The Amazing Kimura Diffusion Operator

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I want to thank the organizers for inviting me to speak in this marvelous Symposium.

Parts of the work I will describe were done jointly with Rafe Mazzeo, Camelia Pop, and Jon Wilkening.
In population genetics we study how the distribution of variants in a reproducing population evolves over time. There are typically four important effects:

1. The randomness in the number of offspring a given individual, or pair, has in a given generation.
2. Mutation from one type to another type.
3. Differences in “fitness” among the different types.
4. Migration in and out of a given environment.
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In this model we assume a fixed population size $N$, and a finite collection of possible types, $\{1, \ldots, M + 1\}$. The state of the population at each time is described by a $M + 1$-tuple: $(n_1, \ldots, n_{M+1})$, giving the number of individuals of each type. Here we assume that $n_1 + \cdots + n_{M+1} = N$, so the state space consists of the integer points in an $M$-simplex.

The evolution of the population is then a Markov process specified by the transition probability:

$$\text{Prob}((k_1, \ldots, k_{M+1})|(n_1, \ldots, n_{M+1})).$$
The simplest haploid case is when there are two types (called alleles) and both types have the same fitness and there is also no mutation. We use $A$ and $a$ to denote the types, and let $X(t)$ be the number of type $a$ and generation $t$. Since $n_a + n_A = N$, in this case the standard Wright-Fisher model is given by the binomial sampling formula:

$$\text{Prob}(X(t+1) = j | X(t) = i) = \binom{N}{j} \left(\frac{i}{N}\right)^{j} \left(1 - \frac{i}{N}\right)^{N-j}$$

(1)
To incorporate mutation and selection, we change the odds. If \( a \) and \( A \) have relative fitness \((1 + s) : 1\), and the rate at which \( a \to A \) is \( \mu_1 \) and the rate at which \( A \to a \) is \( \mu_2 \), then we let:

\[
p_i = \frac{i(1 + s)(1 - \mu_1)}{i(1 + s) + N - i} + \frac{(N - i)\mu_2}{i(1 + s) + N - i}.
\]

We alter the transition matrix to

\[
\text{Prob}(X(t + 1) = j | X(t) = i) = \binom{N}{j} (p_i)^j (1 - p_i)^{N-j} \quad (2)
\]
The main topic of this talk concerns the operators that arise as limits of these sorts of processes as the population $N$ tends to infinity. In the 1d-case, the rescaled processes

$$\frac{1}{N} X^{(N)}([tN]),$$

converge to a continuous time stochastic process parametrized by the interval $[0, 1]$. The “backward” Kolmogorov operator is the second order differential operator:

$$L f(x) = \frac{x(1-x)}{2} \partial_x^2 f + \sigma x(1-x) \partial_x f + m_2(1-x) \partial_x f - m_1 x \partial_x f.$$  

(4)

Where $\sigma = Ns$, $m_1 = N\mu_1$ and $m_2 = N\mu_2$ are assumed fixed, as $N \to \infty$; this is not a biologically meaningful assumption, it just allows us to define the limiting process.
In this limit the second order term,

\[ \frac{x(1 - x)}{2} \frac{\partial^2}{\partial x^2} f, \]

is related to the randomness in the number of offspring; whereas mutation and selection become deterministic forces, represented by the vector field,

\[ \sigma x(1 - x) \frac{\partial}{\partial x} f + m_2(1 - x) \frac{\partial}{\partial x} f - m_1 x \frac{\partial}{\partial x} f. \]

What makes it difficult to study this operator is the fact that the coefficient of the second order term vanishes at the boundary of \([0, 1]\).
What is a Model Good For?

These models make it possible to compute quantities of actual interest in real applications. (When did we diverge from Chimpanzies? What fraction of our genome comes from Neanderthals?) To address these questions requires actually solving these equations numerically with high accuracy.

This is fine if you can write down closed-form expressions for the answer.

But to go beyond that leads to very different concerns from those that arise in the pure math approach to PDE. Today we’ll discuss things along these lines, and tomorrow more traditional PDE questions will be addressed.
In higher dimensions, modeling in population genetics mostly takes place in a very interesting (and very complicated) space called the simplex. The $M$-dimensional simplex is defined to be

$$\Sigma_M = \{(x_0, x_1, \ldots, x_M) : 0 \leq x_j \text{ and } x_0 + \cdots + x_M = 1\}. \quad (5)$$

In population genetics we usually think of $(x_0, \ldots, x_M)$ as the frequencies of $(M + 1)$ possible types.

As defined, $\Sigma_M$ is a closed set, which includes its boundary. The open $M$-simplex is its interior, where all coordinates are strictly positive. $\Sigma_M$ is not a manifold with boundary, but is instead a manifold with corners.
This Markov-chain framework can be used to model populations with any number of types. If there are \( M + 1 \) different types, as noted above, the infinite population limit is a Markov process on an \( M \)-simplex, \( \Sigma_M \), where the coordinates give the frequency of each type. The generator for the stochastic process defining the infinite population limit is then a partial differential operator of the form

\[
Lf = \sum_{i,j} x_i (\delta_{ij} - x_j) \partial_{x_i} \partial_{x_j} + V.
\]

\( V \) is an inward pointing vector field.
The Kimura Operator

We call the second order part

\[ L_{\text{Kim}} f = \sum_{i,j} x_i (\delta_{ij} - x_j) \partial_{x_i} \partial_{x_j} f \]  

(7)

the \textit{Kimura Operator}. In the classical setting the Kimura operator models the changes in frequency of types that occur because of the randomness in the number of off-spring. There are no mutations and no differences in fitness. This is called \textit{genetic drift}. It was something not really included in Darwin’s original thinking.

