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**(54) DISEASE JUDGING SUPPORTING SYSTEM**

SYSTEM ZUR UNTERSTÜTZUNG DER KRANKHEITSBEURTEILUNG

SYSTÈME D'AIDE À L'ÉVALUATION D'UNE PATHOLOGIE

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(56) References cited:  
**EP-A1- 1 506 739 EP-A1- 1 665 985**  
**WO-A1-2005/025421 JP-A- 2003 275 191**  
**JP-U- 3 094 821 US-A- 5 746 204**

- **SUTO ET AL: "Multichannel near-infrared spectroscopy in depression and schizophrenia: cognitive brain activation study" BIOLOGICAL PSYCHIATRY, vol. 55, no. 5, 1 March 2004 (2004-03-01), pages 501-511, XP002605448**
- **MATSUO ET AL.: "Alteration of Hemoglobin Oxygenation in the Frontal Region in Elderly Depressed Patients as Measured by Near-infrared Spectroscopy" J NEUROPSYCHIATRY CLIN NEUROSCI, vol. 12, 1 November 2000 (2000-11-01), pages 465-471, XP002605449**

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**Description**

## Field of the Invention

5 **[0001]** The present invention relates to a system for supporting assessment (diagnosis) of various diseases using results of measurement from a biological photometric device, and particularly to an effective system for the diagnosis of psychiatric disorders such as schizophrenia, bipolar disorder and depression.

## Prior Art

10 **[0002]** The biological photometric device is an apparatus to irradiate near infrared light on the living body and measure the light which passes through the living body or reflects inside the living body. In view of its capability of measuring changes in blood circulation, hemodynamics and the hemoglobin amount easily, simply and with less constraint and damage to the subject, the clinical application of the biological photometric device is strongly expected.

15 **[0003]** It has been reported that the biological photometric device has been applied to the applications such as diagnosis of epilepsy, cerebral ischemia and others and research on linguistic function. Non-patent documents 1 and 2 below report that the optical bio-measurement shows abnormality in the changing pattern of the hemoglobin amount in the frontal lobe of the patients suffering from psychiatric disorders such as depression and schizophrenia. Specifically, it has been reported that the comparison of the integration values of hemoglobin time-domain waveforms when the task was given between healthy persons, depression patients and schizophrenia patients, revealed different characteristics as large, medium and small. It has been also reported that the level of hemoglobin re-increased after the completion of task in schizophrenia patients.

20 **[0004]** On the other hand, the applicant of the present patent proposes a biological photometric device which is equipped with the functions to extract features from the changing patterns of the hemoglobin amount, and numerize and display them by disease (Patent Document 1). The applicant further proposes an apparatus which supports the diagnosis of the subject by calculating the similarity between the feature value data of the patient group whose diagnosis has been finalized and the feature value data of the subject (Patent Document 2). This apparatus provides and displays the probability that the subject is of any particular disease by using the length of Mahalanobis distance from particular disease as a measure indicating the similarity.

30 [Non-Patent Document 1] "Dynamics of local cerebral blood flow in the frontal lobe in psychoneurotic disorders - Study using optical topography" Masato Fukuda, The report of the study supported by the grant from Japan Society for the Promotion of Science in 2001 -2002.

35 [Non Patent Document 2] "Hikari de miru kokoro", Masato Fukuda, "Kokoro to Shakai" vol. 31, Issue 1 Supplementary Volume, Japanese Association of Mental Health.

[Patent Document 1] Japan Published unexamined patents application No.2003-275191 corresponding to EP 1506 739 A1 from which the precharacterising first part of claim 1 starts out.

[Patent Document 2] WO No. 2005/025421

40 Disclosure of the invention

## Problem to be Solved by the Invention

45 **[0005]** However, since the technology described in Patent Document 2 calculates the center of gravity using the feature value for the disease group to be used as a basis of the assessment and its distance from the feature value of the subject, it was difficult to identify the trend of the feature value which demarcates each disease group (including healthy group). It was also difficult to identify where the subject is located in the whole picture of all diseases.

50 **[0006]** Accordingly, the object of the present invention is to provide a disease diagnosis support system which can easily identify the correlation between each disease group and the feature value and the location of the subject in all diseases, and can support to achieve more accurate diagnosis. Means for Solving the Problems

**[0007]** In order to solve the aforementioned problems, the disease diagnosis support system is defined by the claims.

55 **[0008]** The disease diagnosis support system of the present invention is further equipped with a data storage part for storing the feature values of optical bio-measurement data of a large number of subjects including the multiple number of disease groups as dictionary data, wherein a display part displays the analysis results obtained at an analysis part in relation to the dictionary data. The display part produces a scatter diagram for two feature values among plural kinds of feature values, on which one of these values of the dictionary data are plotted along the axis of abscissa and the other values along the axis of ordinate, and displays the two feature values extracted for the subject to be assessed as

superimposed on the scatter diagram.

**[0009]** The disease diagnosis support system of the present invention is equipped with a classification part, which classifies the dictionary data stored in the storage part into several different patterns by using the plural kinds of feature values, and the display part displays the types classified by the classification part as superimposed on the scatter diagram.

**[0010]** In the disease diagnosis support system of the invention, the classification part classifies, for example, the dictionary data by combining threshold values of plural kinds of feature values, wherein the classification is performed by using the combination of threshold values which minimizes the entropy of the distribution of disease groups in the classified types.

**[0011]** In the disease diagnosis support system of an embodiment of the present invention, the display part displays, for example the number of disease groups contain in each types classified by the classification part, together with the scatter diagram. When the data stored in the storage part are updated, the classification part also updates the classification results and displays them in the display part.

**[0012]** Further, the disease diagnosis support system of an embodiment of the present invention comprises a memory part provided in the analysis part, which stores analytical results of data measured for the same subject at different times and displays temporal changes in the analytical data on the display part.

**[0013]** In the disease diagnosis support system of an embodiment of the present invention, the disease groups include, for example, schizophrenia, bipolar disorder and depression. The plural kinds of feature values include the integration values and gradients of the specified part of the optical bio-measurement waveform.

## Effect of the Invention

**[0014]** According to the present invention, by the superimposition display of the feature values of the subject to be examined on the scatter diagram of pre-registered disease dictionary data, it becomes possible to identify instantly in which disease group the subject is likely to be classified and where the subject is positioned in the whole disease group. Particularly, by displaying the area which demarcates the types resulting from the classification on the scatter diagram, said identification can be performed easily.

**[0015]** Further, by adding temporal processing function, not only the data at one time point, but also temporal changes of the data of the subject can be observed. This allows the confirmation of treatment effect, supports the decision making regarding the clinical policy, and provides a very useful system not only for the assessment but also for the treatment of psychiatric disorders.

## Best Mode for Carrying out the Invention

**[0016]** Embodiments of the present invention will be explained below with the reference of the attached drawings.

**[0017]** Figure 1 is a block diagram showing the outline of the disease diagnosis support system 100 of the present invention. This disease diagnosis support system 100 comprises the analyzing part 10 which performs various signal processing and analysis procedures to the hemoglobin change signals measured in the biological photometric device 40, the data storage part 20 which stores the results of analysis of optical bio-measurement data obtained from a number of subjects as disease dictionary data, and the display part 30 which displays the results of analysis by the analysis part 10.

**[0018]** The biological photometric device 40 is an apparatus for irradiating light on the human head, receiving light which is reflected from or scattered at the vicinity of the surface of the head, and measuring change signals of intra-blood substance (hemoglobin in this case) and a multichannel measurement apparatus for measuring signals from multiple positions. The specific structure of the apparatus comprises, as shown in Figure 2, the light source part 41, the light measurement part 43, the control/computation part 44, the display part 45, the memory part 46 and others.

**[0019]** The light source part 41 generates the light with a predetermined wavelength given different modulation depending on the position of measurement, and irradiates it on the head of the subject 50 through the multiple number (omitted in the Figure) of optical fibers 42. Light reflected and scattered in the vicinity of the head part is transmitted to the optical measurement part 43 through the light receiving optical fiber located in the vicinity of the transmitting optical fiber, where it is converted to the intensity of light at every measurement point. Optical measurement is performed by giving predetermined task such as linguistic stimulation and finger tapping to the subject, and the difference in the conditions under the task and without the task is obtained as hemoglobin change signals. The hemoglobin change signals are usually measured for both oxygenated hemoglobin and deoxygenated hemoglobin, and either or the total of both hemoglobin change signals are used depending on the disease to be assessed.

