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Low-Complexity Autoregressive Modeling of the Fast and Slow QT Adaptation to Heart Rate Changes.

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Abstract— **The aim is to develop a new model of the QT interval dynamics behavior related to heart rate changes. Since two kinds of QT response have been pointed out, the main idea is to split the modeling process into two steps: 1) the modeling of the "fast" adaptation, which is inspired by the electrical behavior at the cellular level relative to the electrical restitution curve, 2) the modeling of the "slow" adaptation, inspired by experiments works at the cellular level. Both are modeled as low-complexity autoregressive process whose parameters are computed using an unbiased estimator. The relevance of this approach is illustrated on several ECG recordings where the variations of the heart rate are various (rest, atrial fibrillation episodes, exercise). Significant results are obtained in agreement with the physiological knowledge at the cellular level.**

I. INTRODUCTION

The cardiac period, associated to the RR interval, is widely considered as the origin of the QT interval dynamics [1], [2]. However, the QT interval, which corresponds to the period of ventricular depolarization-repolarization, is mainly influenced by changes in heart rate in addition to the autonomic nervous activity [3], [4], [5].

The QT interval reflects the overall duration of ventricular electrical activity, and is often associated in the literature to the Action Potential Duration (APD) at the cellular level [6], [7]. Some studies have revealed both a "fast" response, and a "slow" response in the APD intervals adaptation to abrupt changes in the cardiac period [8], [9], [10]. As this phenomenon of double adaptation exists at the cellular level, it affects naturally the QT interval dynamics at the ECG level.

The QT response to changes of the heart period was studied during sudden changes by pacing [8]. It was described that 90% of QT interval adaptation to abrupt change in heart rate takes approximatively 2-3 minutes [8]. Considering the influence of preceding RR intervals, the analysis of the relationship QT/RR has been widely studied: Porta *et al.* [11] have proposed a model to quantify the dependence of the duration of ventricular repolarization towards the cardiac period, and considering other factors not directly measurable. This study is however limited under conditions of rest when there is no sudden change in heart period, and was taken over by Almeida *et al.* [12]. Considering only the stable heart periods, a different approach was proposed by Badilini *et al.* [13]. When RR intervals are changing, different works suit to this non-stationary case, such as: El Dajani *et al.* [14], who proposed a model based on neural networks, Larroude *et al.* [15], who studied the QT interval dynamics during atrial fibrillation episodes, and Pueyo *et al.* [16], [17], who proposed a model of the QT response based on the average of previous RR intervals. This latter method makes it possible to adapt a specific model for each subject. Indeed, the QT/RR relationship being different for each subject [18], it is important to model this relationship at an individual basis.

Studying the trends and the variabilities of the QT and the RR intervals, two kinds of QT response to the heart period changes are pointed out [7], [8], [9]: a "fast" phase, which occurs following few heart beats, and a "slower" phase, which occurs following a longer period. However, no study in the literature focus on these two adaptation phases in parallel. Most of them propose a modeling of the "slower" phase by characterizing the evolution of the QT intervals trend.

Therefore, a new modeling of the QT interval dynamics behavior related to the RR one is proposed in this paper. The QT interval dynamics are considered as a weighted sum of two contributions: a fast and a slow adaptation. Both are modeled as a low-complexity autoregressive process, with unknown initial conditions, whose parameters are calculated with an unbiased estimator.

The remainder of the paper is organized as follows. Section II deals with the proposed modeling of the QT adaptations. In Section III, the relevance of this new modeling is illustrated on several real ECG recordings where the variations of the RR-trend and the RR-variability are various: i) resting conditions, ii) atrial fibrillation episodes, iii) exercise conditions. Significant results are obtained in agreement with the physiological knowledge at the cellular level. Finally, a conclusion is made and some perspectives are suggested in Section IV.

II. METHOD

The QT interval response to heart period changes can be considered as a weighted sum of two contributions [9]:

- a "fast" adaptation, which focuses on the variability of QT and RR intervals,
- a "slow" adaptation, which focuses on the trend of QT and RR intervals.

