Quantitative comparison of canine right and left ventricular isovolumic pressure waves

DANIEL BURKHOFF, MARVIN W. KRONENBERG, DAVID T. YUE, W. LOWELL MAUGHAN, WILLIAM C. HUNTER, AND KIICHI SAGAWA
Department of Biomedical Engineering, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205

BURKHOFF, DANIEL, MARVIN W. KRONENBERG, DAVID T. YUE, W. LOWELL MAUGHAN, WILLIAM C. HUNTER, AND KIICHI SAGAWA. *Quantitative comparison of canine right and left ventricular isovolumic pressure waves.* Am. J. Physiol. 253 (Heart Circ. Physiol. 22): H475–H479, 1987.—The mechanical properties of the right and left ventricles (RV and LV) have previously been studied separately. However, because of differences in RV and LV architecture, geometry, and muscle mass, it is not obvious how the properties of the two chambers would relate to each other. This study compared the time courses of RV and LV isovolumic pressure waves (LVP, RVP, respectively) measured simultaneously in the same heart. We compared RVP and LVP in each of five isolated, supported canine hearts after pentobarbital anesthesia. RV and LV volumes were varied independently so that on various beats peak LVP exceeded, equaled, or was less than peak RVP. There was a delay of ~35 ms between the onset of LV and RV pressure waves with atrial pacing, but only 5 ms with ventricular pacing. LVP and RVP were measured and digitized at a sampling rate of 200 Hz. Pressure waves were offset and rescaled by their respective amplitudes so that for each beat the pressure wave had a minimum value of 0% at end diastole and a maximum value of 100% at end systole. RVP was then shifted in time so that its upstroke was synchronous with that of the LVP at the point of 50% of maximal developed pressure. The rescaled, time-shifted RVP was plotted as a function of the rescaled LVP for each point of the cardiac cycle, and the relation between the two was quantified by their root mean square difference (D_{rms}). D_{rms} averaged 2.3 ± 1.5% (SD) for the first half of contraction, 1.5 ± 0.4% for the second half of contraction, and 4.6 ± 1.6% during relaxation. This analysis indicates that the time courses of RVP and LVP generation are nearly identical throughout the cardiac cycle. This near identity implies significant similarities in right and left ventricular chamber properties despite marked anatomic and geometric differences.

end-systolic pressure-volume relationship; time-varying ventricular volume elastance; right ventricular performance; left ventricular performance

THE RIGHT AND LEFT ventricles (RV and LV, respectively) have different geometries, architectures, muscle masses, and activation pathways of the myocardium. In addition, the force generating properties of the RV and LV myocardial fibers may differ and may even vary from region to region throughout both ventricles. Thus it is reasonable to question whether the time courses of pressure development in the two ventricles would be similar. Although RV and LV properties have been studied separately, there has been no previous attempt to compare the relation between the time courses of pressure generation of these two chambers in the same heart.

In a previous study (2) we found that the force-interval relationships of the RV and LV were essentially identical when quantified by normalized contractile indexes. This result suggested that there was a close interrelation between the characteristics of the two chambers as mechanical pumps. To extend our comparison between RV and LV function we tested the hypothesis that the time courses of pressure generation in the two chambers are the same. To obviate the influences of differing ventricular afterloads on the systolic pressure waveforms, we studied isolated, supported canine hearts whose right and left ventricles were made to contract isovolumically.

METHODS

Preparation. Experiments were performed on five isolated hearts. The surgical procedures used to isolate and support the canine heart were identical to those previously reported by Suga and Sagawa (7) and Burkhoff et al. (2). Briefly, two dogs were anesthetized with pentobarbital sodium (30 mg/kg iv). Arterial blood from the support dog perfused the coronary arteries of the heart isolated from the second dog. Coronary venous blood from the isolated heart was returned to the femoral veins of the support dog. The right and left atria of the isolated heart were opened, and the chordae tendinae were freed from both mitral and tricuspid valve leaflets. A metal adapter was sutured to the annulus of both of these valves, through which a water-filled balloon was inserted into each ventricle. The volume of each balloon was maintained at a known constant value by the servosystem described in detail by Suga and Sagawa (8) and Sunagawa et al. (9). A micromanometer (Millar 380) placed inside each balloon measured intraventricular pressure. The pressure signals were electronically filtered with low-pass filters having corner frequencies of 25 Hz.