What makes these models hard to analyze is the fact that the coefficients of the second order derivatives vanish at the boundary. In fact \[ [L x_i] \big|_{x_i=0} = 0 \] for every \( i \).

Nonetheless, or really because of this, the Kimura operator has many remarkable properties, and that is what I would like to discuss today.
A point \((x_0, \ldots, x_M)\) lies on the boundary of the simplex if at least one coordinate is zero. In fact the \(\partial \Sigma_M\) is a stratified space, where the strata are labeled by the number of coordinates that are zero. We let \(\partial \Sigma^k_M\) denote the subset of the boundary where exactly \(1 \leq k \leq M\) coordinates are zero. \(\partial \Sigma^k_M\) is a disjoint union of open \((M - k)\) simplices, whose boundaries lie in the union of the lower dimensional strata:

\[
\partial \Sigma^{k+1}_M \cup \cdots \cup \partial \Sigma^M_M = d \Sigma^{k+1}_M.
\]

One gets the feeling that, in some sense, there is just a single infinite simplex and all other simplices occur as components of the stratification of its boundary.

It’s simplices all the way down!
Some pictures
The simplex has discrete and continuous symmetries. The symmetric group on \((M + 1)\) letters, \(S_{M+1}\), acts by permuting the order of the coordinates. There is also a continuous action by a group of projective transformations

\[
(x_0, \ldots, x_M) \mapsto \frac{(a_0x_0, \ldots, a_Mx_M)}{a_0x_0 + \cdots + a_Mx_M},
\]

(8)

here \((a_0, \ldots, a_M)\) is a positive vector. We will not be too interested in this continuous group action as it does not commute with the operators relevant in population genetics, whereas the action of \(S_{M+1}\) often does.
The “Canonical Operator” on $\mathbb{R}^n$

There are some operators acting on functions defined on some spaces, which are clearly marriages made in heaven. The example that we all know is the Laplace operator on Euclidean space.

$n$-dimensional Euclidean space is $\mathbb{R}^n$ endowed with the Riemannian metric $ds^2 = dx_1^2 + \cdots + dx_n^2$, so that

$$d_{\text{Eucl}}(x, y) = \sqrt{\sum_{j=1}^n (x_i - y_i)^2} = |x - y|^2.$$ The Laplace operator is defined by this metric and is given by

$$\Delta u = \frac{\partial^2}{\partial x_1^2} u + \cdots + \frac{\partial^2}{\partial x_n^2} u.$$ (9)

The metric has a very large isometry group $O(n) \ltimes \mathbb{R}^n$. If $T$ is an isometry, then

$$\Delta \circ T = T \circ \Delta,$$ (10)

and many of the remarkable properties of the Laplace operator follow from this fact and elementary representation theory.
Remarkable properties of the Laplace operator

For example, the “fundamental solution,” that is a solution to \( \Delta G = \delta(x - y) \), is given by \( G(x, y) = c_n |x - y|^{2-n} \), and the fundamental solution to the heat equation is given by

\[
p_t(x, y) = \frac{e^{-\frac{|x-y|^2}{4t}}}{(4\pi t)^{\frac{n}{2}}}.
\] (11)

Indeed similar properties hold for the Laplace operator of any Riemannian space. It always commutes with the full group of isometries, and the distance on the space is always apparent in the heat kernel, at least as \( t \to 0^+ \).

\( L_{\text{Kim}} \) plays a very similar role for analysis on the simplex.
The Boundary of the Simplex, bis

As noted above, if there are $M + 1$ types, then their frequencies define a point in the $M$-simplex, which is most naturally represented in $\mathbb{R}^{M+1}$ by

$$\Sigma_M = \{(x_0, \ldots, x_M) : 0 \leq x_j \text{ and } x_0 + \cdots + x_M = 1\}. \quad (12)$$

For each $1 \leq k \leq M$, each subset of $k$-variables $\{x_{i_1}, \ldots, x_{i_k}\}$ defines a stratum of the boundary given by the equations

$$x_{i_1} = \cdots = x_{i_k} = 0. \quad (13)$$

It is an $M - k$-simplex: if

$$\mathcal{J} = \{j_1, \ldots, j_l\} = \{0, \ldots, M\} \setminus \{x_{i_1}, \ldots, x_{i_k}\},$$

then on this boundary stratum

$$x_{j_1} + \cdots + x_{j_l} = 1. \quad (14)$$

We denote this stratum of $\partial \Sigma_M$ by $\sigma_{\mathcal{J}}$. 
In our formula for $L_{\text{Kim}}$ we are not too specific about the range of indices. For now let’s suppose that

$$L_{\text{Kim}}f = \sum_{0 \leq i, j \leq M} x_i (\delta_{ij} - x_j) \partial_{x_i} \partial_{x_j} f.$$  \hspace{1cm} (15)

