the TIF refocusing. Left panel shows focused waveforms obtained in a process of TIF refocusing: (a) TRA focused signal in the location 2 mm away from focus, TIF refocused signal using regularization factor equal to 16 (b), 1024 (c), 524000(d). Right panel compares the TIF refocusing in different regimes: normal – obtained with analogue TRA system and binary – obtained with binary TRA system. The graph provides amplitude dependence of the TIF refocusing relative to the TRA focusing as a function of the regularization factor.

For small regularization factors the focused waveforms have low level of the side lobes, while large values yield less confined waveforms with larger side lobes level. The overall trend is shown in Figure 4. In agreement with computer simulations, the Tikhonov regularization factor was set to $\zeta = 10^5$ in order to maximize the amplitude of the TIF refocusing and minimize the side lobes. The effectiveness of the TIF refocusing was evaluated in two different regimes: using analogue TRA system, capable of producing an arbitrary waveform signals, and binary TRA systems with fast switching time and only two levels of excitation. Both regimes produced good quality refocusing. Right panels of the Figure 4 show the waveforms labeled normal and binary, obtained using analogue binary TRA systems respectively.

The spatial quality of the TIF refocusing was characterized in a series of two dimensional hydrophone maps and compared with the TRA focusing. The temporal peak acoustic pressure amplitude was measured over 10 mm by 10 mm region in a horizontal plane. Each map consisted of 400 by 400 measurements. The distance to the mapping plane from aluminum cone was about 20 mm. Figure 5 shows the focal pattern achieved by the TRA focusing and TIF refocusing techniques. First, TRA focusing was constructed in the middle or the region of interest and hydrophone map was recorded. Next, similar maps were obtained using the TIF refocusing in two diagonally shifted locations. The acoustic pressures were consistently higher during the TIF refocusing compared to TRA focusing. Within the measurements uncertainty the spatial focal peak widths were identical for both TIF and TRA methods.
FIGURE 5. Two-dimensional maps of peak acoustic peak recorded in the process of TRA focusing and TIF refocusing. From left to right the hydrophone maps show spatial focus due to: a) TIF refocusing in the third quadrant at the point (-3, -3) mm, b) TRA focusing in the middle at (0, 0) mm, c) TIF refocusing in the first quadrant at (3, 3) mm.

The efficiency of the TIF refocusing was further evaluated over larger distances in a series of linear peak acoustic pressure scans. Signals were constructed to focus at discrete locations 10 mm apart along the horizontal line, starting from zero that corresponded to the position closest to the aluminum cone. The spatial profiles of the peak acoustic pressure obtained by TRA focusing and TIF refocusing are shown in Figure 6. The spatial range up to 80 mm was investigated. In each discrete location the three step procedure was followed. First, the TRA focusing was constructed at the point of interest and respective spatial profile of the maximum acoustic pressure was recorded. Second, the hydrophone was moved to coordinate zero and the TRA focusing was repeated without spatial scan. Third, the hydrophone was moved back to the location of interest, where TIF refocusing was performed and another spatial profile was recorded. In the studied configuration, both TRA and TIF techniques demonstrated a wide spatial range of focusing. The peak amplitudes varied by about 20%, while the focal width increased by 137% from the center to 30 mm location. In each discrete location the peak amplitudes obtained by TIF refocusing consistently exceeded TRA focusing by few percent, in agreement with computer modeling.

FIGURE 6. Lateral scans of the peak acoustic pressure achieved by TRA focusing (solid lines) and the TIF refocusing (dashed lines). The TIF profiles were obtained by first focusing in the middle at X=0, then moving and refocusing in the new location.
CONCLUSION

The results indicate that TIF refocusing can become an alternative to the TRA focusing method for ultrasonic applications in which acoustic feedback is available and continuous delivery of acoustic energy is important. While in dynamically changing environment the TRA focusing of acoustic energy quickly decreases, the TIF refocusing technique has an advantage. Our experiments demonstrate the ability of TIF refocusing technique to restore spatial and temporal parameters of the focused waveforms and potentially compensate for tissue anatomy volatility and physiological movements. Such in situ TIF refocusing can be applicable in power delivery to implantable wireless cardiac pacemakers, percutaneous devices and various therapeutic applications.

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