ANALYSIS OF EIGENIMAGES:

CAPTURING CORTICAL SPIRAL WAVE DYNAMICS

by

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THESIS
Presented to the Faculty of the
Honors College
The University of Texas at San Antonio
In Partial Fulfillment
Of the Requirements
For the Degree of

BACHELOR OF SCIENCE IN BIOLOGY
WITH HIGHEST HONORS IN THE HONORS COLLEGE

THE UNIVERSITY OF TEXAS AT SAN ANTONIO
College of Sciences
Department of Biology
December 2011

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ACKNOWLEDGEMENTS

I would like to thank my thesis advisor, Dr. David Senseman for giving me the opportunity to work in his lab and for his guidance throughout this project. He has been a wonderful mentor to me, giving support and advice in regards to my studies and future career path. I am also very grateful to Dr. Kay Robbins for sharing her knowledge of computer science and serving as a thesis reader. Lastly, I would like to thank Dr. David Jaffe for serving as a thesis reader.

December 2011

ABSTRACT

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In turtles, voltage-sensitive dye (VSD) imaging has shown that visual simulation evokes waves that propagate rostrocaudally across the dorsal cerebral cortex. Generally, such waves have a planar structure with a roughly linear wave front but more complex rotating spiral waves with a 2π phase angle gradient across the active cortical surface have been reported. The spatiotemporal dynamics of rotating cortical spiral waves were studied using a large-scale GENESIS computational model of the turtle visual cortex. In this model, propagating planar waves can be converted into rotating spiral waves by brief stimulation of a subpopulation of inhibitory interneurons that served to block part of the advancing wave front. To help characterize the spatiotemporal dynamics of cortical spiral waves, movies of wave activity were subjected to Karhunen-Loeve (KL) analysis. KL analysis decomposed the wave motion into a series of eigenfunctions or basis images with rather complex spatial and temporal relationships. To clarify these relationships, a parallel series of experiments were done in which KL analysis was applied to simple example of rotatory motion, a rotating Fermat spiral. Basis images obtained from the rotating Fermat spiral came in orthonormal pairs that appear to capture the *x* or "cosine" movement and the *y* or "sine" movement of the rotating image. Using the results obtained from the Fermat spiral as a framework, it was possible to discern a similar orthonormal cosine/sine relationship between the KL basis images obtained from the rotating cortical spiral data.

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CHAPTER 1: INTRODUCTION

Traveling electrical waves within the cerebral cortex are of theoretical interest with respect to their possible function(s) in the processing of sensory and motor information. Spiral waves are especially interesting (Ermentrout and Kleinfield, 2001) and have been observed and characterized in tangential slices of disinhibited mammalian cortex (Huang *et al*., 2004). Within the intact brain, spiral waves have been recorded in the turtle cerebral cortex in response to visual stimulation using voltage-sensitive dye (VSD) imaging (Precthl *et al*. 1997). In addition to the cerebral cortex, spiral patterns have also been investigated in a variety of excitable tissues including hippocampal slices (Harris-White et al., 1998), retina (Gorelova and Bures, 1983), and cardiac muscle (Davidenko et al., 1992).

One way that spiral waves can be studied is to use Karhunen-Loeve (KL) decomposition. This technique finds an optimal basis or orthogonal coordinate system for a collection of vectors (Robbins *et al.* 2004). KL is closely related to several statistical techniques such as principal component analysis (PCA), proper orthogonal decomposition (POD), and singular value decomposition (SVD). KL decomposition has been used to study propagating cortical waves in the turtle (Senseman and Robbins 2001). In this study, KL was shown to capture wave movement by the algebraic addition of two or more static basis images. A fundamentally important point about this technique is the production of translationally invariant modes. Each mode may change in its individual contribution to the overall movement, but they will remain unchanged over time.

KL has been used to analyze propagating cortical waves as described and non-biological spiral waves (Robbins *et al.* 2004), but it has not yet been applied to spiral cortical waves. The

first goal of this experiment was to apply KL decomposition to a rotating spiral wave produced by our turtle visual cortex model. Due to the relatively complex modes of the rotating spiral wave, a well-behaved synthetic movie of a Fermat spiral was created. The secondary goal of this experiment was to apply the KL analysis to this synthetic movement and then use the produced modes to better understand the basis images of the cortical wave related to a well-defined geometric system.

