Harnack inequalities for degenerate diffusions

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Based on joint work with Charles Epstein

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Outline

Wright-Fisher processes

Kimura processes

Harnack inequality

Selected references
Population genetics

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$1 - X(t)$ the frequency of gene $a$ at time $t$
Models for gene frequencies

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Models for gene frequencies

\[ X(t) \] the frequency of gene \( A \) at time \( t \)

- One of the simplest models to describe the evolution of the gene frequency \( X(t) \) was studied by Fisher (1922, 1930) and Wright (1931).
- The original Wright-Fisher process is a discrete Markov chain.
- In practice, we often work with continuous limits of the discrete Wright-Fisher process (Fisher, Wright, Kolmogorov, Kimura, Feller, Karlin, Ethier, Shimakura, Athreya, Bass, Barlow, Perkins, ...).
Questions of interest

Let \( p(t, x, dy) \) denote the transition probability distribution of the frequency of gene \( A \), which is \( x \) at \( t = 0 \), and is in the interval \([y, y + dy)\) at time \( t \).
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1. Find closed-form expressions for the transition probabilities distributions, whenever possible.
2. Describe the regularity properties and the singularities of the transition probabilities.
3. Understand the stationary distributions, when they exist.
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The Wright-Fisher process

- A version of the Wright-Fisher model:

\[ dX(t) = \sqrt{X(t)(1 - X(t))} \, dW(t) + [\beta_0(1 - X(t)) - \beta_1 X(t)] \, dt, \]

where \( \{W(t)\}_{t \geq 0} \) is a one-dimensional Brownian motion, and \( \beta_0 \) and \( \beta_1 \) are nonnegative constants.
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\frac{dX(t)}{dt} = \sqrt{X(t)(1 - X(t))} \, dW(t) + [\beta_0(1 - X(t)) - \beta_1 X(t)] \, dt,
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- Following Kolmogorov (1931) and Feller (1936, 1952), the transition probability distributions are solutions to the **backward** and **forward** Kolmogorov equations.
The backward Kolmogorov equation

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- The backward Kolmogorov equation: for all $(t, x) \in (0, \infty) \times (0, 1)$,
  \[
  p_t(t, x, y) = \frac{1}{2} x(1 - x)p_{xx}(t, x, y) + [\beta_0(1 - x) - \beta_1 x]p_x(t, x, y),
  \]
  \[ p(0, x, y) = \delta(x - y). \]
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- The infinitesimal generator: for all $x \in (0, 1)$,
  \[ Lu(x) = \frac{1}{2} x(1 - x)u_{xx}(x) + \left[ \beta_0(1 - x) - \beta_1 x \right] u_x(x), \]
The Wright-Fisher process with $\beta_0 = \beta_1 = 0$

The Wright-Fisher process with random drift:

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- The transition probabilities:

$$p(t, x, dy) = \psi^0(t, x)\delta_0(y) + \psi^1(t, x)\delta_1(y) + p^D(t, x, y) \, dy.$$
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- The stationary distributions are $\delta_0$ and $\delta_1$. 
The Wright-Fisher process with $\beta_0, \beta_1 > 0$

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The stationary distribution is the Beta distribution with parameters $(2\beta_0, 2\beta_1)$. 

A parabolic problem for the Wright-Fisher operator

- Consider now the **parabolic problem** defined by the Wright-Fisher infinitesimal generator $L$:

$$u_t = Lu \quad \text{on } (0, \infty) \times (0, 1)$$
$$u(0) = f \quad \text{on } (0, 1),$$
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The function

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u(t, x) = \int_0^1 f(y) p(t, x, dy) = \mathbb{E}_t^{x}[f(X(t))]
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- Solutions are unique without imposing any boundary condition on the parabolic boundary of the domain, $(0, \infty) \times \{0, 1\}$.
Extensions

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- The Wright-Fisher operator is self-adjoint on a suitable domain of the weighted Sobolev space

\[ L^2((0, 1); y^{2\beta_0-1}(1 - y)^{2\beta_1-1} \, dy). \]
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- We will study the regularity of solutions to the parabolic equation defined by the generator of multidimensional generalizations of the Wright-Fisher process.
Kimura processes
Multi-dimensional models for gene frequencies

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- Similar processes are studied with other applications (Athreya, Bass, Barlow, Perkins, ...).
- The infinitesimal generator of Kimura diffusion preserves the key properties of the infinitesimal generator of the Wright-Fisher process.
- Kimura diffusions live on compact manifolds with corners, which is a generalization of a simplex.
The standard Kimura operator

- Let $S_{n,m} := \mathbb{R}^n \times \mathbb{R}^m$. 

