

Time Series and the Dynamics of Demand Pacing

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Abstract: Motivated by a common practice in cardiology, we analyze the dynamics of a demand paced system where one seeks to create a stable periodic response. By using techniques originally developed for controlling chaotic systems, one can enhance the information contained in time series regarding hidden, unstable periodic orbits. This makes it possible, for example, to track drifts in a system's dynamics.

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1 Introduction

A clinical observation of some importance in cardiology concerns the termination of fast rhythms such as tachycardia by applying periodic stimuli at a rapid rate — a rate faster than the underlying rhythm. By such rapid pacing one can sometimes capture the rhythm. This produces a rhythm that is even faster than the original but whose rate is under the control of the clinician. Sometimes it is possible gradually to slow the stimulation rate while maintaining capture of the cardiac rhythm. If the stimulation rate can be slowed sufficiently while maintaining capture then the stimulation can be turned off, with the cardiac rhythm remaining close to the final slow stimulation rate.

The protocol outlined above, a *capture-slow-release* protocol, has an almost intuitive appeal. Whether the protocol is successful depends on several factors not all of which are known. One of the factors is the rate at which the periodic pacing is slowed. In this communication I will provide a theoretical interpretation of the capture-slow-release protocol that is intended to help in finding out when the release can occur. The theory is based on ideas of chaos control introduced in Garfinkel *et al.*¹ and elaborated on in Kaplan² and Christini and Kaplan³. Along with the theory, I will detail some of the signal processing considerations important to the practical implementation of the theoretical ideas.

The dynamics of fast cardiac rhythms such as tachycardia and fibrillation are quite complex. Perhaps the simplest setting is when there is a well defined anatomical route for circus movement of the wave of activation. But even in this simple setting, the dynamics of recovery

and restitution — how the refractory period and speed of conduction depend on the tissue's activation history — can produce complicated temporal patterns of activation⁴. The more general situation, where the path of activation changes dynamically, is even more complex.

Generic ideas from nonlinear dynamics have been applied to studying tachycardia and fibrillation. When dealing with complex and random-looking rhythms such as fibrillation, chaos has been frequently offered — and challenged — as an explanation.

Whatever the complexity of tachycardia or fibrillation, when such as rhythm has been captured by periodic pacing the dynamics are much simpler; they are periodic.⁵

Periodic dynamics can be studied in terms of an even simpler dynamical structure, the fixed point, by taking a measurement once per cycle. So, the successfully paced heart can be seen as a fixed point. Similarly, when the autonomous cardiac rhythm is periodic, dynamics correspond to a fixed point.

In an abstract view, the dynamics of the capture-slow-release protocol can be seen this way:

Phase 1 The system's dynamics start out with an undesirably rapid and perhaps irregular rhythm.

Phase 2 By an extensive alteration in the dynamics — providing an external source of periodic stimulation — the dynamics are altered to a periodic rhythm.

Phase 3 Slowing the external stimulation while maintaining capture moves the dynamics from a region of state space where the undesirable rhythm in Phase 1 is attractive to a region where a desirable rhythm is attractive. A somewhat more concrete view of “moving the dynamics from one region to another” is that the gradually slowing pacing gives a chance for the slow dynamics of restitution and recovery to alter the properties of the cardiac tissue. Insofar as the variables relevant to restitution and recovery are included in the state space, the change in the properties of the cardiac tissue correspond to a movement from one region to another in the phase space.

Phase 4 Once in a region of the state space where a desirable rhythm is attractive, the pacing stimuli are turned off. The newly established rhythm is then maintained autonomously.

What is the evidence for this interpretation of the capture-slow-release dynamics? Phases 1, 2, and 4 are directly observed clinically. As a justification for the hypothetical Phase 3, I can offer only the following: something must be happening between Phases 2 and 4 to change the autonomous dynamics from the form seen in Phase 1 to the form seen in Phase 4.

The capture-slow-release protocol is unsuccessful when the pacing in Phase 3 fails to change the system in a way that creates the desired stable rhythm in Phase 4. The problem faced by a clinician is to deduce when the autonomous system has a stable rhythm from data collected during pacing. This communication describes one theory for how to do this.

