

Harnack inequalities for degenerate diffusions

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Based on joint work with Charles Epstein

Stony Brook University

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Outline

Wright-Fisher processes

Kimura processes

Harnack inequality

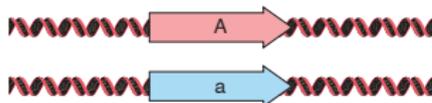
Selected references

Population genetics

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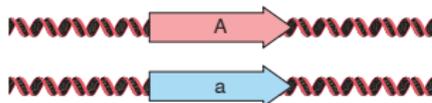
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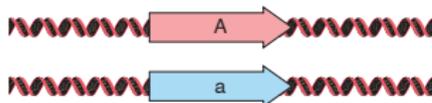
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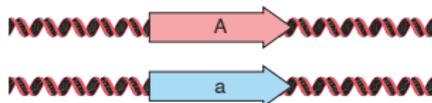
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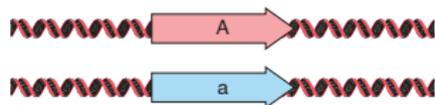
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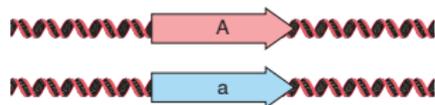
Models for gene frequencies



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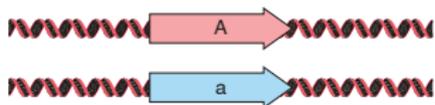
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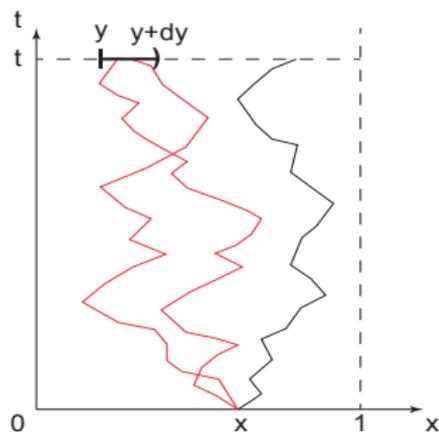


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- The original Wright-Fisher process is a discrete Markov chain.
- In practice, we often work with continuous limits of the discrete Wright-Fisher process (Fisher, Wright, Kolmogorov, Kimura, Feller, Karlin, Ethier, Shimakura, Athreya, Bass, Barlow, Perkins, ...).

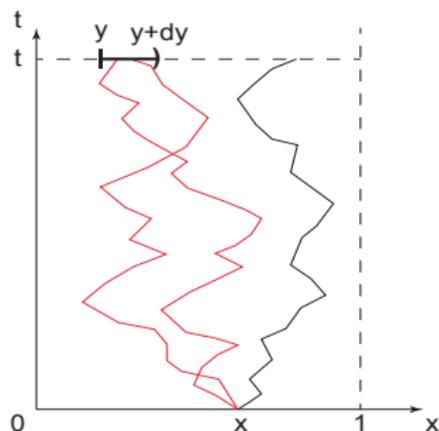
Questions of interest

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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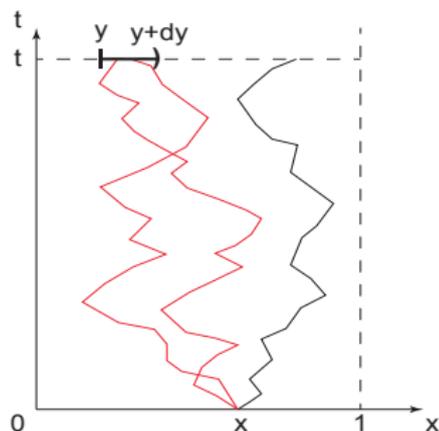
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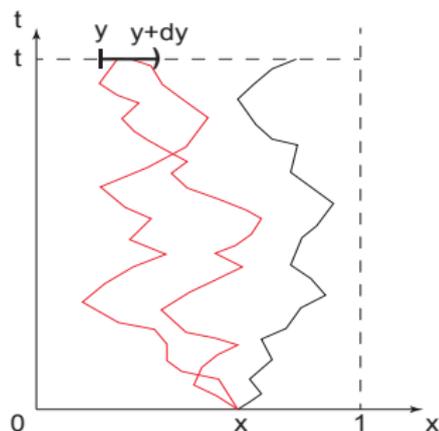
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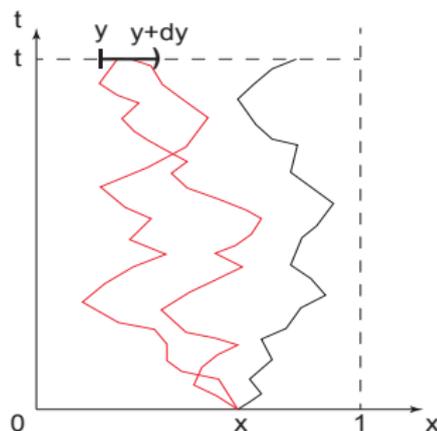
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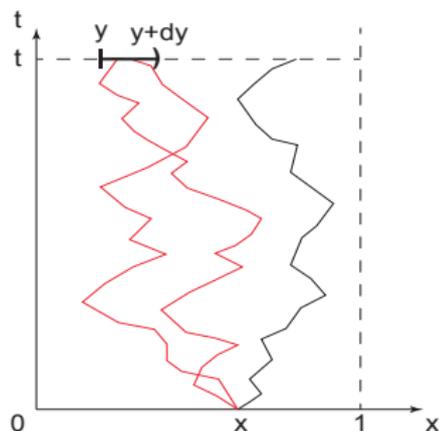
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5. Find the **rate of fixation** or **loss** of a gene in the genome.

