Symmetric Projection Attractor Reconstruction: Inter-Individual Differences in the ECG

Jane V Lyle[1], Manasi Nandi[2], Philip J Aston[1]

[1] University of Surrey, Guildford, UK
[2] King's College London, London, UK

Abstract

The electrocardiogram (ECG) appears highly individual in nature. By applying the Symmetric Projection Attractor Reconstruction (SPAR) method, we obtain a unique visualisation of an individual's ECG and show how the subtle inter- and intra-individual differences observed may be quantified. This preliminary study supports further development of the novel SPAR approach for patient stratification and monitoring.

1. Introduction

An individual's anatomy, endocrinology, autonomic regulation and genetics all contribute to the presentation of their electrocardiogram (ECG). It is well recognised by clinicians that the ECG is influenced by various factors including sex, age and body shape [1], but the resulting differences may not be routinely incorporated into the interpretation of ECG parameters [2]. Furthermore, intra-individual variation will arise due to fluctuations in physiological factors, the presence of disease, changes in behaviour or emotion, and differences in ECG capture [3, 4]. With increasing automated analysis to support clinical decision-making and the use of the ECG in biometric identification [5], there is a renewed focus on subtle inter- and intra-individual differences in the ECG waveform.

The recently developed Symmetric Projection Attractor Reconstruction (SPAR) method [6–8] provides a novel visualisation and quantification of the waveform of an approximately periodic signal, making it an ideal technique to apply to the ECG which has a complex morphology reflecting different biological processes. SPAR analysis has previously been applied to the ECG [9, 10], where it has been shown to supplement standard assessment.

We present here a preliminary study on the unique visualisation of an individual's ECG provided by the SPAR approach and demonstrate how this can be quantified. SPAR is shown to highlight the subtle differences between healthy individuals which allows us to identify an individual using signals recorded in different sessions. We also comment on intra-individual variability and the change observed as a result of treatment with dofetilide, an antiarrhythmic medication [11] that may prolong repolarisation.

2. Methods

2.1. Clinical data

Data was obtained from the Physionet [12] *ecgrdvq* [13] and *ecgdmmld* [14] datasets. These two studies were similarly structured five period (separated by 7 day washout) crossover trials with 10 second, 12 lead, 1,000 Hz triplicate ECG recordings at baseline and post-treatment timepoints. We excluded the 4 subjects who did not complete the study and took the following Lead II signals for the remaining 40 young (19 to 35 years), healthy subjects (18 female):

- 600 (40 subjects $\times$ 5 periods $\times$ triplicate) baseline;
- 120 (40 subjects $\times$ triplicate) post-dofetilide treatment.

Due to differing dosing regimens, we used the timepoint corresponding with the mean peak serum concentration: 2.5 hours for *ecgrdvq* (21 subjects) and 13 hours for *ecgdmmld* (19 subjects).

We also obtained the interval measures provided with the original studies: RR, PR, QRS, QTc, J-T_{peak}c, T_{peak}-T_{end} (taking QTc by Fridericia's correction and J-T_{peak}c as J-T_{peak}/$RR^{0.58}$), and five novel repolarisation measures: early and late repolarisation durations, T wave amplitude, T wave symmetry and flatness [13, 14].

2.2. SPAR attractors and similarity

The SPAR method is described in [6–8] and is extended in [15]. We place $N \geq 3$ points at equal distances of $1/N$ of the average cycle length (cardiac cycle duration) of the ECG and apply Takens' delay coordinate embedding [16] to give a bounded object in N-dimensional phase space. For each N-point embedded object, we generate appropriate two-dimensional projections k where $k = 1, \ldots, \lfloor (N-1)/2 \rfloor$ which display (approximate) rotational

