RESEARCH STATEMENT

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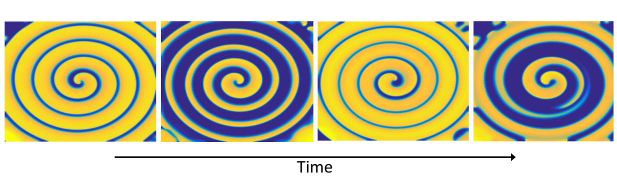
My research interests lie in mathematical biology and dynamical systems, specifically in the formation and stability of spatiotemporal patterns. Motivated by how mathematics can be used to discover and predict relationships in the natural world, I have applied techniques from dynamical systems and numerical methods to study patterns related to cardiac arrhythmias, chemical oscillations, and the migration of blue whales. Summaries of these projects and future directions are below.

1 Summary of Research Projects

Spectral Stability of Spiral Waves: My PhD thesis has focused on using analytical and computational approaches to understand the dynamics of spiral wave patterns that are observed in cardiac arrhythmias and chemical oscillations. Rigidly rotating spiral waves have constant shape and rotational frequency, and can be framed as equilibrium solutions in a rotating frame. This setup allows for both numerical calculation of the waves and a spectral stability analysis of the operator linearized about the spiral wave. We seek to understand bifurcations from rigidly rotating spiral waves, and how the spectral properties of these operators are modified by bounded domains and properties of diffusion. Key findings are summarized below, with additional details in Section 2.

Figure 1: Rigidly rotating spiral wave.

- *Cardiac Arrhythmias and Alternans:* Abnormal cardiac electrical activity results in arrhythmias, with ventricular tachycardia often caused by the electrical activity forming spiral wave patterns. When the spiral destabilizes, the electrical activity can become chaotic and lead to sudden cardiac death (SCD). Higher onset rates of SCD have been clinically linked to alternans, a beat-to-beat oscillation in the action potential duration. Using the two-component Karma Model [1], a simple reaction-diffusion system known to qualitatively reproduce alternans, we analyzed how alternans rhythms arise spectrally, their contribution to spiral breakup, and are investigating whether stable alternans patterns exist.
- *Line Defects in the Rössler System:* The Rössler system qualitatively describes oscillatory interactions between chemical species, and spiral waves formed in these systems have been observed to exhibit stationary line defects. It has been hypothesized that these defects emerged from instabilities of the outer boundary, but has previously not been directly tested [2]. Through a comparison of the full spiral and boundary spectra, we confirm that that line defects are a result of unstable point eigenvalues from the boundary.
- *Systems with Diffusion-less Components:* Theory states that continuous spectra capture the stability of patterns on infinite domains and proves that eigenvalues of spirals on bounded domains should accumulate along predictable curves [3]. If all species in the system diffuse, our numerical results support the theory and predicted convergence. However, if in the limit one or more of the variables is diffusion-less, as is common in ion channel models, the continuous spectra curves exhibit abrupt changes and discrete eigenvalues have unexpected accumulation points. We are using techniques from perturbation theory to investigate the source of the spectral changes.



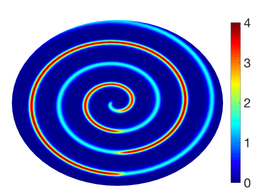


Figure 2: (Left) Development of alternans in the Karma model, as seen in the changing width of spiral bands, leads to spiral breakup. (Right) Stationary line defect in the Rössler system.

A Model for Electrically Excitable Tissue: Due to the dozens of ionic channels that lead to excitable behavior in cardiac cells, conducting experiments on and direct modelling of cardiac tissue are messy. The Cohen Lab at Harvard University developed isradipine Optopatch Spiking Human Embryonic Kidney (iOS-HEK) cells, which express only two ionic channels, but when stimulated, can generate comparable complex electrical spiking behavior and support traveling waves [4]. In collaboration with Harry McNamara and Dr. Adam Cohen, we designed a detailed PDE model for the iOS-HEK cells that reproduces the complex rhythms and dynamical transitions observed in experiments [5].