2 Autonomous Dynamics

We start with a simple model of the dynamics of the autonomous system. Since the goal is to detect when a stable fixed point exists in the system, we'll assume that the autonomous system has a fixed point that might be stable or unstable. At the onset of Phase 3 of the capture-slow-release protocol, this fixed point is unstable. At the end of Phase 3 we release pacing only if the fixed point is seen to be stable.

The autonomous system's dynamics occur in some state space that is not directly accessible to measurement. However, we typically can measure the time between heartbeats, whether this is defined as an RR-interval from the surface ECG or the time between activations detected on an epi- or endo-cardiogram. If we count the activations $t = 1, 2, \dots$, we can denote by τ_t the interactivation time between the activations at t and $t - 1$. As described by Sauer⁶, the sequence of interactivation times can be used to provide a representation of the dynamics in the original, inaccessible state space, by considering τ_{t+1} as a function of previous interactivation intervals τ_t, τ_{t-1} , etc.

The simplest dynamical model with fixed point behavior occurs when τ_{t+1} is a function of τ_t

$$\tau_{t+1} = f(\tau_t). \quad (1)$$

A fixed point occurs for any value of τ_* where $\tau_* = f(\tau_*)$. This fixed point is stable when $|f'(\tau_*)| < 1$. Although this model is indeed simple, it is rather simpler than observed data. For instance, if the model is correct, a plot of τ_{t+1} vs. τ_t should show all the points lying on a one-dimensional curve. This is not the case in practice; such a plot produces a "snowstorm".^{1,7} In addition, the fixed-point dynamics of Eq. 1 show too limited a range of qualitative behaviors: monotonic approach or departure from the fixed point and alternating, back-and-forth approach or departure.

A wider range of dynamics as well as the observed snowstorm structure of the plot of τ_{t+1} vs. τ_t can be had with a slightly more complicated model:

$$\tau_{t+1} = f(\tau_t, \tau_{t-1}). \quad (2)$$

A fixed point occurs at τ_* such that $\tau_* = f(\tau_*, \tau_*)$. Near the fixed point, this model can be approximated as a linear function

$$\tau_{t+1} = a\tau_t + b\tau_{t-1} + c \quad (3)$$

where a , b , and c are constants. (Later, we'll allow a , b and c to vary slowly.) The location of the fixed point is $\tau_* = c/(1 - a - b)$. The stability of the fixed point is given by the eigenvalues:

$$\lambda_{1,2} = \frac{a \pm \sqrt{a^2 + 4b}}{2} \quad (4)$$

When $|\lambda_1| < 1$ and $|\lambda_2| < 1$, the fixed point is stable, otherwise the fixed point is unstable. A variety of types of linear behavior occur depending on λ_1 and λ_2 : monotonic approach or departure, alternating approach or departure, periodic oscillations of any period, saddle-type behavior with approach from one direction and departure in another direction.

One could, of course, consider dynamics with more than two variables, for instance

$$\tau_{t+1} = f(\tau_t, \tau_{t-1}, \tau_{t-2}).$$

We will not do so here partly for the sake of simplicity of the theory, but more importantly because no new dynamical phenomena are introduced by using more than two variables and because, as will be briefly discussed below, the theory is not necessarily modified by the inclusion of more than two variables. The same situation applies to small amounts of random noise in the dynamics.

We are not concerned here with the detailed structure of the function $f()$ away from the fixed points. Indeed, we do not even require that the dynamics be deterministic away from the fixed points. Our model simply states that the dynamics have a fixed point that may be stable or unstable.

3 Dynamics of the Paced System

The addition of external pacing stimuli to the system changes the dynamics. The simplest model of the paced system is arguably

$$\tau_t = \mathcal{C} \quad (5)$$

corresponding to fixed rate pacing with a stimulus every \mathcal{C} seconds and where *the rhythm is completely captured by the pacing*.

