

## Mathematical model in task of recurrent laryngeal nerve identification by electrophysiological method

**Abstract.** The method of constructing the mathematical model for visualization the recurrent laryngeal nerve positioning during neck surgery is described in this paper. Proposed model shows the dependence between the amplitude of information signal as response on stimulation the recurrent laryngeal nerve and the coordinates of stimulation point based on interval data analysis.

**Streszczenie:** Poniższy artykuł opisuje metodę konstrukcji modelu matematycznego do wizualizacji, podczas operacji, położenia nerwu krtaniowego wstecznego. Proponowany model pokazuje zależność między amplitudą sygnału informacyjnego, jako odpowiedzią na symulację nerwu krtaniowego wstecznego a współrzędną punktu symulacji bazującego na interwałowej analizie danych. (Model matematyczny w zagadnieniu identyfikacji nerwu krtaniowego wstecznego na podstawie metody elektrofizjologicznej)

**Keywords:** neck surgery, recurrent laryngeal nerve, mathematical model, interval analysis.

**Słowa kluczowe:** chirurgia szyi, nerw krtaniowy wsteczny, model matematyczny, analiza interwałów

### Introduction

Amount of patients that had surgical operations on the cancer of thyroid or parathyroid gland in the clinics of the world increases incessantly. The most common postsurgical complication is an injury of recurrent laryngeal nerve (RLN) which is a very important problem, especially for insurance medicine. Therefore, it is relevant to apply hardware and software tools for decreasing the risk of nerve damage. Main task of mentioned tools is monitoring of area of surgical operation in the process of surgery with a purpose of identification and visualization of RLN location and in such a way to avoid its damage.

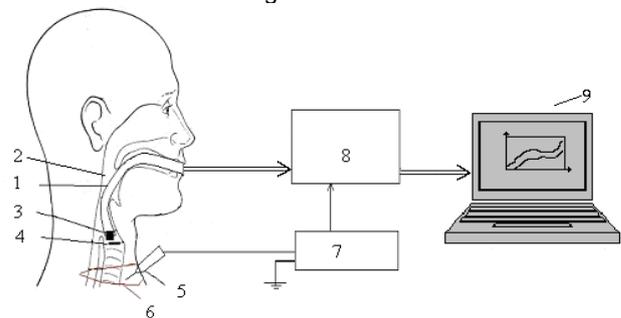
On the First World Congress of Neural Monitoring in Thyroid and Parathyroid Surgery, which took place in Krakow in September 2015 [1], it has been systematized presented methods, hardware and software tools for identification of RLN location in a surgical wound. Functioning principle of such tools based on the electrophysiological method of stimulation of surgical wound tissues by a direct or alternating current and on the registration and processing of stimulation results with the purpose of identification of informative characteristics of tissue type. For development of software for these tools, it is important to use adequate mathematical models of informative characteristics of tissue in surgical operation area. Methods, tools and mathematical models for the RLN identification are considered in papers by V. Riddell, J. Galivan, J. Basmajian, W. E. Davis [2, 3, 4, 5]. The number of hardware and software tools developed for its monitoring. It is advisable to note universal tools among them: NEUROSIGN, NIM® [6, 7]. In spite of wide range of possibilities and substantial decrease of RLN damage risk during use of these tools, their practical application is limited in first to the high cost and to the necessity of the third stage of anesthesia for patient, which is especially dangerous for life.

Lately, in papers by V. O. Shidlovsky, M. P. Dyvak and O. L. Kozak [8] the mathematical models and tools for RLN monitoring, which are based on stimulation the tissues in surgical wound by an alternating current and on the analysis of informative characteristic of signal as response on stimulation are considered. Thus, a maximal amplitude of the signal chosen as its informative characteristic as reaction on surgical wound tissues stimulation. This does not provide a minimization of RLN damage risk due to neglect the errors of positioning the stimulation points. This

fact stipulates further development of RLN monitoring tools that based on an electrophysiological method and described in paper [8].

### Statement of the problem

In paper [8] it is substantiated the use of new perspective method and hardware for development of the RLN monitoring systems based on stimulation of surgical wound tissues by an alternating current and registration of results of stimulation by sound sensor that inserted into an endotracheal tube above vocal cords. The scheme of the noted method shown in Fig. 1.



