QT interval extraction by two-dimensional signal warping

M. Schmidt[1], M. Baumert[2], H. Malberg[1] and S. Zaunseder[1]
[1]Institute of Biomedical Engineering, TU Dresden, Dresden, Germany, Martin_Schmidt@tu-dresden.de
[2]School of Electronics and Electrical Engineering, University of Adelaide, Adelaide, Australia

Abstract

We propose a novel two-dimensional warping technique to match two one-dimensional patterns. Our approach, referred to as two-dimensional signal warping (2DSW), extends the basic ideas of known warping techniques such as dynamic time warping and correlation optimized warping. By employing two-dimensional piecewise stretching 2DSW is able to capture inhomogeneous variations of one-dimensional signals in direction of abscissa and ordinate. In order to prove the applicability of our method we apply 2DSW for tracking changes in beat-to-beat variability in QT intervals (QTV). Using simulated data we demonstrate the robustness of our approach. Analysis of long-term ECG from the DEFINITE trial on circadian rhythms demonstrated the sensitivity of the proposed algorithm to track changes in the QT interval. Using repeated measure ANOVA and Holm–Bonferroni corrected paired Student's t-test for post-hoc analysis we found statistically significant differences in QTV between 1 a.m. to 8 a.m. and 10 a.m. to 11 p.m.

1 Introduction

In signal and image processing *warping* is a well-known technique to find an optimal alignment between two patterns. By allowing certain variations to one pattern's shape, warping accounts for temporal shifts to occur within patterns. A cost function guides the search for the optimal alignment, i.e. the one that results in closely matched patterns. Warping originated from the field of automatic speech recognition, where different speeds of pronunciation of identical phoneme imposes the need for correction techniques. Dynamic Time Warping (DTW), introduced by Vintsyuk in 1968 [1], is the most famous warping algorithm. DTW performs a sample-to-sample mapping of one pattern to a reference pattern that aims at minimizing the Euclidean distance between the patterns.

The QT interval in the electrocardiogram (ECG) represents complex processes affecting the repolarization of ventricular myocardium. Changes in duration and morphology are influenced by a variety of factors. Increased beat-to-beat variability in QT intervals (QTV) was shown to be a strong predictor of cardiac mortality [2]. A major concern regarding QT variability analysis is the correct identification of subtle beat-to-beat QT interval changes. The most commonly used methods to extract the QT interval on a beat-to-beat basis are template-based methods. The adaption of the template typically relies on shifting and/or homogeneous stretching of signal excerpts to optimize the similarity between a beat under consideration and a template [3]. The QT interval can be deduced from the optimal stretching/shifting factors based on manually or semiautomatically defined QT interval borders in the template. A widely used algorithm to determine beat-to-beat QTV is the algorithm proposed by Berger *et al.* [4]. The algorithm is based on homogeneously stretching the ST-T segment of the beat under consideration until it matches best a ST-T template.

From a physiological point of view such homogeneous stretching might not be able to capture all details of morphological changes within the QT interval. Since existing warping techniques do not cover the wide spectrum of physiologically plausible variations, the aim of our work was to develop a technique that complies with the physiological reality by allowing for temporal shifts, stretches and changes in magnitude at the same time. We propose two-dimensional signal warping (2DSW) as a tool that enables complex adaptations to find alignment between two patterns. To exemplify the potential of the proposed method we apply 2DSW to measure QT variability. In the remainder we first give a brief overview on the concept of 2DSW, afterwards we explain its usage in the context of QT interval analysis and apply the technique to simulated and real data.

2 Materials and Methods

2.1 Basic concept of two-dimensional signal warping

2DSW performs the alignment between two patterns by two-dimensional inhomogeneous warping. Our approach extends the basic ideas of shifting and/or homogeneous stretching by segmenting the template with a so-called *warping grid* (see Fig. 1). The inhomogeneous deformation of patterns is realized by shifting the intersection points, so-called *warping points*, and deforming the adjacent areas. By employing two-dimensional piecewise stretching 2DSW is able to capture inhomogeneous variations of shapes. To track fiducial points, the position is marked and subsequently evaluated after deforming the template.

