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Singular Value Decomposition of Optically-Mapped Cardiac Rotors and Fibrillatory Activity

A. Rabinovitch^{a,*}, Y. Biton^a, D. Braunstein^b, M. Friedman^c, I. Aviram^a, S. Yandrapalli^d, S. V. Pandit^d, and O. Berenfeld^d

^aPhysics Department, Ben-Gurion University of the Negev, Beer-Sheva, 84105, Israel

^bPhysics Department. Sami Shamoon College of Engineering, Beer-Sheva, Israel

^cDepartment of Information Systems Engineering, Ben-Gurion University, Beer Sheva 84105, Israel

^dCenter for Arrhythmia Research, University of Michigan, Ann Arbor, MI 48109, USA

Abstract

Our progress of understanding how cellular and structural factors contribute to the arrhythmia is hampered in part because of controversies whether a fibrillating heart is driven by a single, several, or multiple number of sources, and whether they are focal or reentrant, and how to localize them. Here we demonstrate how a novel usage of the neutral singular value decomposition (SVD) method enables the extraction of the governing spatial and temporal modes of excitation from a rotor and fibrillatory waves. Those modes highlight patterns and regions of organization in the midst of the otherwise seemingly-randomly propagating excitation waves. We apply the method to experimental models of cardiac fibrillation in rabbit hearts. We show that the SVD analysis is able to enhance the classification of the heart electrical patterns into regions harboring drivers in the form of fast reentrant activity and other regions of by-standing activity. This enhancement is accomplished without any prior assumptions regarding the spatial, temporal or spectral properties of those drivers. The analysis corroborates that the dominant mode has the highest activation rate and further reveals a new feature: A transfer of modes from the driving to the passive regions resulting in a partial reaction of the passive region to the driving region.

Keywords

Singular Value Decomposition; ventricular fibrillation; rotors; dominant frequency; phase analysis

I. INTRODUCTION

The normal heart activity is driven by electrical beats originating from its natural pacemaker at the sinus node which induces repetitive propagation of electrical pulses (action potentials, AP) throughout the heart and causing its contraction and blood delivery to the body. One of the malfunctions of this rhythmic activity is called fibrillation. Ventricular fibrillation (VF) is the leading cause of sudden cardiac death, accounting for an estimated 300,000 fatalities

*Corresponding author: A. Rabinovitch, Ben-Gurion University of The Negev, Beer-Sheva 84105., avinoam@bgu.ac.il.

annually in the United States of America alone [1]. Atrial fibrillation (AF), yet another form of fibrillation estimated to afflict about 2.5 million Americans, is the most common sustained arrhythmia in humans [2] and is the leading cause of embolic stroke [3]. The efforts to resolve those devastating arrhythmias have attracted a large amount of theoretical, experimental and clinical research. Toward the last third of the previous century, the idea that the complex AP propagation during fibrillation follows a breakup of an organized reentrant activity called a rotor was proposed based on theoretical [4] and experimental [5, 6] studies. In the last 2 decades or so optical, fluorescence-based, mapping of cardiac electrical activation has been developed to increase the resolution of the spatio-temporal characterization of the cardiac fibrillation [7, 8]. Accordingly, an animal heart is excised, kept viable by perfusion of essential nutrients and oxygen and is then stained with potentiometric dye with a transmembrane voltage dependency fluorescence. This fluorescence portraying the local cardiac AP is then photographed via a CCD camera rendering the data in a convenient movie format. Using such methodology the understanding of propagation underlying fibrillation has been shifted to suggest that self-sustained and fast spinning rotors themselves could drive the fibrillation [9–11]. Consequently, recent studies provided evidence that some cases of fibrillations in patients depend on those rotors [12–14] but controversies regarding whether rotors are indeed the mechanism driving fibrillation are still fiercely debated [15, 16].