1 is a respiratory tube, 2 is a larynx, 3 is a sound sensor, 4 are vocal cords, 5 is a probe, 6 is a surgical wound, 7 is an alternator, 8 is an amplifier, 9 is an audioinput of computer sound card

Fig. 1. The method of RLN identification among tissues in surgical wound [8].

The method of RLN identification carries out on set forth below scheme.

In a respiratory tube 1 that located in a patient's larynx 2, a sound sensor 3 inserted above vocal cords 4. By means of probe 5 the tissues in surgical wound 6 are probed. Probe 5 is connected to an alternator 7 with current strength from 0.5 to 2 mA and fixed frequency which provides low conductivity of electric signal by muscular tissues and high conductivity of electric signal by a laryngeal nerve to muscles which control a tension of vocal cords.

An airflow passing through a respiratory tube creates voice vibrations with spectrum that is changing due to modulation of vocal cords vibrations in accordance with frequency of stimulation current. At that, due to low

conductivity of electric signal with fixed frequency by muscular tissues and high conductivity of electric signal with same frequency by a laryngeal nerve, amplitude of modulated sound signal will be proportional to a distance from a point of probing to the laryngeal nerve in a surgical wound. These vibrations are registering by sound sensor 3, converted into an electric signal, amplified by amplifier 8 and sent to a standard audio-input of sound card in computer 9 where this signal is processed.

An output information signal characterizes the closeness of probe location to a laryngeal nerve. Dependence between amplitude of information signal and coordinates actually presents location of RLN in an area of surgical operation since the closer point of stimulation is to RLN the higher is amplitude of sound signal. The noted dependence is a mathematical model of characteristics of surgical operation environment for the RLN identification by the characteristic of maximal amplitude of a signal as reaction on stimulation of surgical wound tissues by an alternating current.

Scheme of obtaining of experimental data for building a mathematical model of surgical operation environment characteristics and then creating area of safe surgical operation represented in Fig. 2.

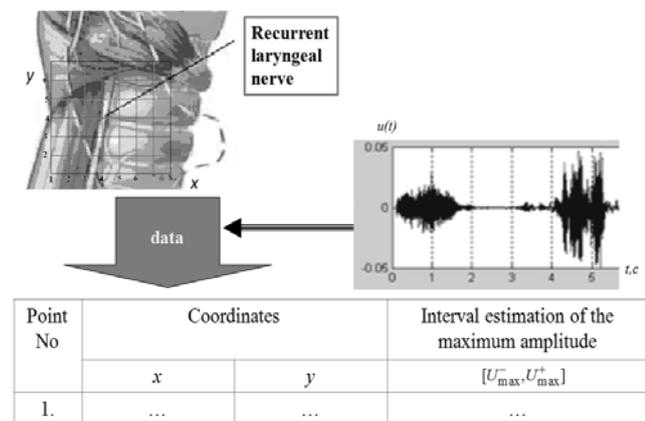


Fig. 2. Scheme of experimental data obtaining [8].

Substantial advantage of the noted tools is a higher level of sensitivity and possibility to execute a surgery using second stage of anesthesia that is safe for patient.

At the same time, the considered method and model of information signal have a number of disadvantages. In particular, for visualization of RLN location in a method that based on the analysis of maximal amplitude of signal as reaction on the stimulation of surgical wound tissues, it is necessary to identify a structure of model of dependence between maximal amplitude of obtained signal and surgical wound coordinates in kind of linear-parametric equation. Procedure of structure identification of mathematical model based on observation results is highly complex from the point of view of calculations. But the worst disadvantages of considered method and model of information signal are necessity of finding dependence between maximal amplitude of sound signal from sound sensor and coordinates of points in a surgical wound and inaccuracy in detecting of coordinates of stimulation point in a surgical wound. As a result, it leads to substantial error in procedure of identification the RLN area location in a surgical wound and accordingly to the increase of risk of its damage.

Considering the above noted, it is necessary to improve the mathematical tools of task of RLN identification in the process of thyroid surgery due to making more accurate a mathematical model of information signal taking into account errors of positioning the stimulation point.

## A mathematical model for the RLN identification by the characteristic of maximal amplitude of information signal

Denote the maximal amplitude of information signal by  $U_{\max}(x, y)$ , where  $(x, y)$  are coordinates of stimulation point in some coordinate system. For example, beginning of a coordinate system can be chosen with linking to some organ in the surgery area.