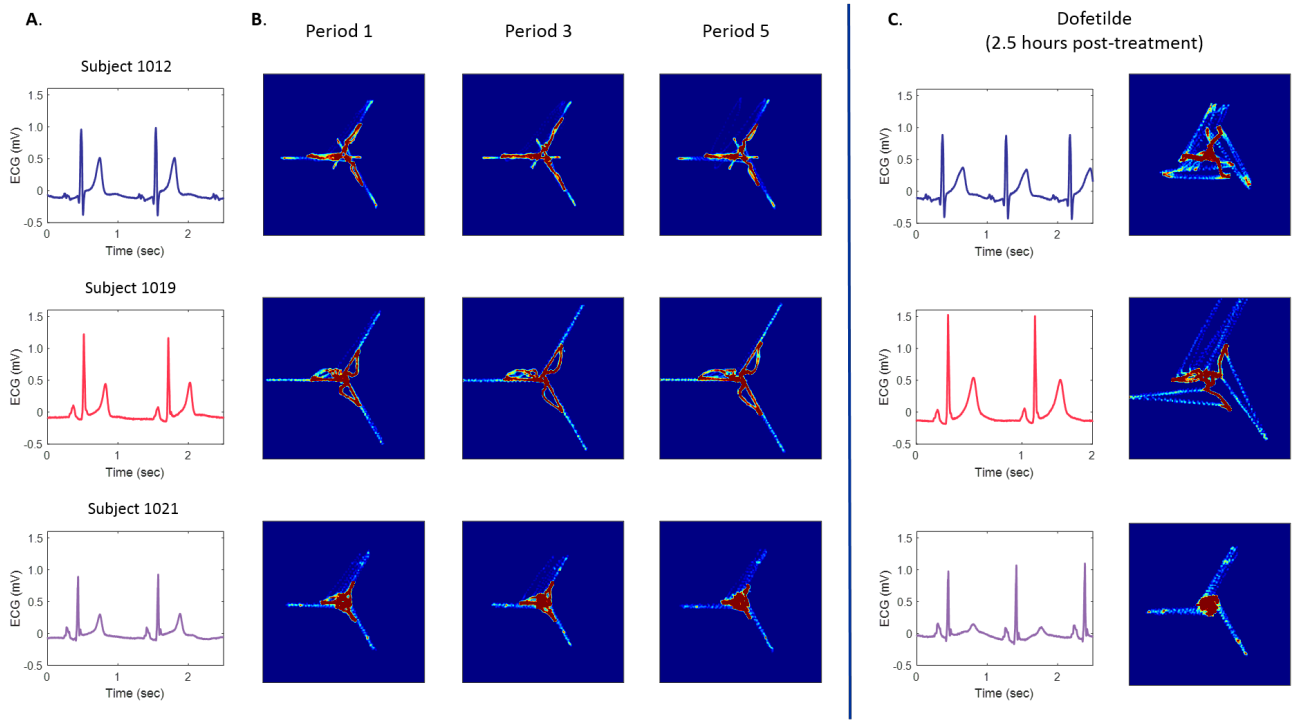

Figure 1. **A**. Excerpt of the baseline ECG (from Week 1) for three male subjects (*ecgrdvq* dataset identifier given). **B**. The $(3, 1)$ attractors generated from 10 second baseline ECG signals from periods 1, 3 and 5. **C**. The post-dofetilide ECG and $(3, 1)$ attractor for the same subjects.

symmetry. These '(N, k) attractors' encapsulate the morphology and variability of the ECG waveform.

For each ECG signal, the average cycle length was taken as the mean of the RR intervals determined by a Pan-Tompkins based algorithm [17]. No further pre-processing was applied. We then generated (N, k) attractors for each signal using $N = 3, \ldots, 10$ embedding dimensions to capture different features of the signal.

We quantified the attractor through its (r, θ) polar coordinates by determining r and θ density distributions. For the r density, we partitioned the distance from the centre to the attractor edge into 50 bins. Similarly for the θ distribution, we divided the angular direction into 100 bins. From these two distributions for each (N, k) attractor created from signal $x(t)$, we formed one attractor vector $\mathbf{d}^x_{N,k}$.