In the past we were able to analyze optical mapping data and link the spatio-temporal fibrillatory activity to the frequency domain, and in particular to the spatial distribution of the local dominant frequency (DF) of the activation rate [17, 18]. However, full understanding of the complex fibrillation dynamics often suffers from optical mapping artifacts undermining a cohesive link between a possible rotor driver, its frequency and the surrounding fibrillatory activity. To improve understanding and address mapping limitations we show here a new approach based on the singular value decomposition (SVD, see [19, 20]) that is capable of ranking the spatiotemporal modes of the fibrillation without any prior assumption on the data structure and underlying relationships as well as any manual arbitrary selections, such as a particular filter or motion cancellation. SVD analyses have been beneficially used in many fields of science: engineering [see e.g. 21], earth sciences [22], biology in general [23] and, in particular, brain research [24]. Previous partial SVD analyses of electro-cardiac activity [25, 26] did not address the link between the modes of the whole system with the driving role of a regional rotor as the underlying mechanisms of the fibrillation. Probably the first SVD use in analyzing VF was carried out by Bayly et al [27] who demonstrated that extraction of the first eigenmodes of VF waves highlights repetitive activation patterns (See Fig. 12 in [27]). Nevertheless that SVD analysis was partial and a more complete SVD reconstruction method was not studied and questions related to the possible applications of the SVD in cardiac fibrillation, and in particular to the ability of the SVD approach to highlight its driving mechanisms, remained. Here we use for the first time the complete SVD method to fill that gap and analyze an experimental dataset of cardiac fibrillation with the purpose of determining its organization and possible driving source; We use an experimental dataset of cardiac fibrillation in which a stable rotor is present at the highest DF across the mapped hearts to demonstrate that this method extracts the dominance of the rotor driving the fibrillation as the most important mode of the system.

Applying the SVD approach to the fibrillating hearts we confirm that, as predicted previously, the highest ranked spatiotemporal modes correspond to the highest local DF in the heart and that a transfer of modes between the driving and the passive regions is characterizing the fibrillating heart as a whole.

II. METHODS

A. Animals and Heart Preparations

Experiments were performed using 10 New Zealand White male rabbits. Animal-handling protocols conformed to the United States National Institutes of Health Guidelines and the European (D2003/65/CE and R2007/526/CE) Guidelines for the Care of Animals Used in Experimental and other Research Purposes and were approved by the University Committee on Use and Care of Animals of the University of Michigan. Following the administration of anesthesia, hearts were quickly removed and immersed in cold (4 °C) cardioplegic solution for further preparation. The aorta was cannulated and connected to a Langendorff system to provide the heart with warmed, oxygenated Tyrode's solution. Oxygenation was carried out with a mixture of 95% O₂ and 5% CO₂. The heart was immersed in the same Tyrode's solution, in a custom-made transparent chamber, and the temperature was maintained at 35.5±1.5 °C. The perfusion pressure was maintained between 60 and 70 mm Hg. Blebbistatin (5–10 µM, Sigma, St. Louis, MO, USA) was added to the perfusate to minimize motion artefact [28].

B. Experimental protocols and data acquisition

Ventricular fibrillation (VF) was induced by pacing at increasing frequencies (2 Hz/sec) in the presence of 30 µM Pinacidil (an I_{K,ATP} opener) in 5 hearts. A 1–2 mL bolus of the voltage-sensitive dye Di-4-ANEPPS (10 µM, Sigma) was added to the perfusion line. Green light from a 532 nm, 1 Watt, laser was directed at the anterior and posterior surfaces of the ventricles and the fluorescence emitted light passed through a 650±50 nm filter before being captured simultaneously with two synchronized 64×64 pixels CCD cameras (Dalsa, Waterloo, ON) at a constant frame rate of 602–604 fr/sec in each animal as described in [28]. The two CCD cameras were positioned to view separated areas of about 2×2 cm² each one on the posterior (dorsal) and anterior (frontal) aspects of the ventricles (PR and AR, respectively, see Figure 1). Following a sustained VF for more than 5 min, 5-sec long movies were recorded. 5 movies showing stable rotors for the entire movie period were selected for analysis. For control, we mapped activation at the AR in additional 5 rabbit hearts during pacing at a cycle length of 200 msec.

