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(54) **SYSTEM FOR MONITORING THE BLOOD SUPPLY TO THE TRANSPLANTED ORGAN**

(57) The system for monitoring the blood supply to a transplanted organ uses its spectral characteristics to monitor the organ's status and, based on the evaluation of the measured results, it robustly classifies blood supply failure regardless of the local variability of blood perfusion. The proposed system is based on the measurement of slow changes in the intensity of the radiation reflected from the organ at several wavelengths in the visible and near-infrared spectral range. The state of the organ perfusion is evaluated on the basis of a common classification of slow changes and amplitudes of pulsations of the measured signals. The measurement accu-

racy is therefore not affected by the intensity of the perfusion, as is the case of pulse oximetry, but the pulse changes in the reflected light intensity can be evaluated. The modulation and demodulation technique applied to the measuring signals significantly increases the useful signal-to-noise ratio, thus allowing for a reduction in the overall system input power and increasing the distance between the sensors while maintaining high measurement accuracy. Due to this and due to the special mechanical concept of the sensor, the system allows to monitor a larger volume of tissue. The system also has low energy demands, making it suitable for battery operation.

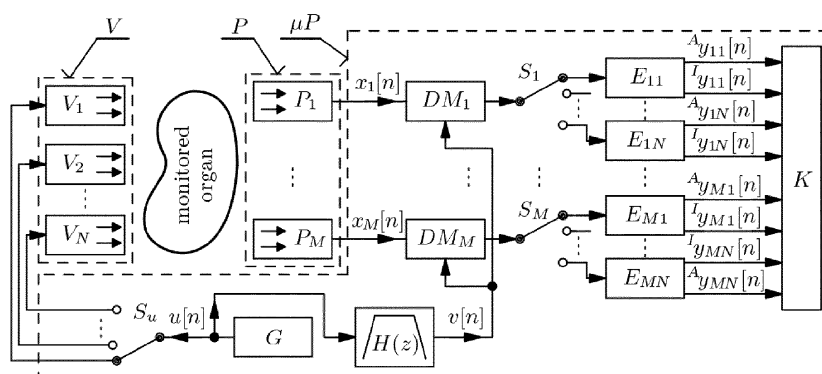


Figure 1

**Description**Background of the Invention

5 **[0001]** The present solution deals with systems for monitoring changes in the function of internal organs by minimally invasive methods. For example, it is a task of monitoring a renal graft perfusion in an early postoperative period using an optical method inside a living organism, especially a human body.

Description of Prior Art

10 **[0002]** At present, ultrasound examination is used in clinical practice to monitor the state of organs during postoperative hospitalization. Besides the need to provide personnel and the fact that this examination offers only one-off measurement without the capability of automated continuous checking, its main disadvantage is that the accuracy of the determination of the target organ condition depends to a large extent on the experience of the operator and his subjective evaluation.

15 **[0003]** For the purposes of ongoing monitoring of the state of organs, experimental electronic pulse oximetry systems can be used to measure oxygen saturation in internal organs. This topic is discussed in the following studies: Theodor, Michael, et al. "Implantable pulse oximetry on subcutaneous tissue." Engineering in Medicine and Biology Society (EMBC), 2014 36th Annual International Conference of the IEEE. IEEE, 2014 and Kyriacou, P. A., M. Hickey, and J. P. Phillips. "Pulse oximetry of body cavities and organs." Engineering in Medicine and Biology Society (EMBC), 2013 35th  
20 Annual International Conference of the IEEE. IEEE, 2013. These systems are based on monitoring the amplitude of quasi-periodic changes in the reflectance or transmittance of the monitored tissue caused by the varying concentrations of oxyhemoglobin and deoxyhemoglobin during a heart cycle. The ratio of the magnitude of these changes on at least two suitably chosen wavelengths, typically 650nm and 900nm, is then proportional to the value of the blood oxygenation. This measurement method has several drawbacks. Changes in the reflectance/transmittance intensity during the heart  
25 cycle are relatively small and can easily disappear in the interference caused by the instability of the optical link between the sensor and the measured tissue, which is often caused by even small and virtually unavoidable mechanical motion of the sensor. Another disadvantage is the unreliability of the measurement at a low perfusion value, see papers Shah, Nitin, et al. "Performance of three new-generation pulse oximeters during motion and low perfusion in volunteers." Journal of clinical anesthesia 24.5 (2012): 385-391 a Barker, Steven J. ""Motion-resistant" pulse oximetry: a comparison of new  
30 and old models." Anesthesia & Analgesia 95.4 (2002): 967-972. In this case, the pulse amplitude is lower and its measurement is unreliable, which may subsequently result in an evaluation of the incorrect oxygen saturation value, which does not indicate a problem with reduced perfusion. Because of these shortcomings, pulse oximetry is not perfectly suitable for monitoring organ perfusion.

35 **[0004]** Another principle applicable to perfusion monitoring is the measurement of the photoplethysmographic PPG signal, as described for instance in Reichelt, Stephan, et al. "Development of an implantable pulse oximeter." IEEE transactions on Biomedical Engineering 55.2 (2008): 581-588. The principle of this measurement is closely related to pulse oximetry - the monitoring of changes in transmissivity of the monitored tissue during the heart cycle is used. However, the measured signal does not indicate the oxygen saturation rate, but only the mentioned volumetric changes of the monitored organ or tissue. The disadvantage of this approach is, as with pulse oximetry, considerable sensitivity  
40 to the mechanical instability of the measuring system. Another difficulty is the possibility of false pulse detection even with reduced perfusion of the monitored organ - e.g. when a renal vein becomes blocked, the pulse of the PPG signal can still be measured both on the renal artery and on the kidney as such because the renal artery and the organ are still affected by change in blood pressure during the heart cycle. Therefore, also the PPG measurement is not a trouble-free approach to monitoring blood organ perfusion.

45 **[0005]** Another possible approach is to monitor the mechanical properties of the monitored tissue and to derive the perfusion from these mechanical properties. This approach is used in US2015208923A1, where the evaluation of mechanical properties is based on the pulse waveform analysis in the measured signal. This approach has a similar disadvantage as the pulse oximetry systems, where the pulsations can disappear due to the interference that is caused by the mechanical movement of the sensor. Moreover, the device described in US2015208923A1 does not contain an  
50 output indicating the tissue perfusion, and the information about the perfusion would have to be derived from the measured mechanical properties, which is not an optimal approach.