The standard Kimura operator

- Let $S_{n,m} := \mathbb{R}^n \times \mathbb{R}^m$.

- The infinitesimal generator of generalized Kimura diffusions takes the following form, in a local system of coordinates in $S_{n,m}$,

$$
Lu = \sum_{i=1}^{n} \left( x_i a_{ii}(z) u_{x_i} + b_i(z) u_{x_i} \right) + \sum_{i,j=1}^{n} x_i x_j \tilde{a}_{ij}(z) u_{x_i} u_{x_j} \\
+ \sum_{i=1}^{n} \sum_{l=1}^{m} x_i c_{il}(z) u_{x_i} y_l + \sum_{l,k=1}^{m} d_{lk}(z) u_{y_l} y_k + \sum_{l=1}^{m} e_l(z) u_{y_l},
$$

where we denote $z = (x, y) \in S_{n,m}$, and we let $u \in C^2(S_{n,m})$. 
Features of the standard Kimura operator

The main features of the Kimura differential operator, defined for all \( z \in S_{n,m} = \mathbb{R}_+^n \times \mathbb{R}^m \), are:

1. The second order matrix-coefficient is not strictly elliptic;
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\[ + \sum_{i=1}^{n} \sum_{l=1}^{m} x_i c_{il}(z) u_{x_i y_l} + \sum_{l,k=1}^{m} d_{lk}(z) u_{y_l y_k} + \sum_{l=1}^{m} e_l(z) u_{y_l}, \]

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3. The drift coefficient \( b_i(z) \) is nonnegative in a neighborhood of the boundary \( \{ x_i = 0 \} \), for all \( i = 1, \ldots, n \);
4. The domain \( S_{n,m} \) is non-smooth (it has corners and edges).
Parabolic equations defined by the Kimura operator

Theorem (Epstein-Mazzeo (2010, 2013))

Let $P$ be a compact manifold with corners.
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Given $g \in C_{WF}^{k,\alpha}([0, T] \times P)$ and $f \in C_{WF}^{k,2+\alpha}(P)$, there is a unique solution, $u \in C_{WF}^{k,2+\alpha}([0, T] \times P)$, to the initial-value problem

\[
\begin{align*}
    u_t - Lu &= g \quad \text{on } (0, T) \times P, \\
    u(0, \cdot) &= f \quad \text{on } P.
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$$u_t - Lu = g \quad \text{on } (0, T) \times P,$$

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Moreover, there is a universal constant, $C$, such that

$$\|u\|_{C_{WF}^{k, 2+\alpha}([0, T] \times P)} \leq C \left( \|g\|_{C_{WF}^{k, \alpha}([0, T] \times P)} + \|f\|_{C_{WF}^{k, 2+\alpha}(P)} \right).$$
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Anisotropic Hölder spaces

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- One of the main differences between the classical Hölder spaces and the anisotropic Hölder spaces is the change in the distance function on $S_{n,m}$.

The "fundamental form" $ds^2_{WF} = \sum_{i=1}^{n} dx_i^2 + \sum_{l=1}^{m} dy_l^2$ induces a Riemannian distance on $\bar{S}_{n,m}$ that is equivalent to $d_{WF}( (x, y), (x', y') ) = \sum_{i=1}^{n} |\sqrt{x_i} - \sqrt{x_i'}| + \sum_{l=1}^{m} |y_l - y_l'|$. 
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- The “fundamental form”

$$ds^2_{WF} = \sum_{i=1}^{n} \frac{dx_i^2}{x_i} + \sum_{l=1}^{m} dy_l^2$$

induces a Riemannian distance on $\tilde{S}_{n,m}$ that is equivalent to

$$d_{WF}((x, y), (x', y')) = \sum_{i=1}^{n} \left| \sqrt{x_i} - \sqrt{x'_i} \right| + \sum_{l=1}^{m} |y_l - y'_l|.$$
Our research