C. General Data Analysis Methods

All movies were masked to exclude low signal pixels in the periphery of the ventricles. Raw fluorescence (F) time-series data were processed with a temporal moving average filter (MAF; 3 time and 5 space points' kernels) and then subjected to background subtraction (F) and normalization to maximal dynamic range, resulting in dimensionless movies of F/F. Phase representation of raw, MAF and SVD processed movies were obtained based on Hilbert transform [14, 18, 29].

The optical data of the VF in the rabbit was also subjected to spectral analysis in which the dominant frequency (DF) of each pixel was determined as the frequency (in the 5–40 Hz band) with the maximal power following a 2048-points FFT [17, 18]. The highest DF across the mapped areas is designated as the DFmax. In the present study movies of about 5 sec long duration were analyzed for DF. In all movies studied here the DFmax resides in the rotor region.

D. The SVD Analysis Method

Sub-segment of 1-sec long movies of VF and pacing from the 10 rabbit hearts were processed with the singular value decomposition (SVD) method. The SVD analysis is based on the method of snapshots [19, 20]. Consider a movie format dataset containing the time sequence of a large number of frames, each frame containing space information at a particular instant. The collection of frames represents the evolution of a phenomenon - in our case the spatiotemporal patterns of action-potential (AP) propagation across the surface of the heart during fibrillation. Each 2D space frame, termed a “snapshot”, at time t_i , $i=1 \dots I$ is discretized into a grid of M rows and N columns, indexed m and n , respectively, resulting in $J = M \times N$ pixels carrying the entire spatial information at this time. The total number of data points is therefore IJ . Each point is attributed a value identifying a color in a selected color scale depicting the action potential (AP) value there. For the analysis the data are arranged in a rectangular matrix (B) in the following manner: The column vectors of B are ordered vectors $u(x, t_i)$ each at time t_i , arranged in an ordered 1D sequence of length J , indexed by the letter $j=1, \dots, J$, where each location, j (discretized $x=j \times \Delta x$), contains the AP value of the pixel. There is a total of J rows and I columns (of space distribution at each time) in B . The SVD procedure then decomposes the matrix B by a left and right side (LHS and RHS, respectively) diagonalization into a product of three matrices: $B=USV^{-1}$ where U is a square matrix of size $J \times J$, whose J orthonormal eigenvectors pertain to the spatial part of the problem. The square matrix V is of size $I \times I$, where the V 's are the orthonormal RHS vectors pertaining to the temporal part of the problem. S is a rectangular diagonal matrix of the same size as B whose diagonal elements S_l are the eigenvalues ranking the order of importance of the corresponding vectors. Sorting these S 's in a decreasing order and rearranging the corresponding vectors accordingly, we arrive at the final SVD “diagonalized” form. The left hand eigenvectors, $U_l(x)$ are the spatial and time-averaged modes mentioned above which constitute the *vector-basis* for the phenomenon. Each eigenvector can be re-converted into a spatial “picture” of the respective eigenmode. The projection of the original movie on each of the $U_l(x)$'s yields a time-dependent projection coefficients, $a_l(t)$. Since the $U_l(x)$'s obtained in the SVD process are orthonormal, the $a_l(t)$'s are obtained by a scalar product between the original $u(x, t_i)$ and the $U_l(x)$'s:

$$a_l(t_i) = \sum_{j=1}^J U_l(x) u(x, t_i) \quad (1)$$

Note that the summation is actually on x (or j) and dimensions of all $a_l(t)$ are those of $u(x, t_i)$ (in our study $u(x, t_i)$ describes F/F of the electrical activity in the hearts and therefore $a_l(t)$ is dimensionless).

