ABSTRACT
The ventricles of open-chest anesthetized dogs were stimulated at a constant frequency to simulate ventricular parasystole. When the stimulation frequency was approximately half the spontaneous discharge frequency of the sinoatrial node, the natural pacemaker became synchronized with the artificial pacemaker. During such entrainment, the parasystolic rhythm resembled bigeminy with fixed coupling. Numerous instances of concealed bigeminy were also observed. Characteristic changes in arterial blood pressure always accompanied the repetitive ectopic beats, and these changes in blood pressure, acting mainly through the baroreceptor reflexes, were principally responsible for the synchronization. When the cardiac autonomic neural pathways were interrupted, synchronization usually could not be achieved. The biological feedback control system producing synchronization may be represented as follows. (1) The difference in timing between the firings of the sinoatrial node and the ectopic focus is the coupling interval. (2) This interval is a determinant of the stroke volumes of the premature and the postextrasystolic beats. (3) The stroke volumes affect the arterial blood pressure. (4) The level of blood pressure influences the neural activity in the baroreceptor reflex arc. (5) This activity in turn alters the frequency of the sinoatrial node. (6) Finally, sinoatrial nodal frequency affects the coupling interval to close the feedback loop.

KEY WORDS analog computer concealed bigeminy extrasystole arrhythmia heart rate premature ventricular contraction artificial pacemaker baroreceptor reflex sinoatrial node

In the more common type of ventricular extrasystole, the coupling interval between the premature contraction and the preceding normally conducted beat tends to be fixed, whereas in parasystole the coupling interval is usually quite variable. However, numerous instances of parasystole have been reported in which there was a distinct tendency for the coupling interval to become fixed temporarily (1-6). Langendorf and Pick (4) divided such parasystoles into two groups: in group I the dominant pacemaker and the parasystolic focus are mutually protected from each other, but in group II the parasystolic impulses can reach the dominant pacemaker and reset it. In some of the cases in group I, fixed coupling was ascribed to a simple numerical relation between the basic and the parasystolic rhythms, the presumption being that such a simple relation existed solely on the basis of chance.

A sustained relation between two apparently independent rhythms is unlikely, since slight disparities very quickly evince obvious phase shifts. More probably, persistent synchronization between two rhythmically discharging foci indicates that there is some interaction responsible for the entrainment. In studies of isorhythmic atrioventricular (AV) dissociation, the baroreceptor reflexes were found to be principally responsible for synchronizing atrial and ventricular pacemakers in complete AV block (7-9). The present study was designed to determine whether a similar mechanism could account for synchronization.

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of sinoatrial (SA) nodal and ventricular parasystolic pacemaking foci.

**Methods**

Experiments were conducted on 16 mongrel dogs anesthetized with morphine sulfate (2 mg/kg, im) followed 30 minutes later by chloralose (75 mg/kg, iv) dissolved in polyethylene glycol. A tracheal cannula was inserted, and intermittent positive-pressure respiration was instituted. The chest was opened by a transverse incision at the fourth intercostal space. A bipolar electrode catheter was introduced into the right ventricular cavity to register the ventricular electrogram, and bipolar needle electrodes were placed in the left ventricular wall to permit stimulation. Blood pressure was recorded from a femoral artery with a Statham P23AA strain gauge.

The arterial blood pressure, the right ventricular electrogram, and the pacing signal were recorded on an eight-channel oscillograph (Brush Mark 200) and on analog magnetic tape (Honeywell model 7600). The right ventricular electrogram and the pacing signal also served as inputs to a parallel-logic analog computer (EAI 580). The computer was programed to measure the intervals between ventricular activations (R-R intervals) and the times from the beginning of a QRS complex to the beginning of a stimulus delivered to the left ventricle (R-St intervals). The program was a modification of one which has been described previously (7).

