Ventricular Response in Atrial Fibrillation
A MODEL BASED ON RETARDED EXCITATION

By M. ten Hoopen

ABSTRACT
The data on durations of the intervals between successive R-R waves in the ECG from patients during atrial fibrillation, reported by Horan and Kistler (Circulation Research 9: 305, 1961) show that the larger the mean and modal value in a record the larger were the shortest and longest durations. The finding that the latter extreme was usually a few times larger than the former has been used in an attempt to organize the data with the help of a probabilistic model. It is assumed that a sequence of intervals is generated, the durations of which are symmetrically distributed, but in fibrillation the process is distorted from time to time and larger intervals occasionally occur. The effects of atrial impulses on conduction through the A-V node are discussed. A mathematical expression describing this phenomenon is derived.

ADDITIONAL KEY WORDS
A-V transmission electrocardiography arrhythmia
statistics man

Horan and Kistler (1) have made a rather extensive study of the irregularity of pulse in patients with atrial fibrillation, with particular attention to the frequency distribution of the R-R interval durations. The distribution curves differed considerably in shape; histograms had a single peak, varying from narrow to broad and tailing to the right, or were bimodal with great variation in the relative size of the two peaks. Less common configurations consisted of high plateau-like or long, low, flattened curves. Certain properties of the interval distributions were tabulated in quantitative terms, namely, mean rate, peak interval and interval span. I have attempted to relate this set of data more systematically, using a model that is characterized by a long-tailed interval distribution. In doing so, I am aware of the objection that the quantities just mentioned provide only a rough description of a particular population of intervals, because the proper shape of the interval distribution is not taken into account. I have partly compensated for this by treating the two distributions published by Macrez (2) in more detail, but wish to emphasize that the distribution of intervals is also just a first-order abstraction of the patterning of interbeat durations because a possible ordering of a sequential nature does not find expression in this way. Related to this point is the question whether the series of intervals is stationary in the mathematical sense, a property I shall assume. In fact, any deviation from stationarity complicates an analytical approach.

The problem was studied because, in spite of the reported huge variety of shapes of the distributions, the measured quantities exhibit a systematic interrelationship that may serve as a possible basis for a statistical organization of the data.

A Model

The mean interval duration of each record, the reciprocal of the mean rate, will subsequently be denoted by \( \bar{r} \), and the peak interval or the most frequent interval duration by \( \hat{r} \). The shortest and longest durations are shortened to \( \hat{r} \) and \( \hat{\bar{r}} \). In Figure 1, \( \hat{r} \), \( \hat{\bar{r}} \) and \( \hat{\bar{r}} \) have been plotted, as points, against \( \hat{r} \) and \( \hat{\bar{r}} \). In Figure 1, \( \hat{r} \), \( \hat{\bar{r}} \) and \( \hat{\bar{r}} \) have been plotted, as points, against \( \hat{r} \) for all 47 cases in Table 1 of Horan and Kistler (1), irrespective of disease, treatment, or other factors. At the risk of ignoring essential properties, for the sake of simplification I have treated all double-peaked curves with peaks at \( \hat{\bar{r}} \),

From the Institute of Medical Physics TNO, Utrecht, The Netherlands.
Accepted for publication August 22, 1966.

Circulation Research, Vol. XIX, November 1966
and \( \bar{r}_2 \) as single-peaked ones with \( \bar{r} = (\bar{r}_1 + \bar{r}_2)/2 \). The data of the two histograms given by Macrez (2) are indicated by +.

One observes that, if \( \bar{r} \) decreases, \( \bar{r}_1, \bar{r}_2 \) and \( \bar{r} \) also decrease, on the whole. Furthermore, one has the impression that the three sets of points converge to a single value for small \( \bar{r} \), and I have assumed this to be the case. The limiting time interval, which I have estimated as 0.25 sec, is probably related to the period of absolute refractoriness, which has a duration of this order. The mean \( \bar{r} \) increases when \( \bar{r} \) increases, as do \( \bar{r}_1 \) and \( \bar{r}_2 \), but the latter much more than the former. This peculiarity means that the distributions are asymmetrical to the right for low rates of the pulse, and it has been taken as a starting point for a theoretical treatment. From inspection of Figure 1 we have assumed that \( \bar{r} = 1.00 \) sec is, on the average, associated with \( \bar{r}_1 = 1.10 \) sec, \( \bar{r}_2 = 0.55 \) sec, and \( \bar{r} = 2.30 \) sec.