CHAPTER 2: THESIS STATEMENT

Relatively simple movies can be made that simulate the patterns of movement in an actual cortical wave such as a rotating spiral. A simplified movie representation of a wave can be decomposed by KL analysis into coherent movements to better understand neural response. Comparing the results of KL analysis between the actual rotating spiral wave in the turtle visual cortex and the wave created using a simple Fermat spiral, should show very similar eigenimages and thus give insight into the spatiotemporal dynamics of rotating cortical waves.

CHAPTER 3: METHODS AND APPROACH

3.1 Large Scale Cortical Model

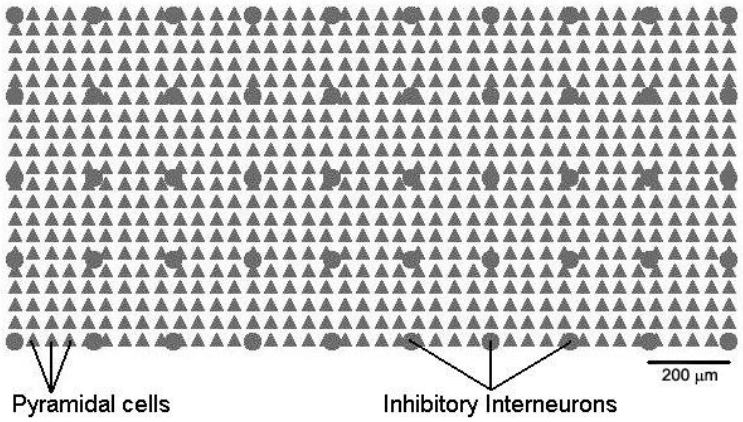


Fig. 1. Spatial organization of the SYM model of turtle dorsal cortex. See text for details.

Movies of rotating cortical waves were generated using the "SYM model" of the turtle visual cortex. The SYM model (Fig. 1) is a somewhat larger version of the original "Nenadic-Ghosh-Ulinski" or NGU model of the turtle visual cortex (Nenadic *et al*., 2003) containing 950 compartmental neurons including 800 pyramidal cells and three types of inhibitory cells (50 stellate, 50 horizontal, and 50 subpial). In contrast to the NGU model–which attempts to place neurons in a biologically realistic (i.e. non-uniform) spatial pattern–the SYM model places neurons in a highly ***symmetrical*** pattern (hence the name "SYM"). Specifically, the 800 pyramidal neurons are symmetrically arranged in 40 columns and 20 rows within a 2 mm x 1 mm grid. Inhibitory neurons are also arranged symmetrically within this grid in ten columns of five.

Pyramidal cells make excitatory synaptic connections with inhibitory neurons as well as with each other. Recurrent excitation between pyramidal cells is mediated by glutamatergic synaptic transmission that accesses both AMPA and NMDA subtypes and provides the

structural/functional basis for wave propagation. Pyramidal cell excitation of adjacent inhibitory stellate and horizontal neurons generates feedback inhibition that "balances" the recurrent excitatory drive. (The third type of inhibitory cell, the subpial neuron, does not contribute under the conditions used to generate spiral waves). The SYM model is written in the GENESIS modeling language.

3.2 Generation of Spiral Waves

Rotating spiral waves in the SYM model were generated in a two-step process. First, a modest depolarizing current pulse (+10 nA, 20 ms) was injected into the leftmost column of pyramidal cells to initiate firing. Due to the recurrent excitation, firing spreads into adjacent pyramidal cells triggering a wave of excitation that propagates left-to-right across the model. This planar wave was converted into a rotating spiral wave by stimulating a small subpopulation of inhibitory neurons in front of the advancing wave front. This causes the wave to "flow around" the inhibited region and transforming it into a rotating spiral (e.g. Huang et al., 2004).

