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► To cite this version:

Sébastien Ménigot, Jean-Marc Girault. Optimization of Contrast-to-Tissue Ratio by Adaptation of Transmitted Ternary Signal in Ultrasound Pulse Inversion Imaging. Computational and Mathematical Methods in Medicine, 2013, 2013, pp.6. 10.1155/2013/297463 . hal-00805020v1

HAL Id: hal-00805020

<https://hal.science/hal-00805020v1>

Submitted on 8 Nov 2013 (v1), last revised 21 Oct 2014 (v2)

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Optimization of Contrast-to-Tissue Ratio by Adaptation of Transmitted Ternary Signal in Ultrasound Pulse Inversion Imaging

Sébastien Ménigot ^{*†‡} and Jean-Marc Girault ^{†‡}

^{*} IUT Ville d'Avray, université Paris Ouest Nanterre La Défense, Ville d'Avray, France

[†] UMR-S930, université François-Rabelais de Tours, Tours, France

[‡] U 930, Inserm, Tours, France

ABSTRACT

Ultrasound contrast imaging has provided more accurate medical diagnoses thanks to the development of innovating modalities like the pulse inversion imaging. However, this latter modality that improves the contrast-to-tissue ratio (*CTR*) is not optimal, since the frequency is manually chosen jointly with the probe. However, an optimal choice of this command is possible but it requires precise information about the transducer and the medium which can be experimentally difficult to obtain, even inaccessible. It turns out that the optimization can become more complex by taking into account the kind of generators, since the generators of electrical signals in a conventional ultrasound scanner can be unipolar, bipolar or tripolar. Our aim was to seek the ternary command which maximized the *CTR*. By combining a genetic algorithm and a closed loop, the system automatically proposed the optimal ternary command. In simulation, the gain compared with the usual ternary signal could reach about 3.9 dB. Another interesting finding was that in contrast to what is generally accepted, the optimal command was not a fixed-frequency signal, but had harmonic components.

Index Terms— Genetic Algorithm, optimal command, pulse inversion, ultrasound imaging, ternary signal.

1. INTRODUCTION

Intravenous injection of ultrasound contrast agents containing microbubbles has revolutionized medical ultrasound imaging in the past twenty years by making possible extraction of physiological and pathological information [1]. Subsequently, the contrast between the tissue perfused by the microbubbles and the non-perfused tissue, *i.e.* contrast-to-tissue ratio (*CTR*), has been improved by taking into account the nonlinear behaviour of microbubbles, as in second harmonic imaging [2], subharmonic imaging [3], super harmonic imaging [4] and attenuation correction [5].

However, the effects of the propagation of the ultrasound wave have limited these improvements since the tissue can generate nonlinearities, thereby reducing the *CTR*. Furthermore, since good separation of the harmonic components requires a limited pulse bandwidth [6], the axial resolution has been limited. To overcome this drawback, certain discrete encoding techniques such as pulse inversion imaging [7], power modulation [8], contrast pulse sequencing [9] and pulse subtraction [10] have been

23 developed to ensure good axial resolution while increasing the *CTR*. Finally, to solve the trade-off between resolution and
24 penetration, other imaging methods such as harmonic chirp imaging [11] have extended this principle for continuous encoding.

25 However, whatever the imaging system used in clinical practise, the fact remains that the excitation settings are manufacturer
26 and user dependant. From our point of view, these settings are not optimal, since they must take into account the explored
27 medium. For adjusting these settings to any examination, it is necessary to correctly adjust this excitation. To do so, the optimal
28 command framework in which the problem takes place is presented. Thus the problem can be written such a way that the
29 optimal command $x^*(n)$ of the ultrasound imaging system provides the best *CTR*:

$$x^*(n) = \underset{x(n)}{\operatorname{argmax}} (CTR(x(n))), \quad (1)$$

30 where $x(n)$ is the signal transmitted and n the discrete time.

