Real-Time Allergy Detection

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***Abstract*— In this paper, we tackle the problem of the food allergic detection in children, based on the analysis of the ECG signal. Through the detection of some changes of this signal, it is possible to detect any reaction before the tested subject experiments any physical reaction or any reaction that could be harmful to his/her life. To be able to realize this process in real-time and with portable devices, it is necessary to reduce the computational cost of the full process, from the ECG analysis to the allergy detection process.**

Keywords*— *Allergy detection; Shimmer; QRS complex detection; Biomedical signal processing.

I. INTRODUCTION (*Heading 1*)

Nowadays, in Ireland, 20000 children are allergic to some kinds of food. The process used to detect these allergies consists in divide the food into several doses with different sizes and give them to the children, leaving between one dose and the next one, an observation interval of 15-20 minutes. This process is called Oral Food Challenge (OFC). During the OFC, some vitals of the subject are recorded: ECG, blood pressure, blood oxygen saturation level and body temperature. Between 3% and 11% of these test end in anaphylaxis [1], which is a danger of the life of the individual if untreated; even if an anaphylaxis don't appear, the stress experienced by both the children and their families is very high. Figure 1 shows an explaining diagram of the steps taken in an OFC.

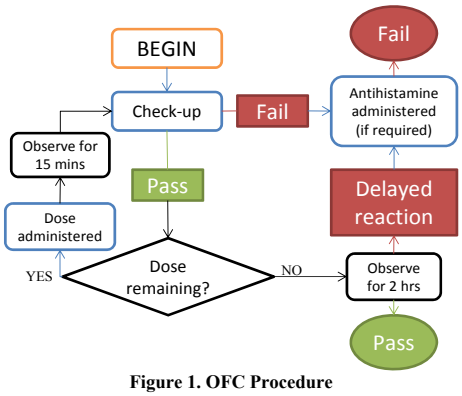

Figure 1. OFC Procedure

Currently, there is only one medical clinic in Ireland which performs allergy detections. As a result, there is a waiting list of 18 months. This fact implies a reduction of the quality of life of the patients and their families, as they are living with unverified fears of the danger of contact with a possible allergen.

This paper explains an allergy detection process based on the measure of the Heart Rate Variability (HRV) during an OFC. The main objective of this work is to reduce the duration of an OFC, thus both reducing the stress suffered by the subject as the extent of the reaction. Moreover, we expect that the existence of this improvement encourage more hospitals to offer food challenge clinics, thus reducing the current length of waiting lists.

The obtained algorithms will be implemented in a mote called Shimmer [2], and executed in real-time. Because of the use of this device, one of the main constrains of our work is the computation complexity, and the needed time to complete the process.

II. PROCEDURE

A. *Data collection*

Ethical approval was secured from the Clinical Research Ethics Committee of the Cork Teaching Hospital to monitor the subjects during the OFC. This monitoring was carried out by using a Shimmer, with which the ECG signal was acquired and sent to a PC trough a Bluetooth connection. The data was the stored in this PC. The ECG was acquired with 3 electrodes arranged in the Einthoven triangle configuration [3], with a sample frequency of 256 Hz. In this way, 24 ECG signals were obtained, 15 of which failed the tests (i.e. they were allergic to some food), and the other 9 pass the OFC. Table 1 summarizes the characteristics of the tested subjects.

B. *Features*

After the acquisition of the ECG, 18 features of the HRV were extracted off-line [4]:

- Time-domain features:
  - Mean heart rate
  - Standard deviation of heart rate
  - Coefficient of variation of heart rate
  - Root mean squared successive difference (RMSSD) of heart rate
  - Percentage of successive QRS points differ by more than 25/50 milliseconds (PNN50/PNN25) of the heart rate
  - Poincaré CSI/CVI: The cardiac sympathetic index and the cardiac vagal index.
  - Sequential trend analysis
- Frequency-domain features
  - Very Low Frequency (VLF) power (0-0.04 Hz)
  - Low Frequency (LF) power (0.04-0.15 Hz)
  - High Frequency (HF) power (0.15-0.4 Hz)
  - High to Low power ratio

Due to the fact that it was known which patient had passed or failed the OFC (the allergic patients suffered a reaction when the tests ended), the changes of each feature on each

subject were checked with the main objective of establish the differences between the allergic and non-allergic subject signals; and between a normal interval and a reaction interval.