From the candidates for an asymmetrical interval distribution offered by the theory of probability, I have not found a convenient one that fulfilled the purpose. The model proposed possesses the required skewness to an appropriate degree. Moreover, it is based on a concept that may be appealing from a purely phenomenological point of view, as it is derived from a symmetrical (Gaussian) distribution by a retardation principle.

The model begins with a mechanism that produces a sequence of intervals, the durations of which are distributed according to a symmetrical function \( \phi(\tau) \). I have inserted a Gaussian function for \( \phi(\tau) \) which has previously been used (3) and is fully defined by only two parameters: mean \( (m) \) and variance \( (\sigma^2) \). For instance, one may think of the cumulative action of basic miniature excitations that produce a ventricular response as soon as a minimum number of them have arrived at the atrioventricular node since the last response, or as soon as their summed effect has reached a certain threshold. The responses then appear in a way that resembles a relaxation type of pulsation. If the basic excitations occur with Gaussian-distributed intervals with a mean duration of \( m/n \) and with a spread \( \sigma/\sqrt{n} \), a threshold value of \( n \) will result in Gaussian-distributed intervals with mean \( m \) and with spread \( \sigma \). Now suppose that from time to time, in an irregular fashion, this process is interrupted in such a way that the amount of excitation summed since the last response is annihilated completely. Immediately thereafter summation restarts and is eventually interrupted one or more times before the next response. Occasionally, then, intervals will occur that are longer than those given by the distribution \( \phi(\tau) \). Furthermore, one may deduce from heuristic reasoning that an excess of large intervals relative to the mean will occur since the last response is annihilated completely. Immediately thereafter summation restarts and is eventually interrupted one or more times before the next response. Occasionally, then, intervals will occur that are longer than those given by the distribution \( \phi(\tau) \). Furthermore, one may deduce from heuristic reasoning that an excess of large intervals relative to the mean will be generated. If the deletion occurs according to a Poisson process with a mean rate \( \mu \), one of the simplest possible assumptions, one can write the result-

\[ 
\text{Circulation Research, Vol. XIX, November 1966}
\]
ing interval distribution $p(\tau)$ in a compact form if expressed in the Laplace transform notation:

$$P(s) = \int_0^\infty p(\tau) \exp(-s \tau) d\tau.$$ 

In the Appendix I have derived

$$P(s) = (\mu + s) \Phi(s + \mu) \left[ \mu + s \Phi(s + \mu) \right]^{-1}$$

with

$$\Phi(s) = \int_0^\infty \phi(\tau) \exp(-s \tau) d\tau$$

and

$$\phi(\tau) = \exp[-(\tau - m)^2/2\sigma^2]/\sigma \sqrt{2\pi}.$$ 

The mean interval duration has been lengthened from a value $m$ to

$$\bar{\tau} = [1 - \Phi(\mu)] \left[ \mu \Phi(\mu) \right]^{-1}.$$ 

The peak interval $\bar{\tau}$ proves to remain about equal to $m$ for the range of parameter values at issue.

**Comparison with Experimental Data**

In accordance with the preliminary observations concerning Figure 1, I furthermore assume that if $m$ increases from the minimum value, 0.25 sec, upwards, $\sigma$ and $\mu$ increase linearly with $m$ from a value zero upwards so that for $m = 1.00$ sec, $\sigma$ equals 0.2 sec and $\mu$ equals 0.2 sec$^{-1}$.

A technical difficulty in comparing theory with experiment arises in interpreting the quantities $\tau$ and $\bar{\tau}$, the shortest and longest interval in each experiment. These are, properly speaking, defined for only a finite sample of intervals, whereas the theory deals with a continuum of interval durations. In the theory, $\tau$ and $\bar{\tau}$ have been selected deliberately as those values for which the cumulative distribution embraces 1% and 99% of the intervals, which are limits often used in statistics. Thus

$$\int_0^\tau p(\tau) d\tau = 0.01$$

and

$$\int_0^{\bar{\tau}} p(\tau) d\tau = 0.99.$$ 

After numerical evaluation of the formulae, one finds an almost linear relation between $\bar{\tau}$ and $\tau$, $\bar{\tau}$ and $\bar{\tau}$, drawn as straight lines in Figure 1. For $\tau = 0.25$ sec, $\bar{\tau}$ and $\bar{\tau}$ are, by definition, equal to 0.25 sec. For $m = 1.00$ sec one finds approximately $\bar{\tau} = 1.10$ sec, $\bar{\tau} = 0.55$ sec, and $\bar{\tau} = 2.30$ sec.