31 Some solutions have been already proposed to solve equation 1 by either minimizing the tissue backscattering, or maxi-
32 mizing the microbubble backscattering. In this context, two interesting approaches have been proposed. On the one hand, time
33 reversal imaging only makes it possible to reduce the nonlinearities of the tissue backscattering [12]. Unfortunately, the for-
34 malism is linear and cannot take into account the microbubble nonlinearities to maximize them. On the other hand, an analytic
35 solution has been proposed for the microbubble backscattering [13]. However, this theoretical solution requires the knowledge
36 of all physical properties about the microbubble, the surrounding medium and the transducer. These *a priori* information which
37 can be accessible with difficulty, even completely inaccessible, led this analytical solution inapplicable in practice.

38 To overcome these limitations, a novel method has recently been proposed. This approach solves equation 1 by transforming
39 a shape optimization into a suboptimal parametric optimization [14]. In this latter work, the parameter to be optimized was the
40 transmit frequency. Thus the optimal frequency was the transmit frequency which optimized the cost-function *CTR*. The com-
41 putation of this optimal frequency was obtained automatically by using a simple algorithm based on the gradient. Although this
42 method is simple, it lays the groundwork of the optimal command. Unfortunately this approach is not completely satisfactory
43 since the initial fixed waveform may not be suitable [15]. Furthermore, this approach does not take into account the specific
44 features of electrical signal generators in conventional ultrasound scanners. For these ultrasound scanners, transmitters are usu-
45 ally unipolar (voltage impulse V), bipolar (voltage -V or V) or tripolar (voltage -V, 0 or V) generators, because their electronic
46 conception is easier. Recently, the nature of the generator have been taken into account in order to improve the signal-to-noise
47 ratio [16] and microbubble detection [17] by combining a binary waveform and an advanced imaging approach. Hovewer, no
48 input optimization process has yet been been proposed to find the optimal command.

49 Finally, no method has been proposed to date to overcome this problem satisfactorily and optimally by taking into account
50 the tripolar transmitter constraint. Since (i) one of the most commonly used ultrasound imaging approaches is pulse inversion
51 imaging and (ii) a conventional transmitter is a tripolar generator, the aim of this study was to determine automatically the

52 optimal ternary command for the ultrasound pulse inversion imaging system to provide the best CTR :

$$x^*(n) = \underset{x(n)=\{-1,0,1\}, \forall n}{\operatorname{argmax}} (CTR(x(n))). \quad (2)$$

53 We therefore modified the current system (including a tripolar ultrasound transmitter) by including feedback. To resolve the
 54 digital waveform optimization, we proposed using a genetic algorithm through simulations. The advantage of the method was
 55 that no *a priori* information was required in order to find the optimal ternary command.

56 2. CLOSED LOOP SYSTEM

57 The principle of pulse inversion imaging including feedback is described in Fig. 1. For an individual solution at the iteration
 58 k , two ternary pulses $x_{k,1}(n)$ and $x_{k,2}(n)$ with opposite phases were transmitted. The sum $z_k(n)$ of the two respective echoes
 59 $y_{k,1}(n)$ and $y_{k,2}(n)$ formed a radiofrequency line l_k . By taking into account the CTR_k estimated on this radiofrequency line l_k ,
 60 a new transmitted ternary signal $x_{k+1}(n)$ was proposed by the algorithm to optimize the CTR_{k+1} .

61 [Figure 1 about here.]

62 2.1. Transmitted Ternary Signal

63 The ternary pulse signal $x_{k,q}(n)$ was digitally computed with Matlab (Mathworks, Natick, MA, USA):

$$x_{k,q}(n) = \begin{cases} A \cdot w_k(n) & \text{if } q = 1; \\ -A \cdot w_k(n) & \text{if } q = 2. \end{cases} \quad (3)$$

64 The ternary signal $w_k(n)$ was defined on a duration T , which corresponded to 100% of the fractional bandwidth of the trans-
 65 ducer. It was thus constructed from N_s samples where each sample could take the value $-1, 0$ or 1 .