One can reconstruct the process in time and space by providing the approximations to any desired accuracy (in a least square difference meaning). As the modes are descending in values and importance, the p^{th} order “best” approximation, $P < J$, to the original vector $u(x, t_i)$ is obtained by:

$$u_p^*(x, t_i) = \sum_{l=1}^P a_l(t_i) U_l(x) \quad (2)$$

If the low ranking modes are related to noise or lower importance in the least square approximations then the *high* modes approximations can actually “enhance” the movie interpretation by highlighting its most significant features. Alternatively, the reconstruction with a subset of *low* eigenvalue modes could assist in interpretation of the non-dominant features of the phenomenon in question.

The eigenvalues (S_l) of the modes are ranked and sorted in descending magnitude order. They are normalized by the sum of all eigenvalues, i.e., presented as $S_l/\sum S_l$.

In presenting the spatial modes U , each mode is self-normalized in such a way that the average is zero; the pixel having the highest value of transmembrane potential (fluorescence) is represented in red-brown while the lowest negative value appears in dark blue. All analyses are performed by adaptation of the SVD package of MATLAB (Mathworks, Natick, MA)

III. RESULTS AND DISCUSSION

A. Baseline Activation Mapping of VF

In Figure 1A we show the anterior and posterior CCD views of sample rabbit ventricles (AR, PR, respectively). A pair of selected pixels from movies obtained simultaneously for the AR and PR show typical F/F, but otherwise unprocessed, time series analog to the transmembrane potential sequence during VF. It is noticeable that relative to the AR signal, the signal from the PR is more regular and with faster activation rate, as found in other cases of VF in animal models [14]. The sequence of frames from the movies of the same VF show unspecific patterns in the AR and a typical, though fuzzy, winding characteristic of rotor activity in the PR.

In typical studies aiming at further characterization of the spatiotemporal activation patterns a moving average filter (MAF) and phase analysis are performed [9, 29]. Figure 2 shows frequency and phase analysis of the VF following MAF (panel A). From the snapshots of the video in Panel B it is clear that the PR consists of a stable rotor (circular arrow). The activity at the AR is less clear. Panel C of Figure 2 shows the DF of all the pixels in the anterior and posterior aspects of the ventricles during the VF. It is clearly seen that while most of the PR is activated at 31.3 Hz (DFmax, which is also the rotor frequency), the AR is fragmented into many smaller domains characteristic of fibrillatory activity. In the following sections, we will demonstrate the effectiveness of the SVD method to extract the features linking the PR and AR, two separated regions that seem so different in their spatio-temporal wave behavior while forming parts of a single system which is the VF in this rabbit heart.

B. The Eigenvalues of the SVD

The singular value decomposition (SVD) approach is conceptually similar to a Fourier expansion. However, in contrast to the Fourier expansion, the SVD approach is not based on any previous knowledge or assumptions about the phenomenon, is constructed solely based on the least square difference between the original and the constructed eigenmodes and it provides a biased-free hierarchical approximation for the original data set. Accordingly, the first spatial SVD eigenmode of a space-time data set refers to the spatial pattern component that appears most often during the analyzing period. The next eigenmode represents the most frequent pattern component to appear in the analyzed period once the first mode has been subtracted and is thus orthogonal to the first one. The rest of the eigenmodes follow a similar meaning. The normalized eigenvalue magnitude, S , of a mode gives the relative retentive power value of the original pattern for a specific mode. Thus, for an S value for a sample mode j of say $S_j=0.3$, if we reconstruct the pattern only by this mode and by the projection $a_j(t)$ of the eigenmode on the original data (which describes the “amount” of the mode j which is present in the pattern at time t) we have captured 30% of the information of the original signal.

In presenting the SVD results, the normalized magnitudes appear first (Figure 3) followed by the first highest-eigenvalue spatial modes (Figures 4 and 5); The projections of the pattern onto these modes, the $a_j(t)$'s (Figure 6); Finally the reconstructions by Eq. (2) of the spatiotemporal patterns by the first 3 modes is shown in Figure 7 and analyzed in Figure 8.