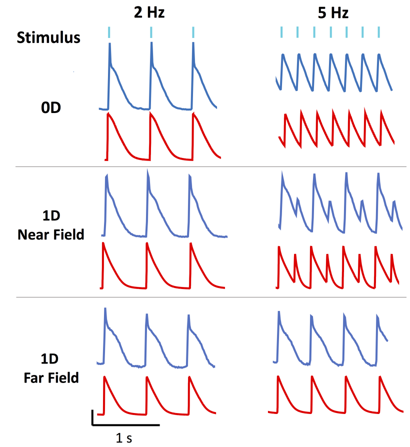


Figure 3: Voltage traces from experimental (blue) and model (red).

The model output captures how the tissue geometry impacts the behavior of propagating waves, suggesting that caution needs to be taken in interpreting results of single cell experiments. There is a one-to-one relationship between stimuli and voltage spikes in a single cell, but in spatially extended arrays of cells, the behavior differs in location near and far from the stimulus.

Migratory Patterns of Blue Whales: As part of the 2018 NSF Graduate Research Internship Program (GRIP), I started working with Dr. Elliott Hazen and Dr. Steven Bograd at the NOAA Environmental Research Division on an individual-based movement model of blue whales in the California current system [6]. Northern Pacific blue whales are a highly migratory species, spending winters in Baja California and summer months as far north as the Oregon-Washington coast, but little is known about how environmental and prey conditions influence the migration patterns. Moreover, the population is endangered and their recovery off the California coast is hindered by increasing ship traffic and changing environmental conditions. Therefore, understanding drivers of migration and the spatiotemporal distribution of individuals is important for implementing effective conservation policies [7].

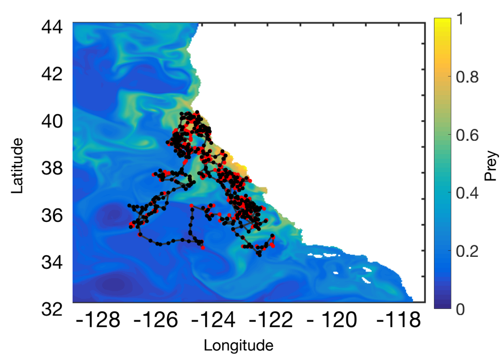


Figure 4: Example simulated track from two-state model.

We developed a two-state agent-based model, with states describing transit and foraging behaviors. States are selected based on preferred environmental conditions and prey levels, and associated with each state is a distribution for step length and turning angle to update whale locations [8]. Both states and locations are updated every six hours, with ocean conditions simulated from a Regional Ocean Modeling System. The model accurately captures the northward migration and yearly differences in the spatiotemporal distribution driven by variations in prey abundance. However, the environmental and prey conditions fail to explain the southward migration, which has been theorized to be precipitated by bioenergetic demands instead of external conditions.

To investigate drivers of southward migration, we expanded the two-state model into a four-state model with additional states representing southward behavior. We tested the impact of prey satiation and proportion of time foraging on southward migration by incorporating these variables into the state transition probabilities. Each strategy leads to contrasting migration behavior, and we are working to compare model results with blue whale observations. The model provides insight into the dynamic behavior of blue whales and opens the door for investigation into other aspects of blue whale behavior, including communication between individual whales and testing robustness of foraging strategies to anomalous conditions.