It doesn’t really matter, because of the following result of Sato: if $u$ is a smooth function on $\Sigma_M \subset \mathbb{R}^{M+1}$ and $U$ is any smooth extension of $u$ to a neighborhood of $\Sigma_M$, then

$$[L_{\text{Kim}}U] \upharpoonright \Sigma_M$$  \hspace{1cm} (16)

is independent of the choice of extension. That is $L_{\text{Kim}}$ is \textit{tangent} to $\Sigma_M$ in a very strong sense.
The Tangency property of $L_{Kim}$, II

In particular, we could take

$$U(x_1, \ldots, x_M) = u(1 - (x_1 + \cdots + x_M), x_1, \ldots, x_M).$$

This is either a function on the projection of the simplex to $\tilde{\Sigma}_M \subset \mathbb{R}^M$, or a function in $\mathbb{R}^{M+1}$, which is independent of $x_0$. With this choice we see $L_{Kim}u$ is computed using the formula

$$L_{Kim}u = \sum_{1 \leq i, j \leq M} x_i (\delta_{ij} - x_j) \partial x_i \partial x_j U.$$  \hspace{1cm} (17)

From a projective representation it is not obvious that the Kimura operator is invariant under the action of $S_{M+1}$, the vertex at 0 “looks special,” but this is an easy consequence of Sato’s theorem.
Tangency property of $L_{\text{Kim}}$, III

The tangency property holds for any stratum of the boundary. If $u$ is a smooth function on a stratum $\sigma_{\mathcal{I}}$, and $U$ is an extension of $u$ to a neighborhood of $\sigma_{\mathcal{I}}$ in $\mathbb{R}^{M+1}$ then

$$[L_{\text{Kim}}U] \uparrow_{\sigma_{\mathcal{J}}}$$  \hspace{1cm} (18)$$

is independent of the choice of extension. That is $L_{\text{Kim}}$ is tangent to every stratum of the boundary of $\Sigma_M$, so in a real sense there is just one Kimura-operator, which is a sum over infinitely many variables, and all others are obtained by restriction to strata of the boundary of this infinite simplex.
As noted above, the boundary of $\Sigma_M$ is a stratified space with each stratum a union of simplices of a single dimension that meet along their boundaries. If $\sigma \subset \partial \Sigma_M$, is a component of a stratum, then we denote by $L_{\text{Kim}}^\sigma$ the restriction of $L_{\text{Kim}}$ to functions defined on $\sigma$. It is well defined by the previous result, and given by the same formula as $L_{\text{Kim}}$ itself by just summing over the variables that don’t vanish identically on $\sigma$. 
To do analysis, we need a metric. The principal symbol of the Kimura operator,

\[ P_{\text{Kim}}(\xi) = \sum_{i,j} x_i (\delta_{ij} - x_j) \xi_i \xi_j \]  

(19)

defines a co-metric on the simplex. The corresponding metric is singular at the boundary, but not complete. The distance it defines is equivalent to

\[ \rho_i(x, y) = \sum_{i=0}^{M} |\sqrt{x_i} - \sqrt{y_i}|. \]  

(20)

The boundary is at a finite distance. The co-metric obviously extends to the boundary, and the metric as well.
This metric turns out to be the natural metric to use when studying the regularity properties of solutions to the equation $L_{\text{Kim}}w = f$, or the related parabolic problem $\partial_t u - L_{\text{Kim}}u = f$. In fact, there is now a well developed theory, which we will discuss tomorrow, based on this metric. Using metric we define two ladders of anisotropic Hölder spaces, $C_{WF}^{k,\gamma}$, and $C_{WF}^{k,2+\gamma}$. For $\lambda > 0$, the maps

$$(L_{\text{Kim}} - \lambda \text{Id}) : C_{WF}^{k,2+\gamma} \rightarrow C_{WF}^{k,\gamma}$$

are isomorphisms. This means that in terms of the intrinsic geometry, defined by the operator itself, the Kimura operator has the “expected” ellipticity properties.
There is another metric on the simplex that is invariant under the action of the projective group. This metric is complete; in 1d it is given by

\[ ds^2 = \frac{dx^2}{x^2(1 - x)^2}, \]  

(22)

as contrasted with

\[ ds^2_{\text{Kim}} = \frac{dx^2}{x(1 - x)}. \]  

(23)
It is very important feature of $ds^2_{\text{Kim}}$ that is not complete. It allows paths of the underlying stochastic process to reach the boundary in finite time. Indeed, once a path reaches the boundary, it stays there, and in fact cascades down through the strata until it reaches a vertex. This happens in finite time, with probability 1, in a randomly reproducing population without mutations. In population genetics this is called “fixation in finite time.”