Table 1. Characteristics of the subjects populating the allergy database

Index	Gender	Age (years)	Allergen	Result
1	male	1.5	wheat	
2	male	6	peanut	
3	male	9	egg	
4	male	1	milk	
5	male	8	peanut	
6	female	9	peanut	
7	male	6	soy	FAIL
8	male	5	peanut	
9	female	8	egg (cake)	
10	male	3	milk	
11	female	6	peanut	
12	female	5	milk	
13	female	3	milk	
18	male	8	soy	
21	female	0.75	wheat	
14	male	6	egg	
15	male	10	egg(cake)	
16	female	4	soy	
17	male	6	peanut	
19	female	1.5	milk	PASS
20	female	0.58	milk	
22	male	1	milk	
23	female	4	wheat	
24	male	2	peanut	

As is explained above, one of the main objectives is to carry out the whole process with the minimum computational cost as possible. After a previous analysis of the variation of all the features and the combination of all of them [5], it was concluded to use just one feature. Among all of them in which variations can be observed, possibly related to the existence of an allergic reaction, the chosen one must be the one that requires the lowest computational cost to be obtained: the mean of the heart rate variability (henceforth, MRR, to avoid confusion). The computation of the MRR is obtained in a window of 60 seconds with a 1-second shift.

C. QRS complex detection

The MRR is the mean of the HRV each minute, so it is based on the measure of each RR interval (heart beat durations). Based on this fact, it is necessary to detect in an accurate way each R peak of the ECG. There are a lot of proposed QRS detection algorithms, but most of them, even those that are designed to work in a real-time environment, require more computational complexity than Shimmer can afford [6–10]. Due to the requirements of our work, it is necessary to find out how to do this in an efficient way from a computational cost point of view.

To reduce low frequency noise due to interferences with the motor unit and with the respiration rate, a derivation is realised at the first point (1). To reduce the high frequency noise, integration is carried out after the derivation as equation (2) shows.

$$x[n] = ECG[n] - ECG[\mathrm{n}-2] \quad (1)$$

$$y[n] = \left(\frac{1}{N} \sum_{i=0}^{N-1} x[n-i] \right)^2 \quad (2)$$

where N is the number of samples to be integrated. This parameter depends on the sample frequency.

Once all the sources of noise are reduced, an adaptive threshold is used. This threshold can, first, avoid the detection of an artefact as an R peak; and second, detect the true R peaks. To control the value of this threshold, a state machine has been designed. This state machine is explained in the flowchart shown in Figure 2. The parameter "*ParamTH*" defines how the threshold decreases its value with each new sample of the ECG signal (State 3). This parameter depends, like N parameter, on the sample frequency, and must be selected depending on the sensitivity and the positive predictability obtained. The relationship between the state of this state machine, the value of the ECG and the value of the threshold is shown in Figure 3.

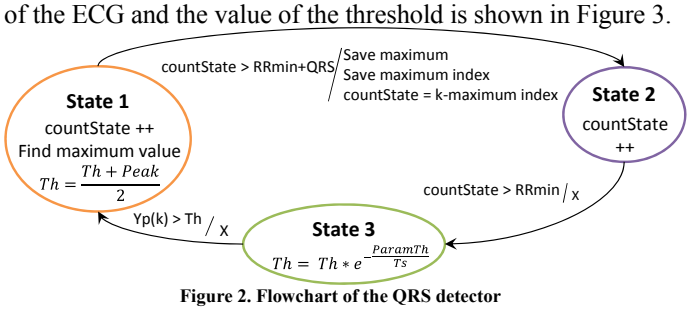

Figure 2. Flowchart of the QRS detector

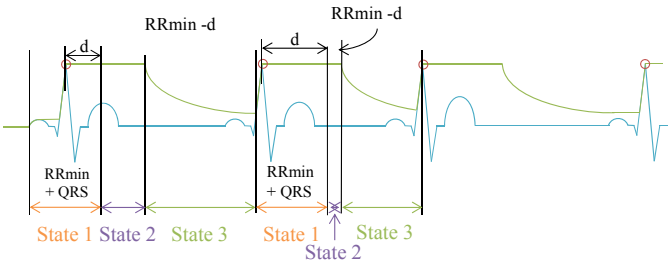

Figure 3. Relationship between the state of the state machine, the ECG and the threshold value.