2 Spectral Stability of Spiral Waves

My research has focused on examining properties of spiral waves found in systems modelled by reaction-diffusion systems of the form

$$\partial_t U = D\Delta U + F(U), \qquad U \in \mathbb{R}^n, \quad D \in \mathbb{R}^{n\times n}, \tag{1}$$

where U is a vector of species which diffuse at rates given by the elements of the diagonal matrix D. Using the rotational symmetry of rigidly rotating spirals, we consider a polar coordinate frame with origin at the spiral center and rotating with frequency ω. In this set up, spiral waves, $U_* = U_*(r,\psi)$, are stationary solutions of the system

$$\partial_t U = D\Delta_{r,\psi} U + \omega\partial_\psi U + F(U). \tag{2}$$

Moreover, in the asymptotic limit as $r \to \infty$, the 2D spiral limits to a 1D periodic traveling wave. That is, $U_*(r,\psi) \to U_\infty(\kappa r - \omega t) = U_\infty(\xi)$, where the wave number κ and frequency ω are selected by the spiral through a nonlinear dispersion relation. Both spiral waves and asymptotic wave trains are numerically calculated by phrasing them as equilibrium solutions and using Newton's Method.

Stability is analyzed by examining the spectrum of the operator $\mathcal{L}_*$ created by linearizing (2) about the spiral wave solution

$$\mathcal{L}_* V = D\left(\partial_{rr} + \frac{1}{r}\partial_r + \frac{1}{r^2}\partial_{\psi\psi}\right)V + \omega\partial_\psi V + F'(U_*)V$$

and considering the resulting eigenvalue problem $\mathcal{L}_* V = \lambda V$ for eigenvalues $\lambda \in \mathbb{C}$. When the spiral is set on an unbounded domain, stability properties are captured by the continuous essential spectrum and discrete eigenvalues of the point spectrum. On bounded domains, discrete eigenvalues converge to asymptotic limits given by the absolute spectrum as the domain size tends to infinity [9]. The main portions of my thesis involve studying the essential, absolute, and point spectra to investigate instabilities observed in rigidly rotating spiral waves.

Unexpected Spectral Behavior in Systems with Diffusion-less Components: Many reaction-diffusion systems describing biological systems, such as ion channel models, have one or more species which do not diffuse. Often, unphysical diffusion is added to these components, but the effect this addition has on the spectral properties has not been studied. We test the impacts of removing diffusion from one species in the Barkley model, a two-component reaction-diffusion system of the form

$$\begin{aligned} u_t &= \Delta u + f(u,v) \\ v_t &= \delta\Delta v + g(u,v) \end{aligned} \tag{3}$$

where $u = u(x,y,t)$, $v = v(x,y,t)$ and v diffuses at the slow rate of $0 < \delta \ll 1$. Numerically, as $\delta \to 0$ we find that the continuous spectra of a spiral wave solution changes from having infinite to finite limits, with the change occurring sharply at $\delta = 0$ (Figure 5). Furthermore, when $\delta = 0$ the point eigenvalues converge to end points of the essential spectrum instead of the predicted absolute spectrum.

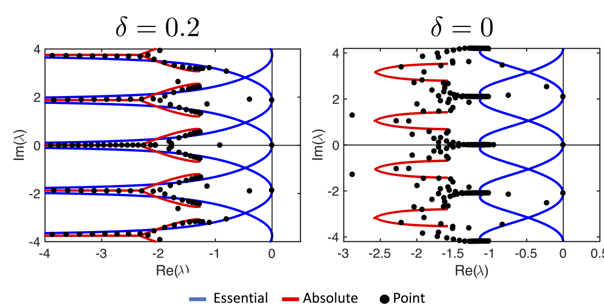


Figure 5: Spiral spectra for $\delta > 0$ and $\delta = 0$.

The continuous spectra depend only on the far-field dynamics and are computed by considering solutions of the form $V(r,\psi) = e^{\nu r}V_\infty(\kappa r - \psi)$, $V_\infty(\xi + 2\pi) = V_\infty(\xi)$ to the eigenvalue problem in the limit that $r \to \infty$, i.e. V_∞ are periodic solutions of

$$\lambda V = D\left(\kappa\partial_\xi + \nu\right)^2 V + \omega\partial_\xi V + F'(U_\infty)V \tag{4}$$

[3, 9, 10]. The essential spectrum is characterized by setting $\nu = i\gamma$, $\gamma \in \mathbb{R}$ in (4), and along the curves $|\gamma| \to \infty$. Dividing (4) by γ^2 and defining $\alpha = 1/\gamma$, we use methods from perturbation theory to analyze how the eigenfunctions and eigenvalues change as $\alpha \to 0$. The results are summarized in the theorem below.

