Virtual biosensors for the estimation of medical precursors

Salvatore Baglio[1], Alessandro Cammarata[2], Petramay Cortis[4], Lucia Lo Bello[1], Pietro Davide Maddio[2], Salvatore Nicosia[3], Gaetano Patti[1], Stephen Sciberras[4], Johann Scicluna[4], Vincenzo Scuderi[3], Rosario Sinatra[2], Carlo Trigona[1]

[1]D.I.E.E.I., Dipartimento di Ingegneria Elettrica Elettronica e Informatica, University of Catania, Viale Andrea Doria 6, 95125, Catania, Italy

[2]D.I.C.A.R., Dipartimento di Ingegneria Civile e Architettura University of Catania, Viale Andrea Doria 6, 95125, Catania, Italy

[3]Azienda Ospedaliero - Universitaria "Policlinico - Vittorio Emanuele" via S.Sofia, 78 - 95123 Catania, Italy

[4]Faculty of Medicine and Surgery, University of Malta, Malta

***Abstract*— The objective of this work concerns the study of virtual biosensors for the estimation of medical precursors. The principle is based on the combination of the signals coming from the patient (vital functions), the transduction of such acquired signals and the processing of the obtained information. The method will use *n* input variables (the classic physiological parameters and/or signals detected by using additive sensors) and one output variable which is correlated with the clinical condition of the patient. A model will produce an association between the input variables and the output variable by using a data set established with the medical team. The proposed methodology improves standard systems such as "track and trigger" and threshold (Early Warning Score) through the adoption of the Fuzzy Set Theory.**

Keywords*— *Virtual biosensors, fuzzy logic, estimation of medical precursors.

I. INTRODUCTION

The study and analysis of vital parameters is extremely important in clinical medicine [1]. There are various guidelines in "clinical practice" and the effort towards programming and developing of new clinical and scientific research is strong [2]. It is worth noting that several solutions have been proposed for clinical methods and specific treatments [3-5]. The evolution of the patient condition in pre-intensive care unit is essential in order to ensure early and rapid action in critical patients that could have a progressive clinical deterioration [6]. In fact, it should be noted that for patients with acute illness [7] (such as acute coronary syndrome, acute heart failure, arrhythmias, hyperkinetic, and hypokinetic disorder), a continuous vital signs monitoring is required [2,8]. Patients in intensive care are in fact subjected to a continuous control (24 hours a day) of the heart rate, blood pressure and, if necessary, they are supported with assisted artificial ventilation, mechanical cardiovascular support, and hemodialysis [9]. In order to ensure pre-intensive care, it is particularly interesting to perform continuous monitoring and measurement of vital functions (physiological parameters) of the patient, including oxygen saturation, blood pressure, body temperature, respiratory rate, diuresis, and consciousness [10]. Typically, such data can be obtained by using sensors and medical instrumentation, such as: the electrocardiograph, which provides the electrocardiogram (the data appear on a video terminal) [11]; a sensor that, connected to a patient's finger, is able to measure the level of oxygen in the blood [12]; a sensor that measures the level of carbon dioxide of the patient [13]; a catheter into the artery to continuously measure blood pressure [14]; sensors for brain activity recording (EEG) [15]; probe to measure the temperature [16], etc.. However, it must be noted that the measure of a single vital sign does not identify the clinical evolution and the state of the patient in pre-intensive care. For this reason, several solutions for the analysis of vital functions by using Early Warning Score (EWS) [17] have been proposed in literature. The basic principle of this method is to collect physical parameters (easily to be measured through sensors) and building a score that allows a rapid evaluation of patient status. The numerical values obtained by using this approach provide an indication of the critical status by supporting and assisting the experience of the doctors, thus allowing the evaluation of the patient's condition. This approach is necessary to define the level of urgency indicating an alert condition and the type of clinical response. However, very often, it is interesting to detect the alterations preceding this stage, predicting critical condition for the patient. The work proposed in this paper is related with this context, in particular the study here conducted regards the phase before the observation study of medical intensive care patients. The basic idea concerns the acquisition of the signals coming from the patient (vital functions), the transduction of such acquired signals and the combination of the obtained information. The proposed methodology is based on advanced mathematical techniques in order to study the signals with variable characteristics in the time domain, using standard systems such as "track and trigger", threshold (EWS) and including the use of the theory of fuzzy sets (Fuzzy Set Theory) [18]. The basic principle is to collect the usual physiological parameters, which are easy to be acquired, and use such information as inputs of a mathematical model (fuzzy system) based on the theory of fuzzy sets and fuzzy logic. The system here proposed will use *n* input variables (the classic physiological parameters and/or signals detected by using additive sensors) and one output variable which is correlated with the clinical condition of the patient. The fuzzy model will produce an association between the input variables and the output variable by using a data set (rules) established with the medical team. The goal