**[0006]** A common problem with some systems using measuring methods similar to oximetry and PPG is also that they use only a limited number of wavelengths. For example, WO2015070162A2 and US2009156918A1 use only two wave-  
55 lengths (US2009156918A1 admits the use of also the third wavelength). Such a limited number of wavelengths does not allow for sufficiently robust monitoring of spectral characteristics, especially when measurements at individual wave-lengths are affected by mechanical movement and vibration. In this case, the robustness of the system can be increased by using multiple wavelengths, at which reflectance and transmittance are measured.

**[0007]** Another problem with some existing devices is that they only work in the red and infrared spectrum range. For

instance, the device described in WO2015070162A2 is limited to wavelengths of 650-1000nm. Better results can be achieved if wavelengths in the remaining visible spectrum are also used. These wavelengths may not reflect the change in the concentration of oxygenated and deoxygenated hemoglobin but here the reference measurements can be made, which the final classifier will use for suppression of the effects of mechanical motion and vibrations of the measuring sensor.

**[0008]** Although pulse oximetry and PPG have a number of drawbacks, the principle of measuring the monitored tissue by means of reflectance and transmittance at various wavelengths does include the information about the perfusion of the monitored organ. The techniques for measuring these parameters are therefore still relevant and their overview is given in the following paragraphs.

**[0009]** A typical arrangement of the reflectance/transmittance measurement used in both pulse oximetry systems and PPG systems always consists of irradiating the organ by transmitting circuit of the system that typically has several sources of radiation, such as LEDs, at different wavelengths, in combination with synchronized reception of the reflected/transmitted radiation from the tissue by a photosensitive sensor at the side of the receiving circuitry block.

**[0010]** For simultaneous measurement at several wavelengths, multiple approaches may be used. Most often, it is a time division multiplex (TDM), where the sources at individual wavelengths are activated sequentially for a predetermined elementary measuring interval, during which the measurement is performed only at a single wavelength, as described for instance in patents US4653498, US4167331, US4883353, US5792052, EP2442709, EP0329196, EP1237467, EP2022394. The result of the measurement is the mean intensity of the detected radiation during the elementary measuring interval. The disadvantage of this approach is that it can be easily affected by external interference such as power-line interference, low-frequency noise of electronics, which is typically a so-called 1/f noise, and a dark current of sensors. Another measurement approach is the frequency division multiplex (FDM), where the sources emit radiation continuously, but their power is amplitude-modulated at different frequencies. This approach is used for example in patents US8150487, US8718737, US9351673, US5482036, US5490505, US5431159, US7062307, EP1709902. After measurement, the signals corresponding to the individual wavelengths are separated by linear filtering. The advantage of this approach is the possibility of avoiding frequency bands with interference, but considerable drawbacks are the high requirements for linearity of the radiation sources and the measuring sensor. If a light source or measuring sensor is non-linear, such as a light-emitting diode or a photodiode, it is no longer possible to separate the individual components by linear filtering, especially if the measurements are made at a greater number of wavelengths. Another, less frequent alternative to the measurement is the phase multiplex described in patent US5349952, wherein the sources emit radiation continuously, while their output is amplitude-modulated by harmonic signals at one frequency with a mutual phase shift, which makes them orthogonal. After measurement, the signals are subsequently separated by a synchronous detector. The disadvantage of this approach is the possibility of using only two wavelengths because the mutual orthogonality on one frequency can only be achieved for one phase shift, namely 90°.

**[0011]** From a mechanical point of view, the implantable systems described for instance in article Theodor, Michael, et al. "Implantable pulse oximetry on subcutaneous tissue." Engineering in Medicine and Biology Society (EMBC), 2014 36th Annual International Conference of the IEEE. IEEE, 2014, or in article Kyriacou, P. A., M. Hickey, and J. P. Phillips. "Pulse oximetry of body cavities and organs." Engineering in Medicine and Biology Society (EMBC), 2013 35th Annual International Conference of the IEEE. IEEE, 2013, typically feature the setback that they measure relatively small volume of the monitored tissue. Measurement systems typically consist of one sensor that measures tissue reflectance/transmittance especially in its immediate vicinity, and the measurement can therefore be affected by a mere local deterioration of the blood perfusion, which however does not reflect the condition of the entire organ.

**[0012]** Overall, none of the currently available solutions for monitoring the blood perfusion of the transplanted organ is without problems. Systems detecting the tissue reflectance/transmittance are primarily designed to measure pulse oximetry or PPG, which however may not reliably indicate the rate of blood perfusion. Reflectance/transmittance measurement techniques as such also have a number of drawbacks, such as noise sensitivity, or high linearity requirements for the sensor used. Last but not least, the mechanical design of the sensor limits the measurement to a small volume of the monitored tissue, which complicates the diagnostics of the organ as a whole.

### Summary of the Invention

**[0013]** The above-mentioned disadvantages are removed by the system for monitoring the blood supply to a transplanted organ according to the presented solution. The system consists of three sections. The transmitting section with transmitters with light-emitting diodes, which irradiate the monitored tissue by radiation of multiple wavelengths, the receiving section with receivers with photosensitive sensors, which detect the radiation reflected from the monitored tissue, and the control section, which generates the excitation pulses for the transmitters and processes signals from the receivers. The main principle of the new solution lies in the following arrangement. Each of the transmitters, which are  $N$  in total where  $N$  corresponds to the number of wavelengths used for irradiation, comprises at its input a digital-to-analog converter connected to the input of the voltage/current converter, the output of which is connected to at least