The "fast" adaptation can be seen as the response to the sum of action potential of ventricular cells. So, it is closely related to the electrical restitution curve at the cellular level, which shows the positive relationship between the Action Potential Duration (APD) and the Diastolic Interval (DI) [9], [19]. The QT interval (or RT interval up to a constant) and

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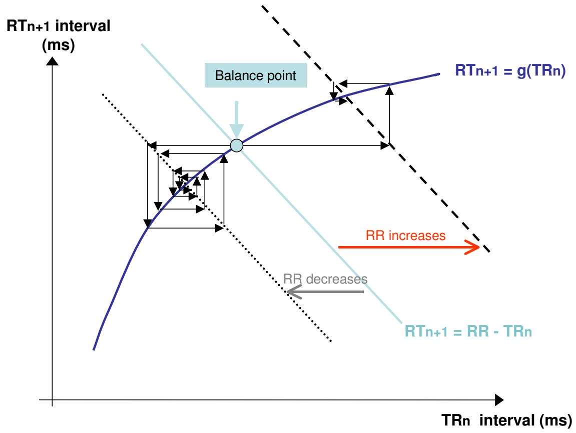

Fig. 1. Restitution curve at ECG level: analogy between the relationship "Action Potential Duration *vs* Diastolic Interval" at the cellular level, and the relationship "RT *vs* TR intervals" at ECG level.

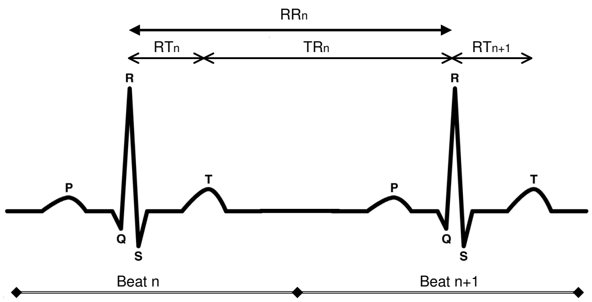

Fig. 2. Schematic representation of normal sinus rhythm showing standard waves and definition of the RR, RT and TR intervals on two consecutive cardiac beats.

the TR interval of ECG can be respectively associated to the APD interval and the DI interval at the cellular level [6], [7]. Then, the relationship between RT and TR can be represented by a restitution curve at the ECG level as in Figure 1. The definition of the notations of the intervals RT_{n+1}, $TR_n \ldots$, is presented in Figure 2. By using the restitution curve (Figure 1), it is graphically possible to put in relation the RT intervals and the cardiac period (RR intervals). Then, according to the definition of the cardiac intervals in Figure 2, we have:

$$RR_{n+1} = RT_{n+1} + TR_{n+1}, \tag{1}$$

or,

$$RT_{n+1} = RR_{n+1} - TR_{n+1}. \tag{2}$$

For a constant heart period, i.e., a fixed RR interval, there is equality between the intervals TR_n and TR_{n+1}. In this case, we can write the equation (2) as follows:

$$RT_{n+1} = RR - TR_n. \tag{3}$$

This latter relationship is represented in Figure 1 by the diagonal lines. The intersection of these lines with the restitution curve defined by $RT_{n+1} = g(TR_n)$ corresponds to the balance point for a fixed RR. We notice that from this balance point, by increasing the heart period (RR increases), the new balance point will be reached quickly, whereas by decreasing the heart period, the new balance point will be reached much more slowly since the slope of the restitution curve is greater for weak RR interval. Also, it is worth noting that if the slope of the restitution curve is greater than 1, there is theoretical instability. However, the minimal and maximal physiological values of the restitution curve are bounded by nature, there will be emergence of a limit cycle generating alternans. In case of a balance point existence (slope sufficiently low), it is possible to make a linear approximation of the restitution curve. It is assumed around the balance point that:

$$RT_{n+1} = aTR_n + b, with \;\; a > 0. \tag{4}$$

By developing this expression, we obtain a relationship between the "fast" adaptation of the RT (or QT) intervals noted RT_f (f for *"fast"*) and preceding RR intervals:

$$\begin{aligned} RT_{f\,n+1} = {} & aRR_n - a^2RR_{n-1} + a^3RR_{n-2} + \ldots \\ & + b - ab + a^2b - a^3b + \ldots, \end{aligned} \tag{5}$$

or in recursive form,

$$RT_{f\,n+1} = -aRT_{f\,n} + aRR_n + b. \tag{6}$$

Neglecting the parameter b in a first step, the filter following the relationship (6) is a high-pass filter of the form:

$$\mathbf{RT_f}(z) = \frac{a}{a+z}\mathbf{RR}(z). \tag{7}$$

Considering the input $\mathbf{RR}(z)$ as a step function, the step response of the filter is:

$$\mathbf{RT_f}(z) = \frac{az}{(a+z)(z-1)} = \frac{\alpha}{(a+z)} + \frac{\beta}{(z-1)}, \tag{8}$$

where the first term of the decomposition, $\frac{\alpha}{(a+z)}$, stands for an "oscillating part" , and the second term corresponds to a shifted step function.

