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## **PHOTOACOUSTIC DETECTION OF SENTINEL LYMPH NODE WITH SENSOR ARRAYS**

Cancer is one of the diseases which cause the highest death rate in XXI century. However, through years techniques and equipment used to fight with this disease improved there are still many opportunity to get better results. Nowadays, the attention is focused on precise cancerous cells place estimation. It is important for effective cancer treatment, but also it allows diminishing the unwanted effects as destruction of healthy cells. One of the promising techniques in obtaining better spatial and temporal resolution of the internal of the human body is the photoacoustic imaging. Combination of the acoustics, ultrasounds or microwaves by the set of ultrasonic detectors can lead to estimation of the localization of the sources of the waves.

The work presents the utilization of the multiple signal classification (MUSIC) algorithm in estimation of angle and distance of microwave or photoacoustic waves sources. The technique presented in the work allows for better prediction of localization of the sources of the detected waves by the sensors array. The proposed application of this technique is detection of sentinel lymph nodes.

### **1. INTRODUCTION**

#### **1.1. PHOTOACOUSTIC AND MICROWAVE DETECTION OF CANCEROUS CELLS**

Unlike most cells cancerous cells proliferate uncontrollably and rapidly, they do not present density dependent growth and posses ability to spread by breaking into blood vessels and moving to other systems [1]. Metastasis which is connected with spreading the cancerous cells leading to abnormal functionality of tissue or organs is the main reason of the worldwide death [2]. Generally cancer can be divided into blood (lymphoma and Hodgkin's disease) or solid types (breast, colorectal, and liver) which form tumors [3]. Early detection of the cancerous cells is helpful in full patient recovery in the preliminary stadium of the disease. Magneto resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) are the examples of the existing techniques for tumors detection. Nowadays cancer is one of the leading cause of the worldwide death, therefore improvements in methods detecting the cancerous cells is so required. One of the promising techniques in obtaining better spatial and temporal resolution of the internal of the human body is the photoacoustic imaging [4-6]. Combination of the acoustics, ultrasounds or microwaves by the set of ultrasonic detectors can lead to estimation of the localization of the sources of the waves.

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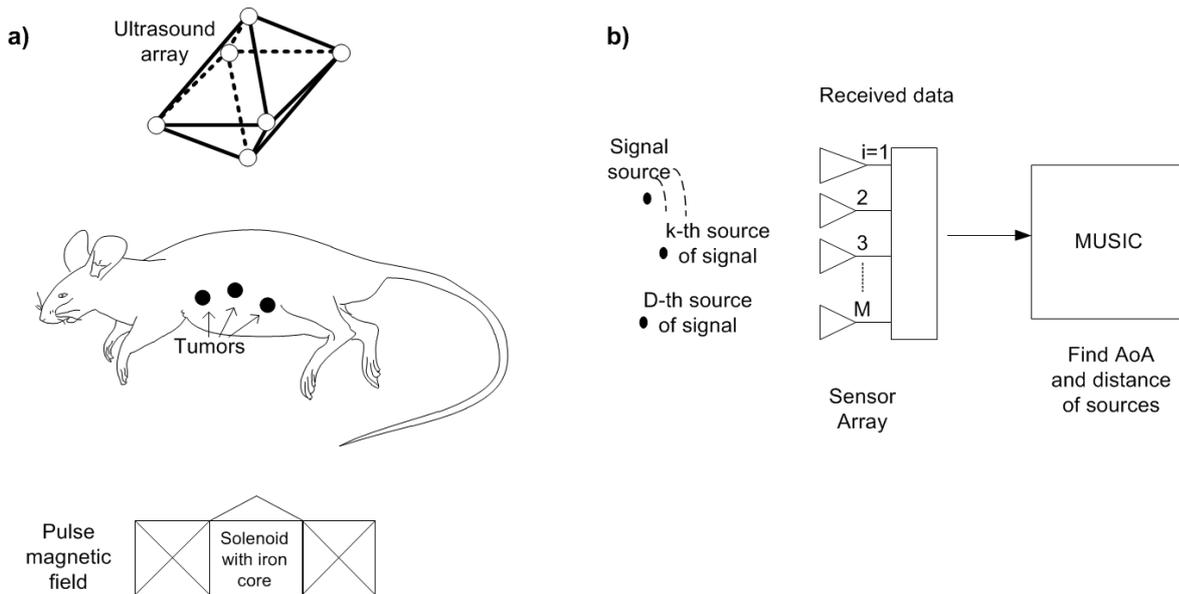