one light-emitting diode for the wavelength of the given transmitter. If multiple light-emitting diodes are used, they are connected in series between the output of the voltage/current converter and the power supply voltage. Each of the receivers in the receiving section, which are  $M$  in total where  $M$  is given by the requirement for the volume of the monitored organ or its part, is formed by the photosensitive sensor, the output of which is connected via the current/voltage converter and via band-pass filter to the input of an analog-to-digital converter. The output of the analog-to-digital converter is the output of the given receiver. Each of the outputs of the receivers is connected to the first input of its corresponding demodulator in the control section. The demodulator comprises at its input a multiplier connected via the integrator with resetting and via the sampling switch to the input of its switcher. Each switcher has  $N$  outputs and to each of them a feature estimator for each wavelength is connected. Each feature estimator is formed by two parallel branches. The first branch is formed at its input by a high-pass filter, the output of which is connected via the squarer circuit to the input of the first low-pass filter, the output of which is the output of the signal corresponding to the amplitude of pulsations of the radiation reflected at the given wavelength. The second branch is formed at its input by the second low-pass filter and its output is the output of the signal corresponding to slow changes of the reflected radiation intensity. The outputs of all feature estimators are connected to the classifier. The control section further contains a digital filter, while its transfer function corresponds to discretized transfer function of the analog band-pass filter. The output of the digital filter is connected to the second inputs of the demodulators, and to its input is connected the output of the generator, which is simultaneously connected to the input of the common switcher, which has outputs for the connection to the inputs of individual transmitters, so that they can be sequentially activated during the elementary measuring interval  $T_p$  by the pulse  $u[n]$  with the sampling frequency  $f_s$  according to the equation

$$u[n] = w[n] \cdot (\sin(\Omega_0 n) + k),$$

where  $w[n]$  is the weight window with length  $N_w$  samples,  $\Omega_0$  is the central normalized frequency of the pulse, and  $k > 1$  is a constant, whereas for the total length of the pulse  $u[n]$  holds that  $T_p \cdot f_s > N_w$ .

**[0014]** In a preferred embodiment, the mechanical design of the unit with sensors of the system that is applied on the monitored organ is implemented in the form of a flexible strip. This strip carries the light-emitting diodes and photosensitive sensors. The light-emitting diodes are arranged into  $L$  groups where each group includes one source for each wavelength. Photosensitive sensors are placed between the individual groups. The higher the number of groups of light-emitting diodes and photosensitive sensors, the larger the volume of the monitored organ, and the whole unit is encapsulated in an optically transparent package.

**[0015]** The proposed system is based on monitoring the tissue reflectance or transmittance, while it includes three innovations that allow for more accurate measurement and more reliable diagnostics of the monitored organ.

**[0016]** The first innovation is the change in the monitored quantities on the basis of which the perfusion in the tissue is evaluated. Instead of the amplitude of the pulsation during the heart cycle, i.e. the quantities measured by the pulse oximetry and the photoplethysmographic PPG signal, the slow and long-term changes of reflectance/transmittance at several wavelengths in the visible and infrared spectra are primarily monitored. While these quantities reflect neither the immediate level of the blood oxygenation nor the tissue volume changes, they reflect changes in the spectral properties of the monitored organ caused by the change in its perfusion. In addition, these changes are even greater by orders of magnitude than changes caused by varying oxy/deoxyhemoglobin concentrations during the heart cycle, and their measurement is therefore less affected by the mechanical instability of the measuring sensors.

**[0017]** As a complementary measurement, the presented device can also measure changes in amplitude pulsation during the heart cycle. However, these are considered as supplementary information only and do not carry the main information which the device functions are based on.

**[0018]** The second innovation is a time multiplex technique with improved modulation of power transmitted between the transmitter and the receiver. This modulation minimizes the effect of added noise, sensitivity to so-called  $1/f$  noise, allowing for robust detection of received pulses of light and infrared radiation. Due to a greater signal-to-noise ratio, this detection method features an increased sensitivity to reflected radiation from the tissue and allows to increase the distance between the transmitters and the receivers, which further increases the irradiated surface of the organ and allows the whole measurement to be carried out in a larger volume of the tissue being monitored.

**[0019]** The third innovation is the concept of the mechanical design of the unit with sensors of the device, allowing for easy measurement at multiple areas of the organ simultaneously, which significantly increases the volume of tissue being monitored and makes the entire monitoring robust to local changes in the organ structure. The mechanical design of the unit with sensors takes the form of a flexible strip and it is proposed in such a way that it can be removed from the patient's body without surgical intervention after the measurement is finished.

Explanation of Drawings

[0020] The system for monitoring the blood supply to a transplanted organ according to the presented solution will be further described by means of drawings. Fig. 1 shows a block diagram of the system for continuous monitoring of perfusion to a target organ. Fig. 2 shows an internal block diagram of the transmitter block. Fig. 3 shows an internal block diagram of the receiver block. Fig. 4 shows an internal block diagram of the demodulator block and Fig. 5 shows an internal block connection of the estimator block. Fig. 6 shows an example of the circuitry implementation of the transmitter and Fig. 7 shows an example of the circuitry implementation of the receiver. Fig. 8 illustrates the excitation signal  $u(t)$  for the light-emitting diodes, while Fig. 9 depicts the arrangement of the implemented mechanical design of the unit with sensors of the device.