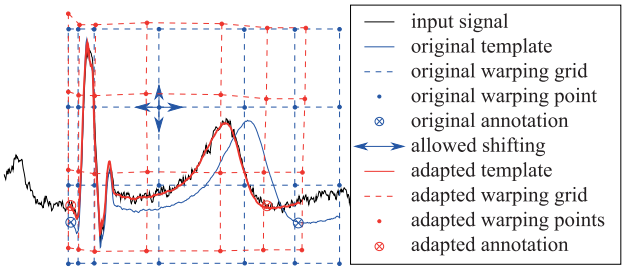


Figure 1 Concept of two-dimensional signal warping (2DSW). 2DSW allows for segmented horizontal and vertical adaptation by shifting of warping points.

Algorithmic Consideration: The *warping grid* splits the beat template in variable areas. The deformation of the areas is realized by shifting the adjacent *warping points* and deforming the adjacent areas (see Figure 2). Each data point is identified by its relative abscissa and ordinate concerning its comprising area. Shifting of *warping points* results in an deformed area. During deforming each relative abscissa and ordinate of data points remain unchanged. The shifting of *warping points* and its resulting deformation aims at minimizing the cost function between the template to be adapted and the reference waveform. As cost function we use the normalized Euclidean distance between the patterns X and Y (with identical length) given by

$$d^{(2n)}(X,Y) = \frac{\sqrt{\sum_{i=1}^{|X|}(X(i)-Y(i))^2}}{|X|}.$$

The propose algorithm results in a complex optimization problem. To deal with that problem we propose a heuristic procedure to find the optimal shifting of *warping points*. *Warping points* are sequentially shifted. The order of shifting is linear and incremented over columns first. Each *warping point* that is located above or to the right from the *current warping* point is moved indirectly in the same way.

2.2 Application to QT interval extraction

The general framework of our approach is similar to the classical template stretching approach [4]: generate a template beat, allocate the QT interval in this template, adapt the template by 2DSW to each single beat and derive from each adapted version of the template the QT interval. *Template generation*: All detected beats occurring in the first 100 s of a record are considered. If data does not contain QRS annotations, the detection algorithm by Alfonso *et al.* [5] is used. Time delay estimation by Improved Woody's Method [6] is applied to adjust the considered beats. For each beat i a predefined QT segment represented by the samples between $t_{begin,i}$ and $t_{end,i}$ is than extracted. Based on Laguna et al. [7] for $t_{begin,i}$ and $t_{end,i}$ are calculated as

$$t_{begin,i} = t_{QRS,i} - 170\ ms$$

$$t_{end,i} = \begin{cases} t_{QRS,i+1} - 240\ ms, & \overline{RR} \geq 720\ ms, \\ t_{QRS,i} + \frac{2}{3}\overline{RR}, & \overline{RR} < 720\ ms \end{cases}$$

where $\overline{RR}$ represents the mean RR-intervall over all considered beats. Based on the normalized Manhanttan distance between each QT segment and the mean QT segment of all considered beats those QT segments where excluded, which exceed a predefined threshold of 30 µV/ms. If less than 50 % of all beats remain for analysis, template construction is again evaluated on the beats of a time window which is shifted by 50 s. The predefined threshold is increased by 20 µV/ms when the end of the signal has been reached and no window with more than 50 % remaining QT segments has been found. The average of the remaining QT segments are used as beat template. For semiautomatic estimation of the QT boarders we used threshold based technique [8]. After a manual verification, the boarders are applied to the beat template.

Grid preparation: Template segmentation refers to all operations that are related to the *warping grid*. In general, 2DSW supports an arbitrary number and arrangement of horizontal and vertical segments. We divided the template in 3 homogeneous vertical segments. In horizontal direction we performed an inhomogeneous segmentation into 6 segments. The segments were fixed automatically based on piecewise linear approximation (PLA) [9]. PLA approximates a signal with straight lines by minimizing the residual. Consequently, line breaks occur where the slope of the signal changes abruptly. We established the segment borders halfway in-between the breaks of approximation lines so that each segment contains some variation in the derivative. The warping range for each point *warping point* in each direction was 20 % of the distance to its neighboring *warping point* in that direction. The temporal resolution for shifting warping points is, depending on the sampling rate, 1 sample. The amplitude resolution was set to 1 µV.

QT interval calculation: Based on the location of the defined QT borders in the optimally warped template the QT interval of the current beat is extracted. To exclude poor matched waveforms caused by noise or ectopic beats from further analysis we calculate the normalized Manhattan distance between the adopted template and the reference waveform. A beat is excluded if the normalized Manhattan distance exceeds 50 µV/Sample. Further information on 2DSW (mathematical consideration, algorithmic implementation) are given in [10].