Taking into account errors of measuring of maximal amplitude of sound signal and errors of detecting of stimulation point coordinates, let's represent results of processing of signal as reaction on tissue stimulation in surgical wound in such kind:

$$(1) \quad ([x_i^-; x_i^+], [y_i^-; y_i^+]) \rightarrow [U_{\max i}^-, U_{\max i}^+], i = 1, \dots, N,$$

where:  $[x_i^-; x_i^+], [y_i^-; y_i^+]$  are interval estimations of stimulation point coordinates;  $U_{\max i}^-, U_{\max i}^+$  are accordingly lower and upper bounds of maximal amplitude of received signal.

With purpose of RLN location identification in surgery area, it is necessary to predict the maximal expected amplitude of signal-reaction on surgical wound tissues stimulation in points that located beyond points of stimulation in surgical wound. Mathematical model that links surgical wound point coordinates with maximal amplitude of sound signal-reaction on stimulation of surgical wound tissues will search in kind of linear parametric function:

$$(2) \quad \hat{U}_{\max}(x, y) = b_0 + b_1 \cdot \varphi_1(x, y) + \dots + b_m \cdot \varphi_m(x, y),$$

where:  $\varphi_1(x, y), \dots, \varphi_m(x, y)$  are base functions from coordinates  $(x, y)$ ,  $b_0, b_1, \dots, b_m$  are unknown parameters of model.

For mathematical model unknown parameters estimation (2), it is necessary to use experimental data in kind (1). The conditions for calculation of estimations of model (2) parameters will formulate to ensure the given accuracy of mathematical model within bounds of interval errors:

$$(3) \quad U_{\max i}^- \leq U_{\max}(x, y) \leq U_{\max i}^+, i = 1, \dots, N.$$

Taking into account the Eq. (2) will obtain from conditions (3):

$$(4) \quad U_{\max i}^- \leq b_0 + b_1 \cdot \varphi_1([x_i^-; x_i^+], [y_i^-; y_i^+]) + \dots + b_m \cdot \varphi_m([x_i^-; x_i^+], [y_i^-; y_i^+]) \leq U_{\max i}^+, i = 1, \dots, N.$$

Obtained system is the interval system of linear algebraic equations (ISLAE). Solution of this system (if it exists) is, in general, non-convex region of the model parameters estimation  $\Omega$ . Every vector of parameters  $\vec{b} = (b_0, b_1, \dots, b_m) \in \Omega$  generates one model and all vectors that belong to this region generate the corridor of interval models in kind:

$$(5) \quad [\hat{U}_{\max}^-([x], [y]), \hat{U}_{\max}^+([x], [y])] = [\min_{\vec{b} \in \Omega} \vec{b}^T \cdot \vec{\varphi}([x], [y]); \max_{\vec{b} \in \Omega} \vec{b}^T \cdot \vec{\varphi}([x], [y])]$$

where  $[x] = [x_i^-; x_i^+], [y] = [y_i^-; y_i^+]$  are interval estimations of stimulation point coordinates.

Taking into account that solution region  $\Omega$  is a non-convex polyhedron, such presentation of parameter estimations region is complex for interval models building. That is why the abandonment of an attempt to find an

“accurate” solution from a methodical point of view is obvious. Instead, it is expedient to search some “rough” solution as approximation of parameters region, scilicet, localization of “accurate” solution.

In an interval analysis, the localization of ISLAE (4) solutions is obtained in a kind of rectangular parallelepiped edges of which are parallel to coordinate axes. Obtained estimations in this case presented in such kind:

$$[b_j^-, b_j^+], j = 1, \dots, m,$$

where  $b_j^-, b_j^+$  are lower and upper guaranteed bounds of possible parameter values accordingly. Then the task of localization formulates in such a way [8]:

$$(6) \quad b_j^- = \min_{\bar{b} \in \Omega} b_j, b_j^+ = \max_{\bar{b} \in \Omega} b_j, \quad j = 1, \dots, m.$$

Evidently, task (6) consists of  $2 \cdot m$  complex tasks of linear programming.