3.3 Generating Movie Data for KL Analysis

A movie is essentially a time series of sequential static images. Generating a series of images that captured a rotating cortical spiral in the SYM model required a very different technical approach than the one used to generating images of a rotating Fermat spiral. For the cortical spiral, the SYM model's GENESIS code was written to log the somatic membrane potential of each pyramidal cell to an ASCII data file at each millisecond time interval. Using a MATLAB script written by Dr. Kay Robbins in the Department of Computer Science at UTSA, the somatic membrane potential of each pyramidal cell was read from this data file at each time

step, normalized, converted to a gray-scale value and then plotted at the appropriate location on a 2-dimensional map of the SYM model to generate one "frame" for the cortical movie (Fig. 2).

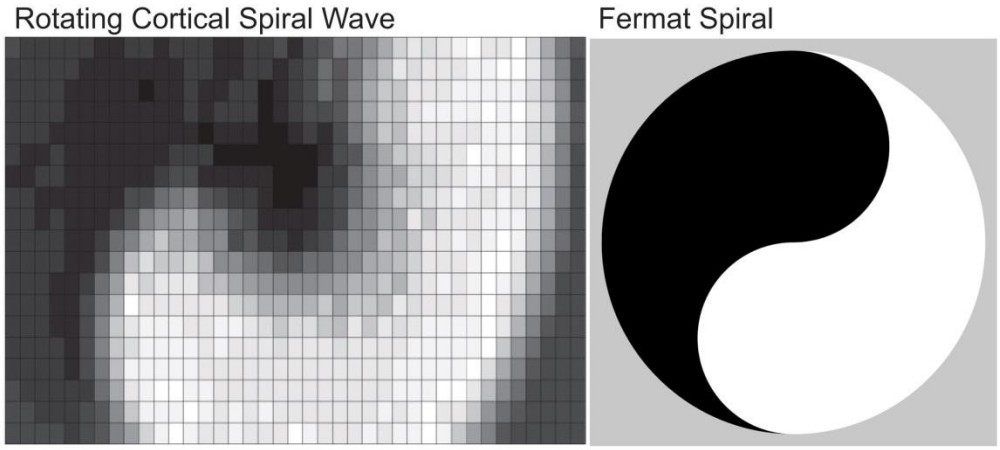


Fig. 2. Examples of "movie frames" analyzed by KL decomposition. The image at left shows a single frame of a continuous movie of a rotating sprial wave generated by the SYM model. The image at the right is a Fermat spiral created using Adobe Photoshop.

Individual movie frames from the rotating Fermat spiral were generated using Adobe Photoshop. A large image of a Fermat spiral (2000 pixels x 2000 pixels) was created in Photoshop (Fig. 3). The purpose of working initially with a relatively large image format was to minimize artifacts that might arise during image rotation. The Fermat spiral itself was composed of a circle with one side "black" and the other side "white" centered in a 50% gray square background. The black and white colors were used to represent maximum positive amplitude and maximum negative amplitude, respectively. A mask the size of the circle was created so that image of the Fermat spiral could be rotated independently of its gray background. A series of 192 images were produced in which the Fermat spiral was sequentially rotated by ~1.8 degrees to generate a complete rotation. The collection of images was reduced from their original large format to a more manageable size of 600 x 600 pixels and converted from Adobe's "RGB mode" to "Index Color mode" (8 bits/channel) prior to KL decomposition.

3.4 KL Analysis of Movie Data

KL decomposition of the two movie data sets was performed using MATLAB scripts that read in the sequence of images, performed the KL decomposition on the complete data set and generated images of the eigenvectors (basis images) that captured the largest amount of the response energy. These scripts were based on a collection of MATLAB scripts originally written by Dr. Kay Robbins that were modified in some details for use in this thesis project. These modifications were generally minor in nature and the KL analytic techniques where essentially identical to those previously published (Robbins, 1998; Robbins & Senseman, 1998; Senseman & Robbins 1999).