XXX-X-XXXX-XXXX-X/XX/$XX.00 ©20XX IEEE

978-1-7281-1273-2/19/$31.00 ©2019 IEEE

is to get a system capable to process the signals (physiological parameters) not only by using a binary logic (thresholds system), but also by using " if-then " rules. The proposed methodology will warn the medical team about condition of patient's deterioration (also in presence of a not dangerous/warning condition). These approaches will also give standardized results correlated with the evolution of the clinical status of the patient. The proposed approach will optimize the medical alert, in particular considering real case of emergencies, predicting acute degeneration conditions, such as cardiac arrest, improving the quality of life and health for all the involved people.

II. Method and Algorithm

A Working principle

Early warning scores (EWSs) are extensively used to identify patients at risk of deterioration in hospital [17,18].
It is worth noting that this method, and several similar approaches, can support clinical decision-making around escalation of care and can provide a clear means of communicating clinical acuity between clinicians and across different healthcare organizations.
EWS systems are based on five measurements of physiological parameters normally performed, as shown in Table I: respiratory rate, oxygen saturation, body temperature, systolic blood pressure, pulse rate, with the addition of the level of consciousness. The last parameter will not be taken into account in the developed algorithm.
Each parameter is graduated in levels, and a numerical value is assigned to each of them. The sum of the numerical values provides the measure of the deviation from the normal physiology. As it is shown in Fig.1 the establishes three levels of clinical alert can be summarized as [19]:

- Low: score from 1 to 4;
- Medium: score from 5 to 6, or a score of 3 for a single parameter;
- High: score ≥ 7.

Depending on the score obtained, the patient's monitoring frequency is determined.
As already mentioned, the classic EWS method is often not able to detect physiological degeneration caused by slow alterations of vital parameters. This is because this method is based on threshold criteria.

B Algorithm

The fuzzy logic allows to associate weights of belonging through the so-called membership functions, that admit values between 0 and 1, unlike Boolean logic which admits only the two above mentioned values. This helps to create rules that are very similar to human language, by moving away from the purely mathematical one.
It is therefore necessary, as a first step, to create membership functions for each physiological parameter. The fuzzy system has been implemented through the *Fuzzy System Designer* included in LabVIEW environment. An example of membership, associated to respiration rate, is shown in Fig.2. As it can be seen, five membership functions have been defined, three of them with triangular shape and the other two (the external ones) with trapezoidal shape. On the horizontal axis the numerical values relating to the vital parameter are shown. RR1 and RR5, in fact, represent the critical values to which, in the Table I, a score of three is associated. On the vertical axis the membership grades μ in the range {0-1} are reported.

NEW score	Clinical risk	Response
Aggregate score 0–4	Low	Ward-based response
Red score Score of 3 in any individual parameter	Low–medium	Urgent ward-based response
Aggregate score 5–6	Medium	Key threshold for urgent response
Aggregate score 7 or more	High	Urgent or emergency response

Fig.1. *EWS aggregate scores and responses*

TABLE I. The EWS scoring system

Parameters	***Score***						
	3	***2***	***1***	***0***	***1***	***2***	***3***
Respiration rate (per minute)	≤8		9-11	12-20		21-24	≥25
SpO_2	≤91	92-93	94-95	≥96			
Systolic blood pressure (mmHg)	≤90	91-100	101-110	111-219			≥220
Pulse (per minute)	≤40		41-50	51-90	91-110	111-130	≥131
Temperature (°C)	≤35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥39.1	