A world comprised of a single species is not something that we see when we look at the world around us, but it is something that occurs in a static environment, like a chemostat filled with bacteria. Provided that we don’t wait too long...
To include other effects in our genetics model, like mutation and selection, we add a vector field $V$ to $L_{Kim}$. It is usually assumed that the vector field is inward pointing at the boundary of $\Sigma_M$. In many applications the vector field takes the form

$$V = \sum_{j=0}^{M} b_j(x) \partial x_j.$$  \hspace{1cm} (24)
In the standard models in genetics the coefficients of $V$ are polynomials; the linear parts $\{b_{1j}(x)\}$ are used to model the effects of mutations. The vector field then splits as

$$V = \sum_{j=0}^{M} b_{1j}(x) \partial_{x_j} + \sum_{j=0}^{M} b_{2j}(x) \partial_{x_j} = V^1 + V^2.$$  \hfill (25)

The vector field $V^2$ is tangent to the boundary of the simplex and models the effects of selection.
Constant weights

An especially simple case for analysis, that often appears in the literature, is where $V^2 = 0$ and

$$V^1 x_j \mid x_j = 0 = b_j,$$

(26)

a constant. We call this the case of constant weights. In the genetics literature it is said that the rate of mutation into the type $j$ is “parent independent,” which is a strange hypothesis....

In the projected model the vector field takes the form

$$\tilde{V}_b = \sum_{j=1}^{M} (b_j - B x_j) \partial x_j,$$

(27)

where $B = b_0 + \cdots + b_M$. We let

$$L_b = L_{\text{Kim}} + V_b.$$  

(28)
Part of what makes the case of constant weights easier to analyze is the fact that the Kimura operator is self adjoint with respect to the weighted measure:

\[ d\mu_b = \prod_{j=0}^{M} x_j^{b_j-1} \, dx_1 \cdots dx_M. \]  

(29)

If all the \(b_j\)s are positive then this is a finite measure, and otherwise it is infinite. In the case of all positive weights, this measure a scalar multiple of the unique “stationary measure.”
Outline

1. The Wright-Fisher Model and Its Diffusion Limit
2. Boundary Conditions
3. Eigenfunctions
4. The Dirichlet Problem
5. Tomorrow’s Lecture
6. Bibliography
Regularity

So far I have not said anything about boundary conditions. Since $L_{Kim}$ is degenerate, the usual Dirichlet and Neumann problems do not make sense. Indeed solutions are better characterized by their regularity properties. This is what makes it very subtle to analyze the solutions to this equation and approximate them numerically.

We say that a function $u$ belongs to $\mathcal{D}^2_{WF}(\Sigma_M)$ if $u \in C^1(\Sigma_M) \cap C^2(\text{int } \Sigma_M)$, and each weighted second derivative

$$x_i (\delta_{ij} - x_j) \partial_{x_i x_j} u$$

(30)

extends continuously to the closure of $\text{int } \Sigma_M$. We also assume that the extension of $x_i (\delta_{ij} - x_j) \partial_{x_i x_j} u$ vanishes where the coefficient $x_i (\delta_{ij} - x_j)$ vanishes.
There are a variety of maximum principles that one can prove for this class of operators. As a consequence one can easily prove:

**Theorem**

Let \( u \in D^2_{WF}(\Sigma_M) \) satisfy \( L_{Kim}u = 0 \) on \( \Sigma_M \), then \( u \) is determined by its values at the vertices of \( \Sigma_M \).

We call a solution to a Kimura equation, \( L_{Kim}u = f \), that belongs to \( D^2_{WF}(\Sigma_M) \) a *regular* solution, because these solutions turn out to be as regular as possible.

The regular null space of \( L_{Kim} \) is spanned by polynomials of degree 1. There is an infinite dimensional space of irregular null-vectors, since, as we shall see, the Dirichlet problem is well posed.
For $L$ a non-degenerate elliptic operator on $\Sigma_M$, and $h$ a smooth and compactly supported function, it is very unlikely that the solution to the initial value problem $\partial_t v - Lv = 0$, with $v(x, 0) = h(x)$, and any reasonable boundary condition will be smooth.

The degeneracies of $L_{Kim}$ are very subtly matched with the singularities of the geometry of $\partial \Sigma_M$. In the next lecture we show that the initial value problem for the heat equation

$$\partial_t u - L_{Kim}u = 0 \text{ with } u(x, 0) = f(x),$$

has a unique solution, for any reasonable initial data, that belongs to $C^\infty(\Sigma_M \times (0, \infty))$.

This is another amazing property of the Kimura operator.
Today I’d like to discuss the solution to the Dirichlet problem

\[ L_{\text{Kim}} u = f \text{ with } u \mid_{\partial \Sigma_M} = g. \]  

Statistical quantities connected to the underlying stochastic process are often found by solving such problems.

And we will try to solve it in a sense that would appeal to biologists, that is:

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Regularity for the Dirichlet Problem

1. It is easy to see that this problem usually does not have a regular solution. If \( \sigma \) is a component of the stratification of \( \partial \Sigma_M \), then a function \( u \in D^2_{WF}(\Sigma_M) \) also belongs to \( D^2_{WF}(\sigma) \), and satisfies

\[
L^\sigma_{\text{Kim}}[u \upharpoonright \sigma] = [L_{\text{Kim}}u] \upharpoonright \sigma .
\] (33)

2. Hence, in order for the Dirichlet problem to have a regular solution, it would have to be the case that, for every boundary stratum \( \sigma \),

\[
L^\sigma_{\text{Kim}}[g \upharpoonright \sigma] = f \upharpoonright \sigma ,
\] (34)

which usually is not true.
1. It is easy to see that this problem usually does not have a regular solution. If $\sigma$ is a component of the stratification of $\partial \Sigma_M$, then a function $u \in D^2_{WF}(\Sigma_M)$ also belongs to $D^2_{WF}(\sigma)$, and satisfies

$$L_{Kim}^\sigma[u \upharpoonright \sigma] = [L_{Kim}u] \upharpoonright \sigma.$$  \hspace{1cm} (33)