Protocol and measurements. The hearts were paced at a constant rate between 120 and 130 beats/min throughout the experiment. Two of the hearts were paced from the right atrium. In the other three hearts, atrioventricular block occurred, and they were therefore paced from the LV apex; the high incidence of atrioventricular block

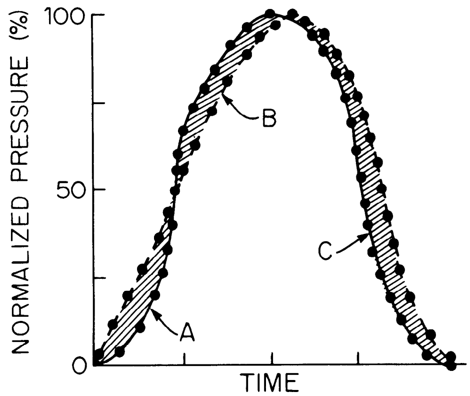

FIG. 1. Method for assessing similarity between time courses of two pressure waveforms. Curves are normalized to similar maximal pressure and are constrained so that the points corresponding to the times of 50% of maximal pressure generation are aligned. Regions *A* and *B* correspond to differences in configuration during first and second halves of contraction. Region *C* shows differences during relaxation.

was probably due to the presence of the metal ring in the tricuspid annulus. Isovolumic RV and LV pressure waveforms were recorded over a wide range of volumes (average range of 22 ml) in both ventricles. The RV and LV volumes (RVV and LVV, respectively) were independently varied so that sometimes RVV was greater than LVV and sometimes LVV was greater than RVV. All signals were recorded on a paper recorder (Gould 2800) and were digitized on-line at a sampling rate of 200 Hz and stored on magnetic tape.

Data analysis. Data analysis was performed off-line using a digital computer (Digital Equipment, LSI 11/23). The RV and LV pressure waves were normalized in magnitude to compare their time courses independent of their magnitude. For each pair of beats analyzed, the waveforms were rescaled to a maximum amplitude of 100% according to the following equation

$$P^*(i) = \frac{P(i) - P_{min}}{P_{max}} \times 100(\%) \qquad (1)$$

where i is the digital index of time (ms), P_{min} is the minimum pressure during the beat (considered the end-diastolic pressure), and P_{max} is the maximum developed pressure (i.e., peak pressure minus end-diastolic pressure) during the beat in the respective ventricle. The rescaled RV developed pressure wave, thus normalized in magnitude, was then shifted in time to match the points of 50% maximal developed pressure, which we defined as t_{50}. The amount of time shift required for this alignment was defined as Δt_{50}.

To define a quantitative index of the similarity between the curves we determined the root mean squared difference (D_{rms}) between the curves at three separate regions as shown in Fig. 1 (*A*, *time 0* until the time of 50% maximum developed pressure; *B*, the time from 50% maximum developed pressure to the time of maximum developed pressure in the LV; and *C*, the time from maximum pressure in the LV to the end of the cycle). The D_{rms} was defined as

$$D_{rms} = \sqrt{\sum_{1}^{n} \frac{[P_{LV}(i) - P_{RV}(i)]^2}{n}} \qquad (2)$$

where $P_{LV}(i)$ is left ventricular pressure at *time i*, $P_{RV}(i)$ is right ventricular pressure at *time i*, and n is the number of data points contained within the particular region of the curve.

We also compared the time durations of the pressure waves at a level of 10% of peak developed pressure (D_{10}) using Student's paired t test. Differences in D_{10} between the RV and LV were termed ΔD_{10}.

RESULTS

Figure 2 illustrates computer-reconstructed isovolumic pressure waves from a single heart at different volumes. As the volume was increased, both the diastolic pressure and the amplitude of developed pressure increased in both LV (Fig. 2*A*) and RV (Fig. 2*C*). When these waves were rescaled (*Eq. 1*), they were virtually superimposable throughout the cardiac cycle for LV (Fig. 2*B*) and for RV (Fig. 2*D*).