Detailed Description of the Preferred Embodiments

[0021] Block diagram of the system is shown in Fig. 1. The system consists of the transmitting section  $\underline{V}$  with transmitters  $V_1$  to  $V_N$  with light-emitting diodes  $D_1$  to  $D_L$  used for the irradiation of the monitored tissue by radiation at various wavelengths, of the receiver section  $\underline{P}$  with receivers  $P_1$  to  $P_M$  with photosensitive sensor  $\underline{D}$  used for the detection of the radiation reflected from the monitored tissue, and of the control section  $\underline{\mu P}$  used for generating the excitation pulses  $u[n]$  for the transmitters  $V_1$  to  $V_N$  and for processing the signals from the receivers  $P_1$  to  $P_M$ . Each of the transmitters  $V_1$  to  $V_N$ , see Fig. 2, which are  $N$  in total where  $N$  corresponds to the number of wavelengths used for irradiation, comprises at its input a digital-to-analog converter  $\underline{DAC}$  connected to the input of the voltage/current converter  $\underline{V/I}$ . The output of this voltage/current converter  $\underline{V/I}$  is connected to at least one light-emitting diode  $D_1$  to  $D_L$  for the wavelength of the given transmitter  $V_1$  to  $V_N$ . If multiple light-emitting diodes  $D_1$  to  $D_L$  are used, they are connected in series between the output of the voltage/current converter  $\underline{V/I}$  and the power supply voltage  $+V_{cc}$ . Each of the receivers  $P_1$  to  $P_M$  in the receiving section  $\underline{P}$ , see Fig. 3, which are  $M$  in total, where  $M$  is given by the requirement for the volume of the monitored organ or its part, is formed by the photosensitive sensor  $\underline{D}$ , the output of which is connected via the current/voltage converter  $\underline{I/V}$  and via the analog band-pass filter  $\underline{PP}$  to the input of the analog-to-digital converter  $\underline{ADC}$ . The output of the analog-to-digital converter  $\underline{ADC}$  is the output of the corresponding receiver. Each of the outputs of receivers  $P_1$  to  $P_M$  is connected to the first input of their corresponding demodulators  $\underline{DM_1}$  to  $\underline{DM_M}$  in the control section  $\underline{\mu P}$ . Individual demodulators comprise at their inputs the multiplier  $\underline{MP}$  connected via the integrator  $\underline{I}$  with resetting and via the sampling switch  $\underline{S}$  to the input of their relevant switchers  $S_1$  to  $S_M$ , each of which has  $N$  outputs each of which is connected to one feature estimator  $\underline{E_{i1}}$  to  $\underline{E_{iN}}$  for each wavelength. Each feature estimator  $\underline{E_{i1}}$  to  $\underline{E_{iN}}$  is formed by two parallel branches. The first branch is formed at its input by the high-pass filter  $\underline{HP}$ , the output of which is connected via the squarer circuit  $\underline{KV}$  to the input of the first low-pass filter  $\underline{DP_1}$ . The output of the first low-pass filter  $\underline{DP_1}$  is the output of the signal corresponding to the amplitude of pulsations of the radiation reflected at the given wavelength. The second branch is formed at its input by the second low-pass filter  $\underline{DP_2}$  and its output is the output of the signal corresponding to slow changes of the reflected radiation intensity. The outputs of all feature estimators  $\underline{E_{i1}}$  to  $\underline{E_{iN}}$  are connected to the classifier  $\underline{K}$ . The control section  $\underline{\mu P}$  further contains a digital filter  $\underline{H(z)}$ , while its transfer function corresponds to the discretized transfer function of the analog band-pass filter  $\underline{PP}$ . The output of the digital filter  $\underline{H(z)}$  is connected to the second inputs of the demodulators  $\underline{DM_1}$  to  $\underline{DM_M}$ , and its input is connected to the output of the generator  $\underline{G}$ . This output is also connected to the input of the common switcher  $\underline{S_u}$ , which has outputs for connection to the inputs of individual transmitters  $V_1$  to  $V_N$ , so that they can be sequentially activated during the elementary measuring interval  $T_p$  by the pulse  $u[n]$  with the sampling frequency  $f_s$ . The generator  $\underline{G}$  synthesizes the signal according to the equation

$$u[n] = w[n] \cdot (\sin(\Omega_0 n) + k), \quad (1)$$

where  $w[n]$  is the weight window with length  $N_w$  samples, and also the total length of the pulse  $u[n]$ , for which holds that  $N_w < T_p \cdot f_s$ ,  $\Omega_0$  is the central normalized pulse frequency and  $k > 1$  is a constant. The pulse  $u[n]$  generated in this way has its energy concentrated into the band with its center on the frequency  $\Omega_0$  and the frequency band width that can be controlled by the choice of the window  $w[n]$ .

[0022] In the described embodiment of the invention, the transmitting section  $\underline{V}$  provides irradiation of the monitored organ and contains  $N$  transmitters  $V_1$  to  $V_N$ , where each block irradiates the tissue by radiation with a specific wavelength. The receivers  $\underline{P_1}$  to  $\underline{P_M}$  of the receiving demodulator  $\underline{P}$  then detect the radiation reflected from the tissue at various places of the organ and convert the detected energy to an electric signal. The control section  $\underline{\mu P}$  ensures the control of the whole measurement process, generation of the excitation pulses for irradiation, and processing of the measured data.

[0023] For simultaneous measurement at several wavelengths, the time multiplex is used. The individual transmitters  $V_1$  to  $V_N$  are sequentially activated by the common switcher  $\underline{S_u}$  for the time period  $T_p$ , which is denoted as an elementary measuring interval and during which the measurement at a single wavelength is performed. During one elementary

measuring interval, the activated transmitting block is excited by the pulse  $u[n]$  with the sampling frequency  $f_s$  according to the equation (1) stated above.

[0024] The individual transmitters  $V_1$  to  $V_N$  subsequently convert the pulse  $u[n]$  to the emitted radiation, which then reflects from or transmits through the monitored tissue and is detected by the receivers  $P_1$  to  $P_M$ . The received signal is subsequently filtered using matched filtering, which suppresses the frequencies not present in the excitation signal  $u[n]$ . Appropriate selection of the  $\Omega_0$  and  $w[n]$  allows for suppression of interfering effects, such as power noise interference and  $1/f$  noise.

[0025] The function of each of the transmitters  $V_1$  to  $V_N$  is illustrated by the diagram in Fig. 2. The transmitters  $V_1$  to  $V_N$  convert the excitation pulse  $u[n]$  by means of the digital-to-analog converter  $DAC$  to the control voltage  $u(t)$  of the voltage/current converter  $V/I$ , the output of which provides the current excitation  $i(t)$  for the total of  $L$  light-emitting diodes  $D_1$  to  $D_L$  connected in series to irradiate the monitored tissue at the total of  $L$  various places simultaneously.

[0026] The function of each of the receivers  $P_1$  to  $P_M$  is illustrated by the diagram in Fig. 3. Each receiver detects the radiation reflected from or transmitted through the tissue by means of its sensor  $D$  and subsequently it converts the current of the sensor by means of the current/voltage converter  $I/V$  to a voltage, which is filtered by the analog band-pass filter  $PP$  in order to remove undesired components, such as low-frequency noises, e.g.  $1/f$  noise. The analog band-pass filter  $PP$  simultaneously serves as an anti-aliasing filter for the analog-to-digital converter  $ADC$ , which converts the received signal into a digital form.