In order to set parameter N and *ParamTH* values, a performance test has been carried out with 3 databases: MIT-BIH Arrhythmia Database, MITDB [11] (48 subjects, sample frequency 360 Hz), Normal Sinus Rhythm Database, NSRDB [11] (18 subjects, sample frequency: 128 Hz) and an allergy database obtained in the paediatric section of the Cork Hospital, ADB (24 subjects, sample frequency: 256 Hz). The performance test is based on the next metrics:

- True Positive (TP): R peak correctly detected
- False Positive (FP): Noise or artefact classified as R peak
- False Negative (FN): R peak no detected
- Sensitivity (Se): Percentage of all R peaks correctly detected.

$$Se = \frac{TP}{TP + FN}$$

- Positive predictivity (+P): Percentage of all the detected peaks which are R peaks

$$+P = \frac{TP}{TP + FP}$$

This test evaluates the performance of the QRS detection algorithm by obtaining Se, +P and mean (Se, +P) over all the subjects with 41 values of *ParamTh* (from 2 to 6, in steps of 0.1), and 15 values of N (from 1 to 15).

Table 2 shows the best results obtained. Figure 4 shows the values of mean (Se, +P) versus *N* and *ParamTh* values with NSRDB database; Figure 5 with ADB database; and Figure 6 with MITDB database.

Table 2. Test performance best results

Database	Fs	N	ParamTH	Se (%)	+P (%)	mean (Se, +P)
NSRDB	128	3	6.0	99.9698	99.9917	99.9808
ADB	256	6	5.9	99.4447	99.0745	99.2596
MITDB	360	10	5.4	99.4349	99.6789	99.5569

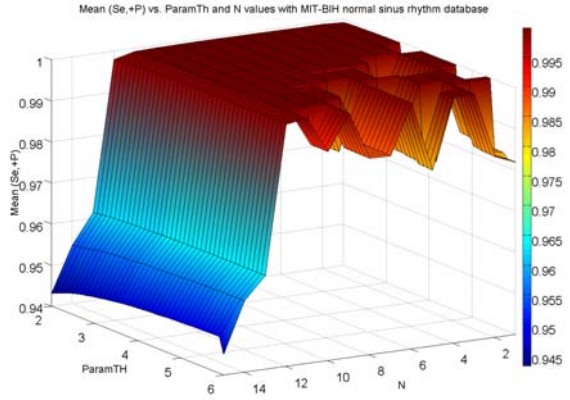

Figure 4. Test performance results with MIT-BIH Normal Sinus Rhythm Database

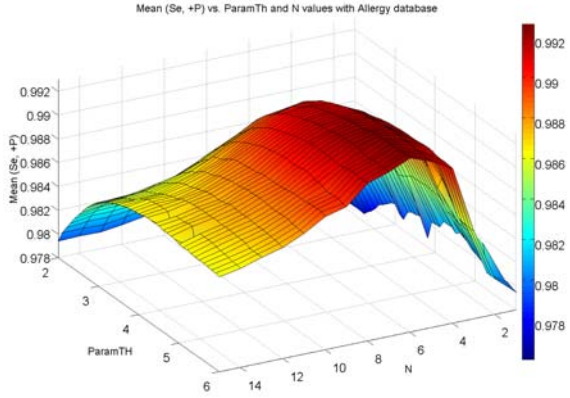

Figure 5. Test performance results with Allergy Database

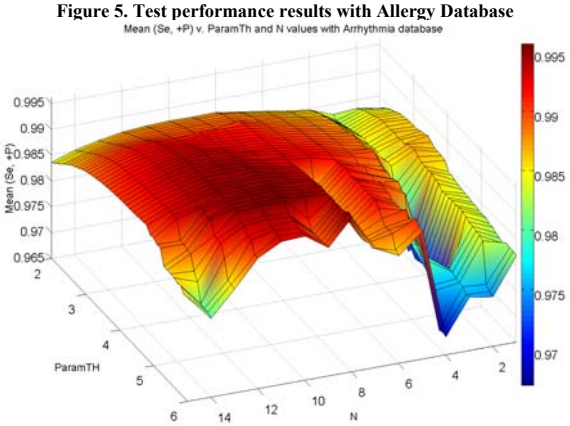

Figure 6. Test performance results with Arrhythmia Database

As we can see in Table 2 and in figures 4, 5 and 6, MITDB is the most restrictive database, so we will use *ParamTH*=5.4, as the results with NSRDB and ADB are still good with this value. *N* value will be set depending on the sample frequency used to acquire the ECG signal.