In addition to decomposing the cortical and Fermat spiral movies into a series of basis images, the MATLAB scripts also computed the "projection" of each basis image on to each frame in the original movie. Used in this context, a projection data set gives the relative contribution of a particular basis image to each frame in the original movie with values ranging from +1 to -1. (Mathematically, the projection value represents the dot product of the basis image with a particular movie frame). A projection value of +1 indicates that the movie frame identical to the projection's basis image at that frame and no other basis images make a contribution. A projection value of -1 also means that a particular movie frame was determined solely by a particular basis image, but in this case by the inverse of the basis image. (The inverse of a basis image is the same basis image but with its light and dark areas reversed). Midway between these two extremes, a projection value of 0 indicates the basis image made no contribution to movie during that frame. It follows that each frame in a movie can be faithfully reconstructed through the algebraic addition of one or more basis images individually weighted by their projection value. Moreover, by extension, an entire movie can be reconstructed using only the information contained in the basis images and in their related projection data sets.

To visualize how two particular basis images change relative to each other during a movie, the projection of one basis image can be plotted against the projection of the other basis image creating a phase plane plot. Microsoft Excel was used to graph both individual mode projections as well as phase-plane plots.

CHAPTER 4: RESULTS AND DISCUSSION

Rotating cortical spiral waves (~ 1.7 Hz) in the SYM model arose when a linear wave front collided with a patch of inhibited pyramidal cells. The center of rotation was not stationary, but slowly meandered over the cortical surface. Basis images derived from KL decomposition of one spiral wave movie is shown in Fig. 3.