Figure 3 and Table 1 illustrate the comparisons between RV and LV pressure waves. Figure 3 demonstrates examples of three typical LV and RV pressure tracings before and after rescaling. Raw data are shown in Fig. 3, *A*, *C*, and *E*, and rescaled data are shown in Fig. 3, *B*, *D*, and *F*, respectively. The data were selected to demonstrate results when LV pressure was greater than RV pressure (Fig. 3, *A* and *B*), was equal to RV pressure (Fig. 3, *C* and *D*), or was less than RV pressure (Fig. 3, *E* and *F*). The rescaled waveforms were highly comparable regardless of the levels of LV and RV pressure. In these three cases, the D_{rms} averaged 3.0 ± 0.6% during the first half of contraction (range 2.6–3.7%), 2.1 ± 0.1% during the second half of contraction, and 4.5 ± 2.3% during relaxation.

The results from all hearts are summarized in Table 1. We compared 120 pairs of RV-LV pressure waves from five hearts. On average, RVV varied from 13.6 to 35.0 ml and LVV varied from 10.8 to 33.4 ml. The Δt_{50}, the time shift required to align the waves, was small in hearts paced from the LV apex (mean value of 6 ms) and large in atrially paced hearts (35.5 ms). The mean D_{rms} values were 2.3% in region *A*, 1.5% in region *B*, and 4.6% in region *C*, indicating a high degree of similarity of the pressure waves during contraction and somewhat less similarity during relaxation.

Figure 4 demonstrates a pair of normalized LV and RV pressures that were selected because the contraction results were more than two standard deviations beyond the mean values for the data in Table 1. The D_{rms} was 5.8% for the first half of contraction, 2.5% for the second half of contraction, and 3.1% for relaxation. In spite of being in the subset of data with the weakest fit, these normalized pressure waveforms had moderately good comparability.

The pacing site had no influence on the goodness of fit of the waveforms. The hearts paced from the LV apex demonstrated the same degree of similarity between RV and LV pressure waves as those paced from the atrium. There was a small difference between the durations of contraction (ΔD_{10}), which was statistically significant ($P < 0.01$) in two hearts but not in the other three.