In our work, we prove the following:

1. For $f \in C(\bar{S}_{n,m})$, there is a unique smooth solution on $(0, \infty) \times \bar{S}_{n,m}$:

   \begin{align*}
   u_t - Lu &= 0 \text{ on } (0, \infty) \times S_{n,m}, \\
   u(0, \cdot) &= f \text{ on } S_{n,m}.
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\]

2. A priori Schauder estimates: for all \( 0 < T_0 < T \) and \( r \in (0, 1) \), there is a universal constant, \( C \), such that

\[
\|u\|_{C^{k,2+\alpha}(\left[T_0,T\right] \times \bar{B}_r)} \leq C \|u\|_{C(\left[T_0/2,T\right] \times \bar{B}_{2r})}
\]
3. **Harnack inequality** for nonnegative solutions: there is a positive constant, $K$, such that for all $(t, z) \in (0, \infty) \times \tilde{S}_{n,m}$ and $r \in (0, \sqrt{t}/4)$, we have that

$$
\sup_{Q^-_r(t,z)} u \leq K \inf_{Q^+_r(t,z)} u,
$$

where we denote

$$B_r(z) := \{ w \in \tilde{S}_{n,m} : d_{WF}(z, w) < r \},$$
$$Q^+_r(t, z) := (t - r^2, t) \times B_r(z),$$
$$Q^-_r(t, z) := (t - 3r^2, t - 2r^2) \times B_r(z).$$
Our research – cont’d

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4. **A stochastic representation formula** for weak solutions to degenerate parabolic equations with unbounded coefficients.
Harnack inequality
Potential applications of the Harnack inequality

- Prove Hölder continuity of solutions, and improve regularity to smoothness.

- Obtain upper and lower bounds for the transition probability distributions (heat kernel estimates).

- Obtain optimal regularity of solutions to nonlinear problems (such as obstacle problems).
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Ways to prove the Harnack inequality

- Using the heat kernel estimates when they are available (Fabes-Stroock (1986), Nash (1958), Koch (1999), ...).

- Moser’s iterations (1964): for operators in divergence form; also generalizations to non-divergence form operators (Sallof-Coste, Grigor’yan, Sturm, ...).

- Krylov-Safonov (1979, 1980): does not need divergence structure for the operator; needs certain $L^p$ estimates.

- Sturm (1994): probabilistic proof based on viewing $L$ as a lower order perturbation of an operator $\hat{L}$ for which we already know that Harnack inequality holds; need to know stochastic representation of solutions.
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How to choose the perturbation operator $\hat{L}$?

- The divergence form operator $\hat{L}$ (Epstein-Mazzeo (2014)):

$$\hat{L}u = Lu + \sum_{i,j=1}^{n} f_{ij}(z)x_i \ln x_j u_{x_i} + \sum_{i=1}^{n} \sum_{l=1}^{m} f_{n+l,j}(z) \ln x_j u_{y_l}.$$
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  \]

- There is a symmetric bilinear form $Q(u, \nu)$ such that

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  (\hat{L}u, \nu)_{L^2(S_{n,m};d\mu)} = Q(u, \nu),
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- There is a symmetric bilinear form $Q(u, v)$ such that

$$(\hat{L}u, v)_{L^2(S_{n,m}; d\mu)} = Q(u, v),$$

- A simplified form of the bilinear form $Q(u, v)$ is:

$$Q(u, v) := \int_{S_{n,m}} \left( \sum_{i=1}^{n} x_i u_{x_i} v_{x_i} + \sum_{l=1}^{m} u_{y_l} v_{y_l} \right) d\mu(z),$$
How to choose the perturbation operator $\hat{\mathcal{L}}$?

- The **divergence form operator** $\hat{\mathcal{L}}$ (Epstein-Mazzeo (2014)):

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  $$d\mu(z) = \prod_{l=1}^{m} \prod_{i=1}^{n} x_i^{b_i(z)-1} dx_i dy_l.$$
What do we mean by a weak solution?