D. Allergy detection process

Before the OFC starts, there is an interval of observation of at least 10 minutes, in which the subjects do not receive any food. The signal during this interval is our background, i.e. whether or not the patient suffers an allergic reaction after these 10 minutes, the signal in this interval is a "normal" ECG signal.

The first step of the process consists in obtaining the mean of the MRR during this interval and, once the food is given to the subjects the process compares the MRR with the last mean obtained. To justify the use of the mean, it is shown at Figure 7, the MRR variation of one of the allergic subjects and, at Figure 8, the same signal of a non-allergic one. In both figures, the green zones correspond to check-up intervals. We do not analyse the MRR during the check-ups because the subject is eating and moving, and it might cause false detections as could happen at the third green zone of the Figure 7.

As can be seen, in the first case (patient 4), the variation of the MRR during a reaction is easily detected, while in the second case (patient 14), there is an important change during all the process.

The allergy detection procedure is divided into the following steps:

1. Computation of the mean of the HRV signal (MRR) in a 60 seconds window with 1 second shift.
2. After each check-up interval, computation of the MRR mean between the immediately two last check-up intervals. As a result, a signal like the green one shown in Figure 7 and in Figure 8 is obtained.
3. Computation of the absolute value of the MRR signals subtracting the last computed mean. The result of this process is the "Normalised MRR", shown in Figure 9.
4. Computation of the areas of the signal obtained in the last step.
5. Division of the areas by their length.
6. If the value of any of these areas is higher than a predetermined value, the system is detecting an allergic reaction (red zone of the Figure 9). The maximum value of the areas of each patient is depicted in Figure 10. In this figure, the values obtained with the allergic subjects are plotted in orange, while the green bars are the maximum value of the areas obtained with the non-allergic subjects. The mean of the maximum areas of the allergic subjects is 27.132, while the mean of the non-allergic ones is 8.142.

III. RESULTS

A. QRS detector results

As is explained above, the QRS detector was tested over 3 databases in order to set ParamTH and N values. Once these values are fixed, the results obtained with MIT-BIH normal sinus database are shown in

Table 3; with allergy database in Table 4; and with MIT-BIH arrhythmia database in Table 5. In these tables, subjects with sensitivity or positive predictivity with a value below 99.00% have been highlighted.

In the case of arrhythmia database, the reason of these results is that, mostly of the early peaks has low amplitude so, when this happens, they don't reach the threshold value. The state machine continues decreasing the threshold's value, so the next peak that is detected is a noise or an artefact. This adds one FP and one FN, decreasing the value both of the sensitivity and the positive predictivity (Figure 11).