**[0020]** The hemoglobin change signals are obtained, as shown in Figure 3, for example, as the waveform 300 showing changes (mMmm) in signal intensity at given times in the period before, during and after the provision of the task. Two vertical lines shown in Figure 3 represent the task starting point 301 and the task completion point 302, respectively. The task, with the combination of its loading and suspending as one set, is repeated for several times. Hemoglobin waveforms obtained by several measurements are averaged and subjected to pre-processing such as smoothing and

baseline processing where appropriate. Figure 3 shows a hemoglobin change waveform, and in case the biological photometric device 40 is a multiple channel device, said waveform is obtained for each channel.

**[0021]** The control/computation part 44 controls the actions of the light source part 41 and the light measurement part 43, as well as performs necessary processing for displaying hemoglobin change signals from the light measurement part 43 on the display part 45. The memory part 46 memorizes the measured hemoglobin change signals and necessary data for processing of the control/computation part 44.

**[0022]** The analysis part 10 comprises the feature value extraction part 11, which inputs hemoglobin change signals produced by the biological photometric device 40 and extracts the feature values, the classification part 12, which classifies a large number of feature values into multiple number of types, the memory part 13, which memorize the feature values of the subject extracted by the feature value extraction part 11, and others. The analysis part 10, though it is not shown in the figure, is equipped with the input device which sends commands to each part, and input data and parameters which are necessary for the action of each part. The function of each component of the analysis part 10 will be described later.

**[0023]** The data storage part 20 stores the feature value data 21, which consists of plural kinds of feature values extracted from optical bio-measurement data of the subjects such as psychiatric patients and healthy subjects, as disease dictionary data. The feature values in this disease dictionary data are of the same kinds with those extracted by the feature value extraction part 11, and are those extracted and produced by the feature value extraction part 11 of the present system or a similar feature value extraction part of the biological photometric device 40 if the device 40 is equipped with the similar feature value extraction part. The number of persons (subjects) constituting the disease dictionary data 21 is not particularly limited, but a number sufficient to be capable of statistical processing. The disease dictionary data 21 can be updated by deletion of data or addition of new data.

**[0024]** The display part 30 displays the feature values of the subject extracted by the feature value extraction part 11, the disease dictionary data 21 (feature value data) stored in the data storage part 20 and the results of classification of said data, and is equipped with the display device such as a display and the display control part (not illustrated in the figure) for controlling the display.

**[0025]** The aforementioned analysis part 10, the data storage part 20 and the display part 30 may be connected directly with the biological photometric device 40 via signal line, or they can be installed as an independent system from the biological photometric device 40. In the latter case, the said system is configured to be able to receive data measured by the biological photometric device 40 through the publicly known data transmission means, including radio transmission and internet. In case that the said system is directly connected with the biological photometric device 40, it is possible to equip the control/computation part 44, the memory part 46 and the display part 45 in the biological photometric device 40 in Figure 2 with the function of the analysis part 10, the data storage part 20 and the display part 20 of the disease diagnosis support system, respectively.

**[0026]** The function of each section of the analysis part 10 will be explained below.

**[0027]** The feature value extraction part 11 extracts the features of waveform from the hemoglobin change waveforms shown in Figure 3, and expresses them in numeric values. When the biological photometric device 40 is a multiple-channel apparatus and the waveform is obtained for each channel, it selects a waveform of the channel showing the strongest feature and performs the principal component analysis as necessary to extract features for one or selected number of hemoglobin waveforms. As the methods of pre-processing of the signals and the analysis of primary components, the method described in the WO 2005/025421 may be used.

**[0028]** In case the disease to be measured is any psychiatric disorder such as schizophrenia, bipolar disorder and depression, the gradient  $d$  immediately after the start of task, the integrated value  $I$  of waveforms while the task is given and the re-rise  $R$  after the task is removed are used as feature values as shown in Figure 3. Figure 4 shows the hemoglobin change waveform (changes in the amount of oxygenated hemoglobin) by psychiatric disease. Figures 4 (a)-(d) represent typical hemoglobin change waveforms for healthy subjects, schizophrenia, depression and bipolar disorder, respectively. As illustrated, the waveform of the healthy subjects signal values dramatically changes upon start of the task and decreases monotonically after the completion of the task, while schizophrenia is characterized by less change during the task than healthy subjects and rising of signal values after the completion of the task. Depression patients show less change in signal values during and after the task. In bipolar disorder patients, changes in signal values are relatively large immediately after the start of the task, but the appearance of peaks, or rise of peaks immediately after the start of the task tends, to be slow. Accordingly, there is the possibility that these disease groups are assessed by the features such as the gradient  $d$  immediately after the start of the task, the integration value  $I$  of the waveforms during the task and the presence or absence of re-rise  $R$  after the completion of the task.

**[0029]** The feature value extraction part 11 obtains the aforementioned features as numeric values by scanning the hemoglobin change signals along the time axis. Specifically, the gradient of the graph immediately after the start of the task is calculated from the signal value at the point when pre-determined length of time (for example, 5 seconds) elapses from the start of the task. The integrated values are calculated by sampling signal values during the task at an appropriate interval and integrating them. Re-rise is considered as "presence", if the integrated value of the waveform area, which

protrudes above the linear line connecting the signals values at the end of the task and the signal values at the end of measurement, is higher than a threshold, whereas it is considered as "absence" if it is lower than the threshold.

**[0030]** The feature extraction by the feature value extraction part 11 is performed for the hemoglobin signals (including signals after processing, such as pre-processing and principal component analysis) of the patient, or subject, and the hemoglobin signals of the healthy subjects and the patients whose diagnosis has been confirmed by other diagnosis method. The feature values obtained for the former are stored in the memory part 13 (or data storage part 20) for displaying them in the display part 30. The feature values obtained for the latter are registered in the disease dictionary data in the data storage part 20. The feature value data registered in the disease dictionary data are classified in the classification part 12.

**[0031]** The classification (a clustering method) by the classification part 12 may use any publicly known method. The embodiment of the present invention employs, however, an automatic clustering method using entropy minimization. This automatic clustering is performed by finding a combination of threshold values which provides largest possible bias in presence probability of each disease group of each type, namely minimum entropy, when the disease groups with different kinds of features are classified into n types by using the combination j of the threshold values of said features.

**[0032]** In the example case where the disease groups of normal cases (NC), schizophrenia cases (SC), depression patients (DP) and bipolar disorder patients (BP) are classified into five types by using gradient and integration values as feature values and combining thresholds of these values, the probabilities of the presence of each patient group for each type,  $p_{NC(j,n)}$ ,  $p_{SC(j,n)}$ ,  $p_{DP(j,n)}$  and  $p_{BP(j,n)}$  satisfy the following equation.

[Formula 1]

$$p_{NC(j,n)} + p_{SC(j,n)} + p_{DP(j,n)} + p_{BP(j,n)} = 1$$

**[0033]** The sum of entropies  $E(j)$  for the combination j of threshold values is expressed with the following equation,

[Formula 2]

$$E(j) = \sum_n p_n E(j,n)$$

$$E(j,n) = - \sum_{\alpha} p_{\alpha(j,n)} \log_2 p_{\alpha(j,n)}$$

$$\alpha = NC, SC, DP, \text{ or } BP$$

where  $p_n$  is the percentage of data contained in type n for the combination j of threshold values. The combination j of threshold values is selected so as to minimize said  $E(j)$ . The classification part 12, in this way, classifies the feature value data registered in the disease dictionary data into multiple types. When new feature value data are added to the disease dictionary data, the classification part 12 re-classifies said data automatically or by the command from the input device and updates the results of reclassification.

**[0034]** Action of the disease diagnosis support system in the abovementioned configuration will be explained below.

**[0035]** Figure 5 shows the flow of the action.

**[0036]** The feature value data, consisting of feature values (gradient, integrated value and presence/absence of re-rise) extracted from hemoglobin change waveforms of many groups of patients whose diagnosis has been confirmed, are registered in the dictionary in advance (Step 1). By classifying the disease dictionary data of these many patient groups by automatic clustering, threshold values are automatically calculated (Step 502). This work can be performed at any point after the adequate number of data for statistical processing is obtained.