When comparing the normalized eigenvalues between the region with the rotor activity and DFmax and the opposing regions at similar modes (Figure 3), it is noticed that the magnitude of the first few modes in the rotors and highest DF side are higher than that in the opposite one. In panel A, the sample VF shown in Figure 1 is analyzed. The 5 first eigenmodes S of the PR, where the rotor and highest DF reside, are larger than those in the AR for the same episode. The sum of those eigenvalues of the first 5 modes in the PR is ~ 1.46 larger than that of the AR. In panel B, cumulative data from VF in 5 different rabbit hearts confirm that the 4 highest ranking eigenvalues in the areas with the rotor (4 PR and 1 AR) are significantly higher than the eigenvalues at the opposing side of the hearts. This difference indicates that fewer modes are needed for the reconstruction of the basic pattern in the rotor area, consistent with the rotor being more organized than the fibrillatory areas of the hearts during VF.

To confirm the assertion that organized spatio-temporal activation patterns is described by fewer modes than less organized activation patterns we compared our VF data to pacing data. In Figure 3C we compare the S values for the VF data to those of 5 additional paced rabbit hearts, in which the activation patterns are the most possible organized [30]. The graph shows that normalized S values for the paced hearts at modes below 3 are larger than those for the VF ($p<0.05$). For modes 5 and higher the paced hearts eigenvalues are lower than those in VF hearts ($p<0.05$). Thus we conclude here that the rotor activity at the highest DF in the heart is the most organized activity during VF and it can be described with fewer modes as compared with at least some of the by-standing areas activated by that rotor activity.

C. The Spatial Modes of SVD during VF

The first three modes of the separated PR and AR of the sample Figure 1 VF are shown in Figure 4. While the modes of the PR exhibit a clear indication of a rotor, it is very difficult to discern any particular activation pattern, and certainly not a vestige of the rotor in the AR modes. To further highlight the dominance and driving role of the PR over the AR in this case, the top six SVD modes of the combined AR/PR video are shown in Figure 5 (In this figure both sides of the heart are processed and normalized together; in all other figures each side is separately processed and normalized.) Thus in Figure 5, each mode is a combined mode of both sides and a direct comparison between the sides is possible. It is immediately clear that the PR is the dominant side; the peak-to-peak amplitudes of the PR side within each mode 1–6 being higher than those of the AR. This difference is diminishing as the mode number is increasing.

D. The Spatial Modes of SVD during Pacing

For more rigorous interpretation of the spatial modes during VF (Figures 4 and 5) we analyzed also 5 rabbit hearts during pacing. In Figure 6A we show 3 sample frames of a movie following a paced beat in a sample heart. As can be appreciated, the excitation in that heart spreads from the tip of the pacing electrodes in almost radial pattern. This pattern repeats itself for all the beats recorded by the CCD camera for an entire movie of 5 sec. In Panel B we show the first 6 spatial modes (whose eigenvalues are shown in Fig. 3C) of a 1-sec segment of that movie. Visual inspection reveals that the modes of the AR show indeed the decreasing spatial similarity to the F/F patterns during the activation as shown in Panel A and an increasing level of details (i.e., increased spatial frequency and possible noise). Fig. 3C, Panels A and B together support the notion that the rotor patterns displayed in Figures 4 and 5 are related to the rotor activity in the original VF movie shown in Figure 1.

E. The Time-dependence of the SVD Modes during VF

The temporal behavior of the modes is proportional to the projections of the spatial modes on the original data (Eq. 1). The projections $a_j(t)$ of the separate PR (red) and AR (blue) patterns onto their respective three dominant modes (1–3) reveal an interesting outcome. These projections are shown in Figure 7 along with their corresponding power spectra. Both a_1 and a_2 projections show lower DF in the AR as compared with the PR which shows a DF of 31.3 Hz, the rotor frequency, but a_3 shows a similar DF of 31.3 Hz in both the AR and PR. The similarity in frequency in the 3rd ranked projection indicates a physiologic link between the two mapped sides that are physically separated and otherwise show different spatio-temporal patterns of activation.