Fig. 1. Detection of localization of magnetic nanoparticles in tumor cells by magneto-motive ultrasound.

The idea of detecting multiple signals produced by magneto-motive ultrasounds generated by iron oxide nanoparticles injected into examined object with tumors is presented in Fig.1a. Nanoparticles which can be injected into the veins travel inside them. They possess ability to penetrate through the veins membranes to lymph nodes and are absorbed by sentinel lymph nodes. When nanoparticles are subjected to pulse magnetic field, the magnetic force acts on the particles and cause their motion [7,8]. The oscillation frequency of the particles is twice bigger than the field excitation frequency what is the additional advantage in measurements [8]. The oscillations of the nanoparticles can be detected by ultrasound receiver, which detects responses for pulse echo signals [9]. Each of the tumors with absorbed nanoparticles can react as the source of the waves. Generated waves can be detected by the array of ultrasound receivers as it is presented in Fig. 1b [10,11]. Finding the localization of the waves impinging on the receiver array can be performed with many digital signal processing techniques. In this work we present application of the multiple signal classification algorithm to simultaneously estimate localization of the signal sources.

## 2. MUSIC ALGORITHM

Problem of finding localization of signal sources is important in disciplines like oceanography, seismology, radio-astronomy and many others [12,13]. There are numerous techniques allowing to estimate the localization of the signal sources [14]. Multiple signal classification (MUSIC) algorithm can simultaneously provide information about source distance and angle of arrival of impinging wave.

The operation of the algorithm, as presented in [15,16], are:

- Collect data from sensor array and create data matrix  $X$ ,
- Calculate eigenstructure of  $X$  in metric of  $X_o$ ,
- Decide the number of incident signals  $k$ ,
- Calculate the orthogonality-measure spectrum matrix  $P$ ,
- Pick  $k$  picks of matrix  $P$ .

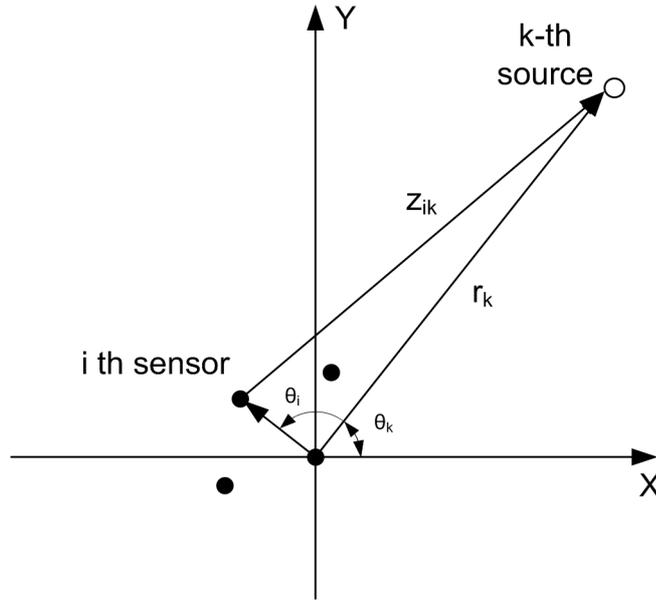


Fig. 2. Visualization of the sensor array and sources used in MUSIC algorithm.