**[0037]** Then, when the results (hemoglobin change waveform) measured for the subject A by the biological photometric device 40 are input in the analysis part 10 (step 503), the feature values, namely gradient, integrated value and the presence/absence of re-rise are calculated from the hemoglobin change waveforms (Step 504). The display part 30 produces a scatter diagram in which the axis of abscissa represents one of the two feature values of the disease dictionary data registered in the dictionary and the axis of ordinate represents the other, and displays individual data positions attached with the label of disease group on the scatter diagram (Step 505). Lines surrounding the combination of threshold values or the area demarcated by the combination of threshold values calculated by the classification 12 are displayed as superimposed on the scatter diagram.

**[0038]** An example of scatter diagram is shown in Figure 6. In the scatter diagram shown in Figure 6, the axes of

abscissa and ordinate show gradients and integrated values, respectively, and the healthy cases, schizophrenia, bipolar disorder and depression are labeled by "+", "□" or "▲", "○" and "\*\*\*", respectively. The combination of threshold values is shown by a dotted line. The example shown here shows the results of clustering disease dictionary data groups including 45 healthy cases, 24 schizophrenia cases, 15 depression cases and 23 bipolar disorder cases, and displays the combination of threshold values classified in the following (1), (2), (4) and (5).

**[0039]**

- (1) The integrated value of 610 or higher or the gradient of 0.006 or higher.
- (2) The integrated value of less than 610, the gradient of less than 0.006, and the integrated value of 93 or higher.
- (3) The integrated value of less than 610, the gradient of less than 0.006 and the integrated value of less than 93.
- (4) The combination of (3) with the gradient of 0.001 or higher.
- (5) The combination of (3) with the gradient of less than 0.001.

**[0040]** These combinations of threshold values were selected such that the presence probability of each disease group contained in each type shows the largest possible bias. The presence probability of healthy case group is high in type (1), while the presence probability of schizophrenia and bipolar disorder patients are high in type (4) and type (5), respectively. However, schizophrenia and bipolar disorder groups are mixed in type (2). There is a difference that the hemoglobin change waveform re-rises after the completion of the task in the schizophrenia group as shown in Figure 4, while it does not re-rise in the bipolar disorder group. Accordingly, in the present embodiment, different colors (□ and ▲) are used to identify whether or not the hemoglobin change waveform re-rises after the completion of the task in the schizophrenia group in order to show the difference from the bipolar disorder group in type (2).

**[0041]** On the other hand, once the feature values similar to the two feature values used for producing the scatter diagram are calculated for the subject A, the position determined based on these feature values is displayed on the scatter diagram with a label of subject A (Step 506). As mentioned above, because the scatter diagram shows the distribution of disease groups and the classification based on the combination of thresholds, by looking the position of the subject A displayed thereon, it is possible to know the type of the subject and identify which disease group the subject is highly likely to belong to. In such case, by adding a clearly identifiable color or mark presenting the third feature to the label of subject A, it is possible to identify whether the schizophrenia group or the bipolar disorder group is more likely even if the two groups are mixed or they are classified as type (2).

**[0042]** The algorithm which is equivalent to such judgment is shown in Figure 7. In the disease diagnosis support system of the present embodiment, the plotting of feature values of the subject on a scatter diagram is equivalent to the implementation of judgment flow from step 701 to step 703, and only when it is classified in the type (2), the integrated value of which is 93 or more and less than 610, the judgment is completed only by confirming the presence or absence of re-rise, the third feature value (step 704). With respect of the step 704, as mentioned above, marking of the presence or absence of re-rise in different color in advance is equivalent to the implementation of judgment flow in step 704. In this case, the presence or absence of re-rise was manually selected by using the value 20, which represents the best classification between the type (2) (schizophrenia) and type (3) (bipolar disorder) in the data group requiring judgment of step 704.

**[0043]** Figure 6 shows only the scatter diagram, but the number of diseases contained in each type can be shown in a bar chart and others, in addition to the scatter diagram. This may help to identify the accuracy of classification. An example of display is shown in Figure 8. The examples shown in Figure 8 displays scatter diagrams similar to Figure 6 (above) and the bar diagrams for the number of patients (bottom). These diagrams show that the presence probabilities of healthy cases, depression patients and schizophrenia patients account for high percentages in type (1), (4) and (5), respectively. Accordingly, the accuracy of judgment is higher if the subject A belongs to either of these types.

**[0044]** According to the present embodiment, it is possible to recognize at a glance which disease group the subject is classified in, and where the subject is positioned in the whole disease group by superimposing the feature values of the subject on the scatter diagram of the disease registration data registered in advance. This recognition becomes even easier particularly by displaying the surrounding lines (area) demarcating the classified type on the scatter diagram.

**[0045]** The second embodiment will be explained below.

**[0046]** Basic functions of the biological photometric device 40, the analysis part 10, the data storage part 20 and the display part 30 in this second embodiment are same with those in the aforementioned embodiment, but the second embodiment is characterized by the addition of temporal data processing functions which show changes in data measured at different points of time for the same subject.

**[0047]** More specifically, the second embodiment is identical with the first embodiment in that a scatter diagram is produced by using the disease dictionary data stored in the data storage part 20, the disease groups are classified into given types and displayed with the scatter diagram in the display part 30 and the feature values calculated for the subject are displayed superimposed on the scatter diagram. However, once the feature value of hemoglobin change waveform of the subject A measured by the biological photometric device 40 is obtained, the temporal data processing part reads

out the feature values of the same subject which have been already extracted, and displays these past feature values with newly obtained feature values. In this case, the data is shown in the way with which temporal change of the data can be known, by using, for example, an arrow indicating the direction from the past to new data. The actions of the temporal data processing part can be performed automatically at the same time with the processing of new data, but it is also possible to send a command to display past data via an input device and to set the number of past data to be displayed.

**[0048]** Figure 9 shows an example of display. In the shown example past two data and newly measured data are displayed in sequence indicated by the arrow. Display of temporal changes may help understanding improvements or aggravation of the conditions of patients, and make them be used in confirming therapy effects and producing a treatment policy including medication.

**[0049]** This embodiment enables the observation of not only the data at one point of the subject but also temporal changes, and provides an extremely useful system applicable not only to the assessment of psychiatric disorders but also to the treatment.

**[0050]** The third embodiment not forming part of the invention will be explained below.

**[0051]** This embodiment differs from the abovementioned embodiment in the point that the third embodiment produces a one-dimensional scatter diagram. In the present embodiment, based on the hemoglobin change waveform measured by the biological photometric device 40, gradient or integrated value is obtained, for example. And as shown in Figure 10, depending on thus obtained value, it is displayed with label on individual data position on the one-dimensional scatter diagram on the display.

**[0052]** For the gradient values shown in Figure 10 (a), the border between range A and range B is the border between type 1 and type 4 in Figure 9. Therefore, the range A and range B are defined as the range for those with suspected disease and the range of healthy cases, respectively. For example, when the gradient value is within the range B as the feature value 810, the subject is a healthy case, and the feature value 810 is displayed as the range of healthy cases. When the gradient value is within the range A, as in the feature value 800, the subject is suspected to have disease, and the feature value 800 is displayed on the one-dimensional scatter diagram.

**[0053]** Similarly, for the integrated values in Figure 10(b), the border between the range C and the range D is the border between the type 1 and the type 2 or 3. Accordingly, the range C and the range D are defined as the range of those with suspected disease and the range of healthy cases, respectively. When the gradient value is within the C range, as the feature values 801 and 811, the subject is suspected to have disease and each value is displayed on the one-dimensional scatter diagram.

**[0054]** Further, psychiatric disorder may be determined and displayed by using two one-dimensional scatter diagrams. If either gradient value or integrated value exceeds a threshold value, the subject is displayed as a healthy case. For example, in case the feature values 810 and 811 are the values for the same subject, since the feature value 810 is in the range B, the subject is judged as healthy and this judgment result is displayed. Also, in case the feature values 800 and 801 are the values for the same subject, since none of them exceeds the threshold values, the subject is judged as having disease and this judgment result is displayed.

**[0055]** As mentioned above, disease conditions can be judged based on the range in which the feature value is positioned on the one-dimensional scatter diagram.