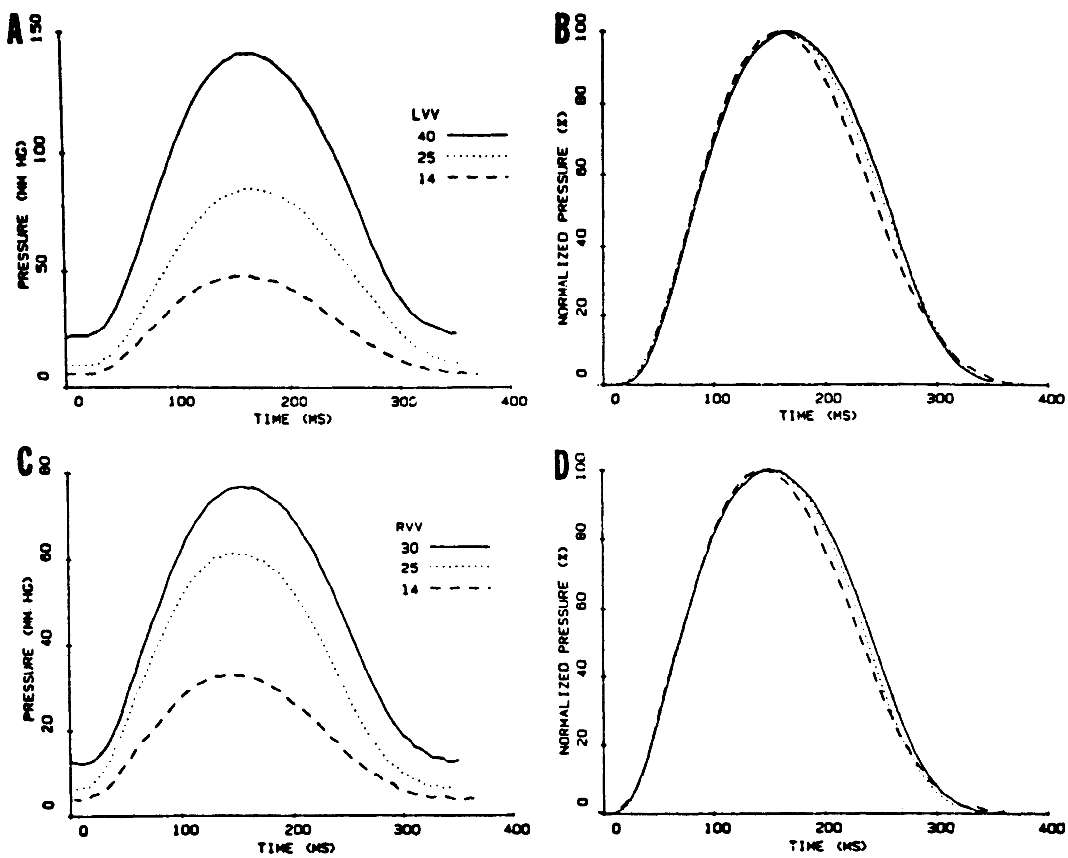

FIG. 2. *A*: computer-reconstructed left ventricular (LV) pressure waves measured at different volumes (LVV) which are specified in inset (all volumes in units of ml). *B*: pressure waves of *A* were offset and rescaled in amplitude. Resulting waveforms were superimposable. *C* and *D* are same as *A* and *B* but for right ventricle (RV) of same heart.

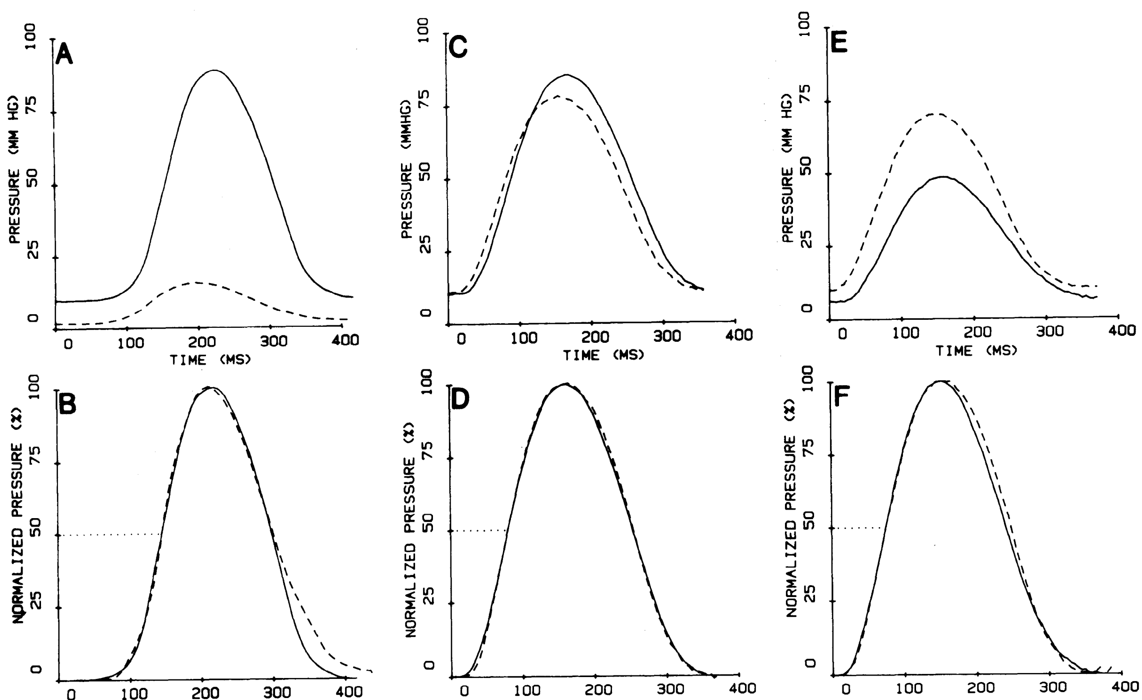

FIG. 3. Simultaneously measured left and right ventricular pressure waves (LVP and RVP, respectively) in cases where LVP exceeded RVP (*A*), equaled RVP (*C*), or was less than RVP (*E*). Normalized pressure waveforms are shown in *B*, *D*, and *F*, respectively. Normalized waveforms were quite comparable, in spite of wide variability in LVP and RVP. *Solid line*, LVP; *dashed line*, RVP; *horizontal dotted lines* (*B*, *D*, and *F*), times of 50% of maximal pressure generation. Please see text for details.