2. Hence, in order for the Dirichlet problem to have a regular solution, it would have to be the case that, for every boundary stratum $\sigma$,

$$L_{Kim}^\sigma[g \upharpoonright \sigma] = f \upharpoonright \sigma.$$  \hspace{1cm} (34)

which usually is not true.
The 1d-case

Let’s first do the 1-d case. A critical observation is that

\[ x(1-x) \partial_x^2 x \log x = 1 - x, \quad \text{and} \quad x(1-x) \partial_x^2 (1-x) \log(1-x) = x. \]  

(35)

If we let

\[ u(x) = x \log x f(0) + (1-x) \log(1-x) f(1) + (1-x) g_0 + x g_1 + \tilde{u}(x), \]

(36)

then \( u \) satisfies the boundary conditions and \( \tilde{u} \) must satisfy

\[ x(1-x) \partial_x^2 \tilde{u} = f(x) - (1-x) f(0) - xf(1) \overset{\text{def}}{=} f^{(1)}(x), \]  

(37)

and \( \tilde{u}(0) = \tilde{u}(1) = 0 \). We note that \( f^{(1)}(0) = f^{(1)}(1) = 0 \), and so there may indeed be a regular solution to this problem, but \( u \) itself is singular at the boundary.
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Shimakura’s formula

In the 1970s and 80s Shimakura studied the eigenfunctions of these operators, which are polynomials. He proved a very useful formula: let \( \mathcal{I} = \{i_1 < i_2 < \cdots < i_{k+1}\} \subset \{0, \ldots, M\} \), and set

\[
w_\mathcal{I} = \prod_{j=1}^{k+1} x^{1-b_{i_j}}. \tag{38}\]

We then have the identities:

\[
L_{b'}(w_\mathcal{I}u) = w_\mathcal{I}[L_{b'} - \kappa_\mathcal{I}]u, \quad \text{where} \tag{39}
\]

\[
\kappa_\mathcal{I} = \left(\sum_{j \in \mathcal{I}} (1 - b_j)\right) \left(k + \sum_{j \notin \mathcal{I}} b_j\right), \quad \text{and} \]

\[
b'_j = \begin{cases} 
2 - b_j & \text{if } j \in \{i_1, \ldots, i_{k+1}\}, \\
b_j & \text{if } j \notin \{i_1, \ldots, i_{k+1}\}. 
\end{cases} \tag{40}\]
To find $\widetilde{u}$ we construct the eigenfunctions of $x(1-x)\partial_x^2$ that vanish as the boundary. These take the form $x(1-x)q(x)$, where $q(x)$ is a polynomial. Using Shimakura’s formula, we see that $q$ must satisfy an equation of the form

$$[x(1-x)\partial_x^2 + 2(1-2x)\partial_x - 2]q = [L_{(2,2)}q - 2q] = \lambda q.$$  \hspace{1cm} (41)

This is a Kimura operator with constant weights $(2, 2)$. A simple calculation shows that if the degree of $q_d$ is $d$, then

$$\lambda_d = -(d + 1)(d + 2).$$
By the self adjointness of \( L_{(2,2)} \) it follows that the eigenfunctions, \( \{q_d\} \), can be found by applying Gram-Schmidt, with respect to the inner product:

\[
\langle p, q \rangle = \int_{0}^{1} p(x)q(x)x(1 - x)dx,
\]

(42)

to the monomials \( \{1, x, x^2, \ldots, \} \); no need to solve ODEs!

More importantly, this implies that there is a 3-term recurrence for computing these functions, which turns out to be stable. That is: the values of eigenfunctions can be accurately computed. NOTE: In general high degree polynomials cannot be evaluated accurately.
Since the nullspace of \( x(1 - x)\partial_x^2 \) is spanned by \{1, x\}, it clear that \{1, x, x(1 - x)q_0(x), \ldots, \} has dense span in \( C^0([0, 1]) \). The function \( \widetilde{u} \) has a series representation of the form

\[
\widetilde{u}(x) = \sum_{j=0}^{\infty} \frac{c_d}{\lambda_d} x(1 - x)q_d(x).
\] (43)

If the \( \{q_d\} \) have unit norm, then

\[
c_d = \int_0^1 f^{(1)}(x)q_d(x) \, dx.
\] (44)

Incidentally \( q_d(x) \propto P_{d}^{(1,1)}(2x - 1) \), where \( \{P_{d}^{(1,1)}\} \) are Jacobi polynomials. Using a similar approach, we now solve this problem in higher dimensions.
$L_{\text{Kim}}$ maps the space of polynomials of degree $d$ to itself for any $d$, and therefore the eigenfunctions of the operator $L_{\text{Kim}}$ are polynomials in many variables.

As such, they can be organized in many different ways. We present a construction that is, in effect a recursion over the stratification of boundary of the simplex. The eigenfunctions are then ordered according to their vanishing properties.