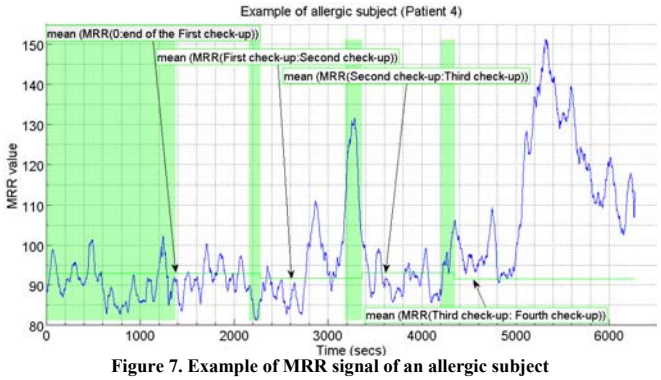

Figure 7. Example of MRR signal of an allergic subject

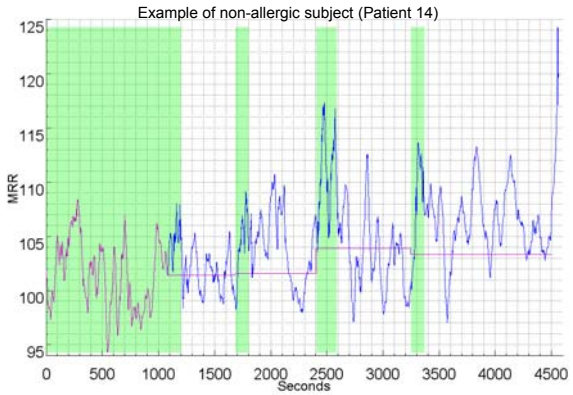

Figure 8. Example of MRR signal of a non-allergic subject

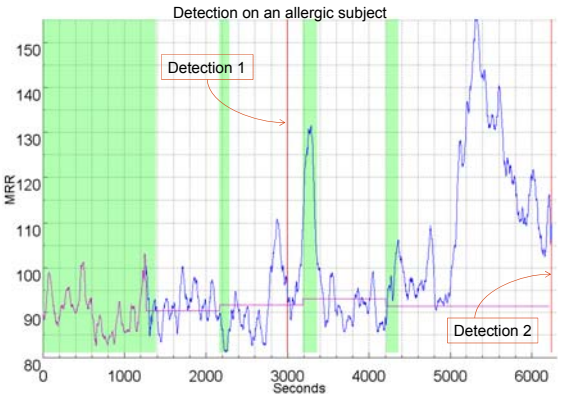

Figure 9. Example of a detection of an allergic reaction

In the case of allergy database the reason of the FP and FN occurrence is the presence of artefacts (Figure 12). Most of these artefacts are due to the subject movement. In further studies artefact detection and removal will be carry out by correlating them with the subject movement, measured by the Shimmer's internal 3-axis accelerometer.

Despite these cases, we obtain an overall result of Se = 99.63 % and +P = 99.57 %, which could be improved by selecting different values of *ParamTh* depending on the sample frequency.

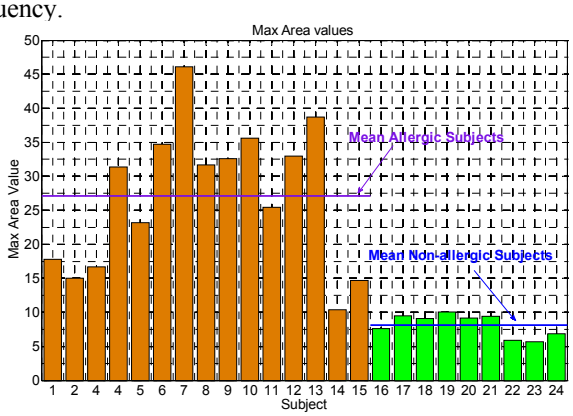

Figure 10. Maximum area value of each subject

Table 3. QRS detector results obtained with MIT-BIH normal sinus rhythm database

Sample	Duration	Total Peaks	FP	FN	TP	Se (%)	+P (%)
16265m	2:10:12	11497	0	0	11497	100,00	100,00
16272m	2:10:12	7987	23	2	7985	99,975	99,713
16273m	2:10:12	10430	1	2	10428	99,981	99,994
16420m	2:10:12	10682	1	2	10680	99,981	99,991
16483m	2:10:12	12162	2	2	12160	99,984	99,984
16539m	2:10:12	9128	0	0	9128	100,00	100,00
16773m	2:10:12	9680	0	2	9678	99,979	100,00
16786m	2:10:12	9510	1	0	9510	100,00	99,990
16795m	2:10:12	10385	2	2	10383	99,981	99,981
17052m	2:10:12	8846	2	1	8845	99,989	99,977
17453m	2:10:12	11256	0	0	11256	100,00	100,00
18177m	2:10:12	11908	0	0	11908	100,00	100,00
18184m	2:10:12	10892	0	2	10890	99,982	100,00
19088m	2:10:12	12289	4	2	12287	99,984	99,968
19090m	2:10:12	10476	1	1	10475	99,991	99,991
19093m	2:10:12	9109	0	0	9109	100,00	100,00
19140m	2:10:12	11293	0	0	11293	100,00	100,00
19830m	2:10:12	14841	0	36	14805	99,757	100,00
Total	**15:03:36**	**192371**	**37**	**54**	**192317**	**99,972**	**99,981**

