

Ultrasonic time-of-flight method for non-invasive physiological monitoring of the human brain

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Abstract

Innovative non-invasive technologies for human brain physiological monitoring which are based on the ultrasonic time-of-flight (TOF) method require zero crossing detection of ultrasound signals. A new zero crossing detection algorithm has been proposed; it evaluates the individual variability of the acoustic path properties. The algorithm is implemented in the Vittamed non-invasive intracranial slow, respiratory and pulse wave monitor and in the Vittamed non-invasive cerebrovascular autoregulation real-time monitor.

Key words: non-invasive physiological monitoring of the human brain, zero crossing detection

Introduction

The available brain physiological monitoring technologies are exceedingly invasive. A non-invasive method of intracranial blood volume measurement using ultrasound is based on the transmission of short ultrasonic pulses from one side of the skull to the other and dynamic measurements of the TOF of ultrasonic pulses. The TOF depends on the acoustic properties of intracranial blood, brain tissue and cerebrospinal fluid. Changes in the volume of any of these components will change the TOF [1, 2].

Detection of zero-crossing of the ultrasonic signal for human brain physiological monitoring

Time-of-flight using a zero-crossing technique is measured by applying the analog to digital conversion of the received ultrasonic signal. After that the received ultrasonic signal, which has been propagated through the human head, is normalized by amplitude using the window with dimensions 1.0 x 1.0. An averaging of the signals provides the necessary signal-to-noise ratio as per safety requirements and the limited acoustic output power of the transmitter. A threshold level is used to detect the first point of the received ultrasonic signal. Then it is searched from that point in a forward direction for the time instance t_{1zc} when the signal $u(t)$ crosses the zero voltage level.

The first point is detected where the received signal $u(t)$ crosses the zero voltage level. In the case of positive and negative peaks, this can be expressed as:

$$\tau_{zc} = \arg [u(t) = 0], \quad (1)$$

where τ_{zc} is the estimated zero crossing time moment of the signal $u(t)$. Such an instant in the time domain, in the case of positive and negative peaks, can be expressed as:

$$y_{zc}(\tau) = \text{sign}(u(t_k) \cdot u(t_{k+1})), \quad (2)$$

where τ is the zero crossing time moment of the corresponding signal $u(t)$, sign is the function for the signal sign estimation of the rising or falling slope and k is the number of the time sample from the sampled signal $u(t)$.

This approach contains the sampling period $\pm \frac{dt_s}{2}$; therefore, for a more precise calculation of the zero crossing instance τ_{zc} , the degree 3 polynomial approximation was used for the 5 samples of the sampled signal $u(t)$ slope to calculate τ_{zc} :

$$y_{p,zc}(\tau_{zc}) = p_1 \cdot t_i^n + p_2 \cdot t_i^{n-1} + p_3 \cdot t_i^{n-2} + p_4, \quad (3)$$

$$i=1.5, n=3,$$

where p_1 and p_2 are the polynomial coefficients and i is the sample number ($i=1.5$) of the sampled signal $u(t)$ slope. By using the aforementioned polynomial approximation and averaging techniques, the sampling error can be reduced.

To estimate the absolute value of the TOF of the ultrasonic signal $u_2(t)$ which has been transmitted through the human head, the difference is calculated between the zero crossing time instants of the reference signal $u_1(t)$ that had been copied from the ultrasonic transducers of the non-invasive monitor using PVDF piezofilms and the received signal $u_2(t)$ (Fig. 1), [3-8]:

$$\hat{t}_{zc} = \hat{t}_{2,zc} - \hat{t}_{1,zc}, \quad (4)$$

where $\hat{t}_{1,zc} = \arg\{u_1(t) = 0\}$, $t \in \left[t_{01} : t_{01} + \frac{T}{2} \right]$,

$t_{01} = \arg\{\min[u_1(t)]\}$,

$$\hat{t}_{2,zc} = \arg\{u_2(t) = 0\}, t \in \left[t_{02} : t_{02} + \frac{T}{2} \right],$$

$t_{02} = \arg\{\max[u_2(t)]\}$ and $u_1(t)$ is the reference signal copied from the ultrasonic transducers using PVDF piezofilms, $u_2(t)$ is the signal transmitted through human cranium, \hat{t}_{zc} is the estimated delay time between the corresponding signals measured by the zero-crossing technique, T_{01} is the period of the signal $u_1(t)$ and T_{02} is the period of the signal $u_2(t)$ (Fig. 1).