[0027] As mentioned above, the control section  $\mu P$  has several functions. The reflected radiation is measured at several wavelengths using the time multiplex where the use of synchronized switching of the common switcher  $S_u$  and the switchers  $S_1$  to  $S_M$  achieves synchronous irradiation of the organ and reception of reflected radiation, always within a single elementary measurement interval with the duration  $T_p$ . The matched filtering for the optimal detection of received pulses of radiation is implemented in the blocks of demodulators  $DM_1$  to  $DM_M$ , the block diagram of which is shown in Fig. 4. In each of the demodulators  $DM_1$  to  $DM_M$  the digitized pulse  $x[n]$  is multiplied by the pulse  $v[n]$  by means of the multiplier  $MP$ . The pulse  $v[n]$  is synthesized by filtering the pulse  $u[n]$  with digital filter  $H(z)$ . The multiplication result is integrated over the entire elementary measurement interval and after its completion, the resulting value is passed over to the subsequent processing via the sampling switch  $S_s$  which serves to capture the resulting sample after demodulation. Subsequently, the integrator is reset before the next integration. From the samples of signals thus obtained, which correspond to the reflected radiation at  $N$  wavelengths, the blocks of the feature estimators  $E_{i1}$  to  $E_{iN}$  continuously estimate the features for classification of the state of blood circulation in the organ. Each of the feature estimators  $E_{i1}$  to  $E_{iN}$ , see Fig. 5, processes the signal in two parallel branches. One branch estimates slow changes of the reflected radiation intensity by filtering the signal in the low-pass filter  $DP_2$ . The other branch estimates the amplitude of pulsations by means of the cascade connection of the high-pass filter  $HP$ , the squarer circuit  $KV$ , and the low-pass filter  $DP_1$ . The output signals of the first branch and the second branch respectively, of the estimator  $E_{ij}$  will further be marked as  $^s y_{ij}[n]$ , and  $^A y_{ij}[n]$  respectively. The state of blood supply to the measured organ is determined in the block of classifier  $K$  based on the evaluation of the non-linear kernel of the classifier for the vectors of the selected input features and the monitoring of the time evolution of this metrics. The non-linear kernel of the classifier  $K$  takes on the form of the function

$$f(^s y_{11}[n], \dots, ^s y_{1N}[n], \dots, ^s y_{MN}[n], ^A y_{11}[n], \dots, ^A y_{1N}[n], \dots, ^A y_{MN}[n]),$$

where for example the multi-dimensional Gauss function may be used as the non-linear function  $f()$ .

[0028] An example of the preferred circuitry implementation of the transmitters  $V_1$  to  $V_N$  is shown in Fig. 6. The input of the transmitter is connected to the digital-to-analog converter  $DAC$ , the output of which is then connected to the inverting input of the operational amplifier  $OA$ , which together with the transistor  $T$  and the resistor  $R$  form a controlled current source for excitation of the light-emitting diodes  $D_1$  to  $D_L$  connected in series.

[0029] An example of the preferred circuitry implementation of the receivers  $P_1$  to  $P_M$  is shown in Fig. 7. The photo-sensitive sensor  $D$  is connected to the resistor  $R_1$ , which together with the capacitors  $C_1$  and  $C_2$ , resistor  $R_2$ , and the operational amplifier  $OA$  forms a current-to-voltage converter with frequency transmission, which acts as a band-pass filter. Its output is against the reference voltage  $V_{ref}$  connected to the input of the analog-to-digital converter  $ADC$ .

[0030] The mechanical design of the unit with sensors serves as a robust and flexible platform for the light emitters and sensors with the ability to conform to the shape of the monitored organ. It creates a stable homogeneous optical link between the optical sensors and the illuminated surface and ensures the waterproof separation of the electronics from the living tissue. In addition, it is designed in such a way that when the subject's monitoring is finished, it is possible to easily remove the complete set out from the body along with the drains without any additional surgical intervention.

[0031] The mechanical arrangement of the unit with sensors is illustrated in Fig. 9. The base is a printed circuit board 1 in the form of a flexible strip, which holds the individual parts and interconnecting elements 2 - that is a cable or a flexible printed circuit interconnecting the electrical elements on a printed circuit board inside the body with the electronics located outside the body. On the printed circuit board 1 the rows of the light-emitting diodes  $D_1$ , to  $D_L$  are located, where

each row includes one diode for each wavelength used. The number of light-emitting diodes  $\underline{D}_1$  to  $\underline{D}_L$  in series in each of the transmitters  $\underline{V}_1$  to  $\underline{V}_N$  corresponds to the number of rows of diodes in the mechanical arrangement, thus determining the size of the monitored volume of the tissue. Between these series of light-emitting diodes there are photosensitive sensors  $\underline{D}$  of the receivers  $\underline{P}_1$  to  $\underline{P}_M$ . The complete set is then encapsulated in the optically transparent package  $\underline{g}$  up to the connector connecting this part to the control electronics. Moreover, on the sides of the optically transparent package  $\underline{g}$  extensions  $\underline{9}$  are created, providing increased stability of the unit with sensors and possible fixation to the monitored organ. The unit with sensors can be fixed by suturing these extensions to the organ in such a way that will not harm the monitored organ when removing the strip out from the body.

#### Industrial Applicability

**[0032]** The invention can be used for monitoring of changes of the function of internal organs using minimally invasive methods. For example, the invention is intended for monitoring perfusion of a transplanted renal graft in an early post-operative period. Its advantage is a robust detection of perfusion changes in the monitored organ. A simple structure of the unit with sensors with a flexible profile for conformation to the surface of the monitored organ inside a living body during surgery, the possibility of continuous monitoring of an organ in the postoperative period and the subsequent easy removal of the unit with sensors out of the body together with the drains without surgical intervention make this system an attractive candidate for inclusion to the indispensable equipment of the postoperative departments in hospitals.