- Let $\Omega \subseteq S_{n,m}$ be a (possibly unbounded) domain, and denote

  \[
  \partial_1 \Omega := \partial \Omega \cap S_{n,m} \quad \text{non-degenerate boundary}
  \]

  \[
  \partial_0 \Omega := \text{int} (\partial \Omega \cap \partial S_{n,m}) \quad \text{degenerate boundary}
  \]

  \[
  \Omega := \Omega \cup \partial_0 \Omega.
  \]

- Roughly speaking, a weak solution to the parabolic equation:

  \[
  u_t - \hat{L}u = 0 \quad \text{on } (0, \infty) \times \Omega,
  \]

  \[
  u = 0 \quad \text{on } (0, \infty) \times \partial_1 \Omega,
  \]

  \[
  u = f \quad \text{on } \{0\} \times \Omega,
  \]

  is a measurable function such that at each time $t$, $u(t)$ has only first order derivatives in the spatial variables, $(x, y)$, and the derivatives are belong to suitable weighted Sobolev spaces.
Theorem (Stochastic representation – Epstein-P. (2014))

Let $u$ be the unique weak solution to the homogeneous initial-value problem,

$$
\begin{align*}
  u_t - \hat{L}u &= 0 \quad \text{on } (0, \infty) \times \Omega, \\
  u &= 0 \quad \text{on } (0, \infty) \times \partial_1 \Omega, \\
  u &= f \quad \text{on } \{0\} \times \Omega,
\end{align*}
$$

where $f$ and is a Borel measurable and bounded function. Then $u$ satisfies the stochastic representation,

$$
  u(t, z) = \mathbb{E}_{\hat{P}_z} \left[ f(\hat{Z}(t)) \mathbf{1}_{\{t < \tau_\Omega\}} \right], \quad \forall (t, z) \in [0, \infty) \times \bar{S}_{n,m},
$$

where

$$
  \tau_\Omega := \inf\{s \geq 0 : \hat{Z}(s) \notin \Omega\},
$$

and $\{\hat{Z}(t)\}_{t \geq 0}$ is the unique weak solution to the singular Kimura equation with initial condition $\hat{Z}(0) = z$. 

Kimura stochastic differential equation with singular drift

Theorem (Kimura equation with singular drift – P. (2014))

Let \( z \in \bar{S}_{n,m} \). The singular Kimura stochastic differential equation,

\[
d\hat{X}_i(t) = \left( b_i(\hat{Z}(t)) + \sum_{j=1}^{n} f_{ij}(\hat{Z}(t)) \sqrt{\hat{X}_i(t) \ln \hat{X}_j(t)} \right) dt \\
+ \sqrt{\hat{X}_i(t)} \sum_{k=1}^{n+m} \sigma_{ik}(\hat{Z}(t)) \, d\hat{W}_k(t), \quad \forall \, i = 1, \ldots, n,
\]

\[
d\hat{Y}_l(t) = \left( e_l(\hat{Z}(t)) + \sum_{j=1}^{n} f_{n+l,j}(\hat{Z}(t)) \ln \hat{X}_j(t) \right) dt, \\
+ \sum_{k=1}^{n+m} \sigma_{n+l,k}(\hat{Z}(t)) \, d\hat{W}_k(t), \quad \forall \, l = 1, \ldots, m,
\]

has a unique weak solution, \( \{\hat{Z}(t)\}_{t \geq 0} \), that satisfies the Markov property with initial condition \( \hat{Z}(0) = z \). Moreover the solution satisfies the strong Markov property.
Review of previous results on stochastic representations

Stochastic representations of weak solutions are proved in Bensoussan-Lions, Friedman, Petrenko, Sturm, among many others, under the assumptions:

- The diffusion matrix is strictly elliptic.

Note that in our framework:

- The diffusion matrix is degenerate.
- The drift coefficients are unbounded functions.
- We only know that the weak solutions belong to the weighted Sobolev space ($H^1_0(\Omega; d\mu)$), and we have no information about the regularity of the second order derivatives.
- $L^p$-theory is not developed for the degenerate differential operators that we consider, and our goal is to use the stochastic representation of weak solutions to obtain information about the regularity of solutions, as for example, the Harnack inequality.
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THANK YOU!
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