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 β_0 and β_1 are nonnegative constants.

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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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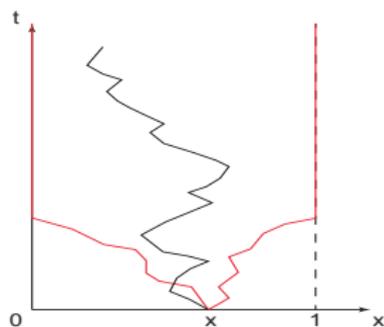
- The infinitesimal generator: for all $x \in (0, 1)$,

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The Wright-Fisher process with $\beta_0 = \beta_1 = 0$

The Wright-Fisher process with random drift:

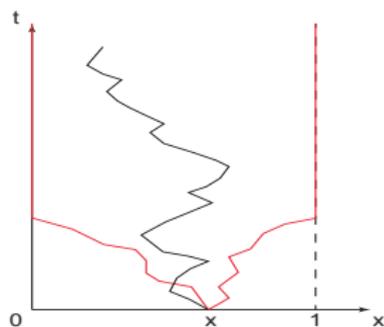
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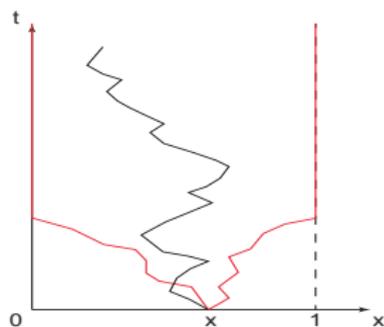
- The transition probabilities:

$$p(t, x, dy) = \psi^0(t, x)\delta_0(y) + \psi^1(t, x)\delta_1(y) + p^D(t, x, y) dy.$$

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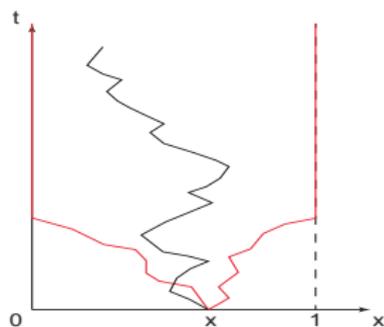
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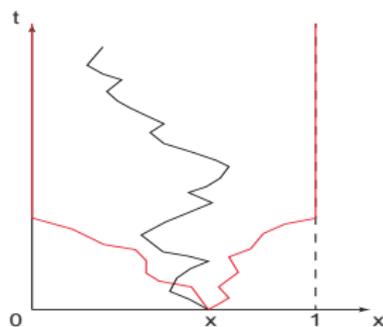
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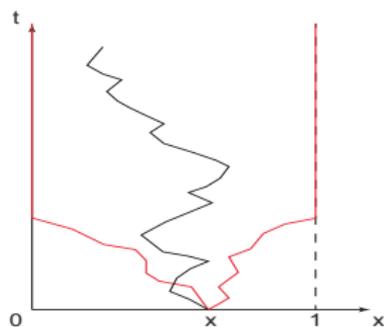
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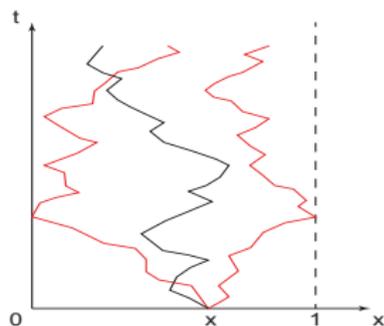
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- The **stationary distributions** are δ_0 and δ_1 .