TABLE 1. *Summary of results in five hearts*

Expt	No. of Beats	Volume Range, ml RV	Volume Range, ml LV	Δt_{50}, ms	D_{rms}, % A	D_{rms}, % B	D_{rms}, % C	ΔD_{10}, ms
1*	36	20–43	11–42	33±4	2.5±7.8	1.6±1.2	7.0±2.2	7.8±10†
2	20	4–31	8–25	5±5	4.8±1.3	2.1±1.1	4.6±1.7	10.0±7†
3*	19	19–36	10–25	38±6	0.9±0.5	0.9±0.6	4.0±3.0	2.4±12
4	18	15–35	15–35	3±3	1.5±0.8	1.4±1.1	4.6±2.6	−1.7±11
5	28	10–30	10–40	10±3	1.8±0.9	1.3±0.6	2.6±1.3	−0.9±7
Means	24.2	13.6–35.0	10.8–33.4		2.3	1.5	4.6	4.6
±SD	±7.7	±6.7 ±5.1	±2.6 ±8.1		±1.5	±0.4	±1.6	

RV, right ventricle; LV, left ventricle; Δt_{50}, difference in time to reach 50% of maximal pressure in RV and LV; D_{rms}, root mean squared difference; *A*, first half of contraction; *B*, second half of contraction; *C*, relaxation; ΔD_{10}, difference in time duration of RV and LV pressure waves at a level of 10% of peak developed pressure. * Paced from atrium; other hearts were paced from LV apex. † Significant difference between RV and LV D_{10} ($P < 0.01$).

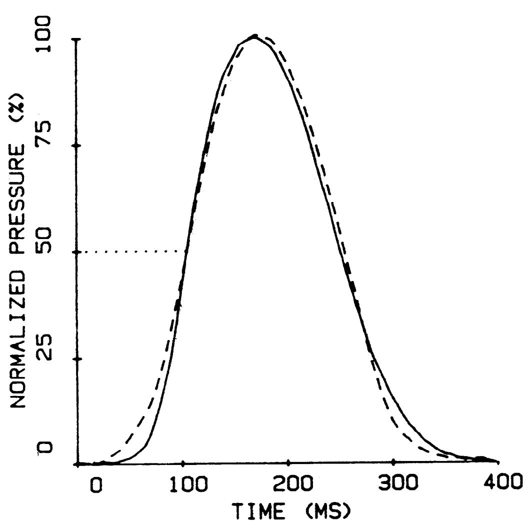

FIG. 4. Normalized pressure waveforms with relatively poor goodness of fit. Root mean squared differences between left (*solid line*) and right ventricular pressure (*dashed line*) during contraction were greater than 2 standard deviations beyond mean values in this study. *Horizontal dotted line*, time of 50% of maximal pressure generation. Please see text for details.

DISCUSSION

Our analysis revealed very similar shapes of canine RV and LV pressure waves during isovolumic contraction (i.e., up to the time of peak tension) after adjustment for peak-developed pressure and for differences in the onset of activation. During relaxation the shapes of the curves were similar, though not fully identical. Also, there was little difference in the durations of RV and LV pressure waves. The similarity in waveforms was observed both in hearts paced from the atrium and in hearts paced from the LV apex. However, with atrial pacing the RV pressure waves lagged behind those of the LV by an average of 35 ms, whereas there was very little delay between the two with ventricular apical pacing.

Recently, we showed that the shape of the LV pressure wave was not influenced by pacing site (3). Thus we expected that the similarity between RV and LV pressure waves would not be affected by pacing site, and indeed this was the case.

Previous studies of the isolated isovolumically contracting and ejecting canine LV demonstrated that instantaneous ventricular pressure, P(t), and volume, V(t), are reasonably well related during the systolic phase of the cardiac cycle by the following equation (7)

$$P(t) = E(t) \times [V(t) - V_0] \quad (3)$$

where $E(t)$ is the time-varying volume elastance of the ventricular chamber, and V_0 is the ventricular volume at which the end-systolic pressure is 0 mmHg. This time-varying elastance representation has also been shown to be a reasonable representation for RV systolic pressure-volume relations (2). However, the relationship between instantaneous ventricular pressure and volume during relaxation is more complex (1) and is not modeled as accurately by the simple relation shown in *Eq. 3* (7).