Then the corridor of interval models after which an area in a surgical wound that guaranteed includes a RLN is built. It will be in such kind:

$$(7) \quad [\hat{U}_{\max}^-(x, y), \hat{U}_{\max}^+(x, y)] = [\bar{b}]^T \cdot \bar{\varphi}(x, y),$$

where  $[\bar{b}] = ([b_1^-, b_1^+], \dots, [b_m^-, b_m^+])^T$  is an interval vector components of which are found from solution of non-convex programming tasks (6).

For this case, it is possible to use methods that described in papers [9, 10, 11]. However, the most effective methods for today are methods of random search of interval estimations of the interval systems of linear and nonlinear equations solutions [12]. Adapt the noted methods for estimation of ISLAE (4) solutions after which, in next stages, an area that guaranteed includes a RLN is built in a surgical wound.

Substitute the task of solving the ISLAE (4) by the task of searching of tolerance interval estimation of its solutions based on such optimization task:

$$(8) \quad F([\bar{b}_k^-, \bar{b}_k^+]) \xrightarrow{\bar{b}_k^-, \bar{b}_k^+} \min, \quad \bar{b}_k^- > 0, \quad \bar{b}_k^+ > 0, \quad [\bar{b}_k^-, \bar{b}_k^+] \subset \Omega,$$

where  $[\bar{b}_k^-, \bar{b}_k^+]$   $\hat{U}_{\max}([\bar{b}_k^-, \bar{b}_k^+], [x_i], [y_i])$  is an interval vector of model parameters obtained on  $k$  iteration of optimization procedure;  $F([\bar{b}_k^-, \bar{b}_k^+])$  is a value of goal function which is built based on ISLAE (4) and, on every iteration, determines an attained “quality” of approximation of parameters vector interval estimation of model of information signal maximal amplitude distribution which meets the requirements  $[\bar{b}_k^-, \bar{b}_k^+] \subset \Omega$ .

Goal function  $F([\bar{b}_k^-, \bar{b}_k^+])$  is determined as a difference of centers of the most remote between each other  $i$  interval of the measured values  $U_{\max}([x_i], [y_i])$  and  $\hat{U}_{\max}([x_i], [y_i])$  that is interval of modeled boundary values of maximal amplitude of information signal when the noted intervals do not intersect. Formally this condition presented in such kind:

$$(9) \quad F([\bar{b}_k^-, \bar{b}_k^+]) = \min_{i=1, \dots, N} \left\{ \begin{aligned} &mid(\hat{U}_{\max}([\bar{b}_k^-, \bar{b}_k^+], [x_i], [y_i]) - \\ &- mid(U_{\max}([x_i], [y_i]))) \end{aligned} \right\}$$

if  $\hat{U}_{\max}([\bar{b}_k^-, \bar{b}_k^+], [x_i], [y_i]) \cap U_{\max}([x_i], [y_i]) = \emptyset$   
 $\exists i = 1, \dots, N$ .

For a case when all intervals of the measured values  $U_{\max}([x_i], [y_i])$  and intervals of modeled boundary values of maximal amplitude of information signal  $\hat{U}_{\max}([x_i], [y_i])$

intersect, the goal function  $F([\bar{b}_k^-, \bar{b}_k^+])$  of “quality” of approximation of parameters vector estimation is determined as the least width of intersection of the noted intervals. Formally this condition presented in such kind:

$$(10) \quad F([\bar{b}_k^-, \bar{b}_k^+]) = \min_{i=1, \dots, N} \left\{ \begin{aligned} &wid(\hat{U}_{\max}([\bar{b}_k^-, \bar{b}_k^+], [x_i], [y_i]) - \\ &- wid(\hat{U}_{\max}([\bar{b}_k^-, \bar{b}_k^+], [x_i], [y_i]) \cap (U_{\max}([x_i], [y_i]))) \end{aligned} \right\}$$

if  $\hat{U}_{\max}([\bar{b}_k^-, \bar{b}_k^+], [x_i], [y_i]) \cap U_{\max}([x_i], [y_i]) \neq \emptyset$ ,  
 $\forall i = 1, \dots, N$ .

$mid(\bullet)$  and  $wid(\bullet)$  in Eqs. (9) and (10) are the standard in an interval analysis operations of determination of interval middle and its width, accordingly.