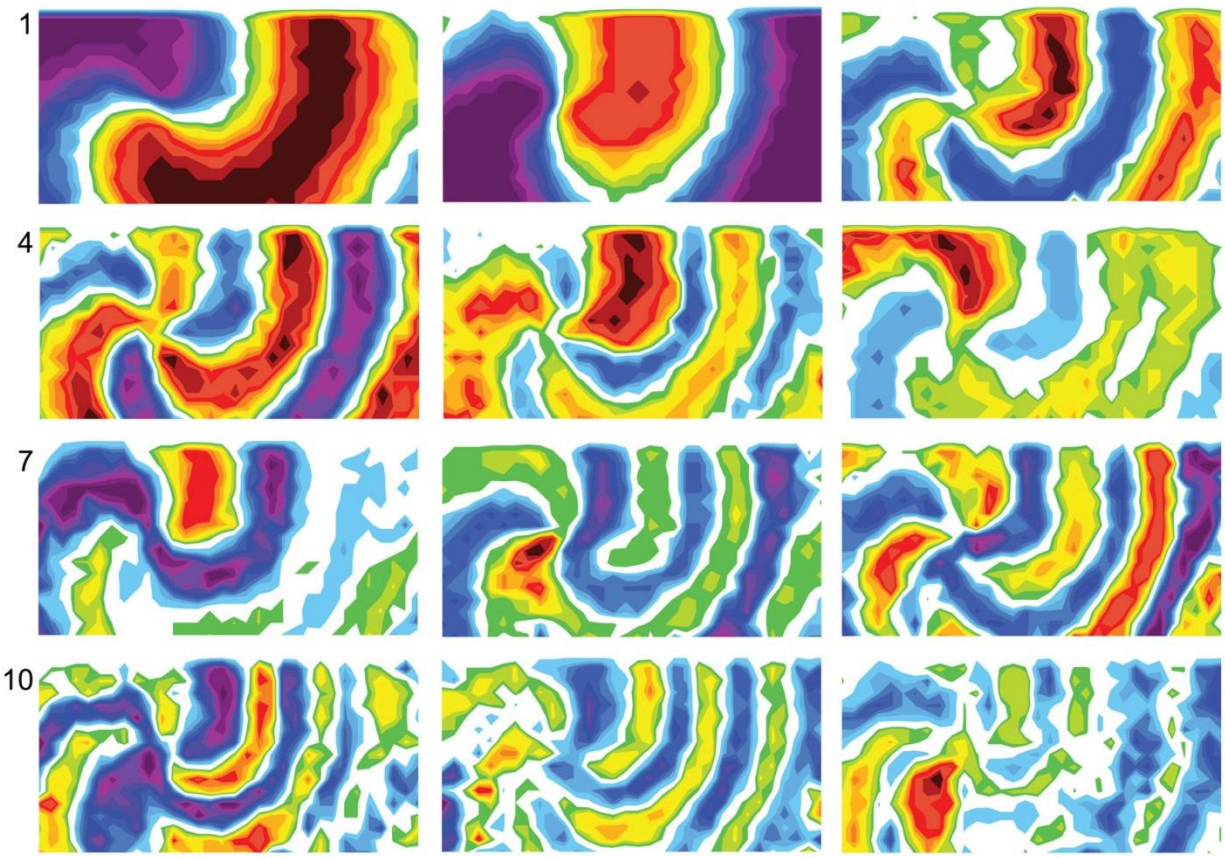


Fig. 3. Basis images derived from KL analysis of a rotating cortical spiral wave in the SYM model. The basis images are organized according to their "energies" with the largest (labeled 1) at the top left and the smallest at the bottom right. The images are pseudo-colored according to a "rainbow" scheme with increasing positive correlation indicated by yellow → orange → red and increasing negative correlation indicated by green → blue → violet. Areas colored "white" indicate regions where correlations were below a threshold of ±10% of the maximal response.

Based upon KL analysis of propagating planar waves in the turtle visual cortex (Senseman and Robbins, ref), it be would expected that basis images of cortical spiral waves

should display evidence of "spatial harmonics". In other words, "higher" basis images (or higher modes) should be geometric multiples of "lower" basis images (lower modes). While visual inspection of these basis images in Fig. 3 appears to show some evidence spatial harmonics, the irregular modal structure, particularly of higher basis images, makes such an analysis problematic.