Table 4. QRS detector results obtained with allergy database

Sample	Duration	Total Peaks	FP	FN	TP	Se (%)	+P (%)
1	0:14:43	2009	4	16	1993	99,204	99,800
2	1:40:19	8056	199	58	7998	99,280	97,572
3	1:34:24	8334	688	234	8100	97,192	92,171
4	1:44:29	10374	29	10	10364	99,904	99,721
5	2:13:19	9958	20	3	9955	99,970	99,800
6	0:36:06	4041	0	13	4028	99,678	100,00
7	0:57:39	5427	7	60	5367	98,894	99,870
8	1:45:58	9318	28	15	9303	99,839	99,700
9	0:50:39	4842	0	1	4841	99,979	100,00
10	1:23:47	7941	1	1	7940	99,987	99,987
11	1:25:56	7614	9	5	7609	99,934	99,882
12	0:41:04	3941	2	3	3938	99,924	99,949
13	1:46:41	11503	4	16	11487	99,861	99,965
14	2:10:12	7860	138	89	7771	98,868	98,255
15	1:42:50	9085	121	47	9038	99,483	98,679
16	2:09:10	14854	43	57	14797	99,616	99,710
17	2:11:34	11078	256	116	10962	98,953	97,718
18	0:32:43	4645	3	17	4628	99,634	99,935
19	1:51:26	14657	18	49	14608	99,666	99,877
20	0:56:40	8005	96	295	7710	96,315	98,770
21	1:37:19	9914	6	37	9877	99,627	99,939
22	1:29:55	8042	72	34	8008	99,577	99,109
23	1:03:08	5745	6	2	5743	99,965	99,896
24	1:33:09	9755	0	0	9755	100,00	100,00
Total	**10:13:10**	**196998**	**1750**	**1178**	**195820**	**99,402**	**99,114**

Table 5. QRS detector results obtained with MIT-BIH arrhythmia database

Sample	Duration	Total Peaks	FP	FN	TP	Se	P+
100m	0:30:05	2271	0	0	2271	100,00	100,00
101m	0:30:05	1864	4	1	1863	99,946	99,786
102m	0:30:05	2186	53	53	2133	97,576	97,576
103m	0:30:05	2083	0	0	2083	100,00	100,00
104m	0:30:05	2228	10	0	2228	100,00	99,553
105m	0:30:05	2572	36	14	2558	99,456	98,612
106m	0:30:05	2026	0	5	2021	99,753	100,00
107m	0:30:05	2137	0	2	2135	99,906	100,00
108m	0:30:05	1774	95	36	1738	97,971	94,817
109m	0:30:05	2531	0	3	2528	99,882	100,00
111m	0:30:05	2124	0	1	2123	99,953	100,00
112m	0:30:05	2539	0	0	2539	100,00	100,00
113m	0:30:05	1794	0	0	1794	100,00	100,00
114m	0:30:05	1879	5	0	1879	100,00	99,735
115m	0:30:05	1953	0	1	1952	99,949	100,00
116m	0:30:05	2391	4	3	2388	99,875	99,833
117m	0:30:05	1534	0	0	1534	100,00	100,00
118m	0:30:05	2278	0	0	2278	100,00	100,00
119m	0:30:05	1986	0	0	1986	100,00	100,00
121m	0:30:05	1863	1	1	1862	99,946	99,946
122m	0:30:05	2476	0	0	2476	100,00	100,00
123m	0:30:05	1518	0	3	1515	99,802	100,00
124m	0:30:05	1620	0	1	1619	99,938	100,00
200m	0:30:05	2597	0	1	2596	99,962	100,00
201m	0:30:05	1999	0	77	1922	96,148	100,00
202m	0:30:05	2135	0	6	2129	99,719	100,00
203m	0:30:05	2979	18	114	2865	96,173	99,376
205m	0:30:05	2655	0	5	2650	99,812	100,00
207m	0:30:05	2329	15	156	2173	93,302	99,314
208m	0:30:05	2953	3	17	2936	99,424	99,898
209m	0:30:05	3004	0	0	3004	100,00	100,00
210m	0:30:05	2648	3	76	2572	97,130	99,884
212m	0:30:05	2746	0	0	2746	100,00	100,00
213m	0:30:05	3249	0	8	3241	99,754	100,00
214m	0:30:05	2261	2	4	2257	99,823	99,912
215m	0:30:05	3362	0	5	3357	99,851	100,00
217m	0:30:05	2207	1	4	2203	99,819	99,955
219m	0:30:05	2153	0	0	2153	100,00	100,00
220m	0:30:05	2047	0	0	2047	100,00	100,00
221m	0:30:05	2426	0	9	2417	99,629	100,00
222m	0:30:05	2428	3	0	2428	100,00	99,877
223m	0:30:05	2604	0	5	2599	99,808	100,00
228m	0:30:05	2052	96	4	2048	99,805	95,522
230m	0:30:05	2255	0	0	2255	100,00	100,00
231m	0:30:05	1570	0	0	1570	100,00	100,00
232m	0:30:05	1779	0	0	1779	100,00	100,00
233m	0:30:05	3077	0	6	3071	99,805	100,00
234m	0:30:05	2752	3	0	2752	100,00	99,891
Total	**24:04:00**	**109894**	**352**	**621**	**109273**	**99,435**	**99,679**