The left ventricle was stimulated electrically (Grass model S4) at frequencies which were approximately half the prevailing frequency of the SA node. Stimuli consisted of 3-msec square-wave pulses approximately 1 v above the diastolic threshold level. After observations were made with the autonomic neural innervation to the heart intact in nine dogs, the experimental procedures were repeated after beta-receptor blockade with propranolol (1 mg/kg, iv) and then after bilateral cervical vagotomy. The completeness of beta-receptor blockade was verified by noting the abolition of the heart rate response to strong stimulation of the right stellate ganglion (10 v, 10 Hz, 2 msec for at least 30 seconds).

**Results**

In all dogs, the experimentally produced parasystolic focus in the left ventricle evoked entrainment of the spontaneously discharging activity. A representative experiment in which three bursts of ectopic activity (manifested by the alternating short and long R-R intervals) were observed by elevations of the arterial blood pressure. Ectopic beats were evoked when the R-St interval (time from the QRS complex to the pacing stimulus) exceeded 0.17 seconds. The left ventricle was paced at 66/min. In view of the constant pacing frequency, any change in slope of the R-St tracing signifies a change in the natural heart rate. The horizontal bar in the middle of the figure indicates that portion of the experiment which is displayed in Figure 2 at a faster paper speed. The downward deflections of the time marker denote 10-second intervals.

![Figure 1](http://circres.ahajournals.org/)

**FIGURE 1**

A representative experiment in which three bursts of ectopic activity (manifested by the alternating short and long R-R intervals) were attended by elevations of the arterial blood pressure. Ectopic beats were evoked when the R-St interval (time from the QRS complex to the pacing stimulus) exceeded 0.17 seconds. The left ventricle was paced at 66/min. In view of the constant pacing frequency, any change in slope of the R-St tracing signifies a change in the natural heart rate. The horizontal bar in the middle of the figure indicates that portion of the experiment which is displayed in Figure 2 at a faster paper speed. The downward deflections of the time marker denote 10-second intervals.

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SA node within a limited range of stimulation frequencies. The precise nature of this synchronization depended on the directional change in arterial blood pressure in response to the premature ventricular contractions.

PRESSURE RISE WITH ECTOPIC BEATS

Figure 1 illustrates an experiment in which left ventricular stimulation at a fixed frequency of 66/min produced three brief episodes of repetitive ectopic beats. During each episode, there was a substantial increase in the arterial blood pressure and, concomitantly, a distinct tendency for the parasystolic rhythm to simulate closely runs of ventricular bigeminy with fixed coupling.

The disparity between the variable frequency of the SA node and the constant frequency of the artificial ventricular pacemaker is reflected by the slope of the R-St tracing (Figure 1, bottom). When the pacing frequency was exactly half the SA nodal frequency, the stimulus occurred at precisely the same point in alternate cardiac cycles, and the R-St tracing was horizontal. When the pacing frequency exceeded half the SA nodal frequency, the stimulus occurred progressively earlier in alternate cardiac cycles, and the R-St tracing had a negative slope. Conversely, when the pacing frequency was less than half the spontaneous heart rate, the slope of the R-St curve was positive.

Near the left border of Figure 1, the spontaneous heart rate was 133/min, and therefore the slope of the R-St curve was positive, reflecting the fact that the pacing frequency (66/min) was less than half the SA nodal frequency. At the beginning of this portion of the experiment, the pacing stimulus occurred very shortly after the beginning of the R wave (i.e., R-St interval = 0), and hence the ventricle was refractory. However, as the R-St interval approached 0.20 seconds, the stimuli finally became effective, and ectopic beats were elicited. The ectopic beats were manifest in two ways: (1) the R-R interval showed alternating short ("coupling interval") and long ("compensatory pause") cycles, and (2) the arterial blood pressure revealed a sharp increase in systolic, diastolic, and pulse pressures.

With the onset of the first episode of ectopic beats, the SA nodal frequency diminished until it briefly equaled twice the constant pacing frequency. This event is indicated by the initial peaking of the R-St tracing. The spontaneous heart rate continued to decline for several seconds, as manifested by the progressive reduction in R-St intervals. As the pacing stimuli began again to fall within the refractory period of the ventricular myocardium, the blood pressure fell. Shortly thereafter, the spontaneous heart rate accelerated, and the slope of the R-St tracing again became positive.