66 The amplitude of the driving pressure A was then adjusted so that the power of the pulse $x_{k,p}(t)$ was constant to $P_{x_{ref}}$ for
 67 all ternary signals transmitted:

$$A = \sqrt{\frac{A_0^2 \cdot P_{x_{ref}}}{P_w}}, \quad (4)$$

68 where the power $P_{x_{ref}}$ was calculated for a signal x_{ref} which was the impulse response of the transducer with a driving pressure
 69 A_0 . The power P_w was the power of the signal $w_{k,p}$. The power of the transmitted wave thus remained constant by adjusting
 70 the amplitude signal A .

71 **2.2. Cost Function**

72 The aim was to maximize the contrast between the tissue perfused by the microbubbles and the non-perfused tissue by selecting
73 the transmitted signal $x(n)$. Since the usual contrast estimator in ultrasound contrast imaging is the CTR , the cost function was
74 CTR_k computed from a line $z_k(n)$:

$$z_k(n) = y_{k,1}(n) + y_{k,2}(n), \quad (5)$$

75 where $y_{k,p}(n)$ is the echo of the transmitted pulse $x_{k,p}(n)$. Thus the CTR_k is defined as the ratio of the power $P_{b,k}$ backscattered
76 by the area of the perfused medium to the power $P_{t,k}$ backscattered by the area of the non-perfused medium [18] as follows:

$$CTR_k = 10 \cdot \log_{10} \left(\frac{P_{b,k}}{P_{t,k}} \right). \quad (6)$$

77 These powers were computed from the lines $z_k(n)$ of the pulse inversion image. Note that the areas were delineated manually
78 before the optimization process, but a segmentation step could be implemented to help the delineate process.

79 **2.3. Genetic Algorithm**

80 The seeking of the optimal excitation $x^*(n)$ consisted in (i) transmitting ternary stochastic signals $w_k(n)$ through the medium
81 and in (ii) selecting the optimal ternary signal which maximized the cost function. However since this latter step required
82 a large number of ternary stochastic signals, to reduce the computational time we proposed using metaheuristic. This meta-
83 heuristic based on the principle of biological reproduction [19] is a genetic algorithm. It found the optimum by setting a
84 chromosome [20], *i.e.* a vector composed of N_s samples of the ternary signal $w_k(n)$.

85 The ternary genetic algorithm was based on a binary genetic algorithm [21]. In our case, at each iteration k , a generation k
86 with M ternary individual solutions (sample vectors) was tested where the probability of the sample value was uniform between
87 $-1, 0$ or 1 . As proposed in [21], the number M of individual solutions per generation was 12.

88 For the next generation $k + 1$, the selection operator only conserved the $M/2$ best individual solutions which maximized
89 the CTR . These vectors became pairs and mates. The best parent was then mixed with one of the $M/2 - 1$ remaining parents
90 by the crossover operator. The offspring was constituted of part of the first parent samples until the crossover point and part of
91 the second parent samples from the crossover point. Note that the crossover point was randomly selected between the first and
92 the last sample. An offspring of $M/2$ new individual solutions thus contained the ternary signal of both parents.

93 Finally 40% samples were mutated so that the optimization was robust. The best individual solution was the optimal ternary
94 command for the generation k . Note a small population and a high mutation rate were chosen to solve the trade-off between
95 robustness and the computation time due to sorting of each individual solution [21].

3. SIMULATION MODEL

97 The simulation model was constructed on the pulse inversion imaging system (Fig. 1). It was composed of different phases:
 98 transmission, 2D nonlinear propagation, nonlinear oscillations of microbubbles and reception [14]. A pulse wave was propa-
 99 gated nonlinearly into an attenuating medium without microbubbles. This wave, composed of harmonic components, excited
 100 a microbubble in the vascular system. The nonlinear oscillations of this microbubble were backscattered and measured by the
 101 receiver.

