SAS® System Visual Performance in Evaluating Arrhythmia Time Series

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ABSTRACT

Visualization techniques are investigated as an adjunct to analytical methods in discerning and characterizing the dynamical aspects of arrhythmia time series. Performance of the SAS graphics packages, SAS/GRAPH®, SAS/INSIGHT®, SAS/DATASCOPE®, and SAS/NVISION®, is scrutinized in melding visual acumen with statistical analysis for distilling the informational content of time series data. The data were collected in a prospective cohort study of 60 healthy adult males undertaken to characterize the spontaneous incidence and temporal aspects of ventricular arrhythmias. Ambulatory circadian recordings of the electrocardiogram, through Holter monitoring targeted for 42 consecutive days, were reduced to hourly rates of ventricular premature beats. These series were assessed for evidence of cyclical, chaotic, and noise content and for the occurrence of clustering. The illustrative, interactive, and animated visual processing, afforded by the SAS graphics packages, is demonstrated in promoting the identification of dynamical structures.

INTRODUCTION

A prospective cohort study was undertaken at the Lilly Laboratory for Clinical Research in a representative sample of its normal, healthy, adult volunteer population to characterize the spontaneous occurrence of cardiac arrhythmias. Holter monitoring, which provides ambulatory, circadian, two-channel analog recording of the electrocardiogram, is often employed in assessing the cardiac safety, or efficacy, of new drug candidates. However, due to cost and inconvenience, the natural incidence of arrhythmias in normal individuals over extended periods has not been previously studied. With the intent of establishing a control data base of arrhythmias as a standard in the clinical evaluation of cardiac electrical disturbances, a cohort of 60 healthy adult males were sequestered and monitored over a targeted period of 42 consecutive days.

The EKG recordings were scanned and reduced to hourly tallies of ventricular premature beats (VPB). The tallies were normalized to a VPB rate based on the total number of heart beats detected over the hour. Where necessary to preserve temporal ordering, missing observations were replaced by the median VPB rate. Hence, the data consisted in 60 time series with more than 1000 observations.

A primary objective in the analysis is to locate each series on the spectrum of dynamical processes that encompass ordered periodic, through deterministic chaotic, to purely random processes. Further, previous clinical experience has suggested the phenomenon of clustering; that is, sporadic activity bursts of arrhythmias. Hence, interest is also directed to determining the appearance and pattern of clustering events.

Preliminary Illustrations

Basic statistical insights into the data were assisted through the illustrations provided by SAS/GRAPH. Logarithm of the average (intra-subject) VPB rate, as a measure of arrhythmia intensity, was displayed as a scattergram over the 60 study volunteers. This illustration reveals that about 10% of the cohort separates out as a high-intensity subgroup. A log-log scatterplot of the variance versus the average VPB rate divulges a distinctively linear trend. This finding supports the tenet of an inverse-power-law relationship between variance and average. Hence, compatibility of the VPB events with a Poisson mechanism can be rejected; rather, such extra-Poisson variability suggests the prevalence of clustering.

Animated Time-Domain Visualization

To enable an overall visual inspection of the time series, SAS/NVISION was employed to provide a 3-dimensional topographical representation of the series with hour, day, and VPB rate as dimensions. A flyover this terrain permits a gestalt perception of intra- and inter-day patterns, such as circadian rhythms, clustering events, and progressive activity with study duration.

In another animation scenario, an additional dimension, representing VPB intensity, was introduced by categorizing VPB intensity into logarithmic sub-ranges. A gradation of colors was employed to correspond to the ordered intensity categories. Subsequently, a topographical tray was constructed formed by time (hour or day) along one tray-plane dimension, intensity category along a second tray-plane dimension, actual intensity along the third (cone-above-tray) dimension. Color was also superimposed on the cone to reflect the intensity category. The redundant use of space and color to capture intensity proved fruitful in quickly and easily following intensity through the animation. To facilitate detection of any temporal trend or rhythm in the VPB rate, both within- and between-days, SAS/DATASCOPE was applied in sequencing through the topographical trays by hours or by days. This multi-dimensional animation suggested the following perceptions. When circadian rhythms were present, they exhibited a pattern of increased activity in the early morning. Generally, no increasing trends in activity over days were evident to correlate with possible stress, or anxiety, with duration of ward confinement.