Two additional episodes of ectopic beats are evident in Figure 1. In both instances, the stimulus continued to "march through" the alternate cardiac cycles at progressively longer R-St intervals, indicating that the ventricular pacemaker did not achieve a sustained entrainment of the SA node during this portion of the experiment. However, the pronounced change in the slope of the R-St tracing during the occurrence of the ectopic beats (with the slope equal to zero for several seconds) demonstrates that there was a transient synchronization. This is analogous to "accrotchage," which is sometimes observed during AV dissociation (7).

The top two tracings in Figure 1, during that portion of the experiment indicated by the horizontal bar, are displayed at a faster paper speed in Figure 2. Also shown are the stimulus event marks (St) and the right ventricular electrogram. The first six stimuli fell during the ventricular refractory period, and no ectopic beats occurred. The arterial blood pressure varied on alternate beats, indicating that there probably was a coincidental mechanical alternans during this period.

The seventh stimulus was effective, as manifested by the inverted premature QRS complex, the shortened R-R (coupling) interval, and the change in arterial blood pressure. For a total of eleven stimuli (St1—St11), the
The electrogram tracing closely resembled bigeminy with fixed coupling. The R-R interval tracing confirmed the apparently fixed coupling interval. In Figure 2, all intervals between the ectopic beats and the preceding conducted beats were within the range of 0.24 to 0.25 seconds. St16, St21, and St26 also evoked ectopic beats, but St18, St20, St22, St23, and St25 did not. The sequence from St17 to St26 resembled "concealed bigeminy," i.e., there were sequences of odd numbers of conducted beats between ectopic beats (2, 10). From St26 to the end of the record, the arrhythmia again resembled bigeminy with fixed coupling.

By using a slightly greater stimulation frequency in this same dog, more prolonged periods of synchronization were obtained which persisted for 1-6 minutes each. Synchronization consisted of repetitive brief runs of premature contractions similar to the first of the three groups of ectopic beats in Figure 1. Each episode of ectopic beats was accompanied by a pronounced elevation of blood pressure that was in turn attended by a temporary reversal of the slope of the R-St tracing, denoting a transient deceleration of the natural pacemaker. This behavior was not appreciably modified by beta-receptor blockade with propranolol, but synchronization was subsequently blocked after bilateral cervical vagotomy.

**PRESSURE DROP WITH ECTOPIC BEATS**

The left of Figure 3 illustrates the tendency toward synchronization in a dog which responded to repetitive ectopic beats with a decline in arterial blood pressure. The cardiac autonomic reflexes were intact at this point in the experiment. At the left margin of the figure, the slope of the R-St tracing was negative, indicating that the constant ventricular pacing frequency was greater than half the spontaneous heart rate. As the pacing stimuli fell progressively earlier in alternate cardiac cycles (as denoted by the bottom tracing), the arterial blood pressure diminished. Within a few beats, the spontaneous heart rate had accelerated first to equal and then to exceed twice the fixed pacing frequency. As the slope of the R-St tracing became positive, the pacing stimuli occurred progressively later in alternate cardiac cycles, and the blood pressure again rose. Concomitantly, the R-St interval reached a peak value and then the slope again became negative. Throughout most of the experiment shown on the left of Figure 3, the R-St interval oscillated slowly.
A representative experiment in which the onset of ectopic beats was attended by a reduction in arterial blood pressure. Left: The cardiac autonomic pathways were intact, and the SA node was synchronized with the ventricular parasystolic focus throughout most of this record. Right: Propranolol was administered and both vagi were transected. The absence of synchronization is manifested by a steady decline in R-St interval, despite the pressure change attending the episode of ectopic beats.