Theorem 1. *Consider a spiral wave solution $U_*(r,\psi)$ with associated asymptotic wave train $U_\infty(\xi)$ to a two-component reaction-diffusion system of the form (3), and assume the linearization $g_v(U_\infty(\xi))$ is constant. Then, when $\delta = 0$, the essential spectrum limits to $\lambda_0 = g_v(U_\infty) + i\omega n$, $n \in \mathbb{Z}$ as $|\gamma| \to \infty$. Moreover, around this limit point, we have the following expansions for the eigenvalues and eigenfunctions, where $\alpha = 1/\gamma$*

$$
\begin{aligned}
u(\xi;\alpha) &= \alpha^2 f_v(U_\infty(\xi))e^{in\xi} + \mathcal{O}(\alpha^3) \\
v(\xi;\alpha) &= e^{in\xi} + \alpha e^{in\xi} + \mathcal{O}(\alpha^2) \\
\lambda(\alpha) &= \lambda_0 + \frac{\alpha^2}{2\pi}\int_0^{2\pi} g_u(U_\infty(s))f_v(U_\infty(s))ds + \mathcal{O}(\alpha^3).
\end{aligned}
$$

A key outcome from the analysis is that periodicity of the eigenfunctions enforces the finite limit points, with the specific values selected by the v-equation.

Ongoing Research: Theorem 1 provides insight into the shifting limits of essential spectrum, but it is still unclear what causes the additional observed spectral changes. We are currently extending the above methods to learn about the unexpected convergence of point eigenvalues.

Period-Doubling Instabilities in Spiral Waves: Alternans and line defects can be considered period-doubling instabilities as new spiral wave must undergo two rotations before returning to the original state. Despite similarities in temporal behavior, we find the mechanisms driving the instabilities are quite different. Using the above framework, we compute the spectra of rigidly rotating spiral waves formed in the Karma and Rössler models at the onset of instability. The focus is on bounded domains where the spiral spectrum is a union of eigenvalues originating from the core region, asymptotic wave trains, and outer boundary, but the essential spectrum also plays a key role in determining the shape of point eigenfunctions [11].

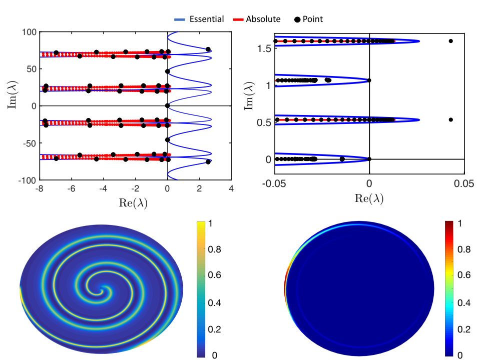


Figure 6: Spectra and unstable point eigenfunction for the (left) Karma and (right) Rössler models.

In the Karma model, we find that the essential spectrum destabilizes first, followed by a complex-conjugate pair of eigenvalues with imaginary part near $3\omega/2$. Alternans and meandering appear as the eigenvalue pair becomes unstable. Moreover, the eigenvalue pair crosses the essential spectrum, meaning that to first order, the associated eigenfunction is given by $V(r,\psi) = e^{i\gamma r}U'_\infty(\kappa r - \psi)$ [11]. The unstable eigenfunction shape, and hence form of the instability, is dominated by the derivative of the wave train, which is highest at wave fronts and backs. Therefore, the growing and shrinking bandwidth associated with alternans emerges from this interaction of the point eigenvalues with the continuous spectrum, and the single pair of eigenvalues suggests the instability is due to the core.