#### Claims

1. A system for monitoring the blood supply to a transplanted organ consists of a transmitting section ( $\underline{V}$ ) with transmitters ( $\underline{V}_1$  to  $\underline{V}_N$ ) with light-emitting diodes ( $\underline{D}_1$  to  $\underline{D}_L$ ), which irradiate the monitored tissue by radiation at various wavelengths, of a receiving section ( $\underline{P}$ ) with receivers ( $\underline{P}_1$  to  $\underline{P}_M$ ) with a photosensitive sensor ( $\underline{D}$ ), which detects the radiation reflected from the monitored tissue, and of a control section ( $\underline{\mu P}$ ), which generates excitation pulses ( $u[n]$ ) for the transmitters ( $\underline{V}_1$  to  $\underline{V}_N$ ) and processes the signals from the receivers ( $\underline{P}_1$  to  $\underline{P}_M$ ), **characterized by the fact that** each of the transmitters ( $\underline{V}_1$  to  $\underline{V}_N$ ), which are  $N$  in total, where  $N$  corresponds to the number of wavelengths used for irradiation, comprises at its input a digital-to-analog converter ( $\underline{DAC}$ ) connected to the input of a voltage/current converter ( $\underline{V/I}$ ), the output of which is connected to at least one light-emitting diode  $\underline{D}_1$  to  $\underline{D}_L$  for the wavelength of the given transmitter ( $\underline{V}_1$  to  $\underline{V}_N$ ), and if multiple light-emitting diodes ( $\underline{D}_1$  to  $\underline{D}_L$ ) are used, they are connected in series between the output of the voltage/current converter ( $\underline{V/I}$ ) and the power supply voltage ( $+V_{cc}$ ), each of the receivers ( $\underline{P}_1$  to  $\underline{P}_M$ ) in the receiving section ( $\underline{P}$ ), which are  $M$  in total, where  $M$  is given by the requirement for the volume of the monitored organ or its part, is formed by the photosensitive sensor ( $\underline{D}$ ), the output of which is connected via a current/voltage converter ( $\underline{I/V}$ ) and via an analog band-pass filter ( $\underline{PP}$ ) to the input of an analog-to-digital converter ( $\underline{ADC}$ ), while its output is the output of the given receiver, and each of the outputs of the receivers ( $\underline{P}_1$  to  $\underline{P}_M$ ) is connected to the first input of its respective demodulator ( $\underline{DM}_1$  to  $\underline{DM}_M$ ) in the control section ( $\underline{\mu P}$ ), the demodulators ( $\underline{DM}_1$  to  $\underline{DM}_M$ ) comprise at their inputs the multiplier ( $\underline{MP}$ ) connected via the integrator ( $\underline{I}$ ) with resetting and via a sampling switch ( $\underline{S}$ ) to the input of their relevant switchers ( $\underline{S}_1$  to  $\underline{S}_M$ ), while each of them has  $N$  outputs and each of these outputs is connected to one feature estimator ( $\underline{E}_{i1}$  to  $\underline{E}_{iN}$ ) for each wavelength, and each feature estimator ( $\underline{E}_{i1}$  to  $\underline{E}_{iN}$ ) is formed by two parallel branches, where one branch is formed at its input by a high-pass filter ( $\underline{HP}$ ), the output of which is connected via a squarer circuit ( $\underline{KV}$ ) to the input of the first low-pass filter ( $\underline{DP}_1$ ), and the output of the first low-pass filter ( $\underline{DP}_1$ ) is the output of the signal ( $\underline{A}_y[n]$ ) corresponding to the amplitude of pulsations of the radiation reflected at the given wavelength, and the second branch is formed at its input by the second low-pass filter ( $\underline{DP}_2$ ) and its output is the output of the signal ( $\underline{I}y[n]$ ) corresponding to slow changes of the reflected radiation intensity, and the outputs of all feature estimators ( $\underline{E}_{i1}$  to  $\underline{E}_{iN}$ ) are connected to a classifier ( $\underline{K}$ ), while the control section ( $\underline{\mu P}$ ) further contains a digital filter ( $\underline{H(z)}$ ) and its transfer function corresponds to the discretized transfer function of the analog band-pass filter ( $\underline{PP}$ ), where the output of the digital filter ( $\underline{H(z)}$ ) is connected to the second inputs of the demodulators ( $\underline{DM}_1$  to  $\underline{DM}_M$ ), and its input is connected to the output of the generator ( $\underline{G}$ ), which is simultaneously connected to the input of the common switcher ( $\underline{S}_u$ ), which has the outputs connected to the inputs of the individual transmitters ( $\underline{V}_1$  to  $\underline{V}_N$ ) so they can be sequentially activated during the elementary measuring interval  $T_p$  by the pulse  $u[n]$  with the sampling frequency  $f_s$  according to the equation

$$u[n] = w[n] \cdot (\sin(\Omega_0 n) + k),$$

where  $w[n]$  is the weight window with length  $N_w$  samples,  $\Omega_0$  is the central normalized frequency of the pulse, and  $k > 1$  is a constant, while for the total length of the pulse  $u[n]$  holds that  $T_p \cdot f_s > N_w$ .

2. The system according to claim 1 **characterized by the fact that** the mechanical design of the unit with sensors of the system that is applied on the monitored organ is implemented in the form of a flexible strip that carries the light-emitting diodes ( $D_1$  to  $D_L$ ) and photosensitive sensors ( $\underline{D}$ ), and the light-emitting diodes are arranged into  $L$  groups where each group includes one source for each wavelength, and the photosensitive sensors ( $\underline{D}$ ) are placed between the individual groups, while the whole unit is encapsulated in an optically transparent package (8).