Will conduct an analysis of goal function depending on the attained quality of the current approximation of parameters of interval models of information signal maximal amplitude. Will use Fig. 3 for this purpose. The graphical illustration of both cases of calculation of goal function (Eqs. (9) and (10)) presented on the figures. As we can see from Fig. 3 (a), in the first case (calculation using Eq. (9)), the measured intervals of maximal amplitude values  $U_{\max}([x_i], [y_i])$  in points with coordinates  $[x_i^-, x_i^+]$ ,  $[y_i^-, y_i^+]$  and the intervals of modeled estimations of boundary values of maximal amplitude of information signal  $\hat{U}_{\max}([\bar{b}_k^-, \bar{b}_k^+], [x_i], [y_i])$  for discrete values of calculating procedure, substantially differ from each other. We see the largest deviation between the centers of these intervals for a point  $i=2$ . Module of this deviation determines the value of goal function.

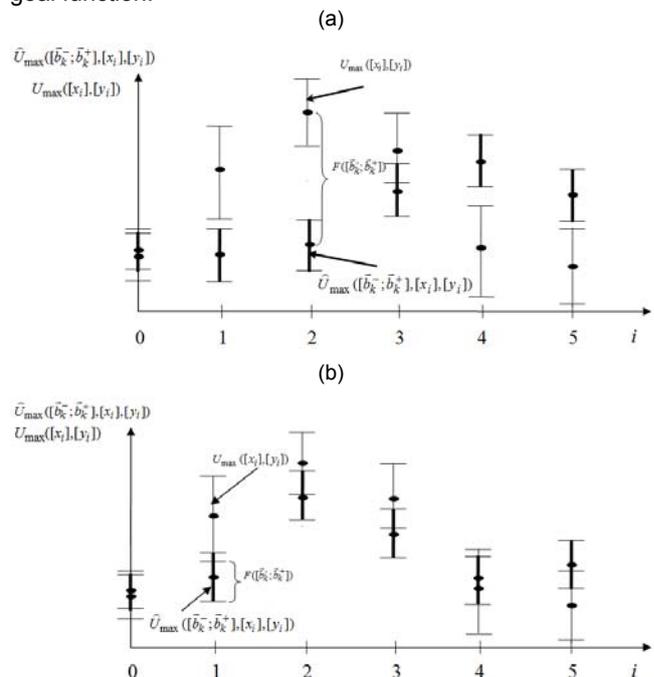


Fig. 3. Graphical illustration of calculation of the goal function value: a) using Eq. (9); b) using Eq. (10).

As soon as the parameter estimations of the system are specifying in the process of calculations, then the intersections of interval estimations of modeled and measured maximal amplitude of information signal for each point become not empty sets as it shown in Fig. 3(b). Then the goal function calculates by Eq. (10). As we can see from Fig 3(b), the largest deviation is between the measured interval of values of maximal amplitude  $U_{\max}([x_i],[y_i])$  and interval of modeled estimations of boundary values of information signal maximal amplitude  $\hat{U}_{\max}([\bar{b}_k^-, \bar{b}_k^+],[x_i],[y_i])$  for a point  $i=1$ . This deviation calculated by Eq. (10) determines the value of goal function on the current iteration of optimization procedure.

### Method of model parameters identification

It is expedient to execute the search of unknown vector of parameters of interval models corridor by methods of random search. The methods of random search was considered in many papers. The noted methods and their practical application for the optimization tasks were analyzed. Therefore, it is expedient to adapt the method of random search of estimations of parameters with the use of director cone [12] for calculation of interval estimations of parameters of mathematical model of dependence between maximal amplitude of obtained signal and stimulation point coordinates.

Consider a calculation scheme in procedure of random search of a minimum of goal function  $F([\bar{b} + \bar{b} \cdot \delta \bar{b}^-; \bar{b} + \bar{b} \cdot \delta \bar{b}^+])$  with the use of director cone.

On the initial iteration of random search ( $k=0$ ) set the initial approximation of parameters vector  $\bar{B}_0 = [\bar{b} + \bar{b} \cdot \delta \bar{b}^-; \bar{b} + \bar{b} \cdot \delta \bar{b}^+]$ . In a neighborhood of this approximation on a surface of imaginary hypersphere with radius  $r$ , scilicet, in the distance  $r$  from a point  $\bar{B}_{k=0}$  in space of parameters based on uniform distribution law generate  $n$  random points:

$$(11) \quad \bar{B}_n = \bar{B}_{k=0} + r \cdot \bar{\xi}_n, n=1, \dots, N.$$

Among generated points, we choose one that provides the minimum value of goal function:

$$(12) \quad \bar{B}_{k=1} = \arg \min_{n=1, \dots, N} (F([\bar{b}_0 + \bar{b}_0 \cdot \delta \bar{b}^-; \bar{b}_0 + \bar{b}_0 \cdot \delta \bar{b}^+] + r \cdot \bar{\xi}_n)).$$