This is very useful both for the stable evaluation of the eigenfunctions, and their usage to solve the inhomogeneous Dirichlet problem.
As in the 1d-case, we will try to construct these polynomials by using Gram-Schmidt. But note that the measure on $\Sigma_M$ with respect to which $L_{\text{Kim}}$ is self adjoint, is

$$d\mu_0 = \frac{dx_1 \cdots dx_M}{x_0 \cdots x_M},$$

which is not a finite, measure, so one cannot just apply Gram-Schmidt to polynomials in a straightforward way to get these eigenfunctions.

Recall that $\Sigma_M^k$ denotes the union of the closed $k$-simplices in $\partial \Sigma_M$. It is connected, but $\Sigma_M^k \setminus \Sigma_M^{k-1}$ is a disjoint union of open simplices with boundaries lying in $\Sigma_M^{k-1}$. 
Choose indices $0 \leq i_1 < i_2 \leq M$. We first look for polynomial eigenfunctions of the form $x_{i_1} x_{i_2} q_d(x_{i_1})$. As polynomials they are globally defined; not only do these solve the 1d-eigenfunction equation defined above, but, thought of as functions in the whole simplex, they also solve the $M$-dimensional equation

$$L_{\text{Kim}}[x_{i_1} x_{i_2} q_d(x_{i_1})] = \lambda_d x_{i_1} x_{i_2} q_d(x_{i_1}).$$ (46)

Finally observe that these functions vanish identically on every component of the 1-skeleton, $\Sigma^1_d$, of $\partial \Sigma_M$, except for the one on which $x_{i_1} + x_{i_2} = 1$. 
We repeat this construction for every stratum of the boundary: choose indices \( \mathcal{I} = \{0 \leq i_1 < \cdots < i_{k+1} \leq M\} \). Look for eigenfunctions of the form

\[
w_\mathcal{I} \cdot q_m(x_{i_1}, \ldots, x_{i_k}),
\]

where \( w_\mathcal{I} = x_{i_1} \cdots x_{i_{k+1}} \). Here \( m = (m_1, \ldots, m_k) \) is a multi-index giving the highest order term:

\[
q_m \propto x_{i_1}^{m_1} \cdots x_{i_k}^{m_k} + \text{l.o.t.}
\]

The degree of \( q_m \) is \(|m| = m_1 + \cdots + m_k\).
Using Shimakura’s formula we see that $q_m$ satisfies a different Kimura equation:

$$[L_{I,2}^{T} - k(k + 1)]q_m = -(|m|^2 + (2k + 3)|m|)q_m. \quad (48)$$

The operator $L_{I,2}^{T}$ has all constant weights equal 2. The dimension of the eigenspace of degree $d$ polynomials is

$$\dim \mathcal{P}_d / \mathcal{P}_{d-1}.$$ 

Once again these extend, as polynomials, to all of $\Sigma^k_M$ and continue to satisfy the same equation $L_{\text{Kim}} w_I q_m = \lambda |m|, k w_I q_m$.

Moreover, a simple counting argument shows that each $w_I q_m$ vanishes on all other components of the $k$-skeleton, $\Sigma^k_M$. 
Thus we see that the eigenfunctions of $L_{Kim}$ can be constructed recursively across the stratification of the boundary of the simplex. At the last stage we get eigenfunctions of the form $x_0 \cdots x_M q(x_1, \ldots, x_M)$, which vanish on all the $\partial \Sigma_M$.

At each stage, the eigenfunctions can be constructed by applying Gram-Schmidt to the polynomials with respect to the measure $w_\Omega dx_{i_1} \cdots dx_{i_k}$.

It is clear that the functions obtained in this way are independent, and span the space of all polynomials. Thus, they have dense span in $C^0(\Sigma_M)$ as well. We now show how to use them to find the regular solution to the equation $L_{Kim}u = f$. 
As noted the eigenfunctions in higher dimensions are found by applying Gram-Schmidt to the monomials with a certain weighted measure. Using an approach introduced by Proriol and extended by Wingate and Taylor, we can express these polynomials as products of 1-variable polynomials. The first step is to map the $k$-cube to the $k$-simplex using the change of variables, $T : (X_1, \ldots, X_k) \rightarrow (x_0, x_1, \ldots, x_k)$,}

$$x_j = \prod_{i=1}^{j-1} (1 - X_i) X_j,$$

and $x_0 = \prod_{i=1}^{k} (1 - X_i)$. 

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and $x_0 = \prod_{i=1}^{k} (1 - X_i)$.
The measure on the simplex pulls back to a product measure on the cube.

The eigenfunctions are then found to be products of 1-variable Jacobi polynomials in the $(X_1, \ldots, X_k)$-variables times powers of the $\{(1 - X_i) : i = 1, \ldots, k\}$:

$$p \circ T(X) = \prod_{j=1}^{k} Q_j(X_j)(1 - X_j)^{d_j}.$$  \hspace{1cm} (50)

In principle, the $\{Q_j\}$ are found by applying Gram-Schmidt with a weighted measure on $[0,1]$. In practice they are computed using 3-term recurrences.
1. The measure on the simplex pulls back to a product measure on the cube.

