(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
02 November 2023 (02.11.2023)

WIPO | PCT

(10) International Publication Number
WO 2023/209609 A1

(51) International Patent Classification:
A61B 5/294 (2021.01) *A61B 5/00* (2006.01)
A61B 5/311 (2021.01)

(21) International Application Number:
PCT/IB2023/054322

(22) International Filing Date:
26 April 2023 (26.04.2023)

(25) Filing Language: Italian

(26) Publication Language: English

(30) Priority Data:
102022000008381 27 April 2022 (27.04.2022) IT

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG,

(54) Title: METHOD FOR DETERMINING THE FUNCTIONAL TOPOGRAPHY OF A PERIPHERAL NERVE

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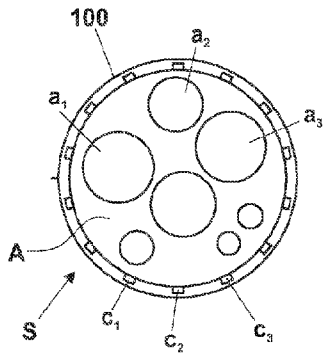
Fig. 2A



(57) Abstract: A method for determining the functional topography of a peripheral nerve (10) of a user comprising the steps of prearranging an electrode (100) comprising a number n of channels c_i, with $i = 1,2..., n$, arranging the electrode (100) in such a way that each channel is in contact with the peripheral nerve (10) at a respective contact point p_i, with $i = 1,2..., n$, generating a model of a cross section S of the peripheral nerve (10) where the area A of the cross section S comprises a number m of areas α_j, with $j = 1,2,..., m$, computing a lead field matrix $L = [R_{j,i}]$, wherein $R_{j,i}$ is a value that describes the electrostatic relationship between an area α_j and a contact point p_i of the cross section S, periodic acquisition, by the electrode (100), of a number n of voltage values V_{ki} at instants t_k, with $k = 1,2,...,S$, obtaining a voltage matrix $V = [V_{k,i}]$, with $i = 1,2,...,n$, where V_{ki} is the voltage value determined by the channel c_i at the contact point p_i at the instant t_k, periodic acquisition, by at least one medical device, of a number r of values of physiological signals $P_{k,h}$ of the user at instants t_k, with $k = 1,2,..., s$, obtaining a matrix of the physiological signals P = $[P_{k,h}]$, with $h. = 1,2,...,r$, where P_k k is the value of the h-th physiological signal determined at the instant t_k, computing a discrimination matrix = $D = [d_{h,i}]$, D being function of the matrices $V = [V_{k,i}]$ and $P = [P_{k,h}]$, where $d_{h,i}$ is the discrimination coefficient which represents the correlation between the h-th physiological signal $P_{k,h}$ and the i-th voltage value $V_{k,i}$ referred to a same instant t_k, computing a spatial filtering matrix $\Phi^{DBF} = [\varphi_{h,j}]$, $\varphi_{h,j}$ being the localization index which represents the correlation between the h-th physiological signal and the area α_j of said cross section S, generating a functional topography of said peripheral nerve (10), for each h-th physiological signal, wherein each area α_j is graphically identified as a function of the

[Continued on next page]

KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE*

corresponding value $\varphi_{h,j}$ associated with it by the spatial filtering matrix Φ^{DBF}.

TITLE

Method for determining the functional topography of a peripheral nerve

DESCRIPTION

Field of the invention

[0001] The present invention relates to the field of neural activity mapping.

[0002] In particular, the present invention relates to the determination of the functional topography of a peripheral nerve for the automatic optimization of spatially selective stimulation protocols with respect to multiple functions.

Description of the prior art

[0003] The autonomic nervous system (ANS) is the part of the peripheral nervous system that interacts with the visceral organs to guarantee the chemical-physical balance (homeostasis) of the organism. The ANS communicates with vital organs including the heart, lungs and digestive tract via nerves, made up of bundles of nerve fibers called fascicles dispersed in a matrix of connective tissue. The "topography" of a nerve is defined as the spatial organization of the fascicles in its cross section.

[0004] The electrical stimulation of a nerve makes it possible to modulate the activity of the organs or to transmit sensory stimuli to the brain, which interprets them

as coming from the target organs of the innervation. Electrical stimulation is performed using electrodes that are surgically applied to the nerve and placed in contact with the outer surface of the nerve (extra-neural electrodes) or inserted into the section of the nerve (intra-neural electrodes). Stimulation is delivered by activating the different conductive contacts of the electrode over time, which cause some electrical activity in the nerve. This variation over time of the currents injected or absorbed by the electrode contacts is called the stimulation protocol. An electrical stimulation protocol acts selectively on a function of the organism if it is capable of significantly modifying this function without altering the other functions controlled by the nerve under stimulation. Since the autonomic nervous system interacts with a large number of vital organs that perform completely heterogeneous functions, non-selective stimulation can produce even serious unwanted effects.

[0005] The scientific community has shown in the past that nerve fibers that interact with a given function often exhibit a certain level of spatial segregation compared to fibers that interact with different functions. The spatial organization of fibers related to different body functions is called functional topography, and its determination in

the least invasive way possible allows the development of spatially selective stimulation protocols.

[0006] By its constitution, the flow of nervous activity that crosses the autonomic system is generated by the simultaneous activity of multiple sources of information. The overall nervous activity crossing a nerve can be recorded using the same electrodes that can be used for stimulation, and therefore without the need to implant additional devices. Nervous activity originating or destined for vital organs such as the heart or lungs can then be related to physiological signals normally recorded in a non-invasive way, such as blood pressure.

[0007] The existing methods of reconstruction of the functional topography of a nerve, based on the use of the electroneurographic signal (ENG), are based on the concepts of lead field matrix and of discriminability index.

[0008] The process of recording an ENG signal, i.e. the electrical activity produced in the cross section of a nerve, can be simulated by calculating a value of the current injected by each segment of each fiber present in the nerve and a constant which relates this segment with the registration contact of the electrode. The constant that establishes the contribution of each fiber in the overall recording can be calculated by finite element analysis (FEA or FEM), so that membrane currents of fibers far from the

recording contact have a smaller contribution within the recorded signal. These constants are characteristic of a given implant (geometry of the implanted nerve and electrode) and must be calculated only once for each application. The constants relating to each recording contact in the implanted electrode (which can be thought of as the "fields of vision" of each contact) are usually collected in several rows of a matrix, called the lead field matrix. Each column of the lead field matrix refers to a single fiber and contains the contribution of this fiber to the signals recorded by each contact of the electrode used. The pseudo-inverse of the lead field matrix has as many columns as there are contacts of the electrode used, and each of these columns represents a spatial filter that converts the signal recorded by a specific contact into a distribution of electrical power in each point of the nerve.

[0009] Document US20110046506A1 describes a triangulation method by spatial filtering ("beamforming", BF), which uses these fields of vision by weighing them by the power of the signal recorded by each contact. Thus, the localization of nerve transmitted power is a weighted sum of the spatial filters for each contact, where contacts registering higher power signals have a higher contribution, since they are likely closer to the source of the power.

[00010] However, in this document the localization procedure does not allow the components relating to a physiological function to be selected and filtered. This can result in off-target activation by electrical stimulation, producing adverse effects that can cause severe discomfort to the patient.

[00011] In the document F. Vallone *et al.*, "Simultaneous decoding of cardiovascular and respiratory functional changes from pig intraneural vagus nerve signals" *J. Neural Eng.*, vol. 18, no. 4, p. 0460a2, Jul. 2021, doi: 10.1088/1741-2552/ac0d42 a method is described for discrimination through potential fields ("discriminative field potential", DFP) which directly uses the lead field matrix. The lines corresponding to each site are weighted with respect to a discriminability coefficient and added together to produce a spatial distribution with higher values in the areas where it is more probable that a given information source is present.

[00012] However, since in this document the inversion of the lead field matrix is not carried out, there is no triangulation: the information coming from the individual contacts is used without eliminating the redundancy due to the fact that the contacts register the same signal from certain locations in the section of the nerve. The localization is therefore limited to the identification of

the zones of influence of the most informative contacts, and there is no construction of a real functional topography of the nerve.

[00013] In the document F. Vallone *et al.*, the discriminability coefficient is defined as a number that is assigned to each contact of the electrode and quantifies the information related to a certain physiological state induced in a subject represented in the ENG signal.

[00014] In the context of such invention, more specifically, the discriminability coefficient is defined as a number that is assigned to each contact of the electrode and quantifies the information related to a certain physiological function present in the ENG signal.

Summary of the invention

[00015] It is therefore a feature of the present invention to provide a method for determining the functional topography of a peripheral nerve of a user which allows to avoid the stimulation of unwanted components and therefore the production of severe adverse effects for the patient.