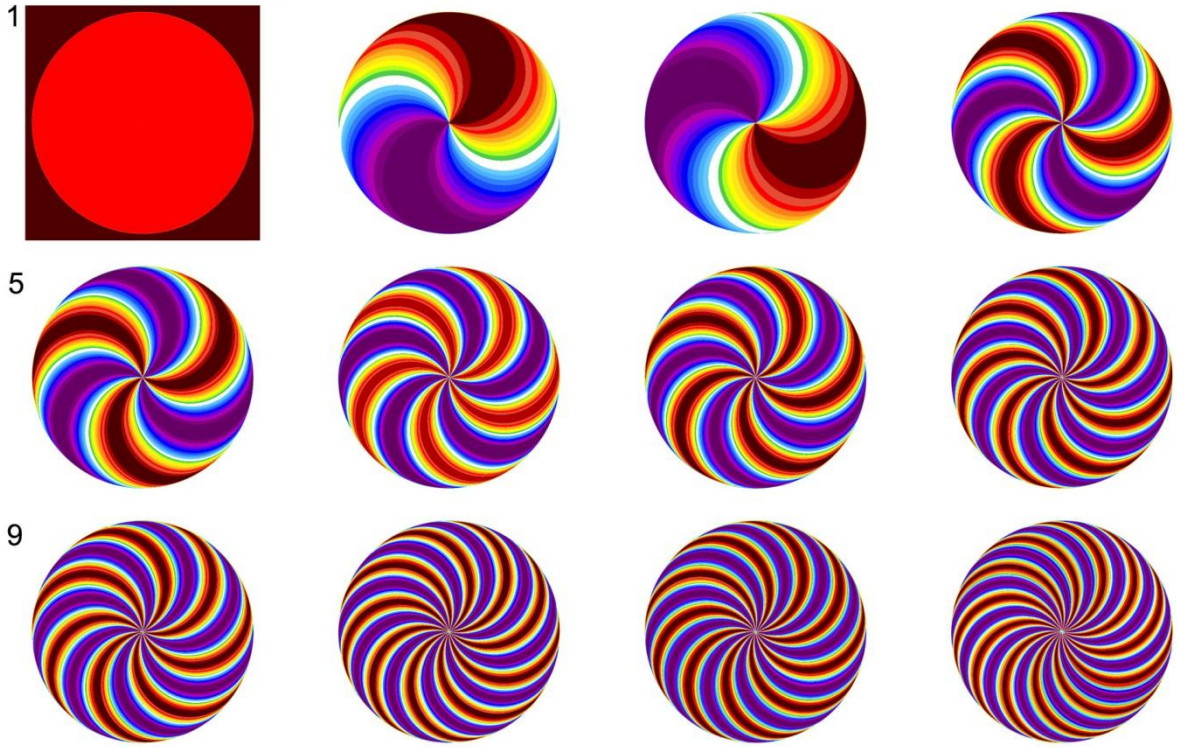


Fig. 4. Basis images derived from KL analysis of a rotating Fermat spiral. The basis images are organized according to their "energies" with the largest (labeled 1) at the top left and the smallest at the bottom right. The images are pseudo-colored according to a "rainbow" scheme with increasing positive correlation indicated by yellow → orange → red and increasing negative correlation indicated by green → blue → violet. Areas colored "white" indicate regions where correlations were below a threshold of ±10% of the maximal response.

By comparison, the spatial harmonic relationships between basis images derived from KL analysis of a rotating Fermat spiral were obvious (Fig. 4). The largest basis image (1 in Fig. 4) is unimodal in structure and captures the overall activity of the movement (e.g. Senseman and

Robbins, 199) and need not be considered further. By inspection of basis images 2–12 is it clear that basis images 2 and 3 are directly related in the sense that the both exhibit only two separate areas: one showing positive correlations ("red") and one showing negative correlations ("blue"). On closer inspection it can also be seen that the two white areas separating the positive and negative areas are orthogonal to each other. In other words the spatial locations of the areas of positive and negative correlation are rotated 90^{o} between the two members of the pair. These two properties: (1) the same number of positive/negative areas of correlation and (2) a rotation of 90^{o} in spatial location is also seen in pairs 4–5, 6–7, 8–9, 10–11 and presumably extends for an infinite series of higher basis image pairs.

That higher order pairs of basis images are "spatial harmonics" of lower order pairs can also be seen by inspection of Fig. 4. It should be noted that the number of areas showing a positive (or negative) correlation increase by n+1 in each higher order pair so that any given basis image can only have an odd number of positive (or negative) regions of correlation.

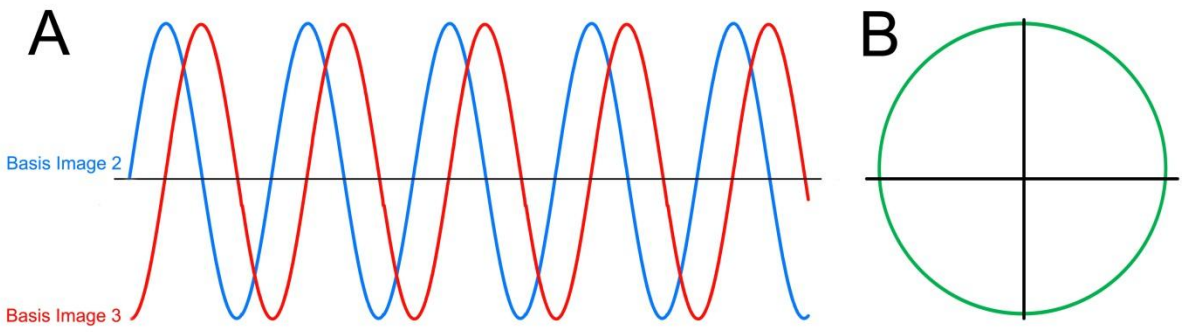


Fig. 5. Projections of Fermat Spiral Basis Images 2 and 3. **A.** Projection of Basis Image 2 (blue) and Basis Image 3 (red) are plotted for 4 rotations of a Fermat spiral. The projections are clearly sinusoidal in structure. **B.** The projection of Basis Image 2 has been plotted as a function of Basis Image 3 to create a phase plane plot which forms a perfect circle.

Fig. 5 shows a plot of the projections for basis image pair 2–3. The waveform structure of both projections plotted independently is clearly sinusoidal (Fig. 5A) with the maximum (or minimum) of one projection corresponding to a zero value for the other. Plotting the two projections against each other generates a phase plane in the shape of a perfect circle (Fig. 5B).