**[0056]** The embodiments mentioned above are explained with the example of psychiatric disorders, but the disease diagnosis support system may be applied to other diseases than psychiatric disorders as far as any correlation with the optical bio-measurement signals is observed.

#### Brief Description of the Drawings

**[0057]**

[Figure 1]

A block diagram showing one embodiment of the disease diagnosis support system of the present invention

[Figure 2]

A block diagram showing one embodiment of the biological photometric device in the disease diagnosis support system of the present invention

[Figure 3]

A diagram showing hemoglobin change waveforms measured by the biological photometric device

[Figure 4]

A diagram showing characteristic waveforms by disease

[Figure 5]

A flow diagram showing actions of the biological photometric device of the present invention

[Figure 6]

A diagram showing an example of a scatter diagram displayed by the disease diagnosis support system of the present invention

[Figure 7]

A diagram showing disease assessment algorithm

[Figure 8]

A diagram showing an example of disease group distribution chart displayed together with the scatter diagram shown in Figure 6.

[Figure 9]

A diagram showing another examples of a scatter diagram displayed by the disease diagnosis support system of the present invention

[Figure 10]

A diagram showing an example of display in the third embodiment of the present invention

Description of Notations

[0058]

100, 150 ... Disease assessment support system, 10... Analysis part, 11... Feature value extraction part, 12... Classification part, 13...Memory part, 20... Data storage part, 30...Display part, 40... Optical bioinstrumentation device

Claims

1. A disease diagnostic support system comprising:

an analysis part (10) comprising:

a feature value extraction part (11) for extracting, from hemoglobin signals measured by optical bio-measurement, feature values including a gradient and an integrated value of a specific part of a hemoglobin waveform,

a classification part (12) for classifying the feature values into multiple types, and

a memory part (13) for memorising the feature values of a subject extracted by the feature value extraction part;

a data storage part (20) for storing the feature values of optical bio-measurement from many subjects including the subjects of multiple disease groups as dictionary data; and

a display part (30) for displaying the results of an analysis performed by the analysis part,

**characterised in that**

the classification part (12) is adapted to classify the feature values into said types by use of a combination of threshold values that may minimise the entropy of the disease group distribution in the classified types for the feature values, the threshold values being automatically calculated by classifying the dictionary data of subjects whose diagnosis has been confirmed, by automatic clustering; and

the display part is adapted to produce a scatter diagram for the gradient and the integrated value, and display the gradient and the integrated value extracted for the subject together with the feature values constituting the dictionary data plotted on the scatter diagram together with lines surrounding areas of the scatter diagram which belong to the types of the classification by the classification part.

2. A disease diagnosis support system according to claim 1,

wherein the display part displays the analysis results obtained by the analysis part in association with the dictionary data.

3. The disease diagnosis support system according to Claim 2,

wherein the display part produces a scatter diagram, on which one of two kinds of feature values among the plural feature values in the dictionary data is plotted on the abscissa, and the other on the ordinate, and two kinds of the feature values extracted for the subject to be examined are displayed superimposed on the scatter diagram.

4. The disease diagnosis support system according to Claim 2 or Claim 3, wherein the display part displays the types

classified by the classification part superimposed on the scatter diagram.

- 5
5. The disease diagnosis support system according to Claim 4, wherein the display part displays the number of disease groups contained in each type classified by the classification part together with the scatter diagram.
- 10
6. The disease diagnosis support system according to any of the claims 4 to 5, wherein the display part updates the results of classification, according to the update of data stored in the storage part, and displays the results of classification on the display part.
- 15
7. The disease diagnosis support system according to any of the claims 1 to 6, wherein the analysis part is equipped with a memory part (13) which stores analysis results of the data measured for the same subject at different times and displays the temporal changes in the analysis results in the display part.
8. The disease diagnosis support system according to any of the claims 1 to 7, wherein the disease group contains schizophrenia, bipolar disorders and depression.

## Patentansprüche

- 20
1. Krankheitsdiagnose-Unterstützungssystem umfassend:
- ein Analyseteil (10) aufweisend:
- 25
- ein Merkmalswert-Gewinnungsteil (11), um aus mittels optischer Biomessung gewonnenen Hämoglobinsignalen Merkmalswerte einschließlich eines Gradienten und eines integrierten Werts eines bestimmten Teils einer Hämoglobin-Wellenform zu gewinnen,
- ein Klassifikationsteil (12) zum Klassifizieren der Merkmalswerte in mehrere Typen, und
- 30
- ein Speicherteil (13) zum Speichern der Merkmalswerte einer Person, die von dem Merkmalswert-Gewinnungsteil gewonnen wurden;
- ein Datenspeicherteil (20) zum Speichern der Merkmalswerte von optischen Biomessungen mehrerer Personen einschließlich Personen verschiedener Krankheitsgruppen als lexikalische Daten; und
- 35
- ein Anzeigeteil (30) zum Anzeigen der Ergebnisse einer vom Analyseteil ausgeführten Analyse,
- dadurch gekennzeichnet, dass**
- das Klassifikationsteil (12) eingerichtet ist, die Merkmalswerte unter Verwendung einer Kombination von Schwellenwerten, die die Entropie der Krankheitsgruppenverteilung in den klassifizierten Typen der Merkmalswerte minimieren kann, in die Typen zu klassifizieren, wobei die Schwellenwerte automatisch durch Klassifizieren der lexikalischen Daten von Personen berechnet werden, deren Diagnose bestätigt wurde, indem eine automatische Clustering stattfindet; und
- 40
- das Anzeigeteil eingerichtet ist, für den Gradienten und den integrierten Wert ein Verteilungsdiagramm zu erzeugen und den von der Person gewonnenen Gradienten und integrierten Wert zusammen mit den die lexikalischen Daten bildenden Merkmalswerten auf dem Verteilungsdiagramm zusammen mit Linien einzuzichnen, die Gebiete des Verteilungsdiagramms umgeben, die zu den vom Klassifikationsteil klassifizierten Typen gehören.
- 45
2. Krankheitsdiagnose-Unterstützungssystem nach Anspruch 1, wobei das Anzeigeteil die vom Analyseteil gewonnenen Analyseergebnisse zugeordnet zu den lexikalischen Daten anzeigt.
- 50
3. Krankheitsdiagnose-Unterstützungssystem nach Anspruch 2, wobei das Anzeigeteil ein Verteilungsdiagramm erzeugt, auf dem unter den Merkmalswerten in den lexikalischen Daten eine von zwei Arten von Merkmalswerten auf der Abszisse und die andere auf der Ordinate eingezeichnet sind und beide Arten von Merkmalswerten, die von der zu untersuchenden Person gewonnen sind, auf dem Verteilungsdiagramm überlagert dargestellt werden.
- 55
4. Krankheitsdiagnose-Unterstützungssystem nach Anspruch 2 oder 3, wobei das Anzeigeteil die vom Klassifikationsteil klassifizierten Typen auf dem Verteilungsdiagramm überlagert

anzeigt.

- 5 5. Krankheitsdiagnose-Unterstützungssystem nach Anspruch 4, wobei das Anzeigeteil zusammen mit dem Verteilungsdiagramm die Anzahl an Krankheitsgruppen anzeigt, die in jeder vom Klassifikationsteil klassifizierten Typen enthalten sind.
- 10 6. Krankheitsdiagnose-Unterstützungssystem nach einem der Ansprüche 4 bis 5, wobei das Anzeigeteil die Klassifikationsergebnisse entsprechend einer Aktualisierung von im Speicherteil gespeicherten Daten aktualisiert und die Ergebnisse der Klassifikation auf dem Anzeigeteil anzeigt.
- 15 7. Krankheitsdiagnose-Unterstützungssystem nach einem der Ansprüche 1 bis 6, wobei das Analyseteil mit einem Speicherteil (13) ausgestattet ist, das Analyseergebnisse der von der gleichen Person zu verschiedenen Zeiten gemessenen Daten speichert, und die zeitlichen Änderungen der Analyseergebnisse am Anzeigeteil anzeigt.
- 20 8. Krankheitsdiagnose-Unterstützungssystem nach einem der Ansprüche 1 bis 7, wobei die Krankheitsgruppe Schizophrenie, bipolare Störungen und Depression enthält.