[00016] It is also a feature of the present invention to provide such a method which allows to accurately determine the spatial/topographical organization in the nerve section of the nerve fibers communicating with different organs which mediate for different functions of the organism.

[00017] It is still a feature of the present invention to provide such a method which allows the relationship between nerve signals and physiological measurements to be used to triangulate the position in the section of the nerve of the fibers which transmit the information relating to each information source.

[00018] These and other objects are achieved by a method for determining the functional topography of a peripheral nerve of a user, said method requiring an electrode (100) comprising a number n of channels c_i, with $i = 1,2,\dots,n$, wherein each channel c_i is in contact with said peripheral nerve at a respective contact point p_i, with $i = 1,2,\dots,n$,

said method comprising the steps of:

- generating a model of a cross section S of said peripheral nerve where the area A of said cross section S comprises a number m of areas a_j, with $j = 1,2,\dots,m$;
- computing a lead field matrix $\boldsymbol{L} = [R_{j,i}]$, wherein $R_{j,i}$ is a value that describes the electrostatic relationship between an area a_j and a contact point p_i of said cross section S;
- periodic acquisition, by said electrode (100), of a number n of voltage values $V_{k,i}$ at instants t_k, with $k = 1,2,\dots,s$, obtaining a voltage matrix $\boldsymbol{V} = [V_{k,i}]$, with $i = 1,2,\dots,n$, where $V_{k,i}$ is the voltage value

determined by the channel c_i at the contact point p_i at the instant t_k;

- periodic acquisition, by at least one medical device, of a number r of values of physiological signals $P_{k,h}$ of said user at instants t_k, with $k = 1,2,\dots,s$, obtaining a matrix of the physiological signals $\boldsymbol{P} = [P_{k,h}]$, with $h = 1,2,\dots,r$, where $P_{k,h}$ is value of the h-th physiological signal determined at the instant t_k;
- computing a discrimination matrix $\boldsymbol{D} = [d_{h,i}]$, $\boldsymbol{D}$ being function of said matrix $\boldsymbol{V} = [V_{k,i}]$ and $\boldsymbol{P} = [P_{k,h}]$, where $d_{h,i}$ is the discrimination coefficient which represents the correlation between the h-th physiological signal $P_{k,h}$ and the i-th voltage value $V_{k,i}$ referred to a same instant t_k;
- computing a spatial filtering matrix $\boldsymbol{\phi}^{DBF} = [\varphi_{h,j}]$, $\varphi_{h,j}$ being the localization index which represents the correlation between the h-th physiological signal and the area a_j of said cross section S;
- for each h-th physiological signal, generating a functional topography of said peripheral nerve wherein each area a_j is graphically identified as a function of the corresponding value $\varphi_{h,j}$ associated with it by said spatial filtering matrix $\boldsymbol{\phi}^{DBF}$.

[00019] The present invention therefore provides a method of discriminative triangulation by spatial filtering ("discriminative beamforming", DBF) which uses the discriminability coefficient to weight the spatial filters used in the triangulation and thus take into account the relative positions of the contacts in the recording electrode. This method makes it possible to obtain a localization measure in the proper sense and to select and filter the components relating to a physiological function by means of the discrimination coefficients.

[00020] In particular, by means of the electrode it is possible to produce currents in the channels c_i such that in correspondence with the desired areas a_j these currents produce a significant effect on the physiological parameters correlated to them.

[00021] Advantageously, a step is also provided of filtering said voltage matrix $\boldsymbol{V} = [V_{k,i}]$ obtaining a filtered voltage matrix $\check{\boldsymbol{V}} = [\check{V}_{k,i}] = filt(\boldsymbol{V})$.

[00022] Advantageously, a step is also provided of extracting features from said filtered voltage matrix $\check{\boldsymbol{V}} = [\check{V}_{k,i}]$ obtaining a neural data matrix $\boldsymbol{X}_{ENG}$.

[00023] In particular, said discrimination matrix $\boldsymbol{D} = [d_{h,i}]$ is function of said neural data matrix $\boldsymbol{X}_{ENG}$.

[00024] In particular, the step of filtering said voltage matrix $\boldsymbol{V} = [V_{k,i}]$ is obtained by the equation:

$$\check{V}_{k,i} = filt(V_{k,i}) = V_{k,i} * H_k = \sum_{\tau=0}^{\tau=L} V_{\tau,i} \cdot H_{k-\tau}$$

where H_k is value of the k-th coefficient, with $k = 1,2,\dots,L$, of the (impulse) response of the filter.

[00025] Alternatively, the step of filtering said voltage matrix $\boldsymbol{V} = [V_{k,i}]$ is obtained by the equation:

$$\check{V}_{k,i} = zscore(V_{k,i}) = \frac{V_{k,i} - \eta_{V_{k,i}}}{\sigma_{V_{k,i}}}$$

where $\eta_{V_{k,i}}$e $\sigma_{V_{k,i}}$ represent respectively the mean and the standard deviation of the i-th neural datum $V_{k,i}$.

[00026] Alternatively, the step of filtering said voltage matrix $\boldsymbol{V} = [V_{k,i}]$ is obtained by the equation:

$$\check{V}_{k,i} = abs(V_{k,i}) = |V_{k,i}|$$

[00027] Alternatively, the step of filtering said voltage matrix $\boldsymbol{V} = [V_{k,i}]$ is obtained by the equation:

$$\check{V}_{k,i} = RMS(V_{k,i}) = \sqrt{\frac{1}{K}\sum_{\tau=k-dk}^{\tau=k+dk} V_{\tau,i}^2}$$

where K represents the number of values taken into consideration.

[00028] In particular, said step of filtering said voltage matrix $\boldsymbol{V} = [V_{k,i}]$ comprises the steps of:

- for each channel c_i, defining a set G_i comprising all the voltage values $V_{k,i}$ taken at said channel c_i;
- applying a filter on said set G_i, obtaining a filtered set $\check{G}_i$ comprising filtered voltage values $\check{V}_{k,i}$;
- obtaining a filtered voltage matrix $\check{\boldsymbol{V}} = [\check{V}_{k,i}] = filt(\boldsymbol{V})$.

[00029] In particular, said step of extracting features from said filtered voltage matrix $\check{\boldsymbol{V}} = [\check{V}_{k,i}]$ comprises the steps of:

- defining a time window $\Delta t_{\tilde{k}} = b * \Delta t_k$, with $\Delta t_{\tilde{k}} = (t_{\tilde{k}+1} - t_{\tilde{k}})$ and $\Delta t_k = (t_{k+1} - t_k)$, where $b \geq 1$ is a predetermined coefficient;
- for each filtered set $\check{G}_i$, selection of filtered voltage values $\check{V}_{k,i}$ acquired in said time window $\Delta t_{\tilde{k}}$, obtaining a number s/b of subsets $\tilde{G}_{\tilde{k},i}$, with $\tilde{k} = 1,2,\dots,s/b$, each subset $\tilde{G}_{\tilde{k},i}$ comprising a number b of filtered voltage values $\check{V}_{k,i}$;
- for each subset $\tilde{G}_{\tilde{k},i}$, extraction of a number f of neural data arranged to define mathematical features of said subset $\tilde{G}_{\tilde{k},i}$, obtaining a number $n * f$ of neural data for each filtered set $\check{G}_i$;
- obtaining a neural data matrix $\boldsymbol{X}_{ENG} = [\tilde{V}_{\tilde{k},\tilde{\imath}}]$, where $\tilde{V}_{\tilde{k},\tilde{\imath}}$ is the $\tilde{\imath}$-th neural datum extracted in the window $\Delta t_{\tilde{k}}$, $\tilde{\imath} = 1,2,\dots,n * f$.

[00030] In particular, a mathematical feature extracted from said subset $\tilde{G}_{\tilde{k},i}$ is the local maximum defined by the equation:

$$\tilde{V}_{\tilde{k},\tilde{\imath}} = \underset{t_{\tilde{k}} < \tau < t_{\tilde{k}+1}}{local\ max}\ \check{V}_{\tau,i} = local\ max\ \tilde{G}_{\tilde{k},i}$$

[00031] In particular, a mathematical feature extracted from said subset $\tilde{G}_{\tilde{k},i}$ is the local minimum defined by the equation:

$$\tilde{V}_{\tilde{k},\tilde{\imath}} = \underset{t_{\tilde{k}}<\tau<t_{\tilde{k}+1}}{local\ min}\ \check{V}_{\tau,i} = local\ min\ \tilde{G}_{\tilde{k},i}$$

[00032] In particular, a mathematical feature extracted from said subset $\tilde{G}_{\tilde{k},i}$ is the number of values above the threshold defined by the relation:

$$\tilde{V}_{\tilde{k},\tilde{\imath}} = \underset{t_{\tilde{k}}<\tau<t_{\tilde{k}+1}}{\#}\ \check{V}_{\tau,i} \geq thr_i = \#\,\tilde{G}_{\tilde{k},i} \geq thr_i$$

where thr_i is the threshold value of the i-th filtered set $\check{G}_i$.