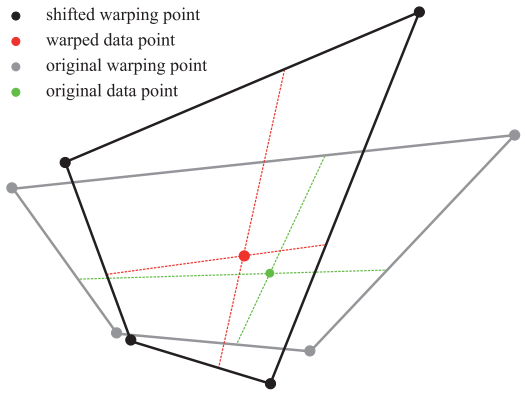
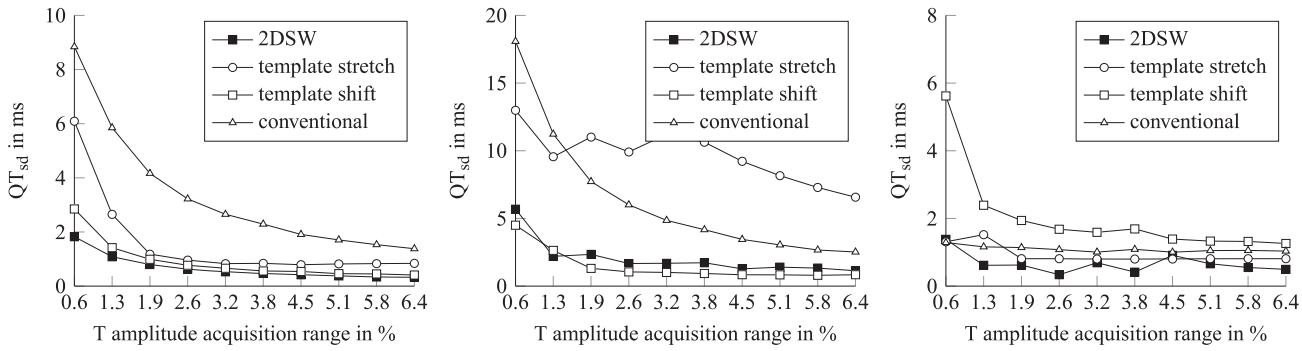


Figure 2 Area before (gray) and after (black) shifting the adjacent *warping points*. Relative abscissa and ordinate is visualized in dashed lines (green - before, red - after warping).



(a) white Gaussian noise. (b) baseline wander. (c) amplitude modulation.

Figure 3 Results obtained with the 2DSW algorithm in comparison to previously published algorithms using simulated data.

2.3 Data

To evaluate the performance of our method with respect to accurateness against typical factors known to affect QT measurement we used simulated data previously described by Porta et. al. [11]. Briefly, a simulated ECG is composed of a single heart beat, which was repeated 500 times (the single beat was extracted from lead II of an ECG recorded at 1000 Hz with 12 bit amplitude resolution). The degree of difficulty to determine the QT interval was varied by lowering the T-wave amplitude A_T of the template beat in steps of 1/10 A_T to 1/10 A_T. Thus, 10 recordings of decreasing T-wave amplitude were obtained. Additionally noise factors, namely white Gaussian noise, baseline wander or sinosoidal amplitude modulation of heart cycles, were introduced resulting in a total of 30 recordings overall. As a single heart beat was used one would ideally expect an algorithm to measure a variability of found QT intervals QTV equal to 0. Baumert et al. [3] compared three algorithms, template stretch [4], template shift [12] and a conventional (derivative) approach [11], and showed that using these data the template based algorithms outperform the other method in most cases.

The Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial randomized 458 patients with nonischemic dilated cardiomyopathy and a left ventricular ejection fraction <36 % to receive standard medical therapy with or without an ICD [13]. For long-term evaluation we used 120 exemplary Holter ECGs (recorded at 500 Hz) from the DEFINITE trial provided by the Telemetric and Holter ECG Warehouse dataset (E-HOL-03-0401-017). Because of highest amplitude of T-wave we used pseudo-orthogonal lead bipolar Z. To prove the flexibility of 2DSW we analyzed the long-term ECGs with focus on circadian rhythms. Therefore, we calculated several QT parameters from date-time aligned QT interval series: hourly mean QT interval (QT_{mean}), hourly QT standard deviation (QT_{sd}), hourly Bazett's corrected mean QT interval (QTc_{mean}) [14] and hourly squared coefficient of variation (QT_{SCV}). In comparison we also calculated hourly mean (RR_{mean}), hourly standard deviation (RR_{sd}) and hourly squared coefficient of variation of (RR_{SCV}) time series. To quantify the relative magnitude of QT interval changes compared to heart rate variability we calculated Berger's QT variability index (QTVI) [4]. To test calculated hourly parameters on statistical differences we applied repeated measures analysis of variance (rANOVA) and paired Student's t-test with Holm–Bonferroni correction.