In addition I have given, in Figure 2, $\bar{\tau}$ and $\bar{\tau}$ versus $1/\tau$ (points) together with the theoretically expected relation as it follows from Figure 1.

Although not furnishing any new information, I have plotted, as did Horan and Kistler (1) in their Figure 4, the relationship $\bar{\tau}$ versus $1/\tau$ in Figure 3 (circles) obtained from their Table I. Two distinct peaks at $\bar{\tau}_1$ and $\bar{\tau}_2$ are represented by two points joined by a line. The curve was obtained from my Figure 1, and furnishes a good check.

The two histograms published by Macrez...
(2) have been replotted in Figures 4 and 5 (circles) from his Figures 1 and 2. From evaluation of $\tau$ and $\hat{\tau}$ I arrived at the following parameter values which seem to give a reasonable fit (curves), although I have not aimed at an optimum solution. As to Figure 4, I have inserted: $m = 0.68$ sec, $\sigma = 0.10$ sec and $\mu = 0.20$ sec$^{-1}$; Figure 5: $m = 0.58$ sec, $\sigma = 0.10$ sec and $\mu = 0.67$ sec$^{-1}$.

Conclusion

Data on durations of the interval between successive R-R waves of the ECG during atrial fibrillation reported by Horan and Kistler (1) have been organized with the help of a simple descriptive model. The model is based on the supposition that a sequence of events whose interval durations are distributed symmetrically round a mean value, is retarded from time to time. As a consequence, the resulting intervals are asymmetrically distributed.

One interpretation is that miniature excitatory events of unspecified nature are accumulated up to the moment that a certain number of these have arrived, after which a ventricular response follows. Events of inhibitory nature interfere in an irregular fashion; these annihilate the effects summed to that time and summation thereafter starts anew.

The use of this concept was initiated by the observation that the interval span, the mean and the peak value of the interval histograms seemed to be about linearly related to each other, and that the longest interval in most instances was rather long, compared with the shortest and mean interval.

The relation between the peak value and the mean rate was compared with the values obtained experimentally.

The two interval distributions published by Macrez (2) were analyzed and were found to fit the theory reasonably well.
Appendix

(In collaboration with H. A. Reuver)

Inhibitory events arrive according to a Poisson process with a mean frequency \( \mu \). Each time a process is set in operation that produces excitatory events occurring with an interval distribution \( \phi(\tau) \). Upon arrival of the next inhibitory event the excitatory process is restarted.

This concept is identical with the model sketched in the text if, in the absence of inhibitory action, the excitatory events occur in such a way that the sum of \( n \) subsequent intervals is distributed according to a distribution \( \phi(\tau) \).

To derive the interval distribution \( p(\tau) \) of the series of excitatory events (responses) thus formed, for convenience we use the auxiliary function \( p_k(\tau) \).

Definition: \( p_k(\tau) \) equals the probability that the interval between two successive excitatory events is in between \( \tau \) and \( \tau + d\tau \), when \( k \) inhibitory events have arrived in the interval \((0, \tau)\).

Then

\[
p_k(\tau) = \frac{1}{\mu} \phi(\tau) \exp(-\mu \tau)
\]

The other terms \( p_k(\tau) \) can be computed with the help of the function \( \pi_k(\tau) \).

Definition: \( \pi_k(\tau) \) equals the probability that the interval between the last excitatory event and the \( k \)th succeeding inhibitory event is in between \( \tau \) and \( \tau + d\tau \).

Then \( p_k(\tau) \) equals for \( k = 1 \)

\[
p_1(\tau) = \int_0^\tau p(\tau) \exp(-\mu \tau) \, d\tau,
\]

where \( \pi_k(\tau) \) can be obtained for \( k = 2 \) from the recurrence relation

\[
\pi_{k+1}(\tau) = \int_0^\tau \pi_k(t) \pi_1(\tau - t) \, dt
\]

with the annotation that

\[
\pi_1(\tau) = \mu \exp(-\mu \tau) \left[ 1 - \int_0^\tau \phi(t) \, dt \right]
\]

After elaboration and using the Laplace transform notation one finds the formula for...
P(s) as given in the text. The mean interval duration follows from
\[ \tau = \frac{dP(s)}{ds} \bigg|_{s=0} \]

References
Ventricular Response in Atrial Fibrillation: A Model Based on Retarded Excitation
M. TEN HOOPEN

Circ Res. 1966;19:911-916
doi: 10.1161/01.RES.19.5.911

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1966 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/19/5/911

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/