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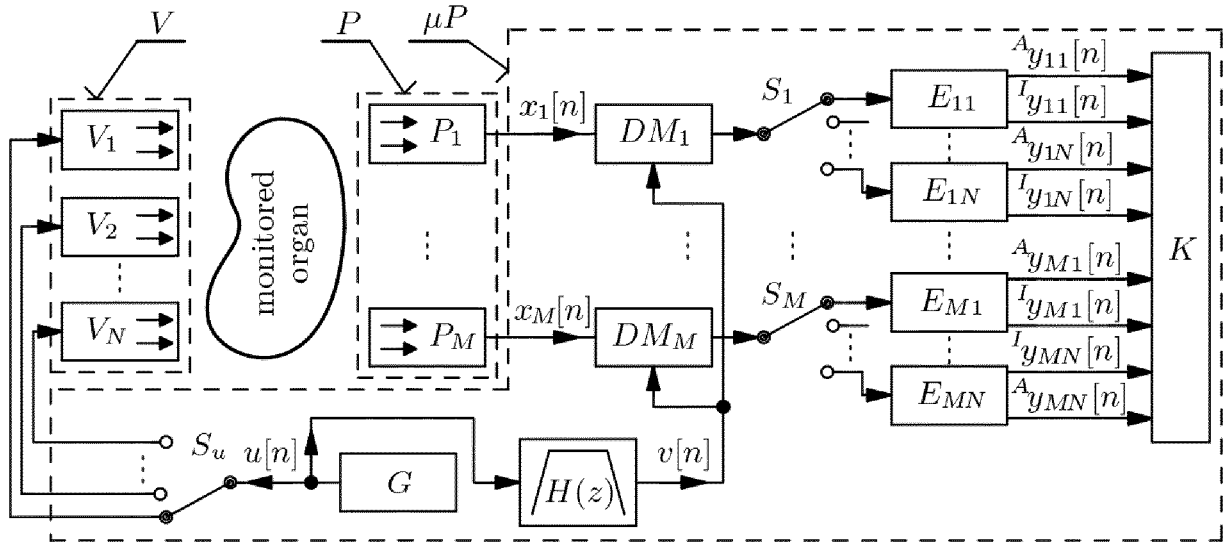