Focusing only on the "oscillating part" of RT_f, which can be associated to the variability of the RT intervals, and noted RT_{hf} (hf for *"high frequency"*), we are looking for the transfer function which links the RT_{hf} and the RR, such as when the input is a step function, the output is oscillating:

$$\mathbf{RT_{hf}}(z) = \frac{\alpha(z-1)}{z(a+z)}\mathbf{RR}(z). \tag{9}$$

By proposing the previous relationship (9), it is clear that for a step input, i.e., $\mathbf{RR}(z) = \frac{z}{z-1}$, then $\mathbf{RT_{hf}}(z)$ corresponds to the oscillating part in (8). From this relationship, the recursive form is deduced:

$$RT_{hf\,n+1} = -aRT_{hf\,n} + \alpha RR_n - \alpha RR_{n-1}, \tag{10}$$

where the term $\alpha RR_n - \alpha RR_{n-1}$ can be seen as a derivative, and can be replaced by γRR_{hf}, where RR_{hf} is the variability of the RR intervals.

Finally, the "fast" adaptation of the RT (or QT) response to RR changes can be split up into:

- an "oscillating part" defined by the relation:

$$RT_{hf\,n+1} = -aRT_{hf\,n} + \gamma RR_{hf\,n}, \tag{11}$$

with a small and positive.

• a shifted step function.

In a first time, only the "oscillating part" $\hat{RT}_{hf}$ is estimated by a least squares method thanks to the observation of the variabilities of the estimated RT and the RR intervals.

The shifted step function will be integrated in the estimation process of the "slow" adaptation which is about the trend of the RT intervals, noted RT_{lf} (*lf* for *"low frequency"*). This "slow" adaptation can be considered as a low-pass filtering of the preceding RR intervals:

$$RT_{lf_{n+1}} = cRT_{lf_n} + (1-c)RR_n, \quad (12)$$

with c less than, but close to 1. This modeling allows to get a "slow" step response similar to the one obtained in the work of Franz *et al.* at the cellular level [9].

After removing the previously estimated "oscillating" part away from the RT intervals, the coefficients relative to the equation (12) and to the residual shifted step function are estimated. Finally, to construct the entire signal, the estimated "oscillating part" of the "fast" adaptation, and the estimated "slow" adaptation should be added.

In conclusion, in order to model the QT adaptation to RR changes, the estimation process is split in two steps:

- the "oscillating part" of the "fast" adaptation, looking at the variabilities of QT and RR intervals;
- the "slow" adaptation and the shifted step function of the "fast" adaptation, looking at the trends of QT and RR intervals.

III. RESULTS

The proposed modeling of the "fast" and "slow" QT adaptations to heart rate changes is applied to real ECG. First of all, a pre-processing method based on a threshold technique applied to the high-pass filtered and demodulated ECG provides us an accurate estimation of the RR intervals [20]. The QT intervals are estimated using the Improved Woody's method developed in [21]. The trends of QT and RR intervals are computed using a MA filtering with a hamming window of 25 beats, and the variabilities of the QT and RR intervals are calculated by substraction of the trends to the considered intervals.

The modeling of the QT adaptation presented in Section II is applied to:

- ECG recorded at rest (see Figure 3), where the trend of the QT intervals is well modeled, whereas the variability of the modeled QT tends to the variability of the observed one (Mean Square Error (MSE) $= 0.79$);
- ECG recorded during atrial fibrillation episodes (see Figure 4), where the trend and the variability of the modeled QT are very close to those of the observed ones (MSE $= 7.24$);
- ECG recorded during rest and exercise on a cyclo-ergometer (see Figure 5), where we observe a large error of modeling when the exercise begins. This modeling error is due to the sudden and significant drop of the RR intervals at the beginning of the exercise (MSE $= 13.86$).

In case of a sudden change of the heart rate as in exercise, a piecewise modeling process is proposed. The ECG recorded in exercise is split into two parts: the rest (from the beginning of the record until the 420^{th} beat in this example) and the exercise (after the 450^{th} beat to the end). The zone between the 420^{th} and the 450^{th} beat is excluded according to the model transition. The result of this piecewise QT adaptation modeling is presented in Figure 6. The MSE of the modeling which was equal to 13.86 considering the whole ECG, is reduced to 5.46. On this example, we observe, in particular in the exercise phase, that the variability of the QT is better preserved. Note that the estimation of the parameter a relative to the "oscillating part" in equation (11) is larger for the exercise than for the resting phase. This observation has been checked on others subjects not provided here.