102 **3.1. Nonlinear Propagation in Tissue**

103 A ternary signal $x_{k,1}(n)$ was generated digitally and filtered by the transfer function of a realistic transducer, centred at $f_c = 4$
 104 MHz with a fractional bandwidth of 75% at -3 dB. The 2D nonlinear wave propagation into the medium was obtained by
 105 solving Anderson's model based on a pseudo-spectral derivative and a time-domain integration algorithm [22]. This solver
 106 required three grids: a grid of mean density of $928 \text{ kg}\cdot\text{m}^{-3}$, a grid of mean speed of sound of $1578 \text{ m}\cdot\text{s}^{-1}$ and a grid of B/A
 107 nonlinearity parameter of 6.7 [23]. The scatterers were generated randomly by weakly modifying the density grid of $\pm 0,5$
 108 $\text{kg}\cdot\text{m}^{-3}$ and the speed grid of $\pm 0,5 \text{ m}\cdot\text{s}^{-1}$. Note that an attenuation of $0.45 \text{ dB}\cdot\text{MHz}^{-1.05}\cdot\text{cm}^{-1}$ was used. Finally, the signal
 109 backscattered by tissue was recorded, and the driving pressure at 15 mm was included into the microbubble model described
 110 below.

111 **3.2. Microbubble**

112 The simulated ultrasound contrast agent had the properties of encapsulated microbubbles used in clinical practice with a mean
 113 diameter of $2.5 \mu\text{m}$ [24] and a resonance frequency of 2.6 MHz [25]. The acoustic response was computed for one microbubble
 114 from Marmottant's model [26] based on the Rayleigh-Plesset equation and the polytropic transformation. Finally, since the
 115 pressure was low in comparison with the transmitted pressure, the echo of the microbubble was deduced from the oscillation [27]
 116 without including nonlinear propagation. Note that in order to simulate the mean behaviour of a microbubble cloud, we
 117 hypothesized that the response of a cloud of N_b microbubbles was N_b times the response of a single microbubble with the mean
 118 properties. To simplify, the microbubble response was thus multiplied by N_b in order to simulate a mean nonlinear behaviour
 119 of a 1/2000 diluted microbubble cloud. Moreover, to be more realistic, the attenuation effects due to the high concentration of
 120 microbubbles were taken into account [28] for this dilution.

121 The echoes from tissue and microbubbles were added and filtered by the transfer function of the transducer to construct the
 122 first echo for the transmitted signal $x_{k,1}(n)$. The simulation process was repeated for the transmitted ternary pulse $x_{k,2}(n)$ to
 123 construct the second echo. Finally, the radiofrequency line l_k was constructed from $z_k(n)$ described by equation 5.

4. RESULTS

The optimization process was applied to the previous simulation model. The driving pressure A_0 was set at 400 kPa. The duration T of the ternary signal represented 100% of the fractional bandwidth of the transducer, *i.e.* $T = 0.3 \mu\text{s}$. According to the sampling rate required by the simulation model, there were 40 samples in $0.3 \mu\text{s}$, therefore $N_s = 40$.

To demonstrate the efficacy of the new method, the results were compared to those of two usual transmitted signals. To construct them, Gaussian-modulated sinusoidal pulses were digitalized to obtain a ternary signal. Their bandwidth represented 100% of the fractional bandwidth of the transducer and their transmitted power was $P_{x_{ref}}$. Their transmit frequencies were set at (i) two-thirds of the central frequency f_c of the transducer [29] ($2/3f_c = 2.67 \text{ MHz}$), and at (ii) the optimal frequency f_{opt} . Note that this optimal frequency f_{opt} enabled to maximize the cost-function CTR as presented in [14].

[Table 1 about here.]

Table 1 summarizes the CTR measured for the optimal ternary signal and the two usual ternary signals. By using frequency optimization, it was possible to achieve a suboptimal solution, better than the transmitted signal at the usual transmit frequency. However, the CTR was higher with the transmitted ternary signal. This CTR value could not be achieved with the usual ternary signal digitalized from a Gaussian-modulated sinusoidal pulse, although the transmit frequency was optimized.