The Wright-Fisher process with $\beta_0, \beta_1 > 0$

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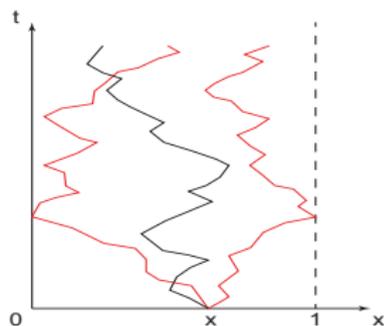
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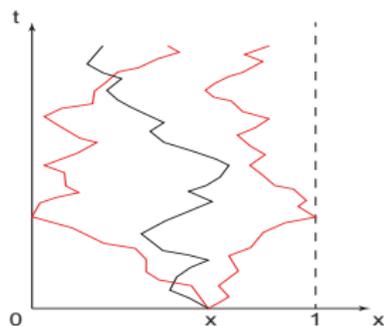
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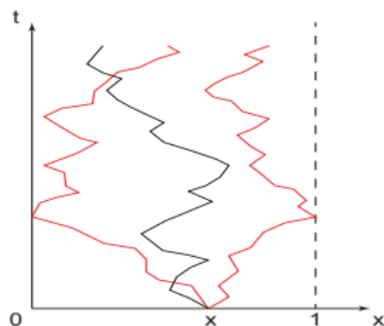
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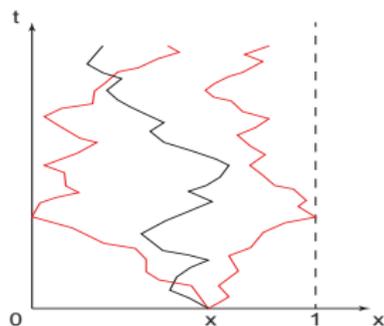
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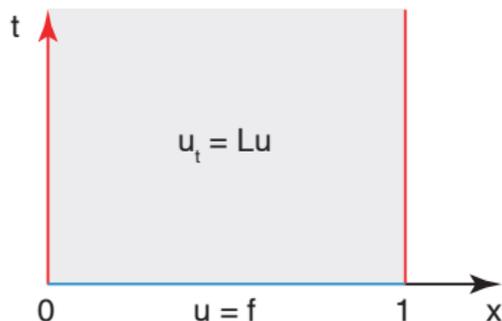
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The **stationary distribution** is the Beta distribution with parameters $(2\beta_0, 2\beta_1)$.

A parabolic problem for the Wright-Fisher operator

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

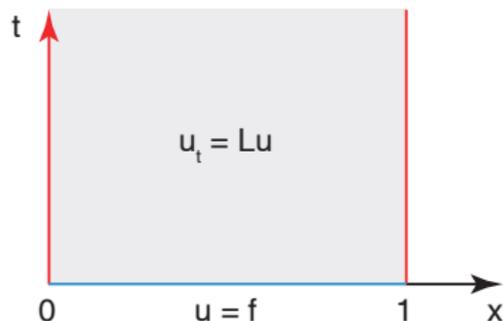
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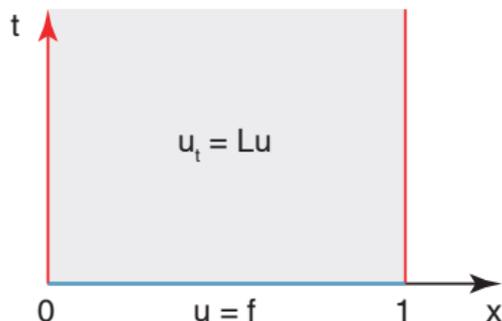
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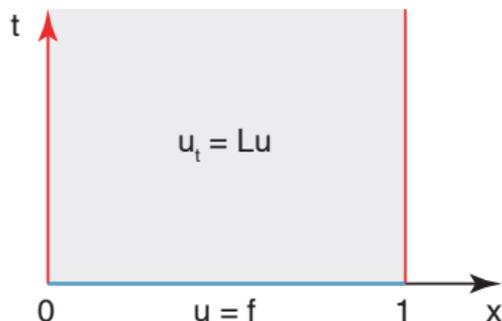
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- Solutions are unique **without imposing any boundary condition** on the parabolic boundary of the domain, $(0, \infty) \times \{0, 1\}$.

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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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Multi-dimensional models for gene frequencies

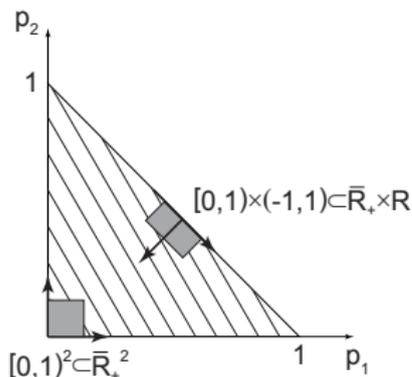
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- Similar processes are studied with other applications (Athreya, Bass, Barlow, Perkins, ...).
- The infinitesimal generator of Kimura diffusion preserves the key properties of the infinitesimal generator of the Wright-Fisher process.
- Kimura diffusions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



The standard Kimura operator

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

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

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,

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

defined for all $z \in S_{n,m} = \mathbb{R}_+^n \times \mathbb{R}^m$, are:

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4. The domain $S_{n,m}$ is **non-smooth** (it has corners and edges).

Parabolic equations defined by the Kimura operator

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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”

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

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

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

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 $(0, \infty) \times \bar{S}_{n,m}$:

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Our research