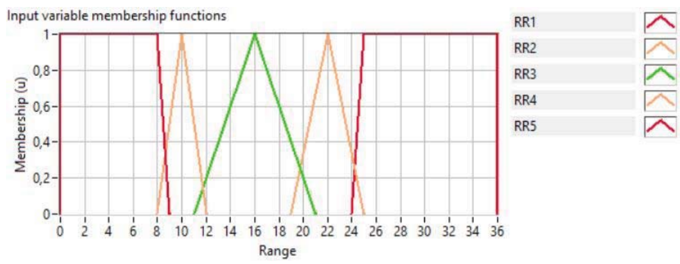


Fig.2. *Membership functions for respiration rate*

The output variables are instead represented only by triangular functions, as it is shown in Fig.3. In order to recall the aggregate scores described in Table I, the functions are defined within the range {0-7}.
Once the functions have been created for all the physiological parameters, they need to be correlated with each other by means of the *if-then* rules. Let us call p the number of physiological parameters and f the number of functions for each of them. The number of rules r is given by

$$r = p^f \qquad (1)$$

Since, in this case, for each vital parameter a number of function equal to five has been chosen, the total number of rules is equal to 3.125. As the implementation of such a high number of rules involves a considerable burden, whether at the debug or testing stage, a coupling of up to two physiological parameters at a time was preferred.

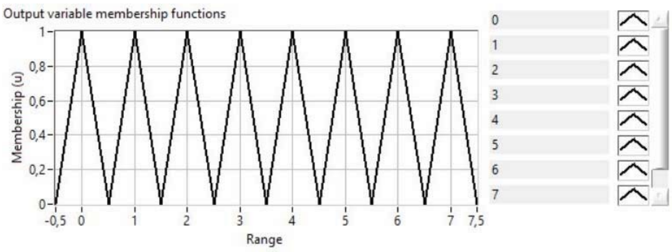


Fig.3. *Membership functions for score*

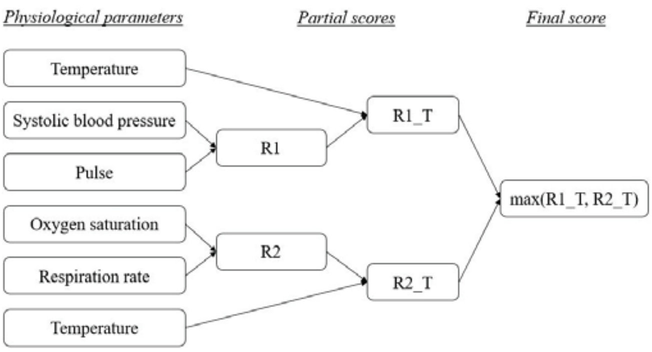


Fig.4. *Synthetic scheme of the algorithm*

In particular, according to the opinion of a medical team, following their clinical observation method, the couplings are as follows:

- Systolic blood pressure + Pulse;
- Oxygen saturation + Respiration rate.

Since the temperature is the last parameter to be taken into consideration, it will be coupled with both results of the above said couplings. The final score will be the maximum value between the results coming from the temperature and the previous coupling combination. This method allows to considerably reduce the number of rules without neglecting the desired correlations. The whole algorithm is synthetized in Fig.4.
A rule is a relationship between input and output variables. It will take the following syntax:

IF *Oxygen Saturation* is S*p3* AND *Respiration rate* is *RR2* THEN *R2* is *5*

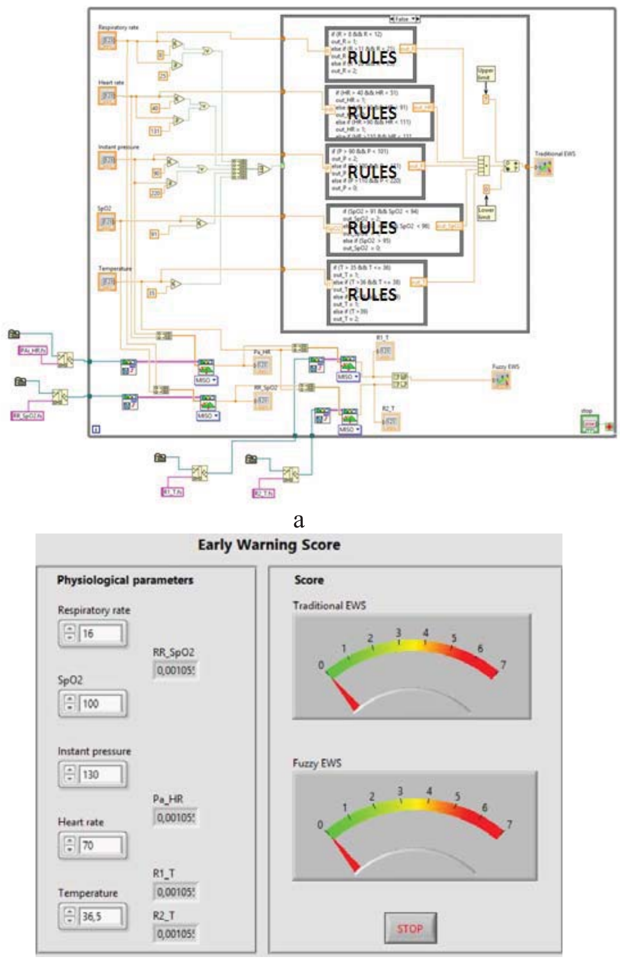
The defuzzification method used to convert the output variables into crisp numerical values is the Center of Area, which calculates the centroid under the weighted sum of the results. This method is the best tradeoff between multiple output linguistic terms.

In order to evaluate the algorithm, a Graphical User Interface in LabVIEW environment has been developed. As it is shown in Fig.5, on the left panel it is possible either to set the values for each physiological parameter manually or get them through a data acquisition (DAQ-6009) board. Moreover, numerical indicators reporting the partial score obtained from the above described couplings can be found. On the right panel, instead, the scores obtained from the standard and the fuzzy methods are compared.

The system was tested by setting a set of some vital parameters as shown in Table II. In the first row we can observe an alteration of three parameters, namely respiration rate, pressure, and pulse. In this case, the standard EWS method produced a score of 2, differently from the fuzzy method which produced a score equal to 4. Increasing the temperature by 2 °C both methods indicate an increase in the score by one point.
In the third and fourth row, instead, the predictivity of the algorithm is appreciated. In the two cases an alteration of oxygen saturation along with a high pulse can be observed. In the first case the traditional method indicates a score of 3, while the fuzzy one gives the score of 4. When increasing the pulse rate, the traditional method does not vary; conversely, with the fuzzy method a clinical degeneration shifting from a score of 4 to a score of five can be noticed.

TABLE II. A COMPARISION BETWEEN THE TRADITIONAL EWS SCORE AND THE FUZZY SCORE

Parameters					*Score*	
Respiration Rate	*SpO$_2$*	*Pressure*	*Pulse*	*Temperature*	*Traditional*	*Fuzzy*
20	*100*	*150*	*124*	*36.5*	*2*	*4*
20	*100*	*150*	*124*	*38.5*	*3*	*5*
12	*94*	*130*	*124*	*36.5*	*3*	*4*
12	*94*	*130*	*126*	*36.5*	*3*	*5*
21	*97*	*200*	*70*	*37.5*	*2*	*4*



a

b

Fig.5. *Implementation of the virtual biosensors for the estimation of medical precursors: a) Labview routine, b) front panel with aggregate scores and responses*

III. CONCLUSION

In this paper virtual biosensors for the estimation of medical precursors have been presented including the model and the implementation through a LabVIEW routine. It is worth noting that the proposed solution improves standard systems such as "track and trigger" and EWS through the adoption of the Fuzzy Set Theory in order to produce an association between the input variables and the output variable by using a data set established with the medical team. The work is in progress with a more exhaustive study based on transducers able to measure the physiological parameters of interest in the perspective to perform a clinical validation of the proposed method.

ACKNOWLEDGMENT

The authors would like to thank INTERREG Italia-Malta European Project MEDIWARN - (CUP E69F18000000005) for funding.

REFERENCES

[1] D. Dias, J. Paulo Silva Cunha, "Wearable health devices—vital sign monitoring, systems and technologies", Sensors, vol. 18, pp. 1-28, 2018.