The dominance of the PR over the AR was manifested by the larger amplitudes of the projections $a_j(t)$ there; since the rotor is the dominant and fastest feature in the PR and also in the combined PR/AR modes (Figure 5), it is expected that the rotor also drives the AR side. The role of an organized rotor in the PR driving fibrillatory, irregular, activity at the AR is corroborated by cross correlation as follows: The main features of the rotor pivoting at 31.3 Hz can be seen as generated by the first 3 modes of the (separate) PR side. Nevertheless, on the AR only the 3rd mode's projection shows a DF at that same frequency (Figure 7). To better describe the mutual effects of modes on each other we calculate the

cross correlations (normalized so that the auto-correlations at zero lag are identically 1.0) between the 3 first projections (a 's) of the corresponding modes in the PR and the first 3 projections of the modes of the separate AR side (see Table 1). We find that the maximal cross correlation between AR and PR modes vary in the 5 animals between 0.853 (Heart 3) and 0.349 (Heart 5; $\text{mean} \pm \text{SD} = 0.585 \pm 0.229$, $p < 0.05$ paired t-test vs. second maximal and $p < 0.01$ one-sample t-test vs. 1). The modes with the highest cross correlations always involved the first 2 highest modes of the area with the rotor; the 3rd highest projection of that area (a_3) never correlated highest with any of the modes on the other side. For example, the first and second projections (a_1 and a_2) of the PR shown in Figure 7 for the VF of Figure 1, correlated at 0.789 and 0.805 with a_3 of the AR, respectively, but the third projection of the PR correlated only 0.445 with a_3 of the AR. When considering all the 5 animals, the 3rd projection of the side with the rotor correlated at most at 0.456 (in Heart 1, see Table 1) with any other projection on the other side ($\text{mean} \pm \text{SD} = 0.359 \pm 0.085$, lower than 2nd ranked correlation, $p < 0.05$, paired t-test). Note that the correlations refer to whole modes and *not to specific positions* within a particular area in the heart (i.e., in the AR and PR). This is an unusual concept which considers the *modes* as the carriers of information. Since we know that the highest modes multiplied by their respective projections can accurately reconstruct the rotor in the PR, the less than 1 value of the cross correlations of the corresponding modes are consequence of the disruption of the rotor activity.

F. Enhancement of the Rotor by Top Modes Reconstruction

In Figure 8 we show how using only the first modes of the SVD to reconstruct the patterns (SVDR) by Eq. 2 highlights the leading spiral activity in the PR (see Supplemental Movie 1). Panel A shows 3 sampled snapshots from a F/F movie reconstructed for the PR and AR by the use of only modes 1, 2 and 3 in Eq. (2). Comparing the snapshots here with those in Figure 1B it is clear that in Figure 8 the images are devoid of noise. Comparing them with the snapshots in Figure 2A that were obtained by MAF of the original data, it is noticeable that the rotor features in the PR are enhanced in by the SVDR; indeed, while in Figure 2A the rotor winding features are seen to span only about half of the normalized color scale (from green to red), in Figure 8A the rotor features span the entire scale (from blue to red).

For a quantitative measure, a peak signal to noise ratio (PSNR) [31, 32] test on 5 randomly chosen PR frames, like those shown in panel A, from each movie, yields an $\text{mean} \pm \text{SD}$ PSNR of 23.9 ± 4.7 dB; A similar procedure on AR frames yields a lesser enhancement; the $\text{mean} \pm \text{SD}$ PSNR here is 14.1 ± 2.8 . Namely, the rotor in frames processed by the SVDR is cleaner than the one in the original frames by ~ 24 dB while the AR signal is enhanced by ~ 14 dB. In panel B we present 3 snapshots of the phase movie based on the SVDR movie. Comparing the PR images of the rotor in Figure 8B with those in Figure 2B it is noticeable that the rotor windings following the SVDR are extended to wider areas toward the periphery of the ventricle view, demonstrating again an effective enhancement of the rotor features.