Obtained estimation of parameters vector of static system is an approximation for next iteration. Additionally, calculate memory vector that determines successful direction of search in this procedure:

$$(13) \quad \bar{w} = \text{mid}[(\bar{B}_1 - \bar{B}_0) / r],$$

where  $\text{mid}(\bullet)$  is an operation of determination of middle of interval for further search.

On next iterations build imaginary hypercones in space of parameters with tops in points with coordinates  $\bar{B} = (\bar{b}_k + \bar{b}_k \cdot \delta \bar{b}^-; \bar{b}_k + \bar{b}_k \cdot \delta \bar{b}^+)$  which are the current estimations of parameters vector with the opening angle  $\psi$  and axe  $\bar{w}_k$ . These hypercones "cut off" some surfaces from hyperspheres with centers in points  $\bar{B} = (\bar{b}_k + \bar{b}_k \cdot \delta \bar{b}^-; \bar{b}_k + \bar{b}_k \cdot \delta \bar{b}^+)$  and radius  $r$ . Generate  $n$  random points using Eq. (11) based on uniform distribution law on obtained surfaces in space of parameters and their

tolerances where vector  $\bar{\xi}_n$  is calculated, in this case, based on the cone parameters limitations. Among generated points, we choose one that provides the minimum value of goal function:

$$(14) \quad \bar{B}_{k+1} = \arg \min_{n=1, \dots, N} (F([\bar{b}_k + \bar{b}_k \cdot \delta \bar{b}^-; \bar{b}_k + \bar{b}_k \cdot \delta \bar{b}^+] + r \cdot \bar{\xi}_n)).$$

Obtained vector parameters estimation is approximation for next  $k+1$  iteration of searching procedure. Additionally, redefine the memory vector in this procedure:

$$(15) \quad \bar{w}_{k+1} = \text{mid}[\alpha \cdot \bar{w}_k + \beta \cdot \frac{\bar{B}_{k+1} - \bar{B}_k}{r}],$$

where  $\alpha - (0 \leq \alpha \leq 1)$  is a coefficient of forgetting and  $\beta \delta$  is a coefficient of intensity of taking into account of new information.

The search continuous while the value of goal function is decreasing. If the value of goal function does not decrease on a certain iteration, then use a hypersphere instead of cone as it is on an initial iteration for given vector of parameter estimations. If it is impossible to find a point that provides decreasing of the goal function among the generated points in farther, then in this case reset the length of step  $r$ , as usually, decrease it.

Thus, as a result of applying of the above described method and algorithm of calculation of interval parameters estimations  $[\bar{b}] = ([b_1^-, b_1^+], \dots, [b_m^-, b_m^+])^T$ , will obtain the corridor of interval models (7).

### Algorithm of building the RLN location area

The corridor of interval models (7) with the guaranteed accuracy describes distribution of maximal amplitude of information signal (reaction on the surgical wound tissues stimulation by an alternating current) on the surface of surgery area. The largest values of maximal amplitude will be in a surgical wound points that represent RLN. Decreasing of these values will be observed when increasing distance between stimulation points and RLN. Graphical illustration of the noted corridor (7) shown in Fig. 4.

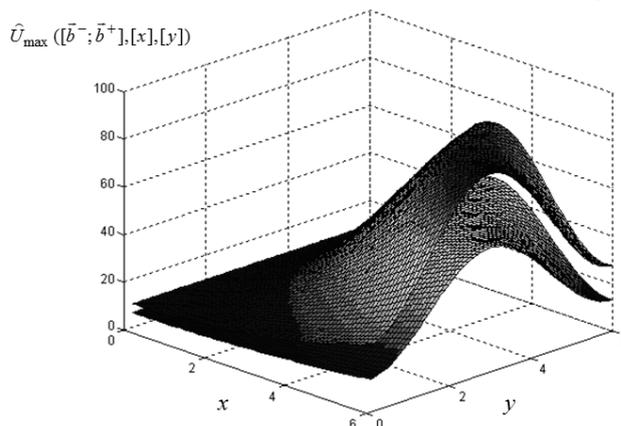


Fig. 4. Graphical illustration of corridor of interval models for RLN visualization

It should be noted that an Eq. (7) for the calculation of this distribution is much simpler than in papers where similar approach for identification of allowable area of surgery is considered.