Figure 1

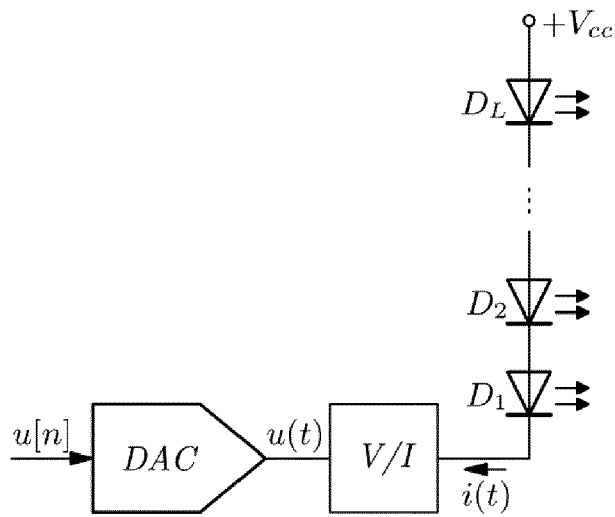


Figure 2

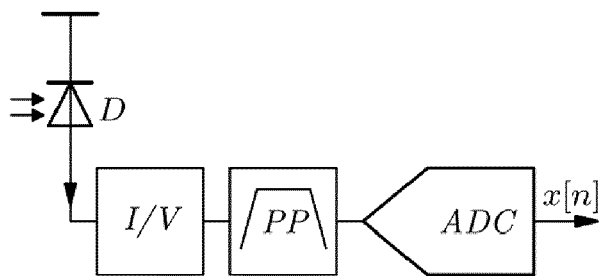


Figure 3

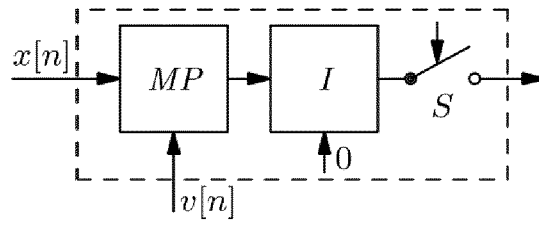


Figure 4

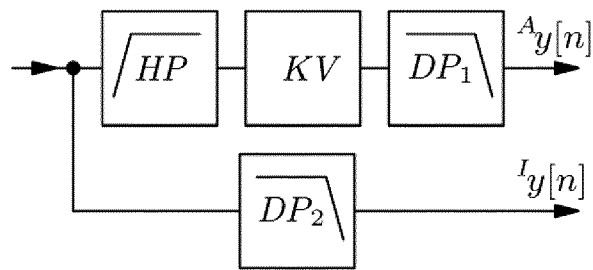


Figure 5

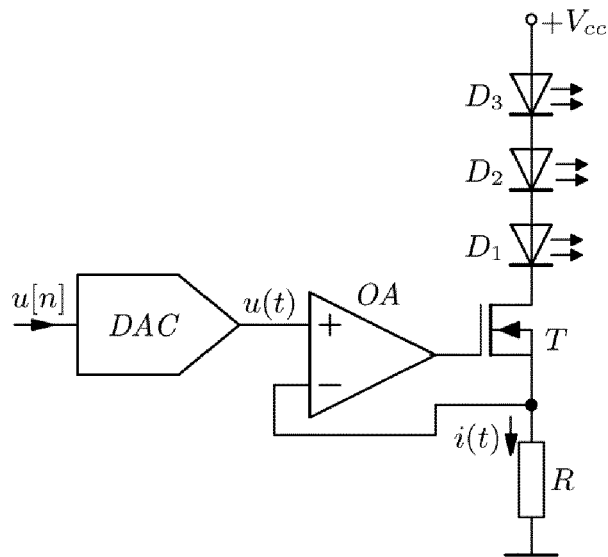


Figure 6

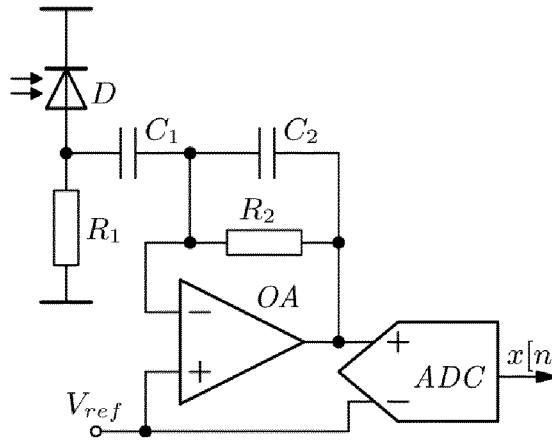


Figure 7

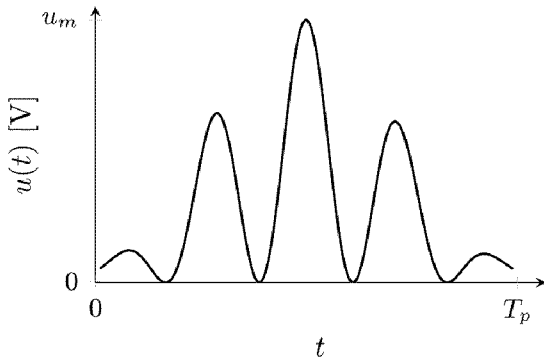


Figure 8a

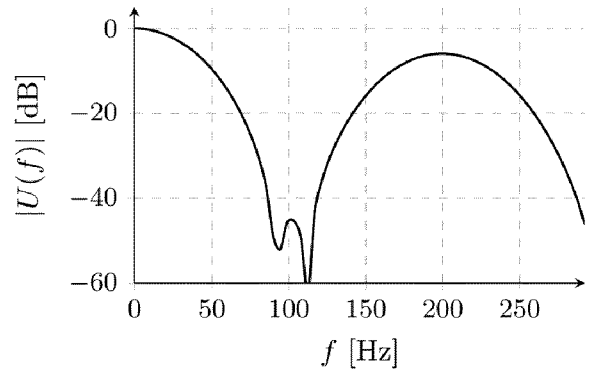


Figure 8b

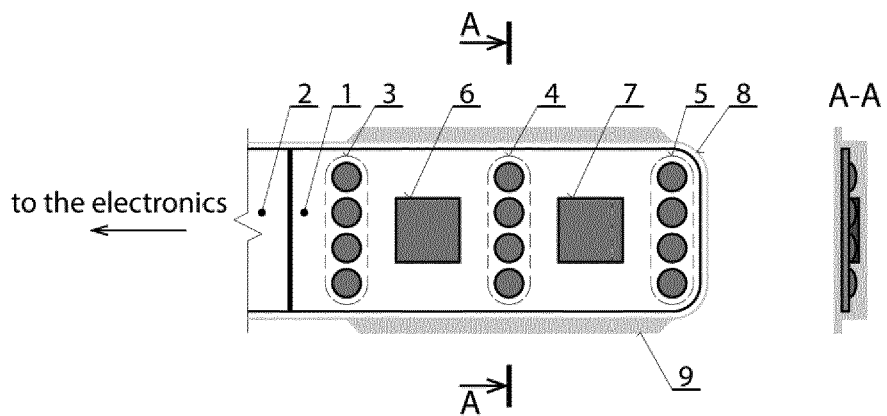


Figure 9



EUROPEAN SEARCH REPORT

Application Number  
EP 18 18 3024

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	WO 2015/070162 A2 (UNIV HOUSTON SYSTEM [US]) 14 May 2015 (2015-05-14) * paragraphs [0009] - [0013], [0032] - [0038] * * figures 1a-1d, 5 *	1,2	INV. A61B5/026 A61B5/00
A	US 2015/208923 A1 (AKL TONY J [US] ET AL) 30 July 2015 (2015-07-30) * paragraphs [0011], [0012], [0037], [0047] * * figure 1 *	1,2	
A	US 4 653 498 A (NEW JR WILLIAM [US] ET AL) 31 March 1987 (1987-03-31) * column 2, lines 39-55 * * column 5, line 30 - column 6, line 62 * * figures 1, 2, 3 *	1,2	
			TECHNICAL FIELDS SEARCHED (IPC)
			A61B
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 3 September 2018	Examiner Trattner, Barbara
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

1  
EPO FORM 1503 03/82 (P04C01)

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ON EUROPEAN PATENT APPLICATION NO.**

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03-09-2018

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WO 2015070162 A2	14-05-2015	US 2015164347 A1 WO 2015070162 A2	18-06-2015 14-05-2015
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US 4653498 A	31-03-1987	NONE	

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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专利名称(译)	用于监测移植器官的血液供应的系统		
公开(公告)号	<a href="#">EP3434182A1</a>	公开(公告)日	2019-01-30
申请号	EP2018183024	申请日	2018-07-11
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当前申请(专利权)人(译)	捷克布杰约维索克塔UCENÍTECHNICKÉV PRAZE		
[标]发明人	BORTEL RADOSLAV HOSPODKA JIRI SEBEK JAN FRONEK JIRI JANOUSEK LIBOR MALY STEPAN		
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IPC分类号	A61B5/026 A61B5/00		
CPC分类号	A61B5/0059 A61B5/0261 A61B5/7217 A61B5/7235		
代理机构(译)	KRATOCHVIL , VACLAV		
优先权	2017430 2017-07-26 CZ		
其他公开文献	EP3434182B1		
外部链接	<a href="#">Espacenet</a>		

摘要(译)

用于监测移植器官的血液供应的系统利用其光谱特征来监测器官的状态，并且基于对测量结果的评估，其无论血液灌注的局部变化如何都对血液供应失败进行稳健地分类。所提出的系统基于在可见光和近红外光谱范围内的几个波长处从器官反射的辐射强度的缓慢变化的测量。根据测量信号的缓慢变化和脉动幅度的共同分类来评估器官灌注的状态。因此，测量精度不受灌注强度的影响，如脉搏血氧测定的情况，但可以评估反射光强度的脉冲变化。应用于测量信号的调制和解调技术显著地增加了有用的信噪比，从而允许降低整个系统输入功率并增加传感器之间的距离，同时保持高测量精度。由于这一点并且由于传感器的特殊机械概念，该系统允许监测更大量的组织。该系统还具有低能量需求，使其适用于电池操作。

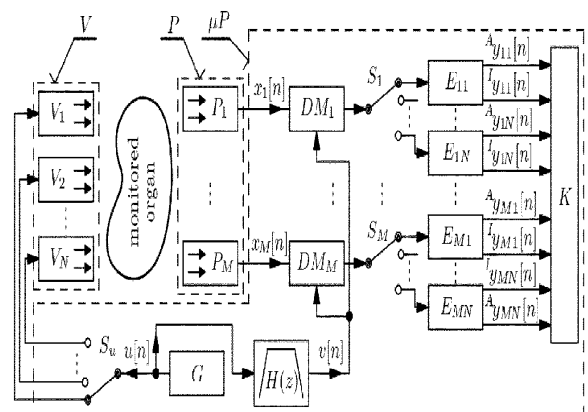


Figure 1