Fig. 2 shows the best CTR as a function of generation k . As an illustration, this result was compared with the two usual ternary signals. After 239 generations, the CTR achieved an optimal value that was higher than the frequency setting cases. The gain reached 3.9 dB in comparison with the usual fixed-frequency transmitted signal, and 0.8 dB in comparison with the transmitted signal at the optimal frequency f_{opt} .

[Figure 2 about here.]

Fig. 3a shows the optimal ternary command $w_{opt}(n)$. As an illustration, Fig. 3b shows the signal $p(n)$ at the transducer output (Fig. 1) transmitted to the tissue when $w(n)$ was the optimal ternary signal (Fig. 3a) and the corresponding backscattered signal was shown in Fig. 3c. Their respective spectra were presented in Fig. 3d. Unlike an usual fixed-frequency transmitted signal, the optimal transmitted signal had nonlinear components. Note that the nonlinear components backscattered by the tissue and the microbubbles remained, because in pulse inversion imaging the linear component was suppressed.

[Figure 3 about here.]

5. DISCUSSION AND CONCLUSIONS

From results derived from Fig. 2, the optimal command methods, presented in [14] and here, outperformed the non-optimized reference method. Although these two methods are optimal command methods, they presented some significant differences. The first method [14] by imposing a waveform defined by a frequency parameter constitutes an optimal mono-parametric solution,

153 and the second method proposed here by imposing a ternary constraint on the waveform constituted an optimal multi-sample
154 solution.

155 In this latter method, ternary sequences were automatically transmitted through a pulse inversion imaging system in order
156 to optimize the *CTR*. This optimization was performed without taking into account *a priori* information about the medium or
157 the transducer, except the fact that this method required a selection of two regions of interest (with and without microbubbles).
158 The delineation of these regions of interest constituted both the strength of the method since it enabled to define the *CTR* cost-
159 function, and a drawback for fully perfused tissue for which no *CTR* computation is possible. Note that to partly overcome this
160 problem, it can be recommended to change the organ section in a view to delineate an non-perfused area.

161 Nevertheless, by disregarding the latter drawback, the closed loop system had the advantage to provided an optimal ternary
162 command. By using this optimal ternary command, the *CTR* was higher than with usual ternary signals digitalized from
163 Gaussian-modulated sinusoidal pulses at a fixed transmit frequency. This optimal setting proposed a filtered ternary wave
164 composed of harmonic components transmitted to the medium being explored. While most researchers have focused on using
165 a fixed-frequency transmitted signal, the better solution was to find a transmitted signal composed of harmonic components.
166 These harmonic components present in the transmitted signal did not affect the *CTR*, because the pulse inversion properties
167 ensured the extraction of nonlinearities generated only by the medium. This property may explain the compromise between
168 maximizing microbubble backscattering and minimizing tissue backscattering. Furthermore, since the transducer bandwidth
169 was not broad enough, the double frequency of the second harmonic component was not present in the backscattered signal.
170 However since the process reached the optimum without the presence of the double frequency of this component, the only
171 presence of a linear interaction acting on the transmitted second harmonic component seemed to play a crucial role in the
172 optimization process.

173 Finally the last advantage which seemed to be important was that the method automatically adjusted the transmitted ternary
174 signal for any nonlinear and attenuating medium to be explored. The reason of this benefit was that the cost-function, exclu-
175 sively computed from the mean power of the output system, was independent of the microbubble size distribution. Indeed, as the
176 backscattered mean power corresponds to an average operating on the whole spectrum, thus its value is independent of the fre-
177 quency distribution whether the spectrum had a narrow bandwidth (same microbubble size) or a large bandwidth (polydisperse
178 microbubble size). Thus, even if the assumptions of the simulation model were simplified, the process of the *CTR* optimization
179 completely ignored the nature of different underlying processes as the multiple scattering or the microbubble speckle. The
180 method can therefore be applied to any medium to be explored.