[00033] Advantageously, a step is also provided of filtering said matrix of the physiological signals $\boldsymbol{P} = [P_{k,h}]$ obtaining a filtered matrix of the physiological signals $\check{\boldsymbol{P}} = [\check{P}_{k,h}] = filt(\boldsymbol{P})$.

[00034] Advantageously, a step is also provided of extracting features from said filtered matrix of the physiological signals $\check{\boldsymbol{P}} = [\check{P}_{k,h}]$ obtaining a functional data matrix $\boldsymbol{X}_{PHYSIO}$.

[00035] In particular, said discrimination matrix $\boldsymbol{D} = [d_{h,i}]$ is function of said neural data matrix $\boldsymbol{X}_{PHYSIO}$.

[00036] In particular, the step of filtering said matrix of the physiological signals $\boldsymbol{P} = [P_{k,h}]$ is obtained by the equation:

$$\check{P}_{k,h} = filt(P_{k,h}) = P_{k,h} * H_k = \sum_{\tau=0}^{\tau=L} P_{\tau,h} \cdot H_{k-\tau}$$

where H_k is value of the k-th coefficient, with $k = 1,2,\dots,L$, of the (impulse) response of the filter.

[00037] Alternatively, the step of filtering said matrix of the physiological signals $\boldsymbol{P} = [P_{k,h}]$ is obtained by the equation:

$$\check{P}_{k,h} = zscore(P_{k,h}) = \frac{P_{k,h} - \eta_{P_{k,h}}}{\sigma_{P_{k,h}}}$$

where $\eta_{P_{k,h}}$e $\sigma_{P_{k,h}}$ represent respectively the mean and the standard deviation of the h-th functional datum $P_{k,h}$.

[00038] Alternatively, the step of filtering said matrix of the physiological signals $\boldsymbol{P} = [P_{k,h}]$ is obtained by the equation:

$$\tilde{P}_{k,h} = abs(P_{k,h}) = |P_{k,h}|$$

[00039] Alternatively, the step of filtering said matrix of the physiological signals $\boldsymbol{P} = [P_{k,h}]$ is obtained by the equation:

$$\check{P}_{k,h} = RMS(P_{k,h}) = \sqrt{\frac{1}{K}\sum_{\tau=k-dk}^{\tau=k+dk} P_{\tau,h}^2}$$

where K represents the number of values taken into consideration.

[00040] In particular, said step of filtering said matrix of the physiological signals $\boldsymbol{P} = [P_{k,h}]$ comprises the steps of:

- for each h-th physiological signal, defining a set G_h comprising all the values of said h-th physiological signal $P_{k,h}$ acquired;
- applying a filter on said set G_h, obtaining a filtered set $\check{G}_h$ comprising values of the filtered physiological signals $\check{P}_{k,h}$;
- obtaining a filtered matrix of the physiological signals $\check{\boldsymbol{P}} = [\check{P}_{k,h}] = filt(\boldsymbol{P})$.

[00041] In particular, said step of extracting features from said filtered matrix of the physiological signals $\check{\boldsymbol{P}} = [\check{P}_{k,h}]$ comprises the steps of:

- defining a time window $\Delta t_{\tilde{k}} = b * \Delta t_k$, with $\Delta t_{\tilde{k}} = (t_{\tilde{k}+1} - t_{\tilde{k}})$ and $\Delta t_k = (t_{k+1} - t_k)$, where $b \geq 1$ is a predetermined coefficient;
- for each filtered set $\check{G}_h$, selection of values of filtered physiological signals $\check{P}_{k,h}$ acquired in said time window $\Delta t_{\tilde{k}}$, obtaining a number s/b of subsets $\tilde{G}_{\tilde{k},h}$, with $\tilde{k} = 1,2,\dots,s/b$, each subset $\tilde{G}_{\tilde{k},h}$ comprising a number b of filtered physiological signals $\check{P}_{k,h}$;
- for each subset $\tilde{G}_{\tilde{k},h}$, extraction of a number w of functional data arranged to define mathematical features of said subset $\tilde{G}_{\tilde{k},h}$, obtaining a number $n * w$ of functional data for each filtered set $\check{G}_h$;
- obtaining a functional data matrix $\boldsymbol{X}_{PHYSIO} = [\tilde{P}_{\tilde{k},\tilde{h}}]$, where $\tilde{P}_{\tilde{k},\tilde{h}}$ is the $\tilde{h}$-th functional datum extracted in the window $\Delta t_{\tilde{k}}$, $\tilde{h} = 1,2,\dots,n * w$.

[00042] In particular, a mathematical feature extracted from said subset $\tilde{G}_{\tilde{k},h}$ is the local maximum defined by the equation:

$$\tilde{P}_{\tilde{k},\tilde{h}} = \underset{t_{\tilde{k}} < \tau < t_{\tilde{k}+1}}{local\ max}\ \check{P}_{\tau,h} = local\ max\ \tilde{G}_{\tilde{k},h}$$

[00043] In particular, a mathematical feature extracted from said subset $\tilde{G}_{\tilde{k},h}$ is the local minimum defined by the equation:

$$\tilde{P}_{\tilde{k},\tilde{h}} = \underset{t_{\tilde{k}}<\tau<t_{\tilde{k}+1}}{local\ min}\ \check{P}_{\tau,h} = local\ min\ \tilde{G}_{\tilde{k},h}$$

[00044] In particular, a mathematical feature extracted from said subset $\tilde{G}_{\tilde{k},h}$ is the number of values above the threshold defined by the relation:

$$\tilde{P}_{\tilde{k},\tilde{h}} = \underset{t_{\tilde{k}}<\tau<t_{\tilde{k}+1}}{\#}\ \check{P}_{\tau,h} \geq thr_h = \#\,\tilde{G}_{\tilde{k},h} \geq thr_h$$

where thr_h is the threshold value of the i-th filtered set $\check{G}_h$.

[00045] In particular, said step of computing said discrimination matrix $\boldsymbol{D}$ is obtained solving the system:

$$\begin{cases} \boldsymbol{X_{ENG}} = \boldsymbol{X_{PHYSIO}}\,\boldsymbol{D} + \boldsymbol{\varepsilon} \\ \boldsymbol{D} = \left(\boldsymbol{X_{PHYSIO}}^{\boldsymbol{T}}\boldsymbol{C_{\varepsilon}^{-1}}\boldsymbol{X_{PHYSIO}}\right)^{\boldsymbol{-1}}\boldsymbol{X_{PHYSIO}}^{\boldsymbol{T}}\boldsymbol{C_{\varepsilon}^{-1}}\boldsymbol{X_{ENG}} \\ \boldsymbol{C_{\varepsilon}} = E\{(\boldsymbol{\varepsilon} - \boldsymbol{\eta_{\varepsilon}})(\boldsymbol{\varepsilon} - \boldsymbol{\eta_{\varepsilon}})^T\} \end{cases}$$

where $\boldsymbol{C_{\varepsilon}}$ is the error covariance matrix,

E is the expected value operator,

$\boldsymbol{\varepsilon}$ is the error matrix in which the residuals of the predictive model are present.

[00046] In particular, $\boldsymbol{\varepsilon} = \left[\varepsilon_{\tilde{k},\tilde{\imath}}\right]$ is the matrix error wherein $\varepsilon_{\tilde{k},\tilde{\imath}}$ is value of the error in the prediction of the $\tilde{\imath}$-th neural datum of $\boldsymbol{X_{ENG}}$ at the instant $t_{\tilde{k}}$.

[00047] The above-described equation is valid if there is linear correlation between each value $P_{k,h}$ and a corresponding value $V_{k,i}$ referred to a same instant t_k.

[00048] Alternatively, said step of computing said discrimination matrix $\boldsymbol{D}$ is obtained by the equation:

$$d_{h,i} = corr\left(X_{PHYSIO_{k,h}}, X_{ENG_{k,i}}\right) = \frac{\sigma_{X_{PHYSIO_{k,h}}, X_{ENG_{k,i}}}}{\sigma_{X_{PHYSIO_{k,h}}}\sigma_{X_{ENG_{k,i}}}}$$

where $\sigma_{X_{PHYSIO_{k,h}},X_{ENG_{k,i}}}$ is the covariance of the variables $X_{PHYSIO_{k,h}}$ and $X_{ENG_{k,i}}$,

$\sigma_{X_{PHYSIO_{k,h}}}/\sigma_{X_{ENG_{k,i}}}$ is the standard deviation of $X_{PHYSIO_{k,h}}/X_{ENG_{k,i}}$.

[00049] The above-described equation is valid if there is linear correlation between each value $P_{k,h}$ and a corresponding value $V_{k,i}$ referred to a same instant t_k.