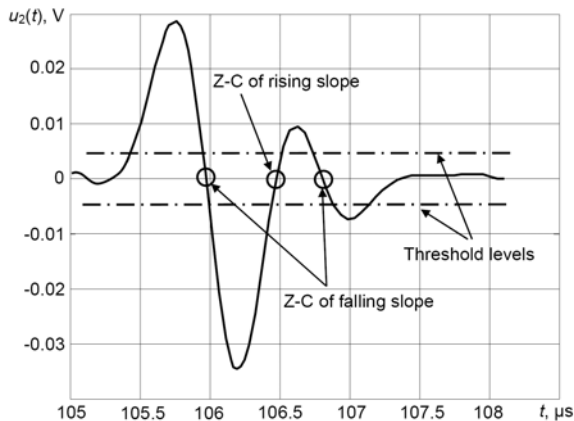


Fig.1. The zero crossing detection and determination of the singular zero crossing time moments according to rising or falling slopes of the signal transmitted through the human head $u_2(t)$

For zero crossing detection of the received ultrasonic signal, the calculation used is of a cross-correlation function between segments of the received signal and the reference signal.

The TOF of the transmitted ultrasonic signal through the human cranium was determined in the following steps:

1. The cross-correlation function $y_{cc}(t)$ was calculated between the reference signal $u_1(t)$ and the signal $u_2(t)$ which has been transmitted through the human cranium (Fig. 2):

$$y_{cc}(\tau) = \frac{1}{T} \int_0^T u_2(t) \cdot u_1(t - \tau) dt, \quad (5)$$

where τ is the time delay between the signals $u_1(t_k)$ and $u_2(t_k)$, k is the number of the sampled signal and T is the duration of the rectangularly shaped time window.

2. The maximal value of the cross-correlation function was determined in accordance to the time delay between the signals:

$$\hat{t}_{cc} = \arg\{\max[y_{cc}(\tau)]\}, \quad (6)$$

where τ_{cc} is the estimated cross-correlation time of the corresponding reflection (Fig. 2).

Maximal values of the cross-correlation function were revised more precisely by an estimation of the zero-crossing time instant of the cross-correlation function derivative, additionally using the 3rd degree polynomial approximation through 5 neighboring points [9-12]:

$$y'_{cc}(\tau) = \frac{dy_{cc}(\tau)}{d\tau}. \quad (7)$$

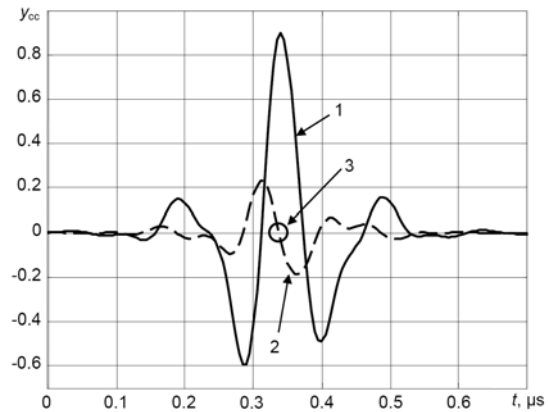


Fig.2. Cross-correlation function of the signal $u_2(t)$ transmitted through the human cranium and the reference signal $u_1(t)$ copied from the ultrasonic transducers of a non-invasive monitor using PVDF piezofilms: 1 - cross correlation function $y_{cc}(t)$, 2 - difference of $y'_{cc}(t) = \frac{dy_{cc}(t)}{dt}$ and 3 - zero-crossing of the cross correlation function difference $y'_{cc}(t)$

Results of the TOF monitoring

Computer modeling was applied to investigate the influence of the TOF measurement uncertainty of the variation in the parameters of each individual layer of the multi-layered biological medium. The variation of the external tissue thickness due to blood flow intake during the cardiac cycle was taken into account. During the analysis, the normalized duration of the cardiac cycle was selected in the range $T=0.1$ s. The waveform of the normalized cardiac cycle sampled with 300 Hz is presented in Fig. 3.

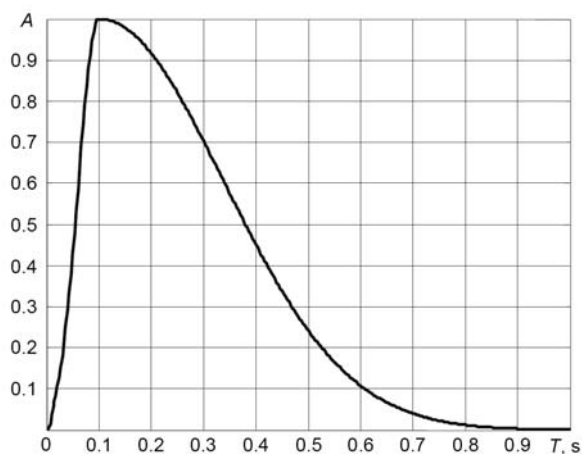


Fig. 3. Cardiac waveform of external blood flow pulsations where A is the amplitude and T is the time duration of the cardiac cycle.