Dynamical Structure Detection and Classification

Analytic time-series methods, entailing estimation of the autocorrelation and spectral density functions, were pursued through SAS/ETS® for assessing process dynamics. As guides in deciphering the autocorrelation and spectral density structures, templates were composed through SAS/GRAPH as depictions of typical patterns manifest over the dynamical spectrum. Templates, constructed for a cyclical process (cosine wave), chaotic processes (Bernoulli and logistic maps), and a random process (Gaussian noise), -served in visually abetting the classification of arrhythmia series as cyclical, chaotic, or random. Further, the tests for white noise, available in the ARIMA and SPECTRA procedures, were noted as additional analytic inputs.

Clustering Assessment

To investigate the phenomenon of clustering, the arrhythmia time series were studied via SAS/INSIGHT. As a first step, the Analyze: Distribution(Y) menu options provided a convenient means of constructing the histogram of hourly VPB rates and to test the empirical distribution for agreement with an exponential distribution. Data histograms assumed the apparent form of an exponential distribution, but generally proved incompatible with it. Frequently a hump was evident in the right tail that apparently correlated with clustering in the series. As a second step, a strategy was adopted to interactively smooth the arrhythmia time series, overlay plots of the raw and smoothed series, and thereby capitalize on visual acuity in identifying sustained periods of intensified activity. Through the Analyze:Fit(Y X) menu selections, nonparametric spline and kernel smoothing fits were explored, while iterating over a variety of smoothing parameter choices. The triangular-kernel smoothing algorithm, with lowest smoothing parameter value, proved optimal in recognizing clustering events.

Animated Attractor Visualization

Usually, cyclicity in a series can be detected through standard time-series methods. By contrast, it is more challenging to discriminate a chaotic process from a random process. As an auxiliary procedure in identifying the presence of chaos, an attempt was made through SAS/NVISION and SAS/DATASCOPE to delineate the structure of the attractor for the series. An attractor in nonlinear dynamical systems is a bounded limit-point region of state space. Chaotic systems are characterized by strange attractors in which trajectories (time course of system state variables) will frequently enter, but also frequently shun, any neighborhood of a limit point. Attractor reconstruction for empirical data can be approximated by employing a phase-space paradigm via the method of delays. The dimensional axes of phase space are made to correspond to lagged variables from the series. For the arrhythmia data, a 3-dimensional phase space was formulated with dimensions corresponding to an hourly VPB rate, the first-order lagged rate, and the second-order lagged rate. The trajectory of such triples of rates, followed through sequential hourly time points, was constructed through the animation of SAS/NVISION. Random arrhythmia series were characterized by near stationarity of the trajectory, periodic series by occasional looping to and from a point of stationarity, and chaotic series by erratic motion of the trajectory within a confined region of phase space.

Another approach employed in chaos theory is to map and study the trajectory crossings of Poincare sections that pass through state space perpendicular to trajectory pathways. In a representation for such crossings of Poincare sections, SAS/DATASCOPE was applied to the phase-space scattergram (portrait) of lagged-rate triples, with color as a 4th dimension to capture serial time increments. Poincare-like sections were examined via planes, perpendicular to a coordinate axis, slicing through the portrait. The color conveys some sense of the timing aspects for the trajectory crossings through the plane. Such cross-sectional maps can convey information about the structure and dynamics of the attractor. Animation was exploited in sequencing through a series of Poincare-like sections along each of the coordinate axes in phase space.

CONCLUSIONS

The functionalities of the various SAS graphics packages proved useful in visually discerning the dynamical content of ventricular arrhythmia time series. In conjunction with the statistical evaluations, classification into the dynamic structures, cyclical, chaotic, and random, were made as well as detection of series with activity clustering. Based on this integrated visual/analytic assessment, the following preliminary classification was obtained.

	Clustering	Non Clustering	Percent
Random	28	5	55%
Cyclical	3	17	33%
Chaotic	2	5	12%
Percent	55%	45%	

REFERENCES

Denton T, Diamond G, Helfant R, Khan S, and Karagueuzian H, (1990), Fascinating Rhythm: A Primer on Chaos Theory and Its Application to Cardiology, American Heart Journal, 120, 1419-1440.

Goldberger A, Rigney D, and West B (1990), Chaos and Fractals in Human Physiology, Scientific American, 262, 43-49.

May R (1976), Simple Mathematical Models with Very Complicated Dynamics, Nature, 261, 459-467.

Ravelli F and Antolini R (1990), Complex Dynamics Underlying the Human Electrocardiogram, Biological Cybernetics, 67, 57-65.

West B (1990), Fractal Physiology and Chaos in Medicine, Teaneck NJ: World Scientific Publisher.

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Editor's Note

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