[00050] In particular, said step of computing said spatial filtering matrix $\boldsymbol{\phi}^{DBF}$ is obtained according to the equation:

$$\boldsymbol{\phi}^{DBF} = \boldsymbol{D}\boldsymbol{L}^{+}$$

with $\boldsymbol{L}^{+} = (\boldsymbol{L}^{T}\boldsymbol{L})^{-1}\boldsymbol{L}^{T}$.

[00051] Alternatively, said step of computing said spatial filtering matrix $\boldsymbol{\phi}^{DBF}$ is obtained according to the equation:

$$\boldsymbol{\phi}^{DBF} = \boldsymbol{D}\boldsymbol{L}_{\Lambda}^{+}$$

with $\boldsymbol{L}_{\Lambda}^{+} = (\boldsymbol{L}^{T}\boldsymbol{\Lambda}\boldsymbol{L})^{-1}\boldsymbol{L}^{T}\boldsymbol{\Lambda}$,

where $\boldsymbol{\Lambda} = [\Lambda_{j,j}]$ is the spatial information matrix, being $\Lambda_{j,j} = 1$ when it is known that the area a_j corresponds to a nonzero value of $\varphi_{h,j}$.

[00052] Alternatively, said step of computing said spatial filtering matrix $\boldsymbol{\phi}^{DBF}$ is obtained according to the equation:

$$\boldsymbol{\phi}^{DBF} = \boldsymbol{D}\hat{\boldsymbol{L}}_{\Lambda}^{+}$$

with $\boldsymbol{L}_{\Lambda}^{+} = (\boldsymbol{L}^{T}\boldsymbol{\Lambda}\boldsymbol{L})^{-1}\boldsymbol{L}^{T}\boldsymbol{\Lambda}$ and $\hat{\boldsymbol{L}}_{\Lambda}^{+}[:,j] \leftarrow \frac{\boldsymbol{L}_{\Lambda}^{+}[:,j]}{\|\boldsymbol{\Lambda}\boldsymbol{L}\boldsymbol{L}_{\Lambda}^{+}[:,j]\|_2}$,

where $\boldsymbol{\Lambda} = [\Lambda_{j,j}]$ is the spatial information matrix, being $\Lambda_{j,j} = 1$ when it is known that the area a_j corresponds to a nonzero value of $\varphi_{h,j}$.

[00053] Advantageously, if there is no linear correlation between each value $P_{k,h}$ and a corresponding value $V_{k,i}$ referred to the same instant t_k, said step of computing said discrimination matrix $\boldsymbol{D}$ is obtained by at least one of the following techniques:

- calculation of advanced similarity metrics;
- indices relating to information theory (e.g. mutual information) or to complexity analysis;
- fuzzy logic techniques;
- artificial intelligence techniques (e.g. neural networks).

[00054] In particular, the step of computing the discrimination matrix $\boldsymbol{D}$ is obtained by the technique of mutual information by the equation:

$$d_{h,i} = \sum_{X_{PHYSIO_{\tilde{k},\tilde{h}}}} \sum_{X_{ENG_{\tilde{k},\tilde{\imath}}}} p_{X_{PHYSIO_{\tilde{k},\tilde{h}}}, X_{ENG_{\tilde{k},\tilde{\imath}}}} log\left(\frac{p_{X_{PHYSIO_{\tilde{k},\tilde{h}}}, X_{ENG_{\tilde{k},\tilde{\imath}}}}}{p_{X_{PHYSIO_{\tilde{k},\tilde{h}}}} p_{X_{ENG_{\tilde{k},\tilde{\imath}}}}}\right)$$

where $\tilde{h} \in h$, $\tilde{\imath} \in i$, $p_{X_{PHYSIO_{\tilde{k},\tilde{h}}}, X_{ENG_{\tilde{k},\tilde{\imath}}}}$ is the joint probability distribution function of $X_{PHYSIO_{\tilde{k},\tilde{h}}}$ and $X_{ENG_{\tilde{k},\tilde{\imath}}}$, $p_{X_{PHYSIO_{\tilde{k},\tilde{h}}}}$ and $p_{X_{ENG_{\tilde{k},\tilde{\imath}}}}$ are the marginal probability distribution functions, respectively, of $X_{PHYSIO_{\tilde{k},\tilde{h}}}$ and $X_{ENG_{\tilde{k},\tilde{\imath}}}$.

[00055] In particular, the step of computing the discrimination matrix $\boldsymbol{D}$ is obtained by the neural networks by the relations:

$$\boldsymbol{X}_{PHYSIO} \approx \Psi(\boldsymbol{X}_{ENG}\boldsymbol{W} - \boldsymbol{b}) + \boldsymbol{\varepsilon}$$

$$\boldsymbol{D} \propto \boldsymbol{W}, \boldsymbol{b}, \boldsymbol{\varepsilon}^{-1}$$

where $\boldsymbol{W} = [w_{\tilde{\imath},u}]$ is the weight matrix,

$\boldsymbol{\varepsilon}$ is the error matrix in which the residuals of the predictive model are present,

$\boldsymbol{b} = [b_{\tilde{\imath},u}]$ is the matrix of bias coefficients, with $u = 1,2,\ldots,q$,

where $w_{\tilde{\imath},u}$ and $b_{\tilde{\imath},u}$ are the values of the $\tilde{\imath}$-th neural datum and of the n-th artificial neuron,

Ψ is the activation function and acts as an approximator of functions, taking the form of a universal function (e.g. tanh, radial basis, etc.).

[00056] Advantageously, said step of generating a functional topography of said peripheral nerve is obtained by associating a plurality of numerical ranges of said values $\varphi_{h,j}$ to respective colours or colour shades.

[00057] Alternatively, said step of generating a functional topography of said peripheral nerve is obtained adopting the technique of field lines (or isolines) to said spatial filtering matrix $\boldsymbol{\phi}^{DBF}$ in order to delineate in said cross section S of the peripheral nerve a perimeter $\prod$ containing the areas a_j correlated to a given physiological parameter.

[00058] Alternatively, said step of generating a functional topography of said peripheral nerve is obtained by assigning to each area a_j a value of statistical significance, obtained by carrying out a statistical test (e.g. t-test), with respect to the activation of this area in relation to the activation of a given physiological parameter.

[00059] In particular, the acquired physiological signals comprise, alternatively or in combination:

- electrophysiological signals that measure the response of the autonomic nervous system: electrocardiogram (ECG), electromyogram (EMG), galvanic response of the skin;
- vital signs of the autonomic nervous system associated with the cardiovascular and respiratory systems: blood pressure, lung volume or other respiratory signals, oxygen saturation;
- other signals capable of measuring the response of the autonomic nervous system: blood glucose level, body temperature.

[00060] In particular, the medical device is selected from the group consisting of:

- wearable or non-wearable electromedical systems for the acquisition of bio-potentials and/or bio-impedances;
- wearable or non-wearable devices for detecting pressure and blood values: photo-plethysmograph, pulse oximeter, electronic meter based on the oscillometric method;
- wearable and non-wearable devices for breath detection: spirometer and devices for mechanical ventilation, impedance or inductance

plethysmograph, piezo-resistive or piezo-electric pneumograph, thermo-couple;

- manual or automatic wearable or non-wearable (needle) blood glucose monitoring systems;
- wearable or non-wearable body temperature monitoring systems: thermo-couple thermometer, resistive sensor thermometer, infrared thermometer.

Brief description of the drawings

[00061] The invention will be now shown with the following description of its embodiments, exemplifying but not limitative, with reference to the attached drawings in which:

- Fig. 1 shows a flow diagram of the successive steps of the method according to the present invention;
- Fig. 2 schematically shows an electrode applied to a peripheral nerve;
- Fig. 2A schematically shows a section of the peripheral nerve to which a first embodiment of the electrode is applied;
- Fig. 2B schematically shows a section of the peripheral nerve to which a second embodiment of the electrode is applied;
- Fig. 3 shows a possible graphical visualization of the functional topography of the peripheral nerve

obtained by the method according to the present invention;

- Fig. 4A schematically shows the process of stimulation, by means of the electrode, of an area of the peripheral nerve assigned to the desired target function;
- Fig. 4B schematically shows the connection between the vagus nerve and some organs responsible for physiological functions which can be stimulated electrically thanks to the functional topography of the nerve obtained by means of the method of the present invention.

Description of some preferred embodiments

[00062] With reference to Figs. 1, 2, 2A and 2B, the method for determining the functional topography of a peripheral nerve 10 of a user, according to the present invention, provides a first step of arranging an electrode 100 comprising a number n of channels c_i, with $i = 1,2,\dots,n$, in contact with the peripheral nerve 10. In particular, the electrode 100 is arranged in such a way that each channel c_i is in contact with the peripheral nerve 10 at a respective contact point p_i, with $i = 1,2,\dots,n$ [301].