We defined the difference between two attractor vectors $\mathbf{d}^x_{N,k}$ and $\mathbf{d}^y_{N,k}$ as

$$\Delta^p_{N,k}(x, y) = \sum_{i=1}^{150} \left(|d^x_{N,k}(i) - d^y_{N,k}(i)| \right)^p$$

where our choice of $p > 0$ is problem-specific. Clearly $\Delta^p_{N,k}(x, y) = 0$ if and only if $\mathbf{d}^x_{N,k} = \mathbf{d}^y_{N,k}$. We then defined the similarity between $\mathbf{d}^x_{N,k}$ and $\mathbf{d}^y_{N,k}$ (assuming $\mathbf{d}^x_{N,k} \neq \mathbf{d}^y_{N,k}$) as

$$\lambda^p_{N,k}(x, y) = 1/[\Delta^p_{N,k}(x, y)]^2,$$

giving an increased weight to smaller differences. Finally, we determined overall similarity Λ^p between signals $x(t)$ and $y(t)$ as

$$\Lambda^p(x, y) = \sum_{N=3}^{10} \sum_{k=1}^{\lfloor (N-1)/2 \rfloor} \lambda^p_{N,k}(x, y)$$

When determining the similarity, we excluded signals from the same triplicate recording and therefore the similarity between ECGs from the same subject was obtained using only recordings from different periods.

3. Results

3.1. Inter-individual differences

Figure 1A. shows that the ECG signals of three healthy young males clearly differ. These differences are amplified by the SPAR approach. Figure 1B. shows how the attractor provides a unique visualisation for each subject that demonstrates considerable distinction between subjects. Applying a k-means clustering ($k = 3$) to the θ distributions from the baseline $(3, 1)$ attractors over the 5 periods for these three subjects indicated a natural separation of the subjects, as shown in Figure 2.

We quantified these visual observations by applying the similarity $\Lambda^p(x, y)$ measure ($p = 1/3$). Figure 3 shows

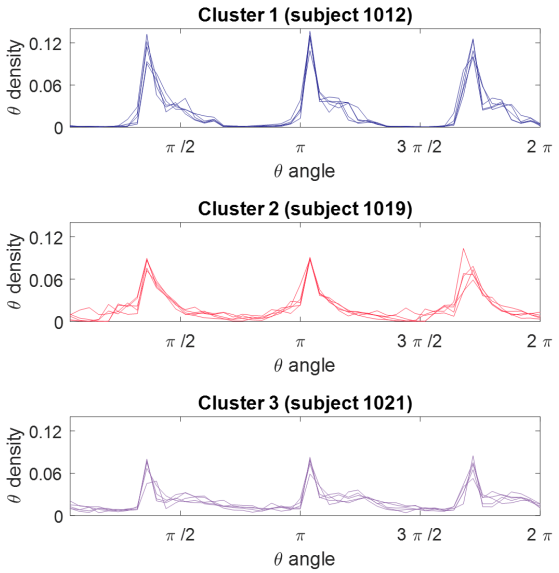

Figure 2. k-means clustering of the θ density distributions of the first $(3, 1)$ attractor over the 5 periods for the three subjects in Figure 1 shows a natural clustering by subject.

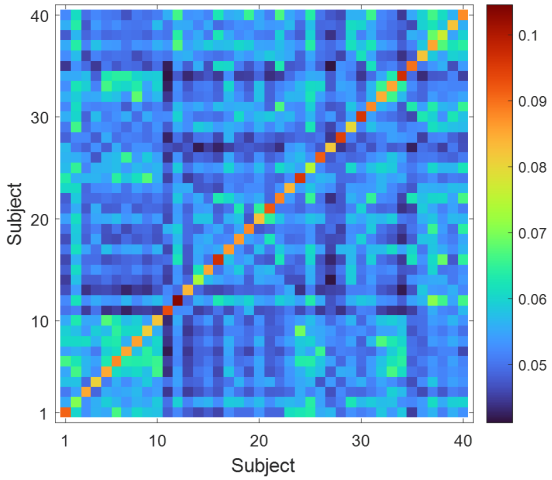

Figure 3. Baseline similarity ($p = 1/3$) between subjects, indicating that a subject is most similar to itself as the highest similarity is seen on the diagonal.