B. Allergy detector results

The metrics used to evaluate the performance of the allergy detector are the following ones:

- Sensitivity: Capability of the detector to detect an allergic subject.

$$Se = \frac{TP}{TP + FN}$$

- Specificity: Capability of the detector to not classify an allergic subject as allergic.

$$Sp = \frac{TN}{TN + FP}$$

with TP: True Positives (Correctly detected allergic subjects); FN: False negatives (No detected allergic subjects); TN: True Negatives (Correct detected non-allergic subjects); FP: False Positives (Non-allergic subjects classified as allergic).

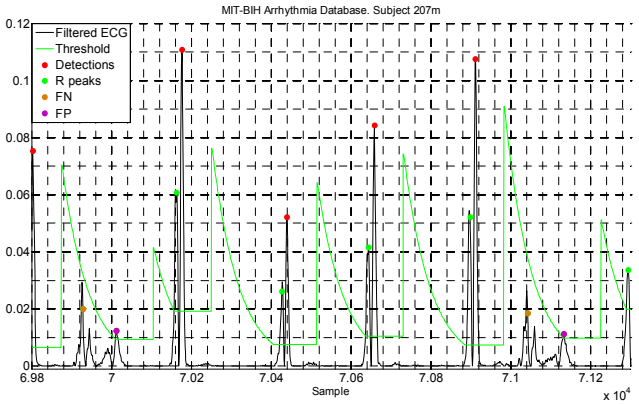

Figure 11. Example of the occurrence of FP and FN in MIT-BIH Arrhythmia Database

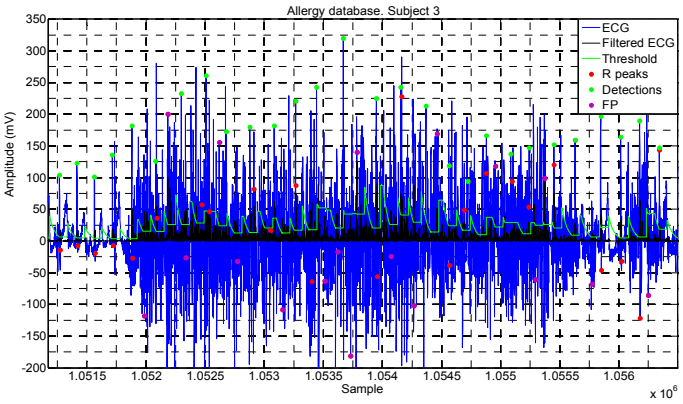

Figure 12. Example of the presence of artefacts in Allergy Database

In this process, the main objective is not to classify any non-allergic subject as allergic (i.e. obtain 100% S_p); so the criteria was chosen taking into account this fact. To differentiate between allergic and non-allergic subjects, we have set a threshold to compare the areas obtained as it is described above. The results as a function of this threshold are shown in Figure 13. As is shown, a value of this threshold between 10.08 and 10.38 allow us to obtain 100% of specificity and 100 % of sensitivity. As can be observed in Figure 10, the most restrictive subject is number 18. The maximum area value of this subject is 10.38, which is closer to the non-allergic mean max area value (8.142) than to the allergic subjects (27.13 with subject 18; 28.33 without subject 18). Another metric to take into account in this process is the time gained and the avoided doses in each one of the allergic subjects (see Table 6). As the areas are computed when the normalised MRR is 0, when a check-up starts, or when the OFC ends, subjects 1,4 and 18 have no time gained, as the max areas of these subjects happen just before the OFC ends. As can be observed in Table 6, the mean time gained taking into account all the detected subjects is 27 minutes and 50 seconds, and the avoided doses, 1.46. If we check only the subjects in which cases the allergy detector avoid any dose the mean doses avoided are 2.44. It should be noticed that the avoided doses are those that are provided in the last part of the OFC, so they are the largest ones and, therefore, those doses can induce more severe reactions. When the allergy detector does not avoid any dose, the mean time gained is 3.5 minutes. So, 3.5 minutes before there is any physic reaction, the allergy detector could generate an alarm to alert the physicians about the existence of a reaction.