This model is unsatisfactory both from a mathematical and a physiological point of view. Physiologically,

there can be a somewhat complicated relationship between the stimulus and the response of the cardiac tissue. For instance, a stimulus can be completely ineffective if it comes too soon after an activation as might happen even at slow pacing rates if an autonomous activation occurs just before the stimulus. If the stimuli are given at a slow pacing rate, autonomous activations may intervene between stimulus-induced activations. Mathematically, the model fails to include any interaction between the autonomous dynamics and the pacing dynamics — when pacing is on there is no hint in the model of the autonomous dynamics, making it impossible to achieve our goal of detecting autonomous fixed points while pacing is on.

In principle, one could elaborate the pacing model by including some coupling with the autonomous dynamics. Since our representation of the dynamics is in the τ_t, τ_{t-1} space, we need to specify some function $g()$ such that $\tau_{t+1} = g(\tau_t, \tau_{t-1})$. But this type of function is doomed to failure mathematically, because it doesn't include any information about the phase of the stimulator at the time the last activation occurred. That is, if activation t occurs autonomously, in order to compute the time of activation $t + 1$ we need to know not the interstimulus interval \mathcal{C} but rather how long after activation t the next stimulus will occur. So, we would need to write the dynamics as a vector-valued function

$$(\tau_{t+1}, \theta_{t+1}) = g(\theta_t, \tau_t, \tau_{t-1})$$

that includes a phase variable θ_t that records the time until the next stimulus at the time of activation t .

Instead of augmenting our dynamics with the variable θ_t , we keep the dynamics simple by changing our pacing protocol to that of demand pacing: after each activation we wait until the next natural activation or until a time \mathcal{C} has elapsed, *whichever comes first*. If time \mathcal{C} has elapsed, we trigger a pacing stimulus, otherwise we reset the waiting clock starting at the time of the natural activation. The effect is to constrain the system to fire every \mathcal{C} seconds or faster. The overall dynamics, including both the external stimuli and the autonomous dynamics are

$$\tau_{t+1} = \min \begin{cases} a\tau_t + b\tau_{t-1} + c & \text{Autonomous dynamics} \\ \mathcal{C} & \text{Pacing stimulus} \end{cases} \quad (6)$$

where we have written the autonomous dynamics in the form that applies near the fixed point. Note that when the autonomous dynamics would lead to an interactivation interval greater than \mathcal{C} , the overall dynamics are identical to those of fixed-rate pacing (Eq. 5).

The nonlinear dynamics of Eq. 6 have been detailed previously by this author^{2,8}. Whenever $a\mathcal{C} + b\mathcal{C} + c > \mathcal{C}$, the dynamics will be simple pacing every \mathcal{C} seconds.⁹ Whether this condition will be satisfied depends on λ_1

and λ_2 of the autonomous dynamics (which depend on the parameters a , b , and c as given in Eq. 4 as well as on the relationship between \mathcal{C} and the autonomous fixed point τ_* .)

The required relationship among λ_1 , λ_2 , \mathcal{C} and τ_* for stable pacing at interval \mathcal{C} is given in the following table:

Type of FP	λ_1	λ_2	\mathcal{C}
Flip saddle	$\lambda_1 < -1$	$-1 < \lambda_2 < 1$	$\mathcal{C} < \tau_*$
Saddle	$\lambda_1 > 1$	$-1 < \lambda_2 < 1$	$\mathcal{C} > \tau_*$
Single-flip repeller	$\lambda_1 > 1$	$\lambda_2 < -1$	$\mathcal{C} > \tau_*$
Double-flip repeller	$\lambda_1 < -1$	$\lambda_2 < -1$	$\mathcal{C} < \tau_*$
Spiral	$\lambda_{1,2}$ complex conjugates		$\mathcal{C} < \tau_*$

According to this model, pacing should be possible whenever the autonomous dynamics have a fixed point that is not a non-flip repeller. One implication of the above table is somewhat counter-intuitive: for non-flip saddles and single-flip repellers, one wants to pace *more slowly* than the autonomous fixed point τ_t in order for pacing to capture the system. (τ_* is the period of firing of the autonomous system when at the system's fixed point.)