3 Results

Figure 3 shows the results that have been obtained by applying 2DSW to simulated data. Our results are compared to those presented in [3]. Our algorithm outperforms the other algorithms in the presence of white Gaussian noise and ECG amplitude modulation. It performs second best during simulated baseline wander. Taken together 2DSW measures 30 % lower QTV than the second best method (paired one-tailed Student's t-test: $p < 0.05$).

Table 1 Results of repeated measures analysis of variance (rANOVA) of hourly segments.

Parameter		***p*-rANOVA**
QT_{mean}	mean QT interval	< 1E-05
QTc_{mean}	Bazett's corrected mean QT interval	0.47
QT_{sd}	standard deviation of QT series	0.06
QT_{SCV}	SCV of QT series	1.00
RR_{mean}	mean RR interval	< 1E-05
RR_{sd}	standard deviation of RR series	< 1E-05
RR_{SCV}	SCV of RR series	< 1E-05
QTVI	Berger's QT variability index	0.09

Table 1 shows the results of the rANOVA between the hourly calculated parameters. The paired Student's t-test showed statistically significant differences ($p < 0.05$, Holm–Bonferroni corrected) between 1 a.m. to 8 a.m. and 10 a.m. to 11 p.m. in QT_{mean} and RR_{mean} and between 8 a.m. and 4 p.m., 5 p.m., 7 p.m., 9 p.m. and 11 p.m. for RR_{sd}. Figure 4 shows our results of QT_{mean} compared with the results of Jensen et al. from 20 healthy subjects [15]. In both curves a characteristic increase between 10 p.m. and 8 a.m. occurs. The standard error of hourly QT_{mean} seems to be higher in our results, which can be attributed to the larger and more inhomogeneous population. Characteristic curves of non significant QT parameters could also be reproduced (not shown here).

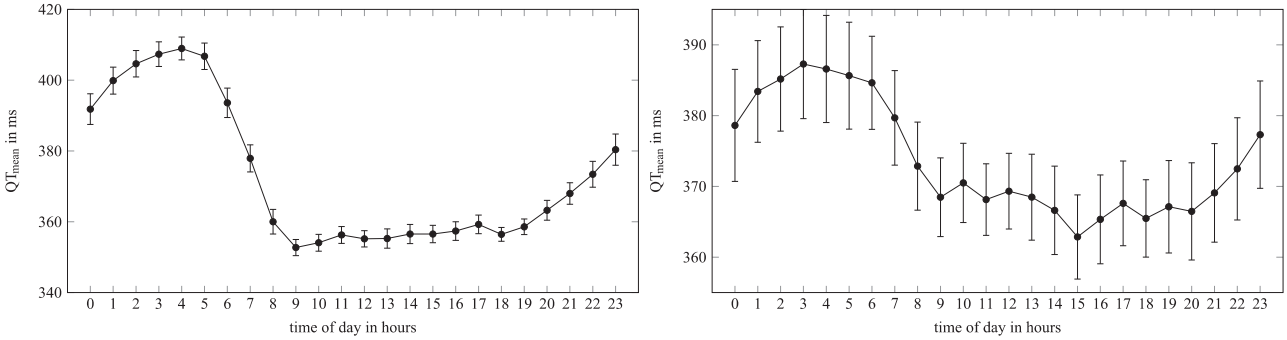


Figure 4 Comparison of the extracted circadian rhythms of the hourly mean QT interval between the results of Jensen *et al.* (left) [15] from healthy subjects and 2DSW results from the DEFINITE trial (right). Shown in hourly group mean and standard error of hourly group.

4 Discussion and Conclusion

Our method proves to be very effective for QT interval extraction. Using simulated data 2DSW outperforms in most cases established algorithms. Using long-term recordings of the DEFINITE trial we demonstrated the adaptability of our approach to measure circadian changes in the QT interval. Taken together, sensitivity and increased robustness, 2DSW is a very promising approach for QT interval extraction.