## 20 Revendications

- 25 1. Système d'aide au diagnostic d'une pathologie comportant :

une partie d'analyse (10) comportant :

30 une partie d'extraction de valeur de caractéristiques (11) pour extraire, à partir de signaux d'hémoglobine mesurés par biomesure optique, des valeurs de caractéristiques incluant un gradient et une valeur intégrée d'une partie spécifique d'une forme d'onde d'hémoglobine,  
une partie de classification (12) pour classer les valeurs de caractéristiques en types multiples, et  
une partie de mémoire (13) pour mémoriser les valeurs de caractéristiques d'un sujet extraites par la partie d'extraction de valeurs de caractéristiques,

35 une partie de stockage de données (20) pour stocker les valeurs de caractéristiques d'une biomesure optique provenant de nombreux sujets incluant les sujets de multiples groupes de pathologies en tant que données de dictionnaire, et

une partie d'affichage (30) pour afficher les résultats d'une analyse réalisée par la partie d'analyse,

### caractérisé en ce que

40 la partie de classification (12) est adaptée pour classer les valeurs de caractéristiques en lesdits types en utilisant une combinaison de valeurs de seuil qui peuvent minimiser l'entropie de la distribution des groupes de pathologies dans les types classés pour les valeurs de caractéristiques, les valeurs de seuil étant automatiquement calculées en classant les données de dictionnaire de sujets dont le diagnostic a été confirmé, par un regroupement automatique, et

45 la partie d'affichage est adaptée pour produire un diagramme de dispersion pour le gradient et la valeur intégrée, et afficher le gradient et la valeur intégrée extraite pour le sujet conjointement avec les valeurs de caractéristiques constituant les données de dictionnaire tracées sur le diagramme de dispersion conjointement avec des lignes entourant des zones du diagramme de dispersion qui appartiennent aux types de la classification par la partie de classification.

- 50 2. Système d'aide au diagnostic d'une pathologie selon la revendication 1, dans lequel la partie d'affichage affiche les résultats d'analyse obtenus par la partie d'analyse en association avec les données de dictionnaire.
- 55 3. Système d'aide au diagnostic d'une pathologie selon la revendication 2, dans lequel la partie d'affichage produit un diagramme de dispersion, sur lequel l'un des deux types de valeurs de caractéristiques parmi la pluralité de valeurs de caractéristiques dans les données de dictionnaire est tracé en abscisse, et l'autre en ordonnée, et deux types de valeurs de caractéristiques extraites pour le sujet à examiner sont affichés superposés sur le diagramme de dispersion.

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4. Système d'aide au diagnostic d'une pathologie selon la revendication 2 ou la revendication 3, dans lequel la partie d'affichage affiche les types classés par la partie de classification superposés sur le diagramme de dispersion.
5. Système d'aide au diagnostic d'une pathologie selon la revendication 4, dans lequel la partie d'affichage affiche le nombre de groupes de pathologies contenus dans chaque type classé par la partie de classification conjointement avec le diagramme de dispersion.
6. Système d'aide au diagnostic d'une pathologie selon l'une quelconque des revendications 4 à 5, dans lequel la partie d'affichage met à jour les résultats de la classification, en fonction de la mise à jour des données stockées dans la partie de stockage, et affiche les résultats de la classification sur la partie d'affichage.
7. Système d'aide au diagnostic d'une pathologie selon l'une quelconque des revendications 1 à 6, dans lequel la partie d'analyse est équipée d'une partie de mémoire (13) qui stocke des résultats d'analyse des données mesurées pour le même sujet à différents instants et affiche les variations temporelles des résultats d'analyse dans la partie d'affichage.
8. Système d'aide au diagnostic d'une pathologie selon l'une quelconque des revendications 1 à 7, dans lequel le groupe de pathologies inclut une schizophrénie, des troubles bipolaires et une dépression.

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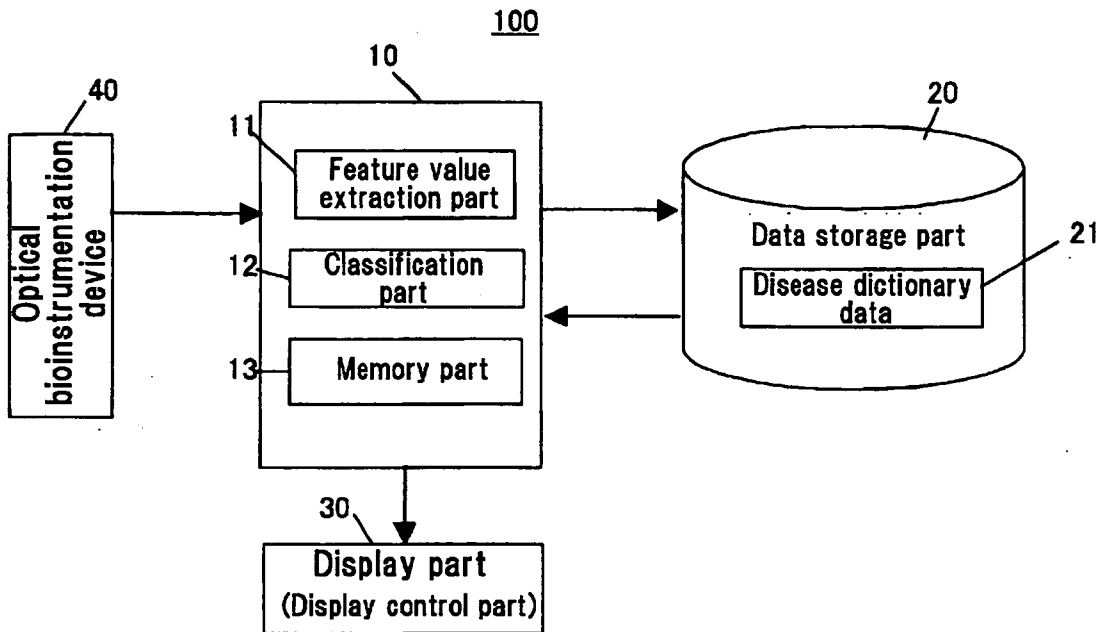
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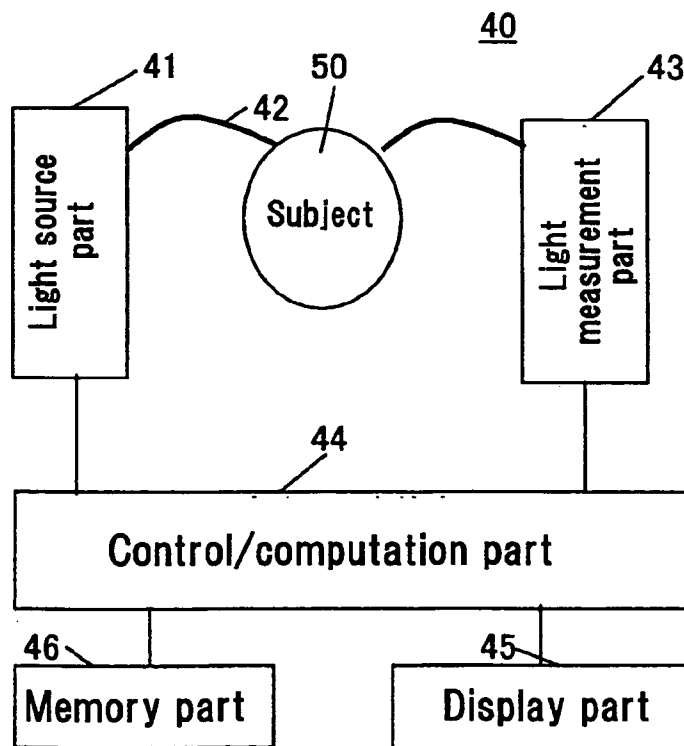
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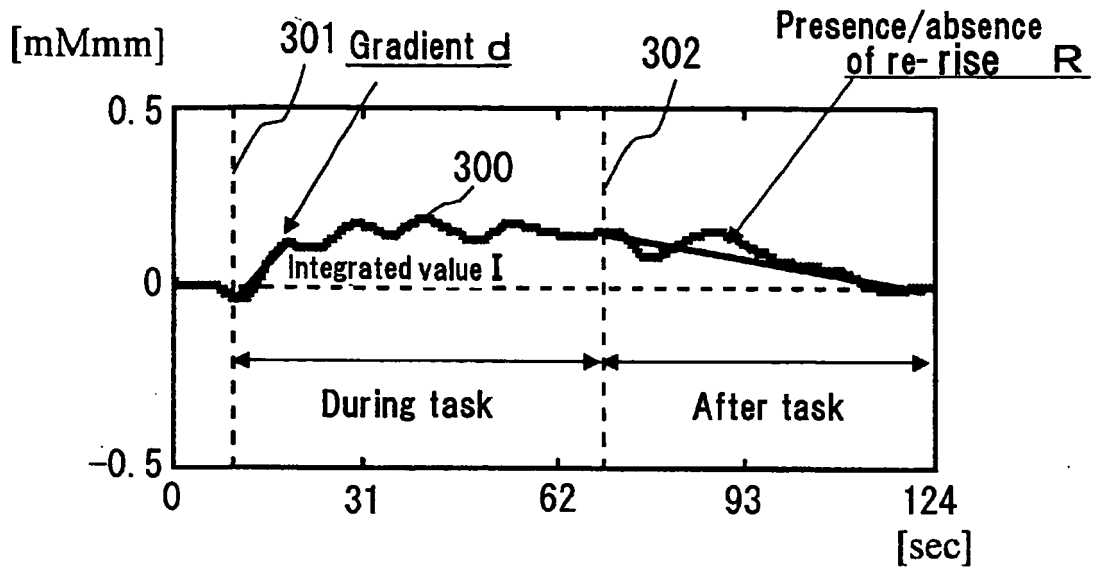
[Figure 1]