[00063] In particular, in Fig. 2A a first embodiment is shown of the electrode 100 where the channels c_i are arranged in contact with the outer surface of the peripheral nerve

10, whereas in Fig. 2B an alternative embodiment is shown where the channels c_i are arranged internally to the section of the peripheral nerve 10.

[00064] The method then provides a step of generating a model of a cross section S of the peripheral nerve 10 where the area A of the cross section S comprises a number m of areas a_j, with $j = 1,2,\dots,m$ [302]. This model, which also includes the electrode 100, allows the subsequent calculation steps of the method.

[00065] The method then provides a step of computing a lead field matrix $\boldsymbol{L} = [R_{j,i}]$, wherein $R_{j,i}$ is a value that describes the electrostatic relationship between an area a_j and a contact point p_i of said cross section S [303]. Such values $R_{j,i}$ depend on the relative spatial arrangement between the peripheral nerve 10 and the electrode 100 and therefore depend on the specific geometry of the electrode 100.

[00066] The method then provides a step of periodic acquisition, by the electrode 100, of a number n of voltage values $V_{k,i}$ at instants t_k, with $k = 1,2,\dots,s$, obtaining a voltage matrix $\boldsymbol{V} = [V_{k,i}]$, with $i = 1,2,\dots,n$, where $V_{k,i}$ is the voltage value determined by the channel c_i at the contact point p_i at the instant t_k [304].

[00067] The method also comprises a step of periodic acquisition, by at least one medical device, of a number r of values of physiological signals $P_{k,h}$ of the user at

instants t_k, with $k = 1,2,\ldots,s$, obtaining a matrix of the physiological signals $\boldsymbol{P} = [P_{k,h}]$, with $h = 1,2,\ldots,r$, where $P_{k,h}$ is value of the h-th physiological signal determined at the instant t_k [305].

[00068] In particular, the medical device, not shown in the figures for simplicity's sake, can be for example a device for acquiring electrophysiological signals that measure the response of the autonomic nervous system or vital signs of the autonomic nervous system associated with the cardiovascular and respiratory systems.

[00069] Once the matrices $\boldsymbol{V} = [V_{k,i}]$ and $\boldsymbol{P} = [P_{k,h}]$ have been obtained, the method provides a step of computing a discrimination matrix $\boldsymbol{D} = [d_{h,i}]$, where $d_{h,i}$ is the discrimination coefficient which represents the correlation between the h-th physiological signal $P_{k,h}$ and the i-th voltage value $V_{k,i}$ referred to the same instant t_k [306]. The discrimination matrix $\boldsymbol{D}$ thus allows to evaluate the degree of correlation between each channel c_i of the electrode 100 and each h-th physiological signal.

[00070] In particular, if there is a linear correlation between each value $P_{k,h}$ and a corresponding value $V_{k,i}$ referred to the same instant t_k, the discrimination matrix $\boldsymbol{D}$ is obtained solving the system:

$$\begin{cases} \boldsymbol{X}_{ENG} = \boldsymbol{X}_{PHYSIO}\,\boldsymbol{D} + \boldsymbol{\varepsilon} \\ \boldsymbol{D} = \left(\boldsymbol{X}_{PHYSIO}{}^{T}\boldsymbol{C}_{\boldsymbol{\varepsilon}}^{-1}\boldsymbol{X}_{PHYSIO}\right)^{-1}\boldsymbol{X}_{PHYSIO}{}^{T}\boldsymbol{C}_{\boldsymbol{\varepsilon}}^{-1}\boldsymbol{X}_{ENG} \\ \boldsymbol{C}_{\boldsymbol{\varepsilon}} = E\{(\boldsymbol{\varepsilon} - \boldsymbol{\eta}_{\boldsymbol{\varepsilon}})(\boldsymbol{\varepsilon} - \boldsymbol{\eta}_{\boldsymbol{\varepsilon}})^{T}\} \end{cases}$$

where $\boldsymbol{C_\varepsilon}$ is the error covariance matrix,

E is the expected value operator,

$\boldsymbol{\varepsilon}$ is the error matrix in which the residuals of the predictive model are present.

[00071] The method then provides a step of computing a spatial filtering matrix $\boldsymbol{\phi}^{DBF} = [\varphi_{h,j}]$, $\varphi_{h,j}$ being the localization index which represents the correlation between the h-th physiological signal and the area a_j of the cross section S [307]. The spatial filtering matrix $\boldsymbol{\phi}^{DBF}$ therefore makes it possible to evaluate which area a_j of the cross section S assigned to the modulation of the h-th parameter physiological.

[00072] The method then provides, for each h-th physiological signal, a step of generating a functional topography of the peripheral nerve 10 wherein each area a_j is graphically identified as a function of the corresponding value $\varphi_{h,j}$ associated with it by the spatial filtering matrix $\boldsymbol{\phi}^{DBF}$ [308].

[00073] With reference even at Fig. 3, the graphic visualization 400 of the functional topography can be obtained by associating a plurality of numerical ranges of the values $\varphi_{h,j}$ to respective colours or colour shades. Furthermore, the graphic visualization 400 can be made more intuitive by adopting the technique of field lines (or isolines) in order to outline in the cross section S of the

peripheral nerve 10 a perimeter $\prod$ containing the areas a_j correlated to a given physiological parameter.

[00074] With reference to Figs. 4A and 4B, it is then possible to use the information contained in the functional topography obtained to accurately stimulate the portion of the peripheral nerve correlated to the physiological signal, and therefore assigned to the modulation of the physiological parameter, on which one wishes to intervene.

[00075] Consulting the functional topography graphed in Fig. 3, for example, it is possible to determine a portion 410 which shows a strong correlation with the target physiological parameter on which it is desired to intervene. Therefore, in this case, the method according to the present invention provides for a selective stimulation on this area by the channels of the electrode 100, for example through an electrical stimulation by the channels most adjacent to this portion 410.

[00076] the foregoing description embodiments of the invention will so fully reveal the invention according to the conceptual point of view, so that others, by applying current knowledge, will be able to modify and/or adapt for various applications such embodiment without further research and without parting from the invention, and, accordingly, it is therefore to be understood that such adaptations and modifications will have to be considered as

equivalent to the specific embodiments. The means and the materials to realise the different functions described herein could have a different nature without, for this reason, departing from the field of the invention. It is to be understood that the phraseology or terminology that is employed herein is for the purpose of description and not of limitation.

CLAIMS

1. A method for determining the functional topography of a peripheral nerve (10) of a user, said method requiring an electrode (100) comprising a number n of channels c_i, with $i = 1,2,\dots,n$, wherein each channel c_i is in contact with said peripheral nerve (10) at a respective contact point p_i, with $i = 1,2,\dots,n$,

said method comprising the steps of:

- generating a model of a cross section S of said peripheral nerve (10) where the area A of said cross section S comprises a number m of areas a_j, with $j = 1,2,\dots,m$;
- computing a lead field matrix $\boldsymbol{L} = [R_{j,i}]$, wherein $R_{j,i}$ is a value that describes the electrostatic relationship between an area a_j and a contact point p_i of said cross section S;
- periodic acquisition, by said electrode (100), of a number n of voltage values $V_{k,i}$ at instants t_k, with $k = 1,2,\dots,s$, obtaining a voltage matrix $\boldsymbol{V} = [V_{k,i}]$, with $i = 1,2,\dots,n$, where $V_{k,i}$ is the voltage value determined by the channel c_i at the contact point p_i at the instant t_k;
- periodic acquisition, by at least one medical device, of a number r of values of physiological signals $P_{k,h}$ of said user at instants t_k, with $k =$

$1,2,\ldots,s$, obtaining a matrix of the physiological signals $\boldsymbol{P}=[P_{k,h}]$, with $h=1,2,\ldots,r$, where $P_{k,h}$ is value of the h-th physiological signal determined at the instant t_k;

- computing a discrimination matrix $\boldsymbol{D}=[d_{h,i}]$, $\boldsymbol{D}$ being function of said matrices $\boldsymbol{V}=[V_{k,i}]$ and $\boldsymbol{P}=[P_{k,h}]$, where $d_{h,i}$ is the discrimination coefficient which represents the correlation between the h-th physiological signal $P_{k,h}$ and the i-th voltage value $V_{k,i}$ referred to a same instant t_k;
- computing a spatial filtering matrix $\boldsymbol{\phi}^{DBF}=[\varphi_{h,j}]$, $\varphi_{h,j}$ being the localization index which represents the correlation between the h-th physiological signal and the area a_j of said cross section S;
- for each h-th physiological signal, generating a functional topography of said peripheral nerve (10) wherein each area a_j is graphically identified as a function of the corresponding value $\varphi_{h,j}$ associated with it by said spatial filtering matrix $\boldsymbol{\phi}^{DBF}$.

2. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 1, wherein they are also provided the steps of:

- filtering said voltage matrix $\boldsymbol{V}=[V_{k,i}]$ obtaining a filtered voltage matrix $\check{\boldsymbol{V}}=[\check{V}_{k,i}]=filt(\boldsymbol{V})$;
- extracting features from said filtered voltage

matrix $\check{\boldsymbol{V}} = [\check{V}_{k,i}]$ obtaining a neural data matrix $\boldsymbol{X}_{ENG}$; and wherein said discrimination matrix $\boldsymbol{D} = [d_{h,i}]$ is function of said neural data matrix $\boldsymbol{X}_{ENG}$.

3. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 2, where said step of filtering said voltage matrix $\boldsymbol{V} = [V_{k,i}]$ comprises the steps of:

- for each channel c_i, defining a set G_i comprising all the voltage values $V_{k,i}$ taken at said channel c_i;
- applying a filter on said set G_i, obtaining a filtered set $\check{G}_i$ comprising filtered voltage values $\check{V}_{k,i}$;
- obtaining a filtered voltage matrix $\check{\boldsymbol{V}} = [\check{V}_{k,i}] = filt(\boldsymbol{V})$.

4. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 2, wherein said step of extracting features from said filtered voltage matrix $\check{\boldsymbol{V}} = [\check{V}_{k,i}]$ comprises the steps of:

- defining a time window $\Delta t_{\tilde{k}} = b * \Delta t_k$, with $\Delta t_{\tilde{k}} = (t_{\tilde{k}+1} - t_{\tilde{k}})$ and $\Delta t_k = (t_{k+1} - t_k)$, where $b \geq 1$ is a predetermined coefficient;
- for each filtered set $\check{G}_i$, selection of filtered voltage values $\check{V}_{k,i}$ acquired in said time window $\Delta t_{\tilde{k}}$, obtaining a number s/b of subsets $\tilde{G}_{\tilde{k},i}$, with $\tilde{k} = 1,2,\dots,s/b$, each subset $\tilde{G}_{\tilde{k},i}$ comprising a number b of filtered voltage values $\check{V}_{k,i}$;

- for each subset $\tilde{G}_{\tilde{k},i}$, extraction of a number f of neural data arranged to define mathematical features of said subset $\tilde{G}_{\tilde{k},i}$, obtaining a number $n*f$ of neural data for each filtered set $\check{G}_i$;
- obtaining a neural data matrix $\boldsymbol{X}_{ENG} = [\tilde{V}_{\tilde{k},\tilde{\imath}}]$, where $\tilde{V}_{\tilde{k},\tilde{\imath}}$ is the $\tilde{\imath}$-th neural datum extracted in the window $\Delta t_{\tilde{k}}$, $\tilde{\imath} = 1,2,\dots,n*f$.

5. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 1, wherein they are also provided the steps of:

- filtering said matrix of the physiological signals $\boldsymbol{P} = [P_{k,h}]$ obtaining a filtered matrix of the physiological signals $\check{\boldsymbol{P}} = [\check{P}_{k,h}] = filt(\boldsymbol{P})$.
- extracting features from said filtered matrix of the physiological signals $\check{\boldsymbol{P}} = [\check{P}_{k,h}]$ obtaining a functional data matrix $\boldsymbol{X}_{PHYSIO}$;

and wherein said discrimination matrix $\boldsymbol{D} = [d_{h,i}]$ is function of said functional data matrix $\boldsymbol{X}_{PHYSIO}$.

6. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 5, wherein said step of filtering said matrix of the physiological signals $\boldsymbol{P} = [P_{k,h}]$ comprises the steps of:

- for each h-th physiological signal, defining a set G_h comprising all the values of said h-th physiological signal $P_{k,h}$ acquired;

- applying a filter on said set G_h, obtaining a filtered set $\check{G}_h$ comprising values of the filtered physiological signals $\check{P}_{k,h}$;
- obtaining a filtered matrix of the physiological signals $\check{\boldsymbol{P}} = [\check{P}_{k,h}] = filt(\boldsymbol{P})$.

7. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 5, wherein said step of extracting features from said filtered matrix of the physiological signals $\check{\boldsymbol{P}} = [\check{P}_{k,h}]$ comprises the steps of:

- defining a time window $\Delta t_{\tilde{k}} = b * \Delta t_k$, with $\Delta t_{\tilde{k}} = (t_{\tilde{k}+1} - t_{\tilde{k}})$ and $\Delta t_k = (t_{k+1} - t_k)$, where $b \geq 1$ is a predetermined coefficient;
- for each filtered set $\check{G}_h$, selection of values of filtered physiological signals $\check{P}_{k,h}$ acquired in said time window $\Delta t_{\tilde{k}}$, obtaining a number s/b of subsets $\tilde{G}_{\tilde{k},h}$, with $\tilde{k} = 1,2,\dots,s/b$, each subset $\tilde{G}_{\tilde{k},h}$ comprising a number b of filtered physiological signals $\check{P}_{k,h}$;
- for each subset $\tilde{G}_{\tilde{k},h}$, extraction of a number w of functional data arranged to define mathematical features of said subset $\tilde{G}_{\tilde{k},h}$, obtaining a number $n * w$ of functional data for each filtered set $\check{G}_h$;
- obtaining a functional data matrix $\boldsymbol{X}_{PHYSIO} = [\tilde{P}_{\tilde{k},\tilde{h}}]$, where $\tilde{P}_{\tilde{k},\tilde{h}}$ is the $\tilde{h}$-th functional datum extracted in the window $\Delta t_{\tilde{k}}$, $\tilde{h} = 1,2,\dots,n * w$.

8. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claims 2 and 5, wherein said step of computing said discrimination matrix $\boldsymbol{D}$ is obtained solving the system:

$$\begin{cases} \boldsymbol{X_{ENG}} = \boldsymbol{X_{PHYSIO}}\,\boldsymbol{D} + \boldsymbol{\varepsilon} \\ \boldsymbol{D} = \left(\boldsymbol{X_{PHYSIO}}^{\boldsymbol{T}}\boldsymbol{C_{\varepsilon}^{-1}}\boldsymbol{X_{PHYSIO}}\right)^{\boldsymbol{-1}}\boldsymbol{X_{PHYSIO}}^{\boldsymbol{T}}\boldsymbol{C_{\varepsilon}^{-1}}\boldsymbol{X_{ENG}} \\ \boldsymbol{C_{\varepsilon}} = E\{(\boldsymbol{\varepsilon} - \boldsymbol{\eta_{\varepsilon}})(\boldsymbol{\varepsilon} - \boldsymbol{\eta_{\varepsilon}})^{T}\} \end{cases}$$

where $\boldsymbol{C_{\varepsilon}}$ is the error covariance matrix,

E is the expected value operator,

$\boldsymbol{\varepsilon}$ is the error matrix in which the residuals of the predictive model are present.

9. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claims 2 and 5, wherein said step of computing said discrimination matrix $\boldsymbol{D}$ is obtained by the equation:

$$d_{h,i} = corr\left(X_{PHYSIO_{k,h}}, X_{ENG_{k,i}}\right) = \frac{\sigma_{X_{PHYSIO_{k,h}}, X_{ENG_{k,i}}}}{\sigma_{X_{PHYSIO_{k,h}}}\sigma_{X_{ENG_{k,i}}}}$$

where $\sigma_{X_{PHYSIO_{k,h}}, X_{ENG_{k,i}}}$ is the covariance of the variables $X_{PHYSIO_{k,h}}$ and $X_{ENG_{k,i}}$,

$\sigma_{X_{PHYSIO_{k,h}}}/\sigma_{X_{ENG_{k,i}}}$ is the standard deviation of $X_{PHYSIO_{k,h}}/X_{ENG_{k,i}}$.

10. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 1, wherein said step of computing said spatial filtering matrix $\boldsymbol{\phi}^{DBF}$ is obtained according to the equation:

$$\boldsymbol{\phi}^{DBF} = \boldsymbol{D}\boldsymbol{L}^{+}$$

with $\boldsymbol{L}^{+} = (\boldsymbol{L}^{T}\boldsymbol{L})^{-1}\boldsymbol{L}^{T}$.

11. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 1, wherein said step of computing said spatial filtering matrix $\boldsymbol{\phi}^{DBF}$ is obtained according to the equation:

$$\boldsymbol{\phi}^{DBF} = \boldsymbol{D}\boldsymbol{L}_{\Lambda}^{+}$$

with $\boldsymbol{L}_{\Lambda}^{+} = (\boldsymbol{L}^{T}\boldsymbol{\Lambda}\boldsymbol{L})^{-1}\boldsymbol{L}^{T}\boldsymbol{\Lambda}$,

where $\boldsymbol{\Lambda} = [\Lambda_{j,j}]$ is the spatial information matrix, being $\Lambda_{j,j} = 1$ when it is known that the area a_j corresponds to a nonzero value of $\varphi_{h,j}$.

12. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 1, wherein said step of computing said spatial filtering matrix $\boldsymbol{\phi}^{DBF}$ is obtained according to the equation:

$$\boldsymbol{\phi}^{DBF} = \boldsymbol{D}\hat{\boldsymbol{L}}_{\Lambda}^{+}$$

with $\boldsymbol{L}_{\Lambda}^{+} = (\boldsymbol{L}^{T}\boldsymbol{\Lambda}\boldsymbol{L})^{-1}\boldsymbol{L}^{T}\boldsymbol{\Lambda}$ and $\hat{\boldsymbol{L}}_{\Lambda}^{+}[:,j] \leftarrow \frac{\boldsymbol{L}_{\Lambda}^{+}[:,j]}{\|\boldsymbol{\Lambda}\boldsymbol{L}\boldsymbol{L}_{\Lambda}^{+}[:,j]\|_2}$,

where $\boldsymbol{\Lambda} = [\Lambda_{j,j}]$ is the spatial information matrix, being $\Lambda_{j,j} = 1$ when it is known that the area a_j corresponds to a nonzero value of $\varphi_{h,j}$.

13. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 1, wherein said step of generating a functional

topography of said peripheral nerve (10) is obtained by associating a plurality of numerical ranges of said values $\varphi_{h,j}$ to respective colours or colour shades.

14. The method for determining the functional topography of a peripheral nerve (10) of a user, according to claim 1, wherein a step is also provided of electrically stimulating, by means of said electrode (100), at least one area a_j of said cross section S, in order to vary the physiological signal $P_{k,h}$ of said user associated with said area a_j.

Fig. 1

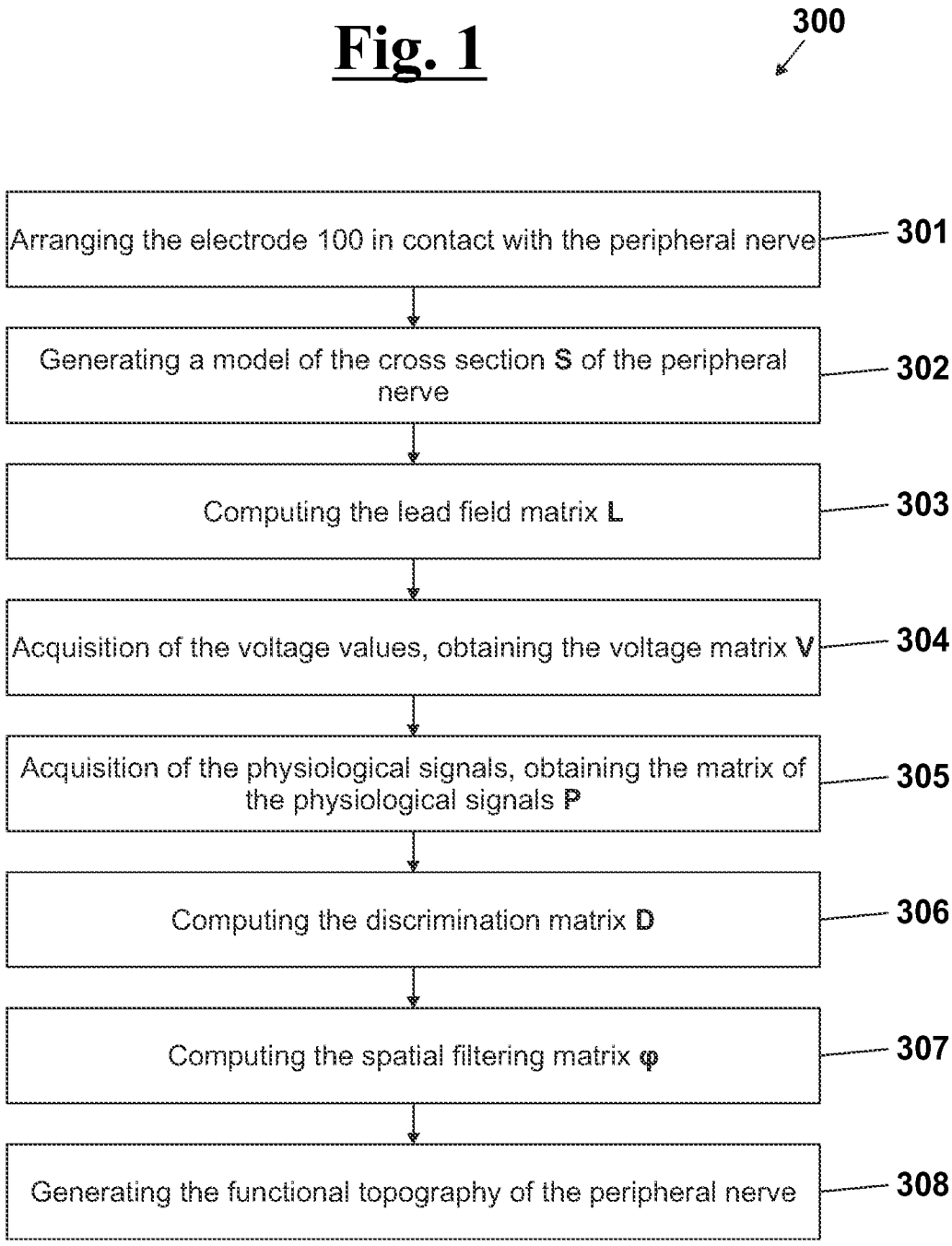

300
Arranging the electrode 100 in contact with the peripheral nerve
301
Generating a model of the cross section S of the peripheral nerve
302
Computing the lead field matrix L
303
Acquisition of the voltage values, obtaining the voltage matrix V
304
Acquisition of the physiological signals, obtaining the matrix of the physiological signals P
305
Computing the discrimination matrix D
306
Computing the spatial filtering matrix φ
307
Generating the functional topography of the peripheral nerve
308