A comparable analysis for basis image pair 4–5 is shown in Fig. 6. Again, the projections are sinusoidal and form a perfect circle when plotted as a phase plane. Although the number of revolutions of the Fermat spiral remained constant (i.e. 4), the number of cycles increases from 4 to 12. This would be expected since there are 3X the number of areas of positive (or negative) correlation in pair 4–5 than in pair 2–3.

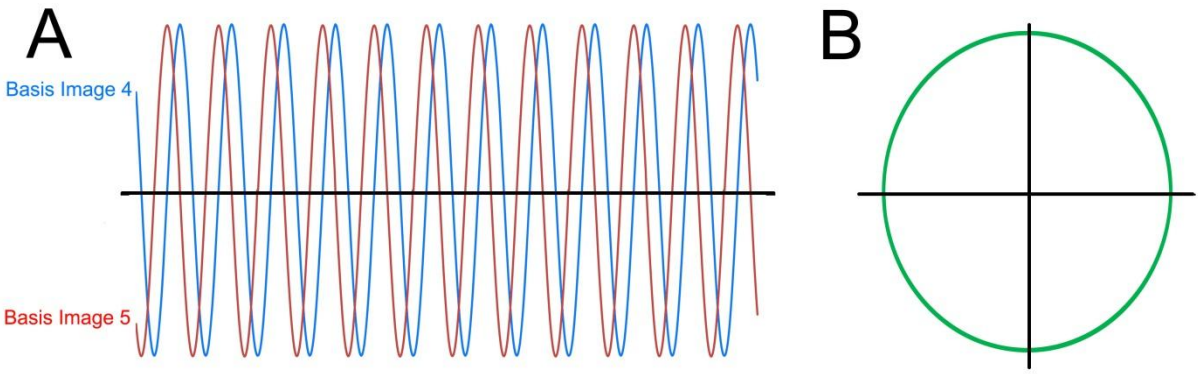


Fig. 6. Projections of Basis Images 4 and 5. **A.** Projection of Basis Image 4 (blue) and Basis Image 5 (red) are plotted for 4 rotations of a Fermat spiral. The projections are clearly sinusoidal in structure. **B.** The projection of Basis Image 5 has been plotted as a function of Basis Image 4 to create a phase plane plot which forms a perfect circle.

There is a direct and rather obvious explanation why KL analysis of a rotating Fermat spiral should generate a series of basis image pairs whose internal structures are spatially shifted by 90^o and whose projections are also phase shifted by a similar 90^o. Since the spiral is moving at a constant angular velocity ω around a circle at a fixed distance from the origin of the x-y

plane, its motion along the x and y coordinates will represent simple harmonic motion with an angular frequency of ω. The behavior of such a system can be described by:

$$x(t) = c_1 \cos(\omega t) + c_2 \sin(\omega t)$$

where c_1 and c_2 are constants determined by the initial conditions.

Since the center of rotation for the Fermat spiral was stationary, the stacked images of the rotating spiral created essentially a circulant matrix. Under such conditions, KL decomposition produces eigenvectors (basis images) that are equivalent to orthonormal Fourier basis functions (sines and cosines) (Kirby, 2001). In essence, KL decomposition of the rotating Fermat spiral produced pairs of orthonormal spatial basis images with one member of the pair capturing the x or "cosine projection", the other pair member capturing the y or "sine projection". Following this reasoning, higher mode pairs (e.g. basis images 4–5) represent "spatial harmonics" of the preceding lower pair (i.e. basis images 3–4). Moreover, as expected of sines and cosines pairs in which the constant c_1 is equal to c_2, the phase plane for modal pairs was circular. These results provide a context in which to interpret KL decomposition data produced by the rotating cortical spiral wave.

A comparison of KL data generated by the rotating Fermat and cortical spirals is shown in Fig. 7. To simplify comparison, basis image 1 for the Fermat spiral (Fig. 4) has been removed with the remaining basis images renumbered to correspond to the cortical spiral images (Fig. 3).