Even in other fields where two-dimensional variations occur to one-dimensional signals, 2DSW might become a valuable tool for signal analysis. Our future work thus will focus on the application of the proposed method for risk stratification by employing long-term ECG as well as the application of 2DSW to other signals.

5 References

[1] T. K. Vintsyuk, "Speech discrimination by dynamic programming," *Cybernetics*, vol. 4, no. 1, pp. 52–57, 1968.

[2] G. Piccirillo, D. Magrì, S. Matera, M. Magnanti, A. Torrini, E. Pasquazzi, E. Schifano, S. Velitti, V. Marigliano, R. Quaglione, and F. Barillà, "QT variability strongly predicts sudden cardiac death in asymptomatic subjects with mild or moderate left ventricular systolic dysfunction: a prospective study.," *Eur Heart J*, vol. 28, no. 11, pp. 1344–1350, 2007.

[3] R. D. Berger, E. K. Kasper, K. L. Baughman, E. Marban, H. Calkins, and G. F. Tomaselli, "Beat-to-Beat QT Interval Variability: Novel Evidence for Repolarization Lability in Ischemic and Nonischemic Dilated Cardiomyopathy," *Circulation*, vol. 96, no. 5, pp. 1557–1565, 1997.

[4] V. X. Afonso, W. J. Tompkins, T. Q. Nguyen, and S. Luo, "ECG beat detection using filter banks," *IEEE Trans. Biomed. Eng.*, vol. 46, no. 2, pp. 192–202, 1999.

[5] A. Cabasson and O. Meste, "Time Delay Estimation: A New Insight Into the Woody's Method," *IEEE Signal Process. Lett.*, vol. 15, pp. 573–576, 2008.

[6] P. Laguna, G. B. Moody, J. García, A. L. Goldberger, and R. G. Mark, "Analysis of the ST-T complex of the electrocardiogram using the Karhunen—Loeve transform: adaptive monitoring and alternans detection," *Med. Biol. Eng. Comput.*, vol. 37, no. 2, pp. 175–189, 1999.

[7] P. Laguna, R. Jané, and P. Caminal, "Automatic Detection of Wave Boundaries in Multilead ECG Signals: Validation with the CSE Database," *Comput. Biomed. Res.*, vol. 27, no. 1, pp. 45–60, 1994.

[8] E. J. Keogh and M. J. Pazzani, "Derivative Dynamic Time Warping," in *In First SIAM International Conference on Data Mining*, 2001.

[9] M. Schmidt, M. Baumert, A. Porta, H. Malberg, and S. Zaunseder, "Two-dimensional warping for one-dimensional signals — Conceptual Framework and Application to ECG Processing," *IEEE T SIGNAL PROCES*, Submitted.

[10] A. Porta, G. Baselli, F. Lambardi, S. Cerutti, R. Antolini, M. D. Greco, F. Ravelli, and D. G. Nollo, "Performance assessment of standard algorithms for dynamic R-T interval measurement: comparison between R-Tapex and R-Tend approach," *Med. Biol. Eng. Comput.*, vol. 36, no. 1, pp. 35–42, 1998.

[11] M. Baumert, V. Starc, and A. Porta, "Conventional QT Variability Measurement vs. Template Matching Techniques: Comparison of Performance Using Simulated and Real ECG," *PLoS ONE*, vol. 7, no. 7, p. e41920, 2012.

[12] V. Starc and T. T. Schlegel, "Real-time multichannel system for beat-to-beat QT interval variability," *J. Electrocardiol.*, vol. 39, no. 4, pp. 358–367, 2006.

[13] A. Kadish, A. Dyer, J. P. Daubert, R. Quigg, N. A. M. Estes, K. P. Anderson, H. Calkins, D. Hoch, J. Goldberger, A. Shalaby, W. E. Sanders, A. Schaechter, and J. H. Levine, "Prophylactic Defibrillator Implantation in Patients with Nonischemic Dilated Cardiomyopathy," *N. Engl. J. Med.*, vol. 350, no. 21, pp. 2151–2158, 2004.

[14] H. C. Bazett, "An analysis of time relations of electrocardiograms.," *Heart*, no. 7, pp. 353–370, 1920.

[15] B. T. Jensen, C. E. Larroude, L. P. Rasmussen, N.-H. Holstein-Rathlou, M. V. Hojgaard, E. Agner, and J. K. Kanters, "Beat-to-Beat QT Dynamics in Healthy Subjects," *Ann. Noninvasive Electrocardiol.*, vol. 9, no. 1, pp. 3–11, 2004.