Equation 3 predicts for an isovolumically contracting LV or RV [(i.e., V(t) = constant)] that the shape of the pressure wave is solely dependent on the shape of the function $E(t)$. The superposition of magnitude-rescaled systolic portions of the pressure waves from either ventricle obtained at different volumes (Fig. 2, *B* and *D*) is in concordance with this prediction.

The term $E(t)$ can be expressed as a product of a factor that characterizes its time variance and a factor that quantifies its magnitude, plus an offset that specifies its minimal value as suggested by Suga and Sagawa (6)

$$E(t) = E_{\max}e(t) + E_{\min} \quad (4)$$

where $E_{\max}$ is the amplitude of developed $E(t)$ at $t = t_{\max}$, $e(t)$ is the descriptor of the time course of $E(t)$ having a magnitude of unity at $t = t_{\max}$ and a value of 0 at end diastole, and $E_{\min}$ is the minimum value of $E(t)$. The results shown in Fig. 3 and Table 1 indicate that in a given heart

$$e_{LV}(t) = e_{RV}(t - \Delta t_{50}) \quad (5)$$

where the subscripts RV and LV denote right and left ventricular properties, respectively, and Δt_{50} is the time delay between the RV and LV pressure waves. Based on the data presented in this study this is accurate for the contraction phase and a reasonable approximation for relaxation. On considering the vast structural differences between the RV and LV, we did not expect that their pressure waves, and therefore $e(t)$'s, would be so consistently similar. There are several possible explanations for this observation. First, it is possible that the time course of ventricular pressure generation is mainly determined by the time course of force generation of the muscle fibers and that this is reasonably uniform in the cells throughout both ventricles, except for a time delay of activation between the ventricles. If this assumption is correct, then the $e(t)$ (*Eqs. 4* and *5*) would reflect the time course of muscle stiffening, and those characteristics of the ventricle which determine the relationship between intrinsic muscle stiffness and ventricular volume-elastance could be accounted for quantitatively by a constant of proportionality; thus if $e(t)$ represents the time course of stiffening, then E_{max} (*Eq. 4*) would account for ventricular mass, geometry, and architecture in determining ventricular volume-elastance properties. Alternatively, the observed similarity between LV and RV pressure waves could result from a more complex relationship between muscle and ventricular properties, such that variable muscle properties throughout the myocardium are transduced into similar time courses of pressure generation by geometrical and architectural factors. Our results and analysis cannot be used to prove which of these, or other possible explanations, is correct. To investigate such details it would be necessary to accurately quantify regional contractile performance, which is not possible at present.

Potential limitations. The method for alignment of waveforms at the time of 50% of developed pressure and the D_{rms} method for describing the similarities between RV and LV pressure waveforms are potential limitations in our data analysis. This 50% point for alignment of the pressure waves appears to us to be the most sensitive and reliable in comparison to other points in the cardiac cycle such as end diastole or time of peak pressure. The definition of end diastole is vague; any definitions based on the characteristics of the pressure wave (e.g., the point at which the derivative rises >0 mmHg/s) are generally not reliable, because they are based on analyses of low magnitude signals, which change relatively slowly. The use of the time at which peak pressure occurs would be more reliable than end diastole but due to the flatness of the pressure wave near peak systole this definition is also relatively imprecise. In contrast, the point at which 50% peak developed pressure is attained is a point at which pressure is changing very rapidly. Therefore, because it can be determined reliably this is a sensitive method for alignment of the pressure waves.

It is difficult to quantitate the similarities or differences between curves. Other methods include linear regression analysis and Fourier analysis. Linear regression analysis is relatively insensitive to subtle differences between curves because there may be shape differences in spite of high correlation coefficients. Fourier analysis is sensitive to shape differences but also requires rescaling the frequency data and shifting right to left to align phase data. Furthermore, constraining Fourier analysis to specific phases of the cardiac cycle (e.g., contraction or relaxation) is not possible. Thus we chose the D_{rms} method as a good compromise, because it achieves sensitivity and requires minimal data manipulation.

Conclusions. Our previous studies (2) indicated that the force-interval relationships of the RV and LV were nearly identical. That result suggested a close correlation between the mechanical properties of the two chambers despite their vast structural differences. The results of the present study further support this concept by demonstrating similar time courses of pressure development of the right and left ventricles.

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Address for reprint requests: D. Burkhoff, Department of Biomedical Engineering, The Johns Hopkins University School of Medicine, Baltimore, MD 21205.

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