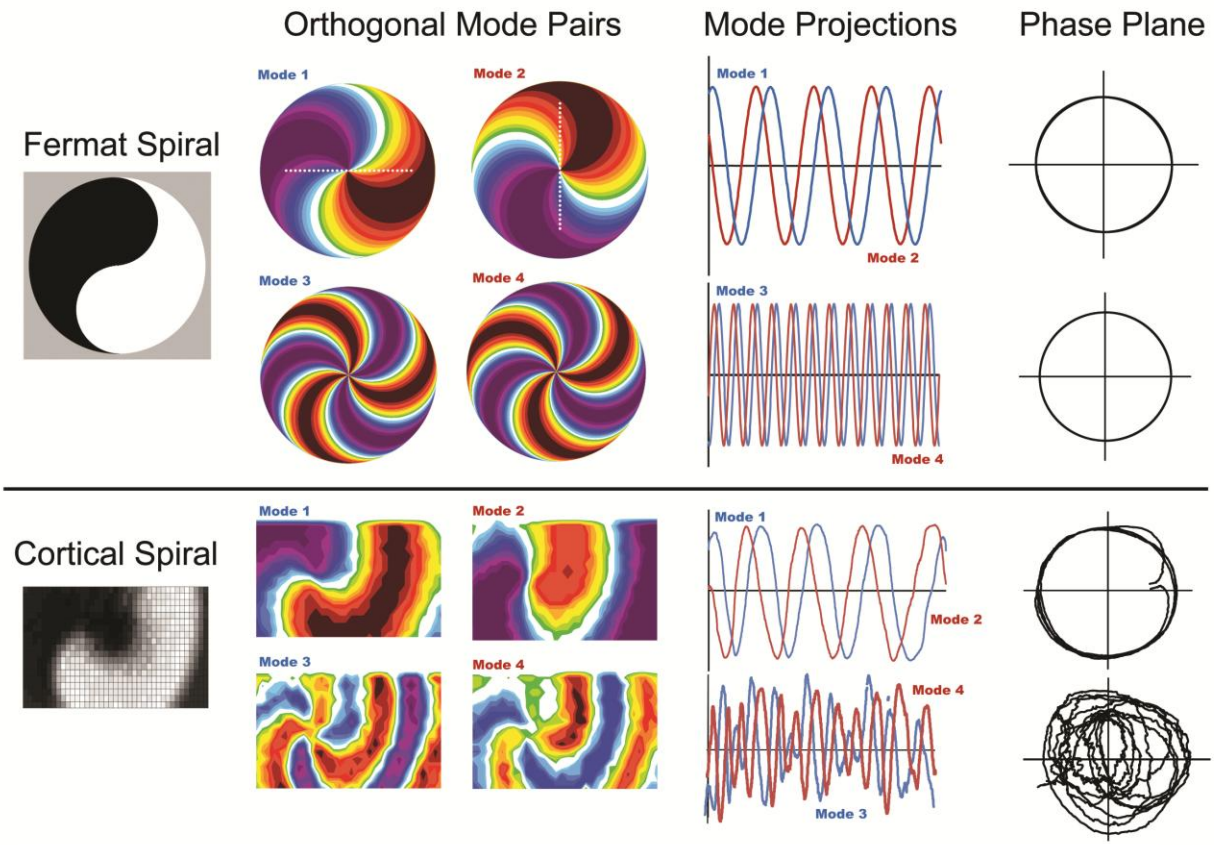


Fig. 7. KL basis images, mode projections, and phase plane plots share similar spatial organization for the rotating Fermat and cortical spiral waves. The first 4 modes are shown for each KL decomposition. Mode pair projections exhibit sinusoidal waveforms offset by ~90^{o} typical of orthogonal pairs. Basis images (modes) for the rotating cortical spiral displays similar patterns but with additional complexity due to a variety of factors including instabilities in the center of rotation.

CHAPTER 5: CONCLUSIONS

KL decomposition provides an efficient way to characterize (nearly) stationary rotating cortical spiral waves. The similarities seen between mode projections and phase planes for the Fermat and cortical spirals led to an increase understanding of how the KL basis images captured the rotational movement the cortical wave dynamics. KL decomposition of rotating spiral waves produces orthonormal pairs of basis images that capture the *x* or "cosine" behavior of the rotation and the *y* or "sine" behavior of the rotation. Higher order basis image pairs represent spatial harmonics of the preceding basis image pair.

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