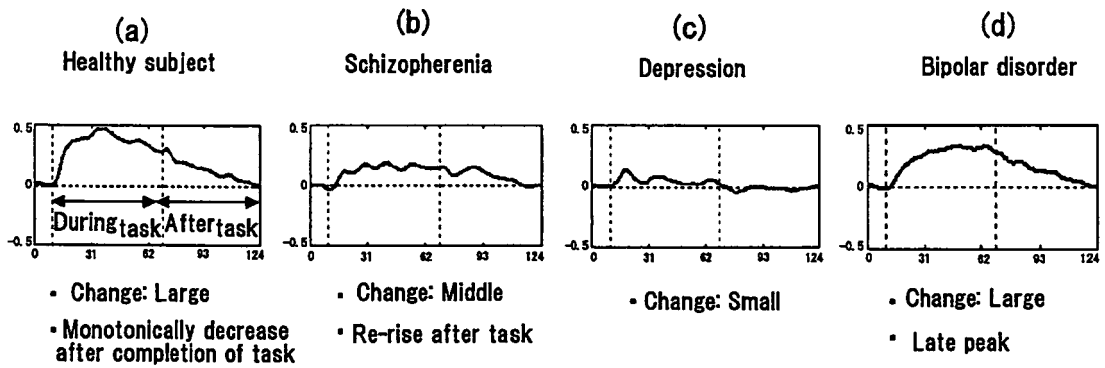
[Figure 2]



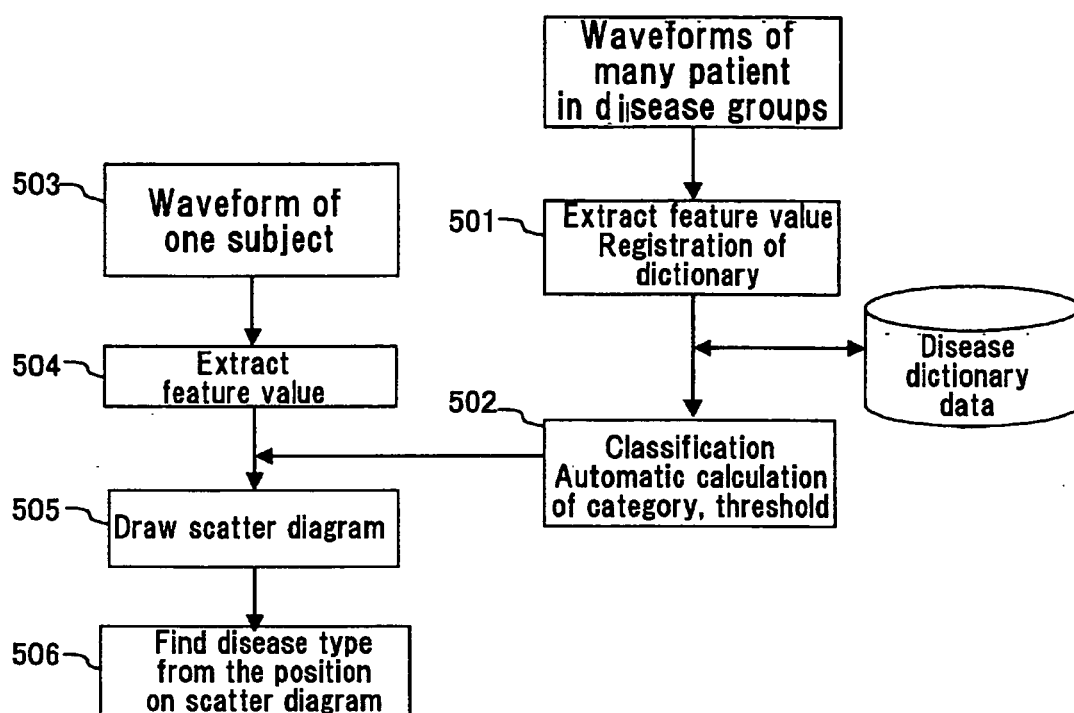
[Figure 3]



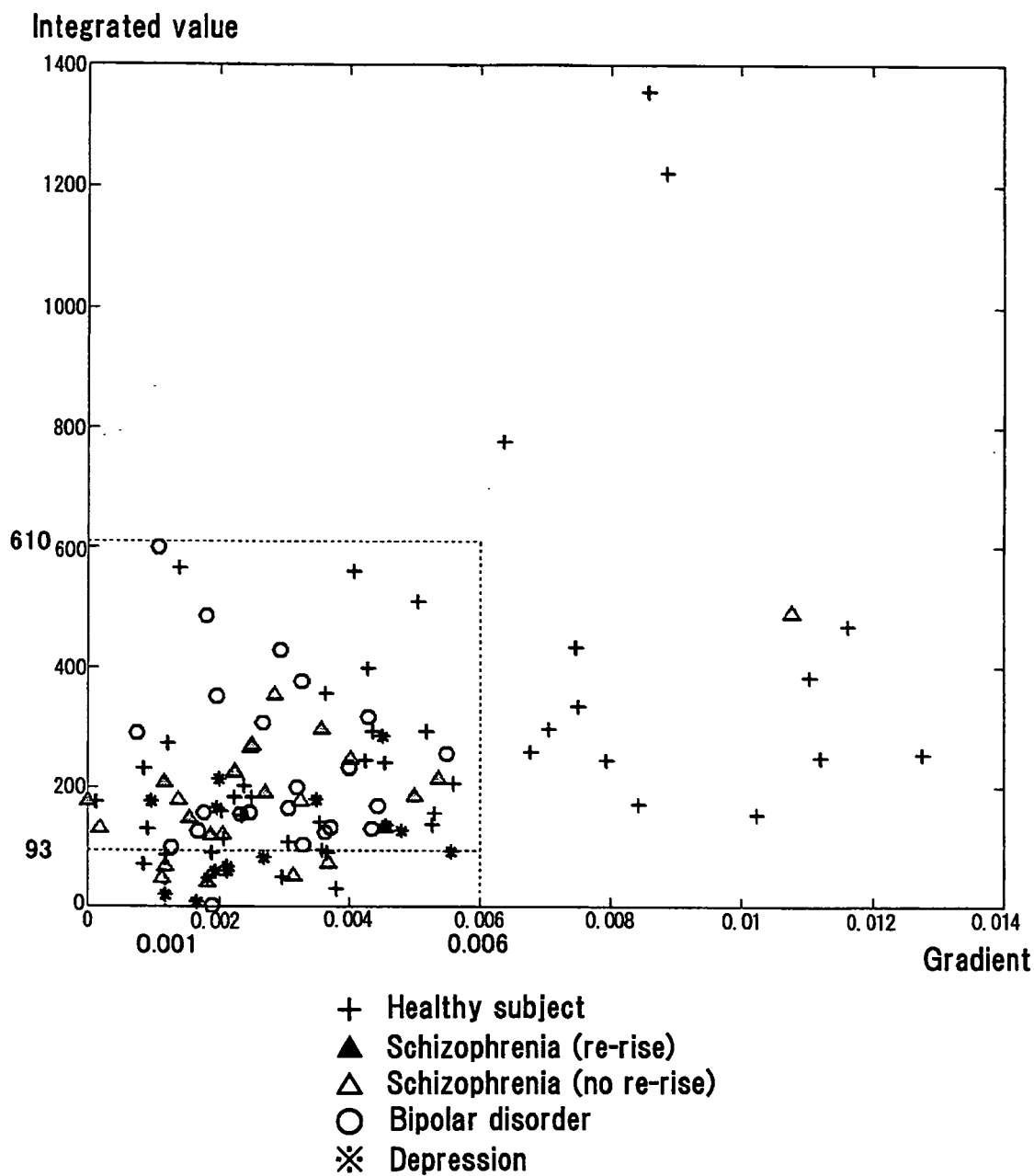
[Figure 4]