During the duration of the rising slope of the cardiac, the thickness of external tissue increases (1.465 μm). Also the ultrasound velocity in such a medium becomes lower 9.37×10^{-4} m/s due to blood inflow 1.0 ml. At the same moment, the thickness of the ultrasonic gel pad thins (also by the same value equal to 1.465 μm) due to the expansion

of external tissue. The initial parameters of the numerical model were taken from our previous work [4].

During the numerical simulation, the reference TOF values of the appropriate reflection from each interface were estimated with a step of the equivalent sampling frequency equal to 1.0 ps. The reference TOF values of the appropriate reflections were estimated in the case of maximum amplitude of blood flow (the blood inflow equal to 1.0 ml) in the external tissue. The ultrasound reflection from the surface between the ultrasonic gel pad and the external soft tissue arrives by 2.0 ns earlier and the reflection from the interface between external tissue and the skull bone arrives by 2.81 ns later (Fig. 4).

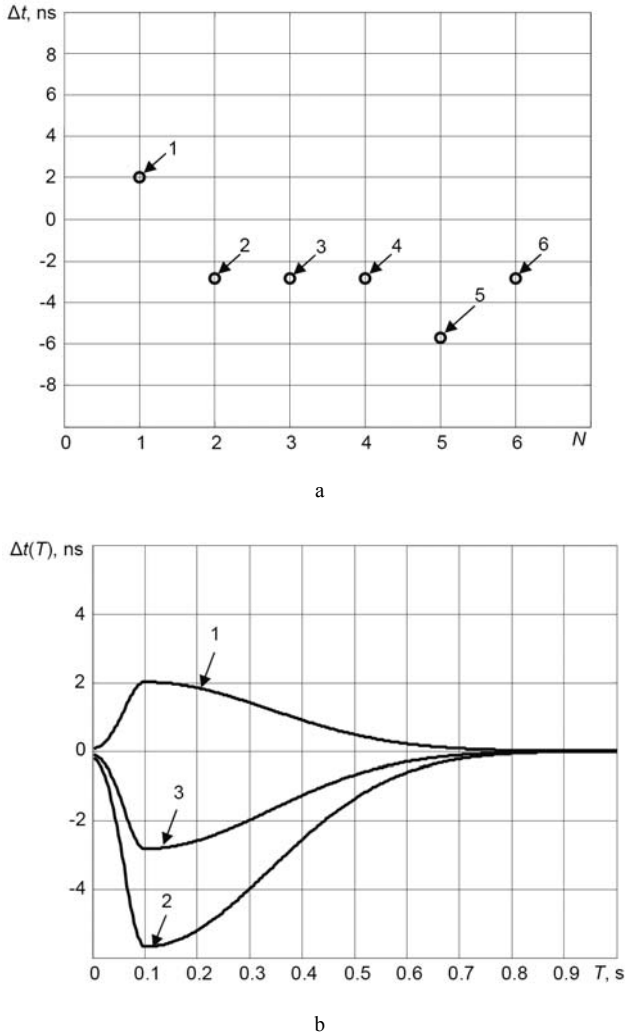


Fig. 4. Expected TOF values of reflections from individual layers: a - TOF values versus the duration of the cardiac pulse cycle, b - maximum values of TOF during the cardiac pulse cycle (assessed while the blood flow pulsations amplitude was maximal in the external tissues) where N is the number of the particular layer, 1 - reflection from the interface between the ultrasonic gel pad and the external tissue (interface No. 1), 2 - reflection from the interface between external tissue and the skull bone (interface No. 2), 3 - reflection from the interface between the skull bone and *dura matter* (interface No. 3), 4 - reflection from the interface between *dura matter* and the layer of cerebrospinal fluid (interface No. 4), 5 - multiple reflections from interface No. 2 and 6 - reflection from the interface between cerebrospinal fluid and brain tissue (interface No. 5)

Such TOF values were obtained by comparing the TOF measurement results in the case of minimum blood flow amplitude (blood inflow equal to 0 ml) in the external tissue. The reflections where TOF values are positive are received earlier than are the reflections in the case of minimal amplitude of the blood flow pulsations (blood inflow equal to 0 ml) in the external tissues.

Such TOF values were compared with the expected TOF measurement values, which had only a 10 ns time resolution. Therefore, an interpolation between the five neighboring points of the received ultrasound signal was performed to reduce the sampling error of TOF measurements down to ± 0.5 ns (the number of averaged TOF values was $n=64$). The results of the differences between the reference TOF values and the expected TOF values, obtained during the aforementioned processing techniques, are presented in Fig. 5.