Let us consider  $D$  spherical signal sources at unknown locations and with arbitrary directional characteristics. Sources are centred around known frequency  $w_0$ , impinge on the array from locations  $\theta_1, \dots, \theta_D$  as it is presented in Fig. 2. The waves emitted by the sources are impinging on the sensor array of  $L$  elements. Array sensors  $L > D$  are positioned at arbitrary locations and directions as it is shown in Fig.1. The waveforms detected at the array elements consists from  $A$  incident wave fronts and noise  $N$ . Data collected at the  $i$ -th sensor can be expressed by its complex envelope as [12]:

$$x_i(m) = \sum_{k=1}^D a_i(r_k, \theta_k) s_k(m) + n_i(m) \quad (1)$$

Where:

$$\begin{aligned} i &= 1, 2, \dots, L \\ m &= 1, 2, \dots, M \end{aligned}$$

where  $a_i(r_k, \theta_k)$  is a steering vector ( $L \times 1$  size) characterized by the sensor array,  $r_k$  and  $\theta_k$  are the unknown range and bearing of the  $k$ -th source with respect to a reference origin,  $s_k(m)$  is the scalar complex waveform of the  $k$ -th incoming signal,  $n_i(m)$  is the additive complex noise vector and  $M$  is the number of snapshots. The complex response in the  $i$ -th sensor element to the  $k$ -th impinging signal can be expressed as:

$$a_i(r_k, \theta_k) = \frac{c_{ik}}{z_{ik}} \exp(-j \frac{2\pi}{\lambda} z_{ik}) \quad (2)$$

where  $j$  is the unitary complex number,  $\lambda$  is the wavelength of the impinging waves, and  $z_{ik}$  is the distance from the  $k$ -th source to the  $i$ -th sensor defined as:

$$z_{ik}^2 = r_k^2 + d_i^2 - 2r_k d_i \cos \theta_{ik} \quad (3)$$

where  $\theta_{ik} = \theta_i - \theta_k$ , and the radial coordinates of sensor ( $i$ ) and source ( $k$ ) are  $(d_i, \theta_i)$  and  $(d_k, \theta_k)$  respectively. The directivity pattern of the sensors and radiating pattern of the sources and its wavelength  $\lambda$  determine the  $c_{ik}$  coefficients. In case when both the sensors and sources are omnidirectional these coefficients are independent and can be set to 1.

Because the observation interval between following samples is larger than the correlation time the finite-sampled data covariance matrix  $R_x(r, \theta)$  can be given as [12]:

$$\hat{R}_x(r, \theta) = \frac{1}{M} \sum_{m=1}^M x(r, \theta; m) x^H(r, \theta; m) \quad (4)$$

Where  $H$  denotes the complex conjugate transpose. The matrix  $\hat{R}_x(r, \theta)$  is the estimate of true data covariance matrix  $R_x(r, \theta)$  given by:

$$R_x(r, \theta) = A(r, \theta) R_s A^H(r, \theta) + \sigma^2 I \quad (5)$$

where  $R_s$  is the signal covariance of the sources. With the additional assumption that noise components are stationary and ergodic Gaussian with zero mean covariance matrix  $\sigma^2 I$ , where  $\sigma^2$  is unknown and  $I$  is the identity matrix.

In signal subspace techniques, it is possible to estimate the number of sources by simply observing the structure of eigenvalues and decide the threshold between the sources and noise if signal to noise ratio is high [12]. In the case when the signal to noise ratio is low it is difficult to determine the difference between the eigenvalues of signal and eigenvalues of noise, therefore the model-selection techniques such as minimum description length (MDL) or Akaike information criteria (AIC) can be used to estimate the number of sources [17,18]. In order to achieve the number of sources it is required to sort in descending order the eigenvalues  $\nu_i$  of  $\hat{R}_x$  and find the threshold between noise and signal eigenvalues or decide the number of sources  $\hat{D}$  by minimalization of MDL or AIC criterion. Let  $u_{D^{\wedge}+1}, u_{D^{\wedge}+2}, \dots, u_L$  be the noise eigenvectors corresponding to the  $(L - \hat{D})$  smaller eigenvalues  $u_{D^{\wedge}+1}, u_{D^{\wedge}+2}, \dots, u_L$ . We construct the noise eigenvectors as:

$$a(r, \theta) = \left[ \frac{1}{z_1} \exp(-j \frac{2\pi}{\lambda} z_1) \cdot \frac{1}{z_2} \exp(-j \frac{2\pi}{\lambda} z_2) \cdots \frac{1}{z_L} \exp(-j \frac{2\pi}{\lambda} z_L) \right]^T \quad (6)$$