The negative slopes of these oscillations were attended by reductions in blood pressure and the positive slopes by elevations in blood pressure. Near the middle of the last oscillation, a brief episode of concealed bigeminy occurred.

Beta-receptor blockade with propranolol did not materially alter the tendency toward synchronization which is evinced in the left of Figure 3. The right of Figure 3 was recorded after subsequent bilateral cervical vagotomy. With cardiac sympathetic and vagal pathways both blocked, the tendency toward synchronization was abolished, as manifested by the absence of any substantial change in slope of the R-St tracing, despite the presence of ectopic beats of continuously changing prematurity and a drop in blood pressure similar in magnitude to those displayed on the left of the figure.

PRESSURE RISE AND FALL WITH ECTOPIC BEATS

A portion of an experiment in which synchronization was attended by alternating periods of rises and falls in arterial blood pressure is exhibited in Figure 4. The direction of the change in blood pressure depended on whether the ectopic beats occurred early or late in the cardiac cycles. At the left border of the figure, the R-St interval increased progressively from 0.44 seconds to a maximum value of 0.72 seconds (i.e., at the end of a cycle). In other words, these stimuli produced ectopic beats with progressively longer coupling intervals, as shown by the progressive rise of the lower border of the R-R interval tracing near the left edge of the figure. The first sharp vertical deflection in the bottom tracing indicates that the next several stimuli were given very early in alternate cardiac cycles. These stimuli were obviously applied during the refractory period; the absence of ectopic beats is indicated by the first horizontal section of the R-R interval tracing. It is evident in the top tracing of the figure that during this period which was free of ectopic beats the arterial blood pressure was greater than it was during the preceding period characterized by late ectopic beats.

As the R-St interval progressively increased from zero to approach a value of about 0.32 seconds, a brief burst of ectopic beats occurred, which produced a rapid rise in the arterial blood pressure attended by an abrupt change in the slope of the R-St tracing from positive to negative. After only two or three beats, the pacing stimuli were delivered late again in alternate cardiac cycles, producing a sharp drop in the arterial blood pressure to a level below that which prevailed when ectopic beats were absent. This sequence, indicated
A representative experiment in which early ectopic beats produced an increase in arterial blood pressure but in which late ectopic beats elicited a fall in pressure. The brief bursts of early ectopic beats caused a deceleration of the SA node, as manifested by an abrupt change in the slope of the R-St tracing from positive to negative. The more prolonged bursts of late ectopic beats caused an acceleration of the SA node as manifested by a more gradual change in the slope of the R-St tracing from negative to positive. The horizontal bar in the middle of the figure indicates that portion of the experiment which is displayed in Figure 5 at a faster paper speed.

In Figure 5, the right ventricular electrogram and the stimulus event marks are also included. St₁ and St₂ were given during the refractory period, but St₃-St₆ evoked early ectopic beats attended by a significant elevation of the systolic blood pressure and the pulse pressure. The ectopic beat elicited by St₅ was an interpolated extrasystole. The abrupt deceleration of the spontaneous heart rate caused a sharp reversal of the slope of the R-St tracing, and consequently St₇ and St₈ again fell during the refractory period. St₆-St₁₅ evoked late ectopic beats accompanied by a substantial drop in the arterial blood pressure.

Subsequent to St₁₅, there was a period of about 15 cycles resembling bigeminy with fixed coupling. This sequence began at the time marked by the right end of the horizontal bar in figure 4. The R-St interval then began to increase again and a similar but briefer episode of early and late ectopic beats was repeated. Two brief intervals of early ectopic beats were then observed, followed by another sequence of early and late ectopic beats near the right border of Figure 4. In all instances, the early ectopic beats caused a rise in the blood pressure and a deceleration of the SA node, whereas the late ectopic beats produced the opposite effects.