To further establish the SVDR enhancement of the rotor dominance appearance in the 5 VFs in different rabbit hearts we analyzed the power spectra of the MAF and SVDR processing schemes used in this study. In Figure 9A we show an example of such analysis for the VF

shown in Figure 1: The relative power in frequencies others than the DF (i.e., the rotor frequency where rotors are present) is seen to be lower following the SVDR as compared to following MAF for both the AR and PR. In panel B of Figure 9 we quantify that relative power distribution by calculating the ratio of the power at the DF to the total power in AR and PR separated movies of the 5 animals studied. The bar graph shows that while MAF doesn't increase significantly that ratio in comparison to the raw movies, SVDR is increasing that ratio both in comparison to raw and to MAF processed data. In other words, while MAF doesn't increase significantly the relative power at the DF, including that of a rotor, in comparison to the raw F/F movies, SVDR with or without MAF increases that relative power significantly and thus is superior to MAF in distinguishing the DF among all frequencies involved in the activity.

IV. SUMMARY

A novel form of SVD analysis has been applied to high resolution optical mapping data in cardiac fibrillation that depends on a fast and stable rotor in rabbit isolated hearts. It has been shown that the fibrillatory activity driven by stationary rotors, as studied here, can be represented more meaningfully by only the *two* top SVD modes; together with their $a(t)$'s they can create a clear reconstruction of the phenomenon. It has been previously shown by Sanghi and Hasan that only two modes are needed also to describe a pure translational movement [29]. Thus we expect that if the rotor as a whole is drifting in one direction in addition to its rotation, then, due to the Doppler effect, one would need two more modes (4 altogether) for an accurate representation. For a meandering rotor, more modes may be necessary but further investigation in such cases is warranted.

The strength of the new method is demonstrated by its ability to rank the dominance of certain areas in the maintenance of the fibrillation without the traditional processing of activation patterns, frequency or directionality, which are often masked by noise in experiments and in the clinic and therefore requiring filtering constrains based on pre-assumptions of the spatio-temporal patterns of the activity. In particular, the SVD analysis performed here reorganizes the complex fibrillation dynamics in hierarchical modes where the two top ranked modes correspond to the driving rotor, but the SVD-based reorganization during VF with unstable rotors needs to be further investigated. The ranked modes enable to reinterpret the primary role of the highest local dominant frequency (DF) as a parameter pointing to the source of the waves during fibrillation and link together distant regions through cross correlations of the time series projections on common modes. Thus, this new application of the SVD method is laying a solid ground for a system-level investigation toward improved understanding and possible improved therapy of the most common atrial and the lethal ventricular fibrillation.

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Figure 1.

Anatomy and raw data. A) Top: Anterior (AR) and posterior (PR) views of the epicardial surface of a rabbit right (RV) and left (LV) ventricles. The dashed line indicates the position of the left anterior descending artery between the RV and LV. Bottom: sample raw $\Delta F/F$ time-series obtained with two synchronized CCD cameras during VF in a sample isolated rabbit heart at the indicated positions (arrows) during ventricular fibrillation (VF, see text). B) Time-series such as in A are combined to provide movies of the spatio-temporal electrical activity on the surface of the heart during VF. Snap shots at the designated times (in ms) show unspecific pattern in the AR, but a winding pattern, characteristic of rotor activity, in the PR (see Movie 1).

Figure 2.

Moving average filtered (MAF) movies of VF. A) A sequence of snapshots from the MAF processed movies from the AR and PR of the same rabbit shown in Figure 1 (see Movie 1). Bottom traces: Sample single pixels time-series recordings of activity during VF from indicated locations in the AR and PR. B) Selected frames from a phase representation of the movie following MAF, whose selected frames are shown in panel A. C) Maps of local activation rate (Dominant frequency, DF) at the anterior (left) and posterior (right) aspects of the rabbit ventricles during the VF. The rotor in the PR has a DF of 31.3 Hz.