More detailed analysis² of the dynamics of Eq. 6 reveals that there is a system bifurcation as the pacing parameter \mathcal{C} passes through the value of the autonomous fixed point τ_* . Depending on the type of the autonomous fixed point, the bifurcation will be of a period-doubling or Hopf type. The implication is that the system will remain under pacing control, although the pacing stimulus may not be evoked each iteration. This means that in some circumstances it may be possible to find τ_* by tuning \mathcal{C} with the system remaining under pacing control. For example, if the autonomous fixed point is of the saddle type, once the system has been captured and is being periodically paced, one gradually increases \mathcal{C} until a period-doubling bifurcation occurs. The value of \mathcal{C} at which the bifurcation occurred is the location of the autonomous fixed point.

4 Tracking Autonomous Dynamics

Our theory of the capture-slow-release protocol imagined that the stability of the fixed point changes during pacing. This means that the parameters λ_1 , λ_2 , and τ_* are all functions of time, although the functions are unknown to us and may depend on the history of the pacing parameter \mathcal{C} . As outlined in the previous section, we can track τ_* by varying \mathcal{C} to find the location of a bifurcation. Beyond the bifurcation point, rather than periodic pacing the system will show an autonomous activation from time to time — every second activation in the case of a flip saddle, for example.

In order to assess the stability of the fixed point, we need to measure λ_1 and λ_2 . During fixed rate pacing this is impossible because the dynamics are simply those of

Eq. 5 which doesn't include any of the autonomous parameters. However, near the bifurcation point there will be autonomous activations. Let's assume that these autonomous activations occur at times k_1, k_2, \dots (We know the times of autonomous activation because no stimulus was applied to trigger these activations.) We can collect triplets of points $(\tau_{k_1}, \tau_{k_1-1}, \tau_{k_1-2}), (\tau_{k_2}, \tau_{k_2-1}, \tau_{k_2-2}), (\tau_{k_3}, \tau_{k_3-1}, \tau_{k_3-2})$, and so on. Using these triplets, we can then fit a model $\tau_{t+1} = a\tau_t + b\tau_{t-1} + c$ using any appropriate regression technique. But note that if the parameter \mathcal{C} is set so that the pacing dynamics are period doubled, then $\tau_{k_i-1} = \mathcal{C}$. This means that we will only be able to estimate the lumped parameter $a\mathcal{C} + c$. We can avoid this problem by jiggling the parameter \mathcal{C} , perhaps randomly, to make it take on a range of values close to the bifurcation point.

By tracking the stability of the autonomous fixed point, we can determine when it becomes stable and therefore when it is appropriate to release the system from the pacing stimuli. In order to track the stability, it is necessary to set the pacing parameter \mathcal{C} close to the bifurcation point that occurs at the autonomous fixed point τ_* .

The process of tracking has a somewhat common-sense interpretation. After capturing the rhythm using demand pacing at a fast pacing rate, we gradually slow the pacing. Whenever capture is about to be lost — as will be indicated by the emergence of a period-doubled response — we speed up the pacing a little and wait. After a while we try slowing the pacing rate again, and do so until the period-doubled response is encountered. We hope that by pacing the system at the slowest rate consistent with capture that the properties of the tissue will gradually change, moving the autonomous fixed point to a larger τ_* and making the fixed point stable. At the time when the fixed point becomes stable an increase in \mathcal{C} will no longer elicit a period-doubled response. Instead, the autonomous system will produce intervals that are shorter than \mathcal{C} and the pacing will no longer be required. In this sense, tracking of λ_1 and λ_2 are not strictly needed, since stability of the autonomous fixed point can be assessed simply by seeing if external stimulation is necessary. However, monitoring λ_1 and λ_2 can indicate whether the protocol is progressing and may help to monitor the effects of additional therapy.

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References

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- [5] This claim depends on one's point of view. During successful periodic pacing the detailed dynamics might still be very complex and irregular, causing fluctuations that are small compared to the pacing period. But, seen from a coarse measurement, the dynamics might appear quite periodic.
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- [9] Note that if the dynamics involved more than two previous values of τ , this condition would be largely the same. For example, if the dynamics were three-dimensional

$$\tau_{t+1} = a\tau_t + b\tau_{t-1} + c\tau_{t-2} + d$$

the condition for stable pacing would be

$$(a + b + c)\mathcal{C} + d > \mathcal{C}.$$

Thus, two-dimensional dynamics can correctly model the stability of pacing when the autonomous dynamics involve more than two dimensions.