The near steering vector  $a(r, \theta)$ , comprises all possible near field steering vectors, that is,

$$z_i^2 = r^2 + d_i^2 - 2rd_i \cos(\theta - \theta_i) \quad (7)$$

To search for the location of sources, we construct a 2-D orthogonality-measure spectrum,

$$P(r, \theta) = \frac{1}{a_H(r, \theta) U_N U_N^H a(r, \theta)} \quad (8)$$

where  $H$  denotes the complex conjugate transpose. The noise eigenvector matrix  $U_N$  is created from  $L - \hat{D}$  smaller noise eigenvectors as  $U_N = [u_{D^{\wedge}+1} \ u_{D^{\wedge}+2} \ \dots \ u_L]$  [12]. The peaks of the spectrum  $P(r, \theta)$  are the locations of the sources  $(r_k, \theta_k), k=1, 2, \dots, \hat{D}$ .

### 3. SIMULATIONS

#### 3.1. VARIOUS NUMBER OF WAVE SOURCES

The algorithm described in previous section can be used to distinguish the angle of incident signals. Simulation of two waves produced by uncorrelated sources incident on the array of five sensors is presented in this section. The wave detected at the array sensor (e.g. piezoelectric sensor) can be simulated as:

$$\xi(x, t) = \alpha_1 e^{i(\omega t - kx)} + \alpha_2 e^{i(\omega t + kx)} \quad (9)$$

where  $k = \omega / c_s = 2\pi / \lambda =$  wave number and  $c_s$  is the speed of light. The amplitude of the outgoing wave from the ultrasound transducer is  $\alpha_1$  and  $\alpha_2$  is the amplitude of the wave reflected from the object (e.g. tumor). The number of positive eigenvector values in logarithmic scale corresponds to the number of detected

signals. Fig. 3a shows eigenvalues describing the signals received on the array in this experiment. Next Fig. 3b presents the estimated angle from which the signals have come. In this case it was 5 and 20 degrees what is in accordance with the parameters of the simulated wave sources.

### 3.2. ESTIMATION OF ANGLE OF ARRIVAL OF INCIDENT WAVE

Modified two-dimensional multiple signal classification (MUSIC 2-D) algorithm is used to provide parameters of multiple wave fronts arriving at an antenna array. This technique enables to provide information about number of incident signals, estimation of directions of arrival (DOA) of signals collected by the array elements. There is possibility to estimate the number of sources and their location by pre-processing the signal subspace.