181 For future integration in an ultrasound imaging system, the time to achieve optimization is crucial. First, the *CTR* compu-
182 tation from regions of interest ($L \times L$ size) in the image required $2(2L + 1)^2 + 1$ operations. Secondly, the genetic algorithm
183 required $0.4(12N_s) + 6$ random selections per generation to achieve the optimum. Taking into account the computing power
184 available for a personal computer, the two last operations must not slow down the optimization process. However, the number
185 of generations to achieve the optimum may be a limiting factor. Since the frame rate can reach 2000 Hz in some ultrasound

186 scanners, this limitation should be relative. We therefore estimated that the optimization should take less than 5 seconds.

187 To conclude, the method reported ensured optimal *CTR* by selecting the appropriate transmitted ternary signal. The method
188 could be applied to ultrasound imaging without using programmable analogue transmitters in contrast to transmit frequency
189 optimization. Manufacturers and clinicians would not themselves need to tune the transmitted signal. This new approach
190 could open up optimal commands for ultrasound imaging. The next step will be to implement it in an ultrasound scanner.
191 Moreover, the future approach should take into account the fact that the optimal transmitted signal must be composed of
192 harmonic components.

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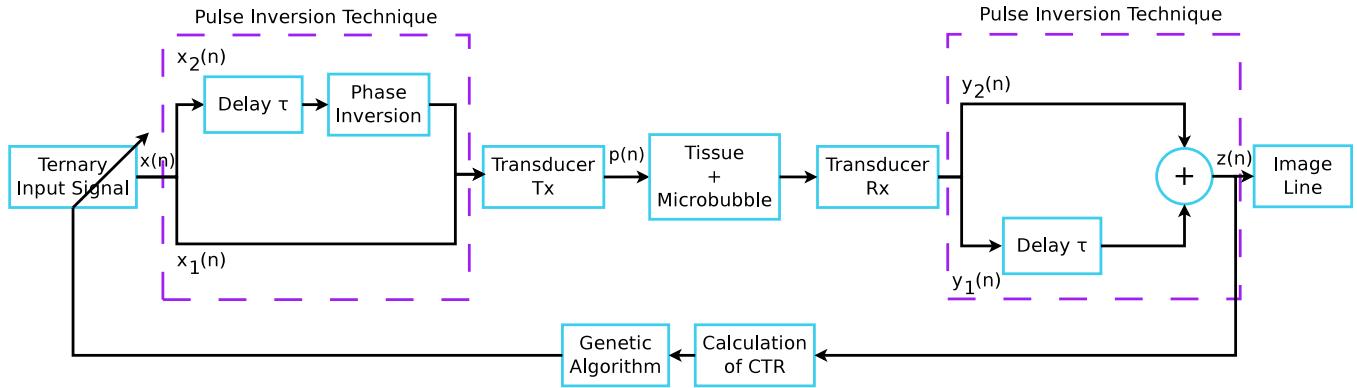


Fig. 1. Block diagram of *CTR* optimization in pulse inversion imaging.