Fig. 2

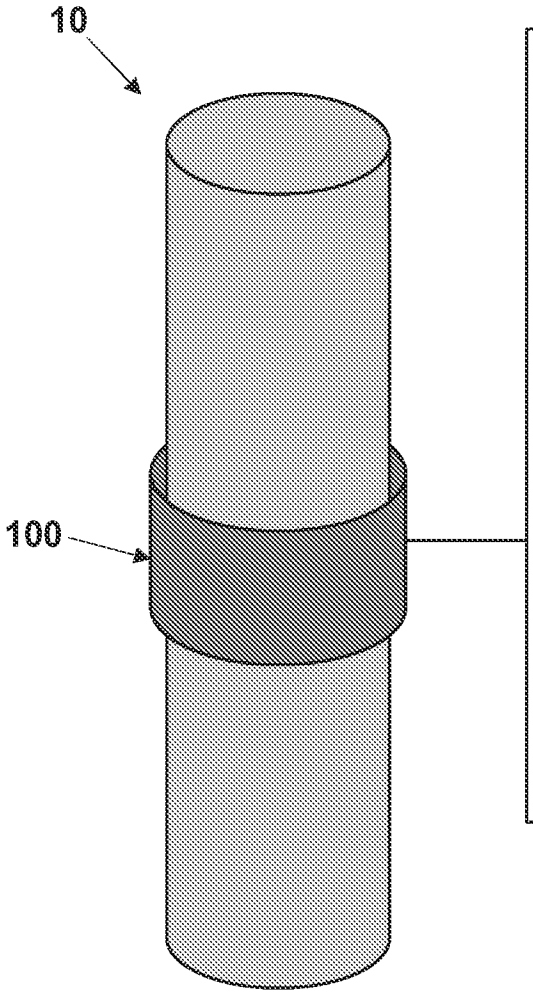


Fig. 2A

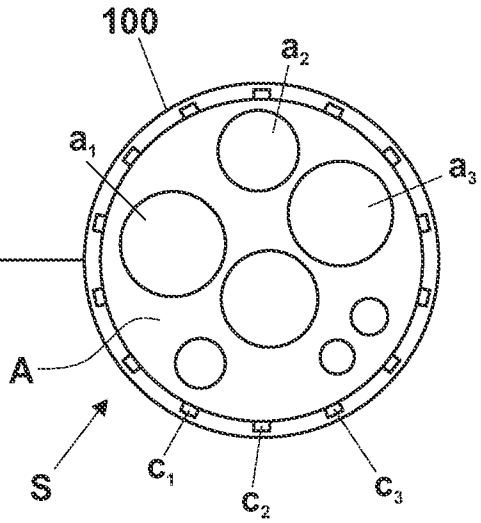


Fig. 2B

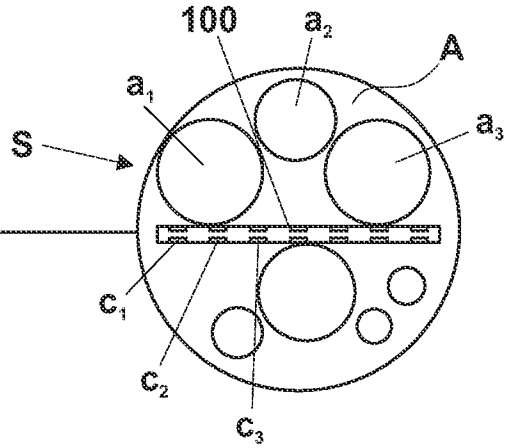
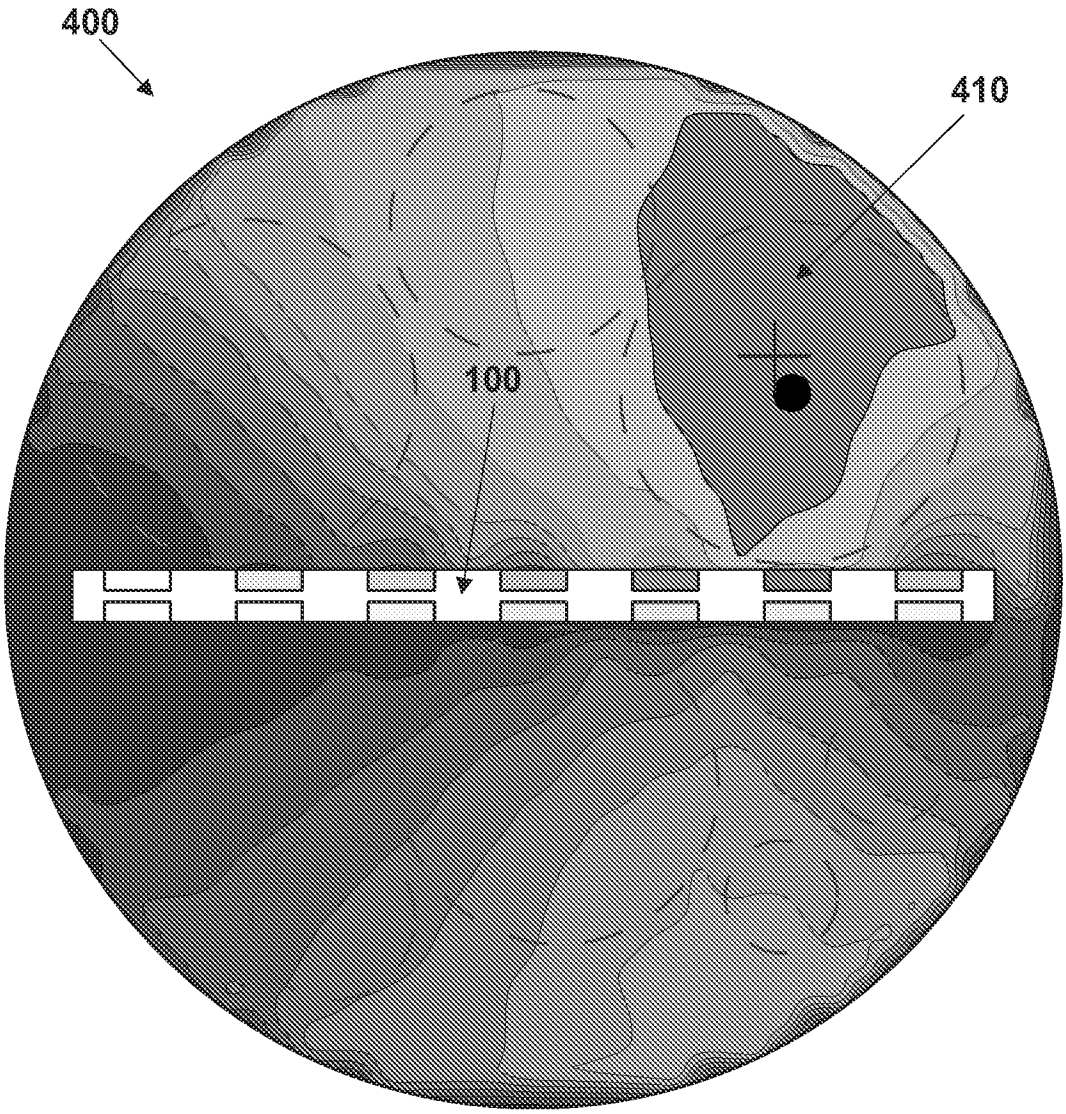


Fig. 3



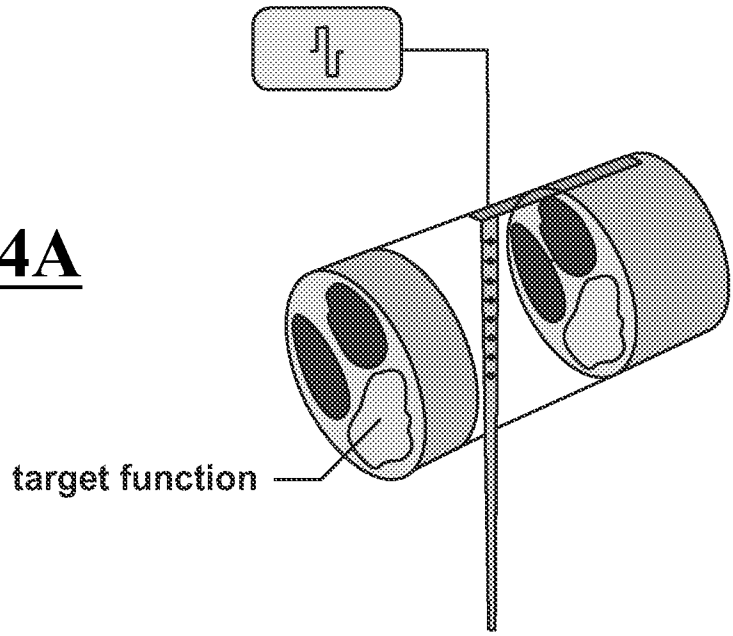


Fig. 4A

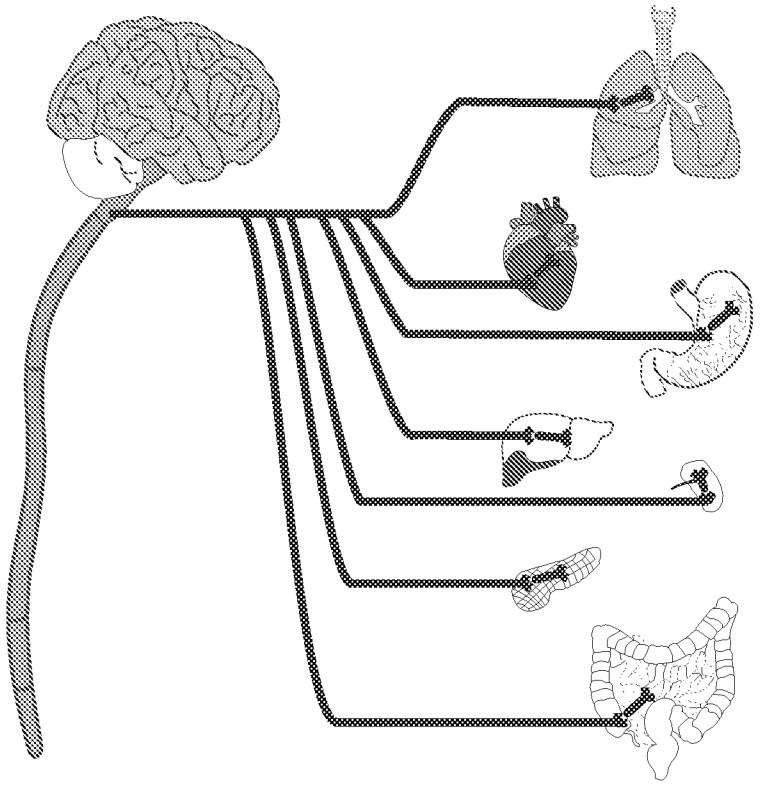


Fig. 4B

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2023/054322

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/294 A61B5/311 A61B5/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KIRILL ARISTOVICH ET AL: "Imaging fast neural traffic at fascicular level with electrical impedance tomography: proof of principle in rat sciatic nerve", JOURNAL OF NEURAL ENGINEERING, INSTITUTE OF PHYSICS PUBLISHING, BRISTOL, GB, vol. 15, no. 5, 23 August 2018 (2018-08-23), page 56025, XP020330973, ISSN: 1741-2552, DOI: 10.1088/1741-2552/AAD78E [retrieved on 2018-08-23] the whole document -----	1-14

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
28 June 2023	19/07/2023

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