COMPOSITE RESULTS

Of the total of 16 dogs which were studied, 4 responded to repetitive ectopic beats with a significant elevation of the arterial blood pressure (e.g., Figs. 1, 2), and 9 displayed an appreciable decline in blood pressure (Fig. 3). The remaining 3 dogs were characterized by a biphasic response, such that early ectopic beats elevated the blood pressure and late ectopic beats lowered the pressure (Figs. 4, 5).
That portion of the experiment denoted by the horizontal bar in Figure 4. St₃–St₁₃ elicited late ectopic beats, which caused a drop in arterial blood pressure and an acceleration of the natural heart rate.

Discussion

The present series of experiments demonstrates that the spontaneous SA nodal pacemaker and a fixed ventricular parasympathetic focus can become synchronized in dogs with intact cardiac reflexes. Such synchronization can be expressed as a simple numerical relation between basic and parasympathetic rhythms (4) or as “a simple mathematical relationship between the sinus and the parasympathetic intervals” (6). The studies described in this paper make it evident, however, that such a simple mathematical relation is not maintained by chance. Indeed, if the spontaneous heart rate was determined before ventricular pacing and then if the ventricles were paced at precisely half this frequency, entrainment probably would not occur. Ventricular pacing would alter the level of arterial blood pressure, which would cause a change in the SA nodal frequency, and the numerical relation would no longer be “simple.” It is evident, therefore, that some negative feedback system must be operative to sustain the synchronization. Furthermore, once synchronization had been established in any given experiment, the ventricular stimulation frequency could be varied over a small range of
values, and the 2:1 ratio of atrial to ventricular ectopic beats would persist. This finding indicates that the SA node was indeed entrained by the ectopic ventricular focus. The consequent tendency for the coupling interval to become fixed in this experimental model simulates that in group I in the classification of Langendorf and Pick (4), i.e., the group in which the dominant and the parasystolic foci are mutually protected from one another. In all the experiments in this series, the ectopic beats were followed by full compensatory pauses, except for an occasional interpolated beat. This finding indicates that the SA node was not reset by the ectopic ventricular stimulus.

The principal biological feedback control system producing entrainment in the present series of experiments can be represented by the block diagram in Figure 6. The two pacemaking sites are located in the upper left corner of the diagram. The natural pacemaker, the SA node, is responsive to a number of neural and humoral influences, whereas the ventricular parasystolic focus is relatively independent of such influences. The phase difference between the SA nodal and the parasystolic pacemakers is, by definition, the R-R interval between the conducted and the ectopic beats, the so-called coupling interval. The coupling interval is, in turn, a critical determinant of the stroke volume of both the premature and the postextrasystolic beats. Stroke volume, heart rate, and peripheral resistance are responsible for the level of arterial blood pressure; the details of this relationship will be discussed below. The arterial blood pressure affects the SA nodal frequency principally through the baroreceptor reflexes, and this interaction completes the feedback loop. There is, of course, a finite delay in the time required for a change in R-R interval to evoke an alteration in heart rate, and this delay is responsible for the periodic oscillations in the coupling intervals observed in Figures 3 and 4. The effect of this delay is analogous to that producing the periodic variations in P-R intervals which occur in isorhythmic AV dissociation (9).

The closed-loop relation between R-R interval, arterial blood pressure, and heart rate depicted in Figure 6 produces the entrainment of the variable-frequency SA node by the fixed- or relatively fixed-frequency parasystolic focus. The precise quantitative relation among coupling interval, blood pressure, and heart rate in the intact dog is complex and has not been adequately investigated. The results of the present study reveal that repetitive pairs of conducted and ectopic beats (bigeminy) can evoke an increase or a decrease in the arterial blood pressure or a biphasic pressure response. However, no matter what the directional change in blood pressure produced by the bigeminal rhythm in any given experiment, there is a range of coupling intervals over which the rate of change in blood pressure per unit change in coupling interval is positive, i.e., a progressive increase in coupling interval is accompanied by a rise in blood pressure or a progressive decrease in coupling interval is accompanied by a fall in blood pressure. For example, in Figure 3, it is evident that the bigeminal rhythm provokes a reduction in blood pressure. The right of this figure shows that as the coupling interval (lower border of the R-R tracing) becomes progressively shorter, the blood pressure decreases over a certain range of coupling intervals, i.e., the rate of change in blood pressure per unit change in coupling interval is positive. Similarly, in those dogs in which the blood pressure rises during the bigeminal rhythm, there is a range of coupling intervals
over which blood pressure increases with increasing coupling interval.