2. The eigenfunctions are then found to be products of 1-variable Jacobi polynomials in the \((X_1, \ldots, X_k)\)-variables times powers of the \(\{(1 - X_i) : i = 1, \ldots, k\} :\)

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3. In principle, the \(\{Q_j\}\) are found by applying Gram-Schmidt with a weighted measure on \([0, 1]\). In practice they are computed using 3-term recurrences.
In order for $L_{\text{Kim}}u = f$ to have a regular solution, it necessary that $f$ vanishes at vertices of $\Sigma_M$. For each component $\sigma \in \Sigma_1$, we first solve the equations

$$L_{\text{Kim}}^{\sigma}u^{1} \upharpoonright_{\sigma} = f \upharpoonright_{\sigma}. \quad (51)$$

There are $\mathcal{M}(\mathcal{M} + 1)/2$ such 1-dimensional boundary components. Since a given family of “1d-eigenfunctions” vanishes on all other components of $\Sigma_1$, and $L_{\text{Kim}}$ is tangent to all boundary strata, each of these equations can be solved independently of the others. This gives a function $u^{1}$ defined on all of $\Sigma_M$, so that

$$L_{\text{Kim}}^{\sigma}[u^{1} \upharpoonright_{\sigma}] = f \upharpoonright_{\sigma}, \quad (52)$$

for each $\sigma \in \Sigma^1_M$. 
Recursively we can find $u^1, u^2, \ldots, u^n$, so that

$$f^{(k)} = f - L_{Kim}(u^1 + \cdots + u^{k-1})$$  \hspace{1cm} (53)$$

vanishes on the $k - 1$-skeleton of $\partial \Sigma_M$, and $u^k$ is then defined to solve

$$L_{Kim} u^k \upharpoonright \Sigma^k_M = f^{(k)} \upharpoonright \Sigma^k_M.$$  \hspace{1cm} (54)$$

As before, this equation can be solved, using the eigenfunctions constructed above, on each component of $\Sigma^k_M$ independently of the others. If we let $u = u^1 + \cdots + u^M$, then $L_{Kim} u = f$ on the entire closed simplex. If $f$ is a polynomial, then so is $u$. Using the regularity results mentioned above, it is easy to show that $u$ is always the regular solution.
Outline

1 The Wright-Fisher Model and Its Diffusion Limit

2 Boundary Conditions

3 Eigenfunctions

4 The Dirichlet Problem

5 Tomorrow’s Lecture

6 Bibliography
We now turn to the solution of the Dirichlet problem, which, as we’ve seen is generally not regular. We are looking for a function \( u \) that satisfies

\[
L_{\text{Kim}} u = f \quad \text{and} \quad u \bigg|_{\partial \Sigma_M} = g. \tag{55}
\]

We extend \( g \) to a function \( \tilde{g} \) defined on all of \( \Sigma_M \), with optimal smoothness, and set \( u = v + \tilde{g} \). The function \( v \) must satisfy:

\[
L_{\text{Kim}} v = f - L_{\text{Kim}} \tilde{g} \quad \text{and} \quad v \bigg|_{\partial \Sigma_M} = 0. \tag{56}
\]

The singular part of the solution is contained in \( v \), as \( \tilde{g} \) could be defined to be \( C^\infty \) in the interior of \( \Sigma_M \).
We say that $v$ solves this homogeneous Dirichlet problem if

$$v \in C^0(\Sigma_M) \cap C^2(\text{int } \Sigma_M),$$

vanishes on the boundary and

$$L_{Kim}v = f - L_{Kim}\tilde{g} \quad \text{in the interior},$$

has a continuous extension to the boundary.

We next show how to find a formula for the leading order singular part of $v$. 
The 2d-case I

We first do this in the 2d-case, for a simpler operator. We work in the positive quadrant, \( [0, \infty) \times [0, \infty) \), with

\[
L_0 v = x_1 \partial_{x_1}^2 v + x_2 \partial_{x_2}^2 v = f(x_1, x_2),
\]

which we assume is supported in \( x_1 + x_2 < R \). Let \( \psi(t) = 1 \) for \( t < R \), and 0 for \( t > R + 1 \). We set

\[
v_1 = \psi(x_1 + x_2) [ f(x_1, 0) x_2 \log x_2 + f(0, x_2) x_1 \log x_1 - f(0, 0) (x_1 + x_2) \log(x_1 + x_2) ].
\]

It is easy to see that \( v_1 \) is continuous in the closed orthant, and vanishes on the boundary. Finally a calculation shows that

\[
L_0 v_1 \upharpoonright_{\partial \mathbb{R}_+^2} = f \upharpoonright_{\partial \mathbb{R}_+^2}.
\]

The key is the function

\[
\eta(t) = t \log t.
\]
To complete the 2d case we observe that $f - L_0 v_1$ has a certain degree of anisotropic Hölder regularity at the boundary. Thus there is a “regular” solution to the equation

$$L_0 v_0 = f - L_0 v_1,$$

which vanishes at the boundary. The sum $v = v_0 + v_1$ solves the original Dirichlet problem. The function $v_0 \in C^{0,2+\gamma}_{WF}(\mathbb{R}^2_+)$, is not smooth up to the boundary, but it is smoother than $v_1$. A similar method works in any dimension and also on the simplex.
To use this approach on the simplex, we work in a neighborhood of one vertex at a time. To that end choose a partition of unity \( \{ \varphi_0, \ldots, \varphi_M \} \) so that \( \varphi_j \) is 1 in a neighborhood of the \( j \)th vertex, and vanishes in a neighborhood of the “opposite” face. We then need to solve the equations

\[
L_{\text{Kim}} v_j = \varphi_j (f - L_{\text{Kim}} \tilde{g}) = \tilde{f}_j.
\]