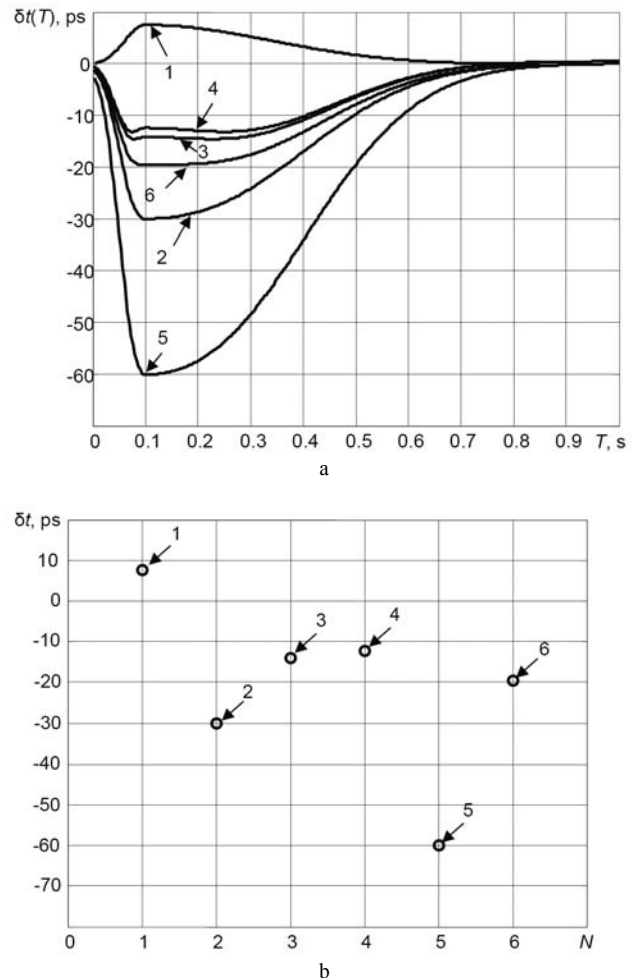


Fig. 5. Numerically estimated errors of the TOF measurement of reflections from individual layers: a - errors versus the duration of the cardiac pulse cycle, b - maximum values of the errors during the cardiac pulse cycle where N is the number of the particular layer, 1 - reflection from the interface between the ultrasonic gel pad and external tissue (interface No. 1), 2 - reflection from the interface between external tissue and the skull bone (interface No. 2), 3 - reflection from the interface between the skull bone and *dura matter* (interface No. 3), 4 - reflection from the interface between *dura matter* and the layer of cerebrospinal fluid (interface No. 4), 5 - multiple reflections from interface No. 2 and 6 - reflection from the interface between the cerebrospinal fluid and brain tissue (interface No. 5).

Conclusions

The variation of external tissue thickness due to blood flow intake during the cardiac cycle was taken into account. During the analysis, the normalized duration of the cardiac cycle was selected in the range $T=0.1$ s. During the duration of the rising slope of the cardiac, the thickness of the external tissue increases. Also the ultrasound velocity in such a medium becomes slower due to blood inflow which was equal to 1.0 ml. Simultaneously the thickness of the ultrasonic gel pad thins due to the expansion of external tissue. In the case of the maximum amplitude of blood flow pulsations in the external tissues which has been caused due to blood inflow 1.0 ml, the reflection from the interface between the ultrasonic gel pad and external tissue arrives by 2.0 ns earlier than it does in the case of the minimum amplitude of blood flow pulsations in the external tissues. The reflection from the interface between external tissue and the skull bone arrives by 2.81 ns later than it does in the case of the minimum amplitude of blood flow pulsations in the external tissues. The values of the TOF sampling errors were evaluated to be close to 0.06 ns.

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Ultragarsinis suvėlinimo laiko matavimo metodas fiziologinei neinvazinei žmogaus smegenų stebėsenai atlikti

Reziumė

Inovatyvi žmogaus smegenų neinvazinės fiziologinės stebėsenos technologija, kuri remiasi ultragarso bangos sklidimo suvėlinimo laiko matavimu, reikalauja aptikti priimtų ultragarsinių signalų perėjimus per nulį. Pasiūlytas naujas perėjimų per nulį aptikimo algoritmas, kuris įvertina daugiasluksnę biologinę struktūrą sudarančių medžiagų savybių individualų kitimą ultragarso bangos sklidimo kelyje. Šis algoritmas įdiegtas *Vittamed* neinvaziniame intrakraniospinaliniame lėtų, kvėpavimo ir pulsinių bangų monitoriuje ir *Vittamed* neinvaziniame cerebrovaskulinės autoreguliacijos realiojo laiko monitoriuje.

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