No matter whether blood pressure increases or decreases during the bigeminal rhythm, if synchronization develops, it will only persist when the coupling interval is within that range over which the rate of change in blood pressure per unit change in coupling interval is positive. Under these conditions, the feedback in the control loop depicted in Figure 6 is negative. The tendency for negative feedback to produce synchronization when the rate of change in blood pressure per unit change in coupling interval is positive is illustrated in Figure 7. The effect of the coupling interval on the systolic and diastolic arterial blood pressures are plotted from the data in Figure 3. It is evident from Figure 7 that over the range of coupling intervals included in the graph, an increase in coupling interval was accompanied by a rise in blood pressure.

Consider first the situation where the ventricular pacing frequency is precisely half the spontaneous SA nodal frequency. If the coupling interval happens to correspond to point A in Figure 7, then all successive coupling intervals will also fall at A as long as the spontaneous SA nodal frequency is precisely double the ventricular pacing frequency. Consider also that the pacing frequency remains constant but that the SA nodal frequency is subject to small, natural variations. If the SA nodal frequency should decrease slightly, the coupling interval would then diminish (e.g., to point B in Figure 7). At the shorter coupling interval, blood pressure would tend to fall, causing a reflex rise in SA nodal frequency. Conversely, should there be a small spontaneous increase in SA nodal frequency, the coupling interval would be prolonged (e.g., to point C). This will induce a rise in blood pressure, which would cause a reflex reduction in SA nodal frequency. Hence, any perturbation of SA nodal frequency will evoke a reflex change in the frequency in the opposite direction; this phenomenon is negative feedback, by definition. The open-loop gain in such a feedback system can be defined as the ratio of the secondary (reflexly induced) change in SA nodal frequency to the initiating change in frequency (i.e., the perturbation itself). Stable synchronization can occur only when the gain of this feedback system is between zero and minus one and when the disparity between SA nodal frequency and twice the pacing frequency is not excessive. In the left of Figure 3, for example, the open-loop gain is between the limits of zero and minus one, and synchronization persisted for about 1 minute.

In the first burst of ectopic beats in Figure 1 and in the five bursts of ectopic beats which led to a sharp rise of blood pressure in Figure 4, negative feedback also prevailed, but the gain was excessive (< -1). The steep rise in blood pressure evoked such a reduction in SA nodal frequency that there was a rapid shift in the relation between SA nodal frequency and ventricular pacing frequency: SA nodal frequency was more than twice ventricular pacing frequency before the onset of the ectopic beats but less than twice the pacing frequency during and immediately after the brief burst of ectopic beats. This phenomenon is manifest in both figures by the reversal in

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**Figure 7**
The changes in systolic ($P_s$) and diastolic ($P_d$) arterial blood pressures which accompanied the changes in coupling interval (RR$_C$) in the experiment in Figure 3.
the slope of the R-St tracing, as described in
the Results. In such experiments with excessive
negative gains, persistent synchronization
could be produced by using a ventricular
pacing frequency significantly less than half
the SA nodal frequency that would prevail in
the total absence of ventricular pacing. When
such ectopic stimuli became effective, blood
pressure would rise abruptly, SA nodal fre-
quency would decrease sharply to a value
less than twice ventricular pacing frequency,
and ectopic stimuli would soon fall in the
refractory period again. There would be
synchronization in the sense that the mean SA
nodal frequency would equal twice the mean
ventricular pacing frequency, and it would be
manifest as brief, repetitive bursts of ectopic
beats. A sequence of three such bursts is
illustrated by the sixth, seventh, and eighth
bursts in Figure 4.