[Figure 5]

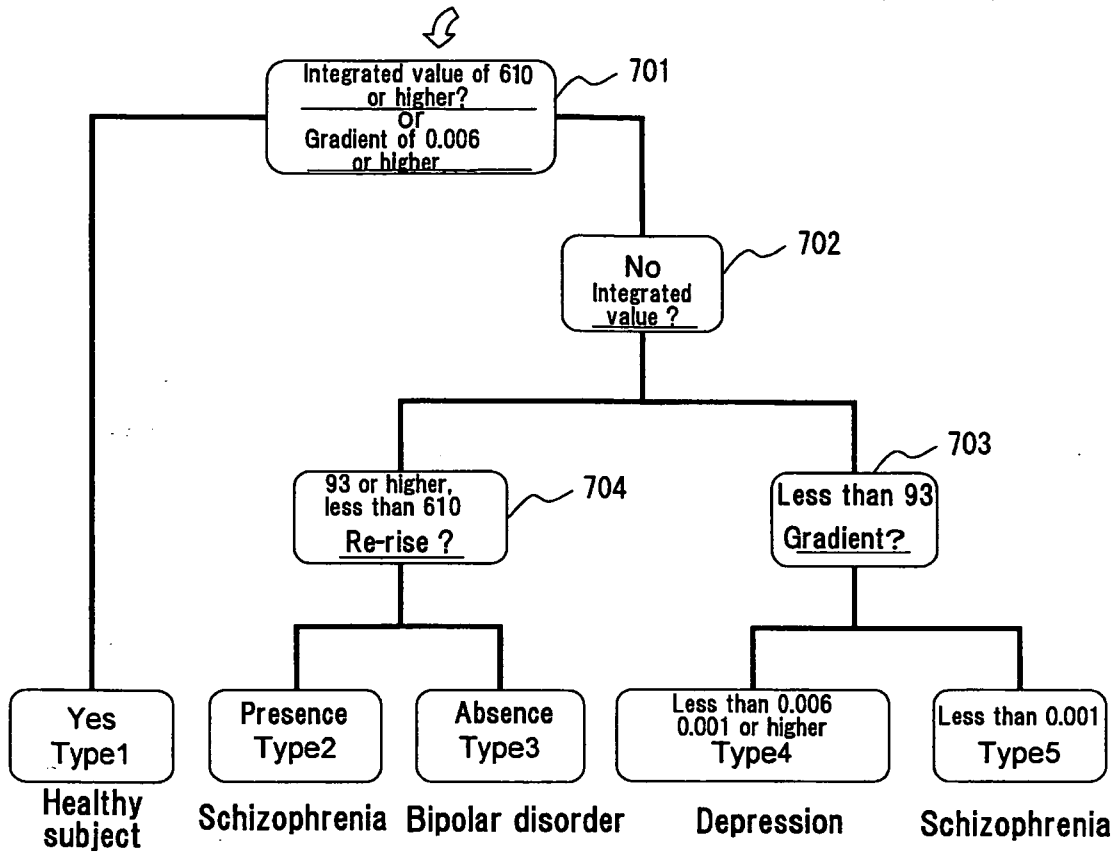


[Figure 6]

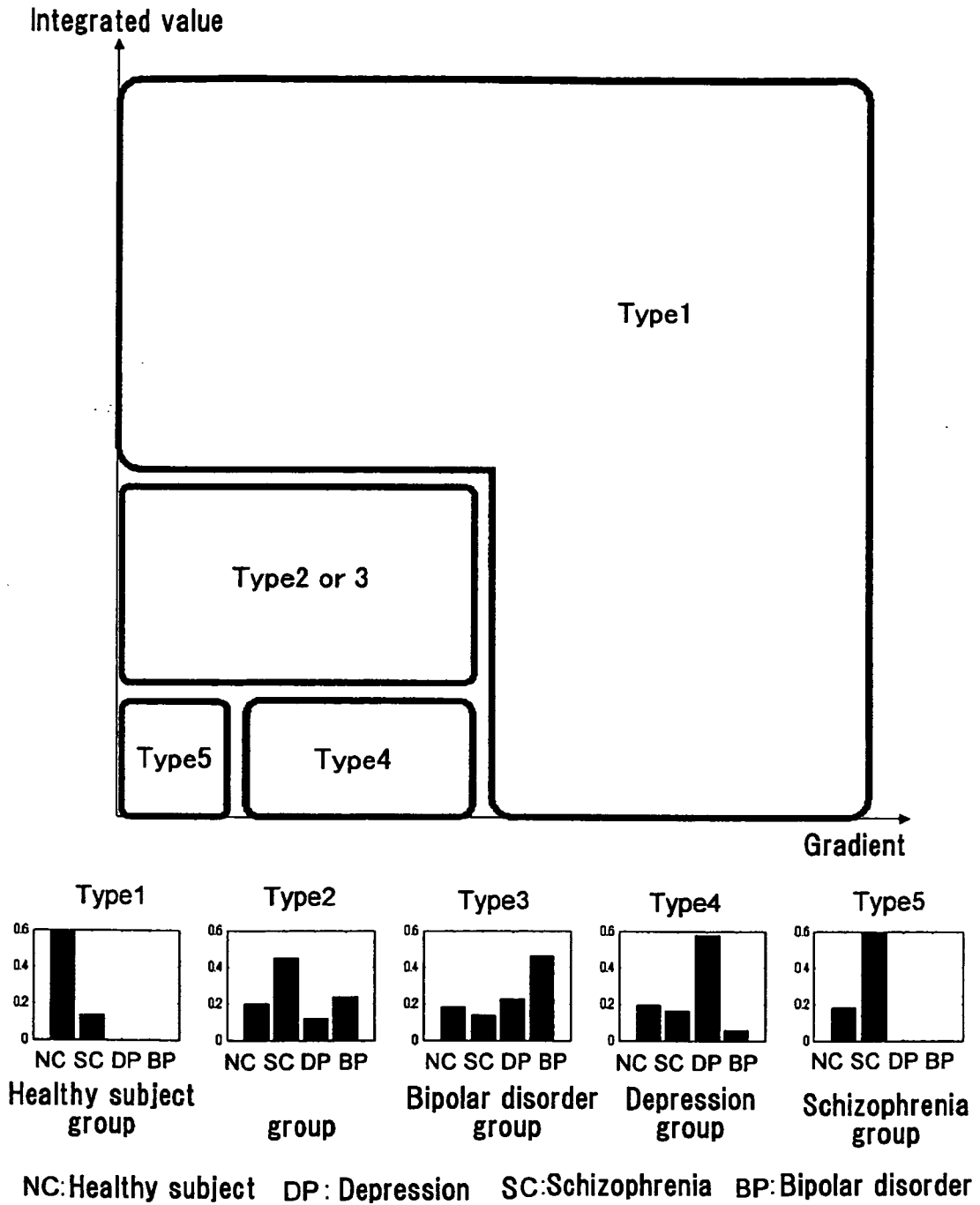


[Figure 7]