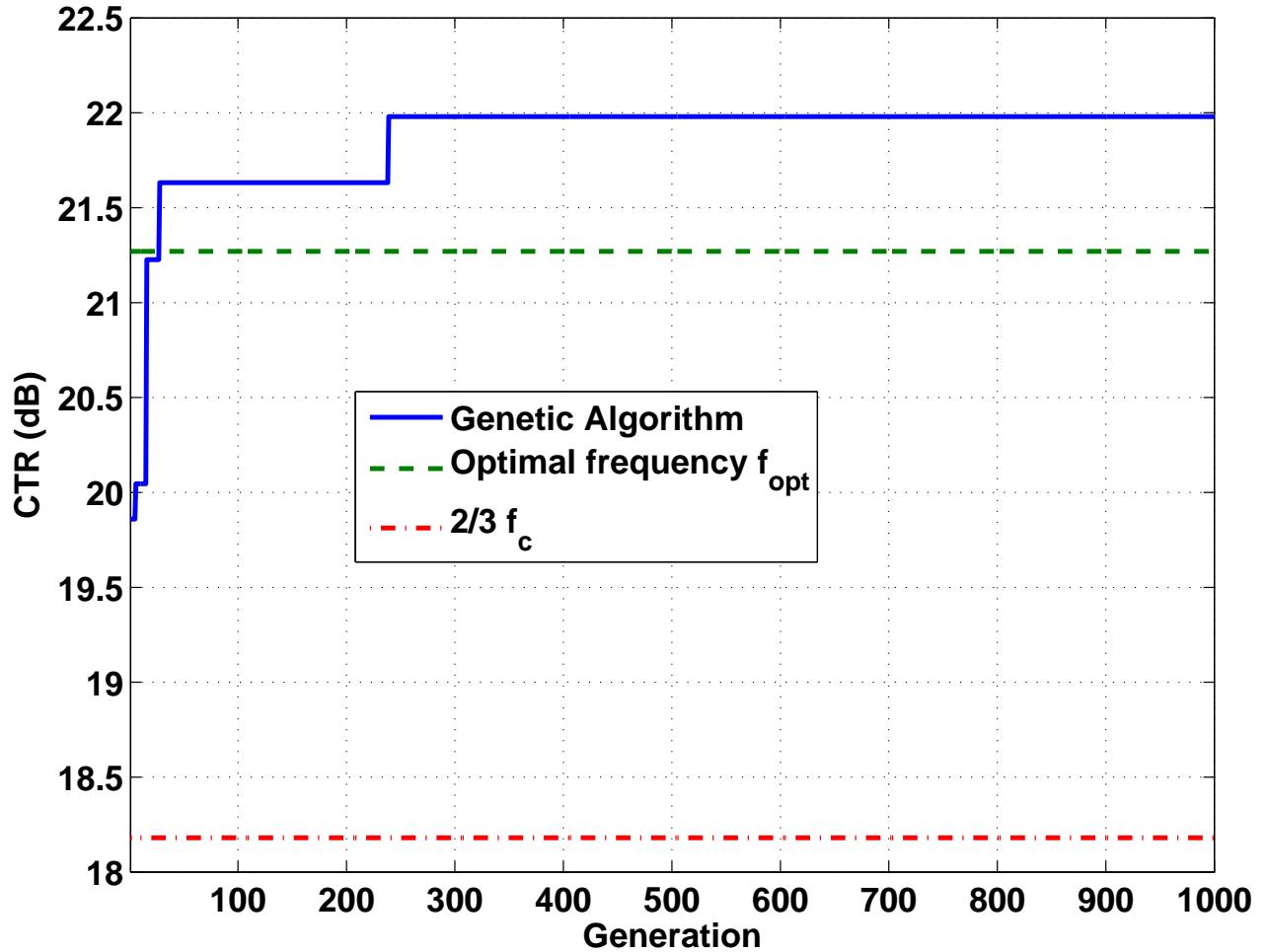


Fig. 2. Simulation of automatic optimization of the contrast-to-tissue ratio (CTR) by a transmitted ternary signal. The optimization was compared to two ternary signals where the transmit frequency was at the optimal frequency and at two-thirds of the central frequency of the transducer.