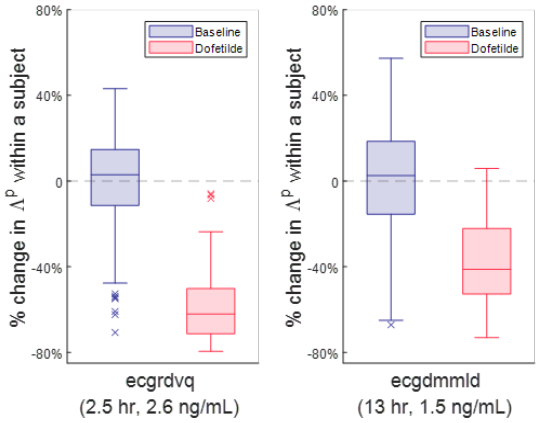

Figure 4. The percentage change from mean baseline Λ^p ($p = 1$ to optimise intra-individual similarity) for baseline and post-dofetilide records within a subject. Plots are split by database (timepoint, mean peak serum concentration).

that the highest baseline similarity was obtained within the same subject. Translating this into a simple subject identification by determining the subject from the record with the highest similarity ($p = 1/3$) provided a 94.3% correct identification over the 600 baseline ECG signals. We emphasise that this result excluded triplicate recordings from the same subject; if we included recordings from the same session, 98.7% of subjects were correctly identified.

As a brief comparison of SPAR with other metrics, we took a vector of the suitably scaled interval and repolarisation metrics and determined the similarity Λ^p, taking $p = 1/2$ to optimise the identification. Using the same approach as for the attractor similiarity, we found that the interval metrics alone gave a correct subject identification of 56.5%, whereas including the novel repolarisation metrics increased this to 80.8%.

3.2. Intra-individual differences

Whilst Figure 1A. shows a remarkable similarity within a subject over time, Figure 2 illustrates that there is some intra-individual variation within this. Figure 4 (blue) illustrates that there is considerable variation in the similarity measure between a subject's baseline records.

We then investigated how the similarity measure is affected when the ECG of a given subject is changed. Figure 1C. shows that treatment with dofetilide (which impacts the potassium ion channels of the heart) has an effect on the ECG signal, which we again see emphasised in changes within the attractor. We found that the similarity was reduced between the post-dofetilide records and the baseline of the same subject, as illustrated in Figure 4 (red). We note that where the mean peak serum concentration attained is lower (*ecgdmmld*), the plot indicates a smaller change. As in the baseline records of subject, there is also considerable variation across the post-dofetilide records.

4. Discussion and Conclusions

We have demonstrated the potential utility of the SPAR method in the intuitive visualisation and quantification of inter- and intra-individual differences in the ECG and

showed that a measure of similarity between attractors allowed us to identify a subject from their ECG. Whilst we observed some variation within the baseline attractors of a subject, we found that the similarity measure could indicate when a more significant change had occurred in the ECG signal post-treatment with dofetilide.

For inter-individual differences, we found that the SPAR similarity measure provided clear discrimination between subjects. This distinction was clearer than that obtained with standard interval and repolarisation metrics, once again showing that SPAR supplements standard assessment [9,10]. However, biometric identification studies typically apply a much larger feature set [5] supporting that the SPAR approach to encapsulate the whole waveform is more applicable here. Importantly, we only compared an ECG to signals of same subject from different recording sessions. Many biometric studies window ECG signals from the same session [5], and, in agreement with our findings, these will tend to have a higher similarity than those from separate sessions and are of less relevance to real-world applications. As SPAR provides an easily implemented means of quantifying the ECG without the challenges and bias of multiple fiducial point identification, it is a candidate for inclusion as a complementary feature in the problem of biometric identification.

Within a subject we observed variation in the baseline similiarity between sessions. To understand the clinical implications of this, further work is needed to separate the inherent natural variability of the ECG of an individual from differences due to ECG capture. Despite this variability, we still found that when a significant change occurred in the ECG of a subject (post-dofetilide treatment), a change was seen in the similarity measure, and it was found that this change was larger where a higher peak serum doeftilide concentration was reached. Whilst further work is needed to evaluate the trajectory of each subject with changing dofetilide concentration [9], the overall findings suggest that the SPAR approach may be helpful in personalising an individual patient's trajectory over time.