In fact we will just find a formula for the leading singular part that also vanishes in a neighborhood of the opposite face. To do this we work in the projection of the simplex to \( \mathbb{R}^M \) wherein the \( j \)th vertex is mapped to the origin.
We assume that $\tilde{f}_j$ is supported in the set $x_1 + \cdots + x_M < 1 - \epsilon$, and let $\psi(t) = 1$ for $t < 1 - \epsilon$ and zero for $t > 1 - \frac{\epsilon}{2}$. For a collection of indices $\mathcal{I} = \{1 \leq i_1 < \cdots < i_k\}$, we let

$$X_{\mathcal{I}}(x) = \sum_{j \notin \mathcal{I}} x_j e_j, \quad S_{\mathcal{I}}(x) = \sum_{i \in \mathcal{I}} x_i.$$  \hspace{1cm} (62)

Note that $X_{\mathcal{I}}$ and $S_{\mathcal{I}}$ are functions of complementary sets of variables, and $X_{\{1, \ldots, M\}} = (0, \ldots, 0)$. The singular part of $v_j$ is given by the sum

$$v_j \psi = \psi(x_1 + \cdots + x_M) \left[ \sum_{\mathcal{I}} (-1)^{|\mathcal{I}| - 1} f_j(X_{\mathcal{I}}(x)) \eta(S_{\mathcal{I}}(x)) \right],$$  \hspace{1cm} (63)

with $\eta(t) = t \log t$, as before. The sum is over all collections of indices $\mathcal{I}$, with $|\mathcal{I}| \leq M$. 


It is again easy to show that $v_{j1}$ is a continuous function on $\Sigma_M$, which vanishes at the boundary. It is also not hard to see that $L_{\text{Kim}}v_{j1}$ is continuous up to the boundary. An easy calculation shows that $L_{\text{Kim}}\eta(S_\mathcal{I}(x)) = 1 - \eta(S_\mathcal{I}(x))$, and from this it is not difficult to show that

$$L_{\text{Kim}}v_{j1} \upharpoonright_{\partial \Sigma_M} = f_j \upharpoonright_{\partial \Sigma_M}. \quad (64)$$

If we let $v_1 = v_{01} + \cdots + v_{M1}$, then $v_1$ and $L_{\text{Kim}}v_1$ are continuous up to the boundary, and

$$L_{\text{Kim}}v_1 \upharpoonright_{\partial \Sigma_M} = [f - L_{\text{Kim}}\overline{g}] \upharpoonright_{\partial \Sigma_M}. \quad (65)$$

The difference $f^{(1)} = f - L_{\text{Kim}}(\overline{g} + v_1)$, is again Hölder continuous up to the boundary, where it vanishes.
Since $f^{(1)}$ vanishes on the boundary, the eigenfunction method used above can be applied to solve

$$L_{\text{Kim}} v_0 = f^{(1)}$$

The solution $v_0$ belongs to $C^{0,2+\gamma}_{\text{WF}}(\Sigma_M)$, and can be chosen to vanish on the boundary.

Thus we can solve the Dirichlet problem, and we have a very explicit expression for the leading part of the singularity, which is, in fact, quite complicated. This yet another very special property of this operator.
Outline

1. The Wright-Fisher Model and Its Diffusion Limit
2. Boundary Conditions
3. Eigenfunctions
4. The Dirichlet Problem
5. Tomorrow’s Lecture
6. Bibliography
Much of what I’ve described today has been known in one form or the other since the 1980s. Though the fact that the regular solution to the parabolic initial value problem, $(\partial_t - (L_{\text{Kim}} + V))u = 0, u(x, 0) = f(x)$, belongs to $C^\infty((0, \infty) \times \Sigma_M)$ was not known.

Indeed, essentially nothing was known about the higher-order regularity of solutions to the parabolic initial value problem.

It was not even known, in 1d, if having $f \in C^k([0, 1])$ implies that the solution is also in $C^k([0, \infty] \times [0, 1])$.

If the coefficients of $V$ were not linear polynomials, then the only existence proof was via the Kato-Trotter product formula, and it gave no useful information about the regularity of these solutions.
The Classical Case

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4. If the coefficients of \(V\) were not linear polynomials, then the only existence proof was via the Kato-Trotter product formula, and it gave no useful information about the regularity of these solutions.
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If the coefficients of $$ V $$ were not linear polynomials, then the only existence proof was via the Kato-Trotter product formula, and it gave no useful information about the regularity of these solutions.
In the lecture tomorrow I will describe our results on the general existence, uniqueness, and regularity of solutions to a class of parabolic equations on manifolds-with-corners, which includes the classical Kimura operators.

In the proofs of these results it was quite essential that we not assume that the underlying is a simplex, or product of intervals, or any other specific space.

For certain cases we can also prove asymptotics for associated heat kernel.
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Thanks for your attention!

And thanks to my sponsors the NSF, DARPA, and the ARO.
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