In contrast, results from the Rössler system show that an infinite number of point eigenvalues with imaginary parts at $n\omega/2$ destabilize, followed by branches of essential spectrum. Localization of the eigenfunctions near the boundary, and the infinite number of point eigenvalues is indicative of instabilities from the boundary conditions, as was hypothesized in [2].

To further test contributions from the core and far-field in the instabilities, we formulated the time periodic 1D asymptotic wave trains on a half-line as a two-dimensional spatiotemporal pattern. This pattern has the same asymptotic wave trains and outer boundary condition as the spiral, but does not contain a core.

Comparing the spectra of the far-field and full spirals, the absolute spectrum align as expected in each system. Both sets of spectra in Rössler contain the eigenvalues responsible for the line defect instabilities, indicating the instability is caused by the boundary. Alternans eigenvalues are only present in the full spiral, further justifying alternans emerge from the core.

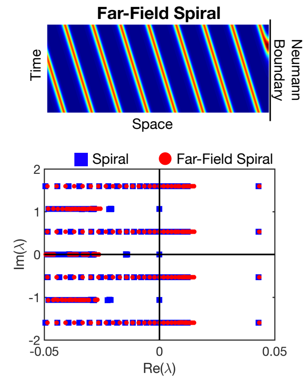


Figure 7: Rössler system

Ongoing Research: Line defects emerge in a supercritical bifurcation, but this property is unknown for alternans. We are working to determine if stable alternans patterns exist by using symmetry properties of the spiral to calculate the bifurcating spiral as a 3D pattern formulated on a disk and periodic in time.

3 Future Research Directions

Pattern Formation and Stability in Reaction-Diffusion Systems: There are two natural directions to broaden my thesis work on spiral waves. The first is to extend the results from qualitative systems to medically applicable settings by considering more realistic models and tissue properties, and there are several questions that can be investigated here. For example, is the interaction of the point and essential spectrum that creates alternans in the Karma model responsible for alternans across all systems? With the added dynamics in realistic models also comes increased complexity and number of variables, making full 2D spectral calculations computationally expensive. If the continuous spectrum can be attributed to formation of alternans, the 1D computation of the essential spectrum provides a more tractable tool for analysis. Additionally, spiral tips are known to pin to defects in the cardiac tissue, leading to the question of how the spectral properties are impacted by an inhomogeneous material.

A second direction is to look at mechanisms for controlling spiral waves and the arrhythmic patterns they induce. In recent years, there have been a number of methods proposed to terminate arrhythmias with external forcing from a series of electrical pulses [12], but there is no formal understanding of when these methods effectively work. By considering how external forcing impacts the stability of spirals in qualitative and then realistic models, I hope to provide the foundation for a rigorous explanation of these methods.

Furthermore, the numerical and analytical techniques that I have applied in my thesis work can be extended to patterns formed in reaction-diffusion systems across a wide variety of applications. I am interested in pursuing additional problems in pattern-forming systems in biology, social systems, and ecology.

Investigating Animal Movement with Agent-Based Models: In addition to exploring drivers of southward migration for blue whales, I am interested in testing environmental factors that can be used as a proxy for prey and using satellite data as input. Although prey is a key driver, there is currently no way to measure prey density across wide spatial areas and instead simulated data is relied upon. Using measurable drivers and current satellite observations would increase the model usefulness by allowing for real-time predictions of whale distributions. Moreover, I would like to test how the seasonal distributions and migrations will be altered with climate change predictions and other anomalous conditions.

The blue whale model highlights the utility of agent-based models to test drivers and understand spatiotemporal distributions of migratory and dynamic animals, both in the marine and terrestrial settings. I want to continue using techniques from agent-based models to investigate questions related to ecology and how systems will respond to a changing climate.

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