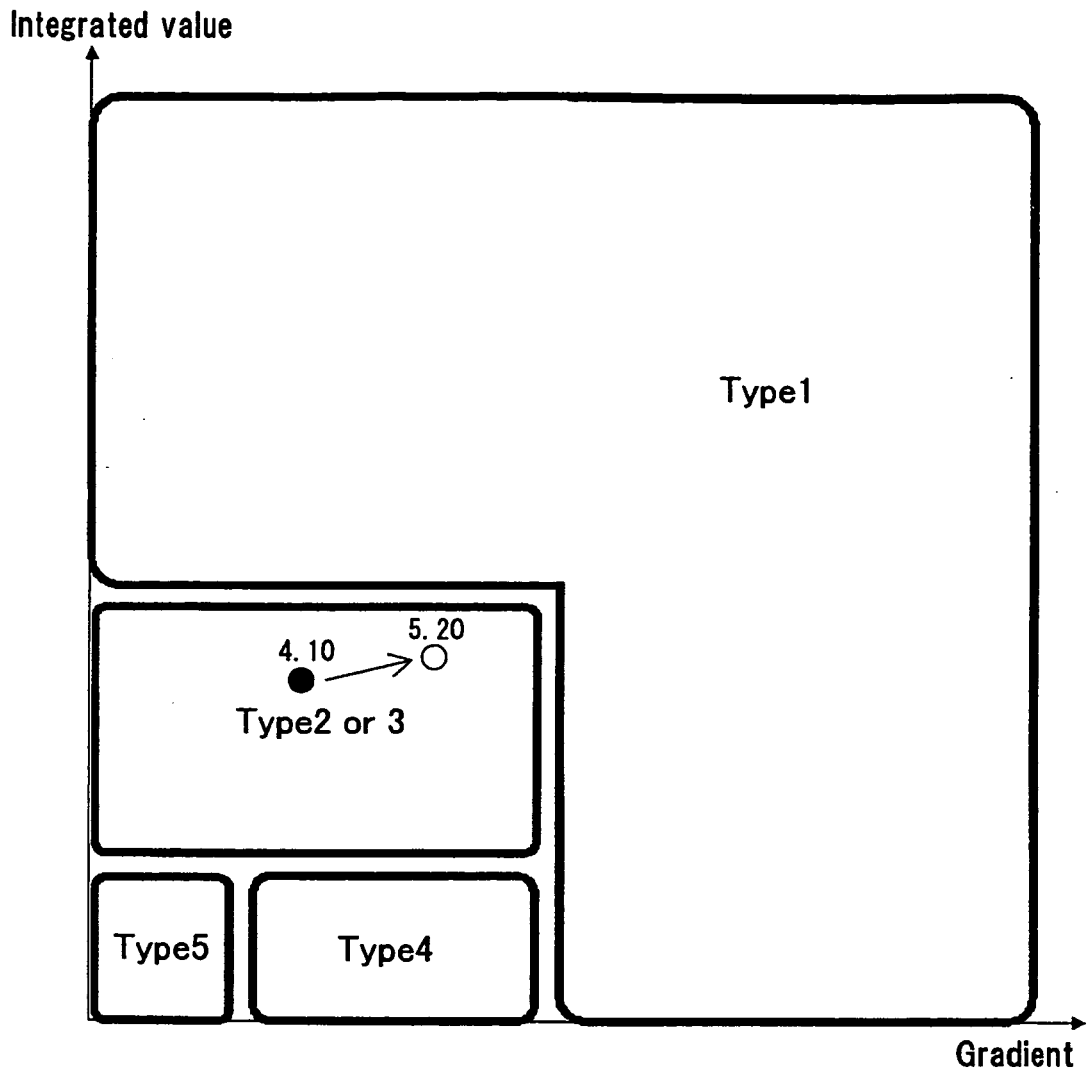
Feature values of waveform (Integrated value, gradient, re-rise)



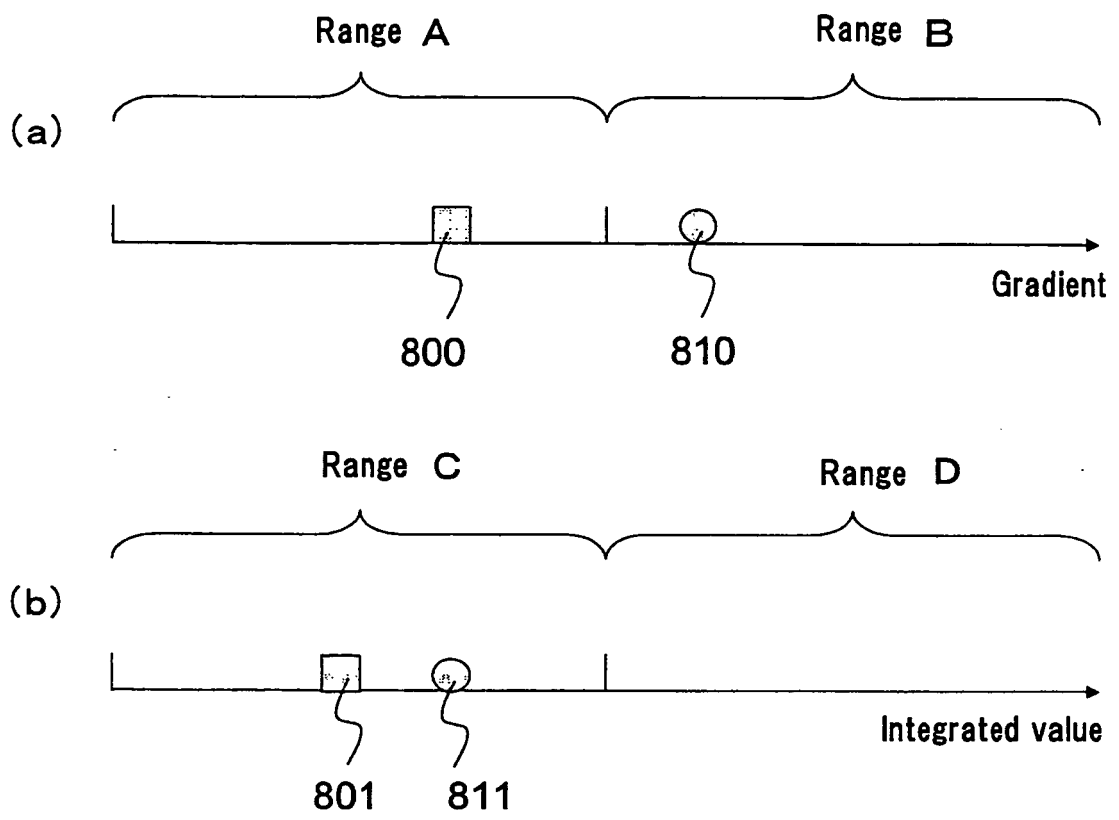
[Figure 8]



[Figure 9]



[Figure 10]



**REFERENCES CITED IN THE DESCRIPTION**

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**Patent documents cited in the description**

- JP 2003275191 A [0004]
- EP 1506739 A1 [0004]
- WO 2005025421 A [0004] [0027]

**Non-patent literature cited in the description**

- Dynamics of local cerebral blood flow in the frontal lobe in psychoneurotic disorders - Study using optical topography. **MASATO FUKUDA**. The report of the study supported by the grant from Japan Society for the Promotion of Science. 2001 [0004]
- Hikari de miru kokoro. **MASATO FUKUDA**. Kokoro to Shakai. Japanese Association of Mental Health, vol. 31 [0004]

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[标]申请(专利权)人(译)	株式会社日立医药 株式会社日立制作所 国立大学法人群馬大学		
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其他公开文献	EP1891893A4 EP1891893A1		
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#### 摘要(译)

提供了一种系统，用于支持评估待检查对象属于哪个疾病组或者受试者所处的整个疾病组中的位置。该支持系统包括存储光学生物的特征值的数据存储部分。包括多个疾病组中的患者的许多受试者的测量数据，从光学生物测量数据中提取多种特征值的分析部分和在与词典数据相关联的分析部分中显示分析结果的显示部分，其中显示部分产生散点图，在该散点图上绘制字典数据的特征值，其中两个特征值中的一个沿横坐标轴绘制，另一个沿纵坐标轴绘制，并显示主体的位置。评估叠加在散点图上的散点图。利用该散点图，可以一眼就知道受试者的特征与疾病组的特征之间的关系。

[Formula 1]

$$p_{NC}(j, n) + p_{SC}(j, n) + p_{DP}(j, n) + p_{BP}(j, n) = 1$$