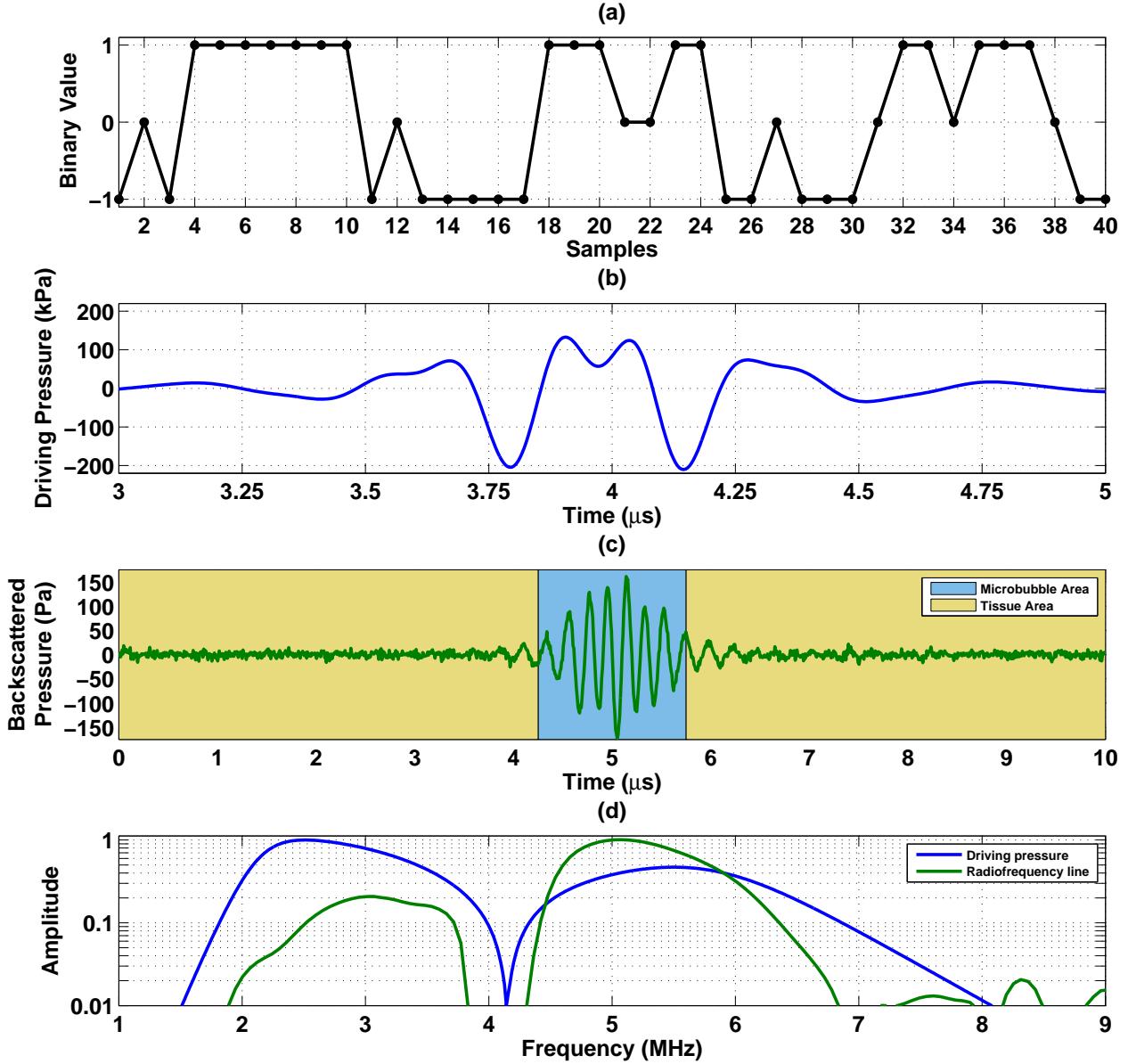


Fig. 3. (a) Optimal transmitted ternary signal $x_1(n)$ obtained by genetic algorithm. (b) Signal $p(n)$ at the transducer output (Fig. 1) when $w(n)$ was the optimal ternary signal, (c) the radiofrequency line and (d) their spectra.

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261	1	<i>CTR</i> measured if the signal transmitted is (i) a ternary signal at two-thirds of the central frequency f_c of the transducer, (ii) a ternary signal at the optimal frequency f_{opt} or (iii) the optimal ternary command.	16
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	$2/3f_c = 2.67$ MHz	$f_{opt} = 1.9$ MHz	Optimal Ternary Signal
CTR (dB)	18.1	21.2	22

Table 1. CTR measured if the signal transmitted is (i) a ternary signal at two-thirds of the central frequency f_c of the transducer, (ii) a ternary signal at the optimal frequency f_{opt} or (iii) the optimal ternary command.