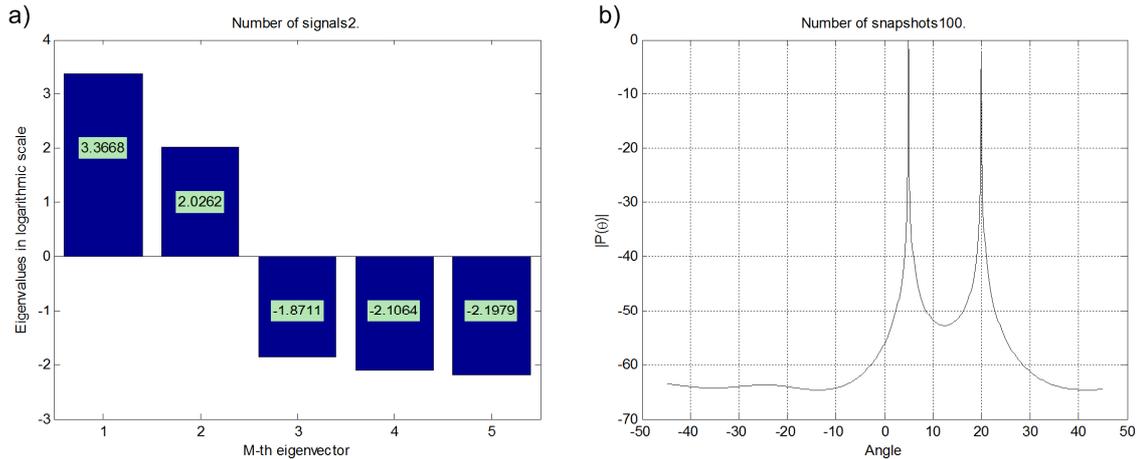


Fig. 3. Estimation of angle of arriving signal and number of incident signals.

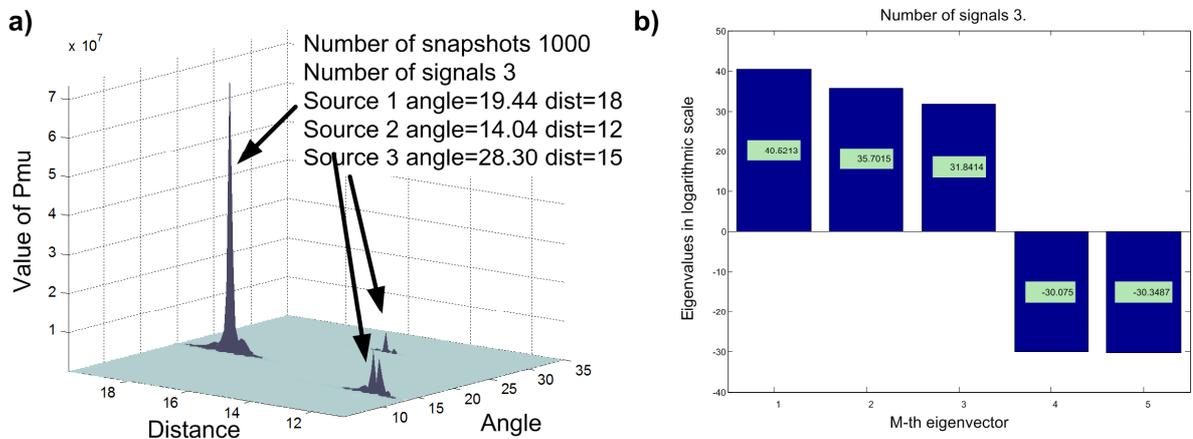


Fig. 4. Simultaneous estimation of angle of arriving signal and location of signals' sources.

Simulations of various numbers of waves incoming from arbitrary localizations have been performed. The example of the simulation of three waves incoming at the array consisting of four sensors is presented in Fig. 4a. In the presented simulation acoustic sources of 200 kHz placed at 18 cm, 14 cm, and 12 cm were exploited. It is possible to find the positions of signal sources with MUSIC algorithm. Appropriate transformation of orthogonal space allows estimating the number of wave sources. Scanning the orthogonal space with the angle and direction allows deriving exact localization of wave sources.

It is possible to estimate the number of incident signals if the signal to noise ratio is high, the logarithmic representation of eigenvectors of covariance matrix of received signal is presented in Fig. 4b. Finding the threshold between signal and noise subspace is easy if number of array elements is higher than number of impinging signals and the received signal is stronger than the noise.

## 4. CONCLUSIONS

The proposed method for detection of sentinel lymph nodes locations is currently the theoretical benchmark. Changes of the various parameters of sensor arrays (such as distance between sensing elements, number of collected snapshots, number of array elements, power of input noise) can influence on the performance of the estimation of wave source localization. Increasing the number of array elements can greatly improve resolution for multiple wave sources. With lower noise, the peaks in orthogonality spectrum become sharper. The presence of added noise causes a spreading effect on the peaks. Increasing the number of snapshots brings an improvement in the estimation of angle and distance. It is believed that proposed methodology improve the quality of detecting the localization of sentinel lymph nodes with photo-acoustic-imaging method.

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