We chose to use only Lead II signals here as many of the potential applications of this approach are in primary care. Given that the post-dofetilide changes impact repolarisation [11], extending this work to more leads is likely to provide a more comprehensive measure of inter- and intra-individual differences. For example we have previously shown that the mid pre-cordial leads have been shown to be particularly discerning in sex classification [18].

The SPAR method was developed in response to the challenge of making better use of existing physiological waveform data. Our successful visualisation and quantification of inter- and intra-individual differences in the ECG supports further development of this novel approach for patient stratification and monitoring.

Acknowledgements

Jane Lyle is grateful for an EPSRC PhD studentship (EP/M508160/1).

References

[1] Simonson E. Differentiation Between Normal and Abnormal in Electrocardiography. 1961.

[2] Macfarlane P. The Influence of Age and Sex on the Electrocardiogram. Sex-Specific Analysis of Cardiovascular Function. 2018:93–106.

[3] Swenne C. Neurocardiological Basis for Intraindividual ECG Variability. J. Electrocardiology. 2002;35(4):239–242.

[4] Simoons ML, Hugenholtz PG. Gradual Change of ECG Waveform During and After Exercise in Normal Subjects. Circ. 1975;Oct:570–577.

[5] Ingale M, Cordeiro R et al. ECG Biometric Authentication: A Comparative Analysis. IEEE Access. 2020;8.

[6] Aston PJ, Christie M, Huang Y, Nandi M. Beyond HRV: Attractor Reconstruction Using the Entire Cardiovascular Waveform Data. Phys. Meas. 2018;39:024001.

[7] Nandi M et al. A Novel Method to Quantify Arterial Pulse Waveform Morphology: Attractor Reconstruction for Physiologists and Clinicians. Phys. Meas. 2018;39:10.

[8] Nandi M, Aston PJ. Extracting New Information from Old Waveforms. Exp. Phys. 2020;105(9):1444–1451.

[9] Lyle JV, Nandi M, Aston PJ. Investigating the Response to Dofetilide with Symmetric Projection Attractor Reconstruction of the Electrocardiogram. Comp. Cardio. 2019;45.

[10] Bonet-Luz E, Lyle JV et al. Symmetric Projection Attractor Reconstruction Analysis of Murine Electrocardiograms. Heart Rhythm O2. 2002;1(5);368–375.

[11] Roukoz H, Saliba W. Dofetilide: A New Class III Antiarrhythmic Agent. Exp. Rev. of Card. Ther. 2007;5(1):9-–19.

[12] Goldberger AL et al. PhysioBank, PhysioToolkit, and PhysioNet: Components of a New Research Resource for Complex Physiologic Signals. Circ. 2000;101(23):e215–e220.

[13] Johannesen L et al. Differentiating Drug-Induced Multichannel Block on the Electrocardiogram. Clin. Pharmacol. Ther. 2014;96(5):549–558.

[14] Johannesen L et al. Late Sodium Current Block for Drug-induced Long QT Syndrome: Results from a Prospective Clinical Trial. Clin. Pharmacol. Ther. 2016;99(2):214–223.

[15] Lyle JV, Aston PJ. Symmetric Projection Attractor Reconstruction: Embedding in Higher Dimensions. [Submitted]

[16] Takens F. Detecting Strange Attractors in Turbulence. Dyn. Sys. and Turb., Lec. Notes in Maths. 1981;898:366–381.

[17] Pan J, Tompkins W. A Real-time QRS Detection Algorithm. IEEE Trans. on Bio. Eng. 1985;BME-35(3):230–236.

[18] Lyle JV, Nandi M, Aston PJ. Symmetric Projection Attractor Reconstruction: Sex Differences in the ECG. Frontiers in Cardiovascular Medicine 2021;8:1034.

Address for correspondence:

Jane Lyle (j.lyle@surrey.ac.uk)
Dept. of Mathematics, University of Surrey, GU2 7XH, UK