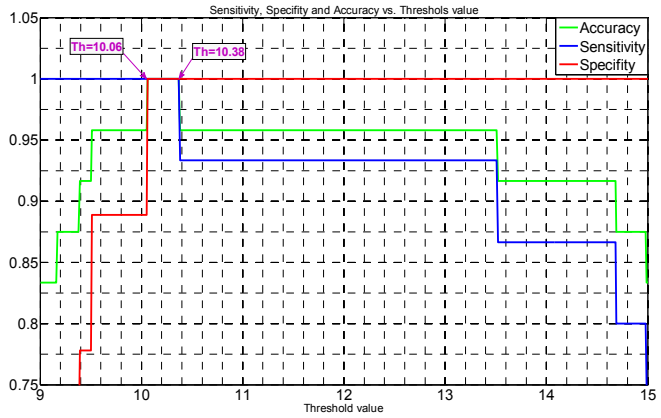

Figure 13. Sensitivity, Specificity and Accuracy vs. Threshold value

Table 6. Time gain and number of avoided doses for each subject

Subject	Time gained (min:sec)	OFC duration (hour:min)	Doses avoided	Doses taken
1	00:00	0:13	0	1
2	55:56	1:35	3	5
3	57:27	1:30	1	5
4	00:00	1:40	0	4
5	32:26	2:00	2	7
6	14:12	0:33	0	1
7	06:43	0:57	0	3
8	43:52	1:40	2	5
9	21:51	0:50	1	2
10	00:08	1:22	0	3
11	35:07	1:25	2	5
12	09:40	0:40	1	2
13	68:10	1:45	4	5
18	00:00	0:33	0	1
21	71:52	1:31	6	7
mean	**27:50**	**0:73**	**1.46**	**3.4**
mean (doses avoided)	**44:02**	**0:86**	**2.44**	**4.88**
mean (doses not avoided)	**03:30**	**0:53**	**0.00**	**2**

IV. Conclusion

A real-time allergy detector with low computation complexity has been proposed in this paper. To get the required low-complexity, a QRS detector has been also presented.

The presence of artifacts in the acquired ECG signals causes mainly the appearance of false positives, but also of false negatives, thus, reducing both positive predictivity and sensitivity of the QRS detector algorithm. In further studies, Shimmer's internal accelerometer will be used. A study will be carried out to link together the user movement with artifact appearance, trying to obtain artifact patterns for subsequent elimination of such artifacts. In this way, it aims to significantly improve the QRS detection algorithm performance. With regard to allergy detection process, it has been demonstrated its utility through its use over 24 patients who have been exposed to OFC at the paediatric section of the Cork Hospital. To confirm the proper performance of this algorithm it is important to increase the number of subjects, as well as to test the algorithm working in real-time during an Oral Food Challenge in the Hospital.

The obtained results show that, even the low-complexity of both subsystems, the full system is accurate enough to carry out the main objectives proposed at the beginning of this paper: to reduce the length of the OFC test without false detections.

Obtained results show that the number of doses are reduced to the 50% of the total ones of the allergic subjects, and the time needed to detect an allergic reaction is reduced by a factor of 0.38 in the case of all subjects; 0.51 in the cases in which, at least, one dose is avoided, and 6 % in the cases in which there are not avoided doses.

Acknowledgment

This work was supported in part by the Spanish Ministry of Economy and Competitiveness (LORIS Project, TIN2012-38080-C04-01) and by the University of Alcalá trough the FPI program.

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