[2] W. Q. Mok, W. Wang, S.Y. Liaw, "Vital signs monitoring to detect patient deterioration: An integrative literature review", International Journal of Nursing Practice, vol. 21, pp. 91-98, 2015.

[3] A.M. Gueli, N. Cavalli, R. De Vincolis, L. Raffaele, S.O. Troja, "Background fog subtraction methods in Gafchromic® dosimetry", Radiation Measurements, vol. 72, 2015, pp. 44-52.

[4] A. Burssens, J. Peeters, K. Buedts, J. Victor, G. Vandeputte, "Measuring hindfoot alignment in weight bearing CT: A novel clinical relevant measurement method", Foot and Ankle Surgery, vol. 22, 2016, pp. 233-238.

[5] G. Mannino, S.O. Troja, G. Asero, G. Burrafato, A.M. Gueli, R. De Vincolis, G. Stella, "3D dosimetry on Ru-106 plaque for ocular melanoma treatments", Radiation Measurements, vol. 46, 2011, pp. 2014-2019.

[6] T. Kredo, S. Bernhardsson, S. Machingaidze, T. Young, Q. Louw, E. Ochodo, K. Grimmer, "Guide to clinical practice guidelines: the current state of play", International Journal for Quality in Health Care, vol. 28, pp. 122-128, 2016.

[7] T.A. Miller, "Health literacy and adherence to medical treatment in chronic and acute illness: A meta-analysis", Patient education and counseling, vol. 99, pp. 1079-1086, 2016.

[8] Y. Khan, A.E. Ostfeld, C.M. Lochner, A. Pierre, A.C. Arias, "Monitoring of vital signs with flexible and wearable medical devices", Advanced Materials, vol. 28, pp. 4373-4395, 2016.

[9] J. Holden, L. Harrison, M. Johnson, "Families, nurses and intensive care patients: a review of the literature", Journal of Clinical Nursing, vol. 11, pp. 140-148, 2002.

[10] R. Paradiso, G. Loriga, N. Taccini, M. Pacelli, R. Orselli, "Wearable system for vital signs monitoring", Stud Health Technol Inform, vol. 108, pp. 253-259, 2004.

[11] A. Fratini, M. Sansone, P. Bifulco, M. Cesarelli, "Individual identification via electrocardiogram analysis", Biomedical engineering online, vol. 14, pp. 1-23, 2015.

[12] K.A. Reddy, B. George, N.M. Mohan, V.J. Kumar, "A novel calibration-free method of measurement of oxygen saturation in arterial blood", IEEE transactions on instrumentation and measurement, vol. 58, pp. 1699-1705, 2009.

[13] A. Cuvelier, B. Grigoriu, L.C. Molano, J.F. Muir, "Limitations of transcutaneous carbon dioxide measurements for assessing long-term mechanical ventilation", Chest, vol. 127, pp. 1744-1748, 2005.

[14] H. Krum, N. Barman, M. Schlaich, P. Sobotka, M. Esler, F. Mahfoud, "Long-term follow-up of catheter-based renal sympathetic denervation for resistant hypertension confirms durable blood pressure reduction", Journal of the American College of Cardiology, vol. 59, pp. E1704, 2012.

[15] E.A. Curran, M.J. Stokes, "Learning to control brain activity: A review of the production and control of EEG components for driving brain–computer interface (BCI) systems", Brain and cognition, vol. 51, pp. 326-336, 2003.

[16] Y. Houdas, E.F.J. Ring, "Human body temperature: its measurement and regulation", Springer Science & Business Media, 2013.

[17] N.E. Pedersen, L.S. Rasmussen, J.A. Petersen, T.A. Gerds, D. Østergaard, A. Lippert, "A critical assessment of early warning score records in 168,000 patients", Journal of clinical monitoring and computing, vol. 32, pp. 109-116, 2018.

[18] M.J. Asiain, H. Bustince, R. Mesiar, A. Kolesárová, Z. Takáč, "Negations with respect to admissible orders in the interval-valued fuzzy set theory", IEEE Transactions on Fuzzy Systems, vol. 26, pp. 556-568, 2018.

[19] https://www.weahsn.net/wp-content/uploads/NEWS_toolkit_njd_19Apr2016.pdf.