Figure 3.

The eigenvalues S of movies during VF and pacing A) The eigenvalues from the example VF shown in Figure 1 show that the highest-ranking eigenvalues (below about mode 5) at the posterior wall, where the highest DF and the driving rotor reside, are higher than the eigenvalues of the anterior wall. B) Cumulative data from 5 hearts show that the areas with the highest DFs and driving rotors have higher highest-ranking eigenvalues than other areas (paired two sample t-test: $p < 0.05$). C) Comparison between VF and pacing data. Normalized cumulative eigenvalue data from 5 VF (blue and red) and 5 paced (black) hearts. At modes

below 3 the paced eigenvalues S are larger than in VF, while at modes 5 and higher the paced eigenvalues are lower than in VF (two sample t-test: $p < 0.05$).

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Figure 4.

The first 3 eigenmodes of the PR and AR. Note the rotor pattern in the PR modes and the rather disorganized electrical activity appearance in the AR modes.

Figure 5.

The first 6 modes of the *combined* AR/PR video during VF. For each mode, the AR appears on the left side and the PR on the right side.

Figure 6. SVD analysis a rabbit AR ventricle view during pacing at a cycle length of 200 ms. A) Three sample frames of the MAF $\Delta F/F$ movie showing radial propagation (white arrows) away from the pacing electrode (gray line). Numbers are time of frames in msec. B) The first 6 modes of the AR show the decreasing spatial similarity to the $\Delta F/F$ patterns during activation in Panel A.

Figure 7.

The projections of the PR (blue) and the AR (red) electrical activity of the VF shown in Figure 1 onto their respective first 3 eigenmodes (a_1 – a_3) and their respective power spectra.

Figure 8. Frames at different time points (numbers in ms) from movies reconstructed with 3 highest SVD modes (SVDR) of the AR and PR movies shown in Figure 1. A) A fluorescence representation of a reconstructed movie. B) A phase representation of a reconstructed movie.

Figure 9.

The effect of the SVD-based reconstruction (SVDR) on the observation of the rotor dominance. A) Power spectra after MAF (red) and MAF + SVDR (blue) processing of the posterior (top) and anterior (bottom) views of the VF shown in Figure 1. The power spectra are normalized to the power at the dominant frequency (DF, maximal power, green arrows) and are logarithmically scaled. It is clear that the addition of the SVDR processing increases the dominance of the rotor with a dominant frequency of 31.3 Hz in the posterior wall. B) Mean $\pm$ standard error summary of increased dominance of the highest DF, corresponding to

a rotor activity in the 2 views in 5 experiments of VF (total 10 movies; only significant differences are marked). While MAF doesn't increase significantly the relative power at the rotor DF in comparison to the raw F/F movies, SVDR with or without MAF increases that relative power significantly.

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Table 1

Cross correlations of modes

Cross correlation values between the first 3 projections a_1 , a_2 and a_3 from the anterior (AR) and posterior (PR) walls of the rabbit hearts during VF. Numbers in bold indicate maximal cross correlations for a particular heart.

PR	AR	Heart 1	Heart 2	Heart 3*	Heart 4	Heart 5
a_1	a_1	0.168	0.363	0.853	0.487	0.260
a_2	a_1	0.187	0.189	0.522	0.144	0.164
a_3	a_1	0.456	0.192	0.315	0.239	0.216
a_1	a_2	0.331	0.263	0.634	0.372	0.084
a_2	a_2	0.275	0.432	0.468	0.171	0.111
a_3	a_2	0.365	0.223	0.338	0.204	0.121
a_1	a_3	0.788	0.332	0.414	0.198	0.349
a_2	a_3	0.805	0.345	0.297	0.173	0.321
a_3	a_3	0.445	0.373	0.337	0.195	0.311

* In heart 3 the rotor and DFmax are in the anterior wall.