Now, obtained corridor of interval models is basis for identification of the guaranteed area without a risk (from a point of view of RLN damage possibility) in surgical operation. For this purpose, it is enough to identify the minimum threshold level of maximal amplitude of

information signal which probably yet may response to point of direct RLN stimulation. Obviously, that this level of amplitude of information signal  $\bar{U}_{\min}$  corresponds to a minimal value on the crest of function for the lower bound of corridor of interval models:

$$(16) \quad \bar{U}_{\min} = \max \left\{ \min_{x_i} \max_{y_j} \hat{U}([\bar{b}^-, \bar{b}^+], [x_i], [y_j]), \right. \\ i = 1, \dots, N, j = 1, \dots, M; \\ \left. \max_{x_i} \min_{y_j} \hat{U}([\bar{b}^-, \bar{b}^+], [x_i], [y_j]), \right. \\ i = 1, \dots, N, j = 1, \dots, M \left. \right\}$$

The rule of choice of the noted threshold (16) is shown in Fig. 5.

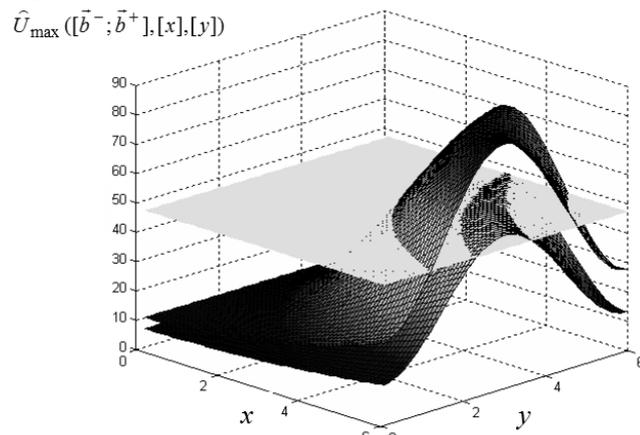


Fig. 5. Illustration of choice of threshold value of information signal amplitude for visualization of RLN location.

Then the guaranteed area of surgery is identifying by equation:

$$(17) \quad \chi = \left\{ \bar{p} = \begin{pmatrix} x \\ y \end{pmatrix} \mid \hat{U}^+(x, y) \leq \bar{U}_{\min} \right\}.$$

Obtained from (17) set  $\chi$  of points  $\bar{p}$  on area of surgery with coordinates  $(x, y)$  identifies the guaranteed area of surgical operation which guaranteed does not include a RLN.

The proposed method of identification of guaranteed safe area of surgical operation has a number of advantages compared to the known methods. In particular, taking into account of errors while detecting the point coordinates for surgical wound tissues stimulation that usually may be up to 50%. As a result, it enables to specify the area of safe surgical operation. Also, an advantage is a more simple from a calculating point of view presentation of corridor of interval models which describes distribution of maximal amplitude of information signal (reaction on the surgical wound tissues stimulation by an alternating current) on the surface of area of surgery with the guaranteed accuracy.

At the same time, the proposed method does not guarantee the decrease of risk of RLN damage in the process of surgical operation to "0" due to the low informativeness of information signal parameter that is its maximal amplitude.

The some noted results obtained within the national scientific and research project (2011). The development of this research started in 2017 in project on topic "Mathematical tools and software for classifying the tissues

in surgical wound during surgery on the neck organs" (Gov.reg. No 0117U000410).

## Conclusions

It was considered the mathematical models of informative characteristic of tissues in surgical wound used for construction the tools of the electrophysiological monitoring the recurrent laryngeal nerve. As distinct from existing method, it is proposed a method, which theoretically decrease the risk of RLN damage due to taking into account the errors of detecting the coordinates of points where stimulating the tissues in surgical wound. Realization of proposed mathematical model and algorithm of search the allowable area of surgical operation based on Raspberry Pi and conducting the approbation of new system during a surgery on a thyroid gland provided for the noted project.

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