According to these results, we observe that the values of the slope a are consistent with the average QT values. This observation is totally consistent with the analysis of the restitution curve at the ECG level in Figure 1: the slope a of the restitution curve is more important when the RR intervals decrease as during exercise.

IV. CONCLUSIONS AND FUTURE WORKS

The problem of modeling the QT adaptation to heart rate changes is considered. Contrary to the previous studies, the modeling focuses both on the "fast" and "slow" QT intervals adaptations. Then, a new modeling based on two processes is proposed: at first the "oscillating part" relative to the QT and RR variabilities, and secondly the "slow" adaptation relative to the QT and RR trends, are modeled. The proposed "fast" adaptation modeling is based on the electrical behavior at the cellular level relative to the electrical restitution curve. In parallel, the "slow" adaptation modeling is inspired by experiments works at the cellular level too.

The results on real ECG recordings in Section III illustrate the feasibility of the modeling of the QT adaptation to heart rate changes. Excepted in case of an abrupt change of the heart rate as in the beginning of exercise for instance, the modeling of both trend and variability of QT intervals are satisfactory according to the applications. In case of large changes in the heart rate, a piecewise modeling process is proposed assuming two stationary intervals in the cardiac period. Future works can tackle this issue: instead of considering the parameter a relative to the "oscillating part" as constant, it would be interesting to consider it time-variant. With this new adaptive parameter a_n, the modeling of the QT adaptation will be more accurate, in particular the variability.

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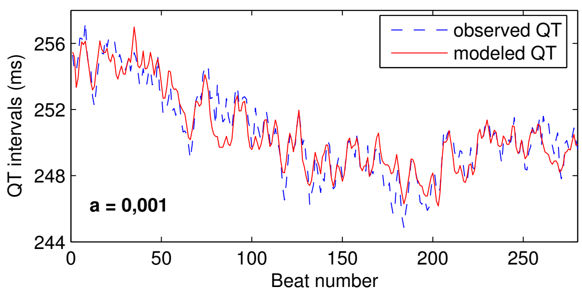

Fig. 3. Example of modeling of the QT adaptation to RR changes on a ECG recorded at rest. MSE = 0.79.

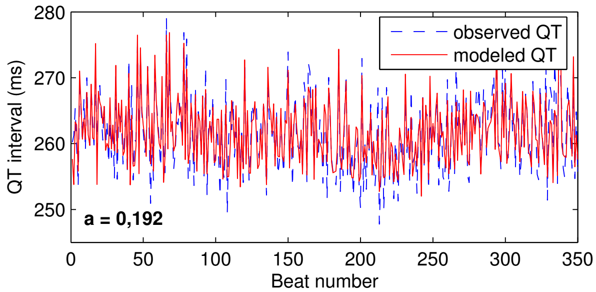

Fig. 4. Example of modeling of the QT adaptation to RR changes on a ECG recorded during atrial fibrillation episodes. Note that the trend and the variability of the modeled QT are very close to those of the observed ones. MSE = 7.24.

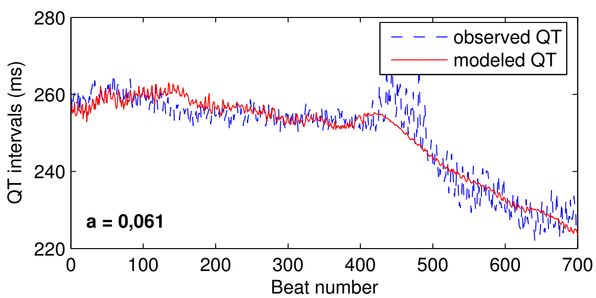

Fig. 5. Example of modeling of the QT adaptation to RR changes on a ECG recorded during exercise. We observe that the modeled QT can not really reach the observed one when the RR drop is too large in the beginning of the exercise for instance. MSE = 13.86.

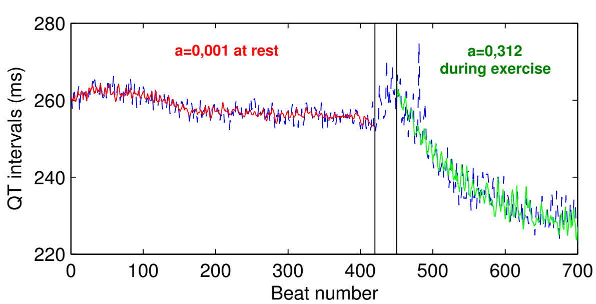

Fig. 6. Example of modeling of the QT adaptation to RR changes on a ECG recorded during exercise. Modeling by piecewise: rest part, and exercise. Exclusion zone of model transition between the two vertical lines. MSE = 5.46.

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