The influence of a series of ectopic beats on
the arterial blood pressure is very complex,
and numerous factors are involved. Some of
the factors tend to diminish blood pressure,
whereas others tend to raise it. The overall
directional change in blood pressure is the
resultant of the interaction of these various
factors. On the basis of the filling time of the
ventricles, it is clear that the stroke volume
will be reduced for a premature beat and
augmented for the following normally con-
ducted contraction, based simply on the
Frank-Starling mechanism (11). Very early
ectopic beats may not develop a peak systolic
ventricular pressure greater than the prevail-
ing arterial diastolic pressure. In this event,
the ventricles eject no blood. A bigeminal
rhythm which included a series of such
ineffictual ectopic beats would then constitute
an effective pumping frequency equal to half
the prevailing SA nodal frequency. At low
prevailing SA nodal frequencies, the effective
pumping frequency of half the SA nodal
frequency would probably result in a reduc-
tion of the mean arterial blood pressure. At
excessively high SA nodal frequencies, on the
other hand, the effective pumping frequency
of half the SA nodal frequency would
probably raise the mean arterial blood pres-
sure. Finally, it is well known that coupled
beats may enhance myocardial contractility.
Such postextrasystolic potentiation is more
pronounced the earlier the ectopic beat (11).
The relation between the degree of prematur-
ity and the tendency toward potentiation
probably accounts for the direction of the
change in blood pressure in the experiment
illustrated in Figure 4. The very early ectopic
beats (short R-St intervals) resulted in an
abrupt rise in blood pressure, whereas the
later ectopic beats (long R-St intervals)
produced a fall in blood pressure.

The fact that synchronization was observed
in two experiments even after complete
cardiac autonomic blockade suggests that the
baroreceptor reflex is not the only mechanism
leading to entrainment. Ancillary mechanisms
have also been described in isorhythmic AV
dissociation (7, 8), and many of these parallel
feedback systems probably also operate to
achieve synchronization during simulated par-
systole.

In most of the experiments in this study,
concealed bigeminy (2, 10) was observed
when the R-St interval just exceeded the
refractory period. An example is shown in
Figures 1 and 2. It is evident in the latter
figure that stimuli St17—St17 were effective in
evoking ectopic beats, whereas St18, St20, St22,
St23, and St25 were ineffective. Figure 1 shows
that the R-St interval was diminishing pro-
gressively over the course of the first three
episodes of concealment (St17—St24 in Fig. 2).
Hence, R-St19 < R-St18, yet St19 evoked an
ectopic beat, but St18 did not. Also R-St21 < R-
St20, R-St24 < R-St22, and R-St24 < R-St23, yet
St21 and St24 elicited ectopic beats, whereas
St20, St22, and St25 did not.

The mechanism responsible for concealed
bigeminy in this experimental model probably
resides in the relation of the duration of the
refractory period to the preceding cycle
length. It has been amply demonstrated that
the duration of the refractory period of
cardiac muscle varies directly with the length
of the preceding cardiac cycle (12, 13). In
Figure 2, R-St17 must just have exceeded the
refractory period, and therefore St17 elicited
an ectopic beat. R-St18 was slightly shorter than R-St17; hence, the myocardium must have been refractory to St18. However, R-St19 was even slightly shorter than R-St18 (from Fig. 1), yet St19 did evoke an ectopic beat. The fact that the myocardium was responsive to St19 but not to St18 is almost certainly ascribable to the duration of the preceding R-R interval. The R-R interval preceding St18 was long as a consequence of the compensatory pause following the ectopic beat evoked by St17. Consequently, the refractory period was prolonged, and St18 was ineffectual. Since St18 did not elicit an ectopic beat, the subsequent cycle was not prolonged. Hence, the refractory period for the next beat was evidently not as prolonged as it was at the time of St18, and therefore St19 did produce an ectopic beat. The prolongation of the refractory period may persist for more than one beat after a long R-R interval (13), although the persistence of such an effect after a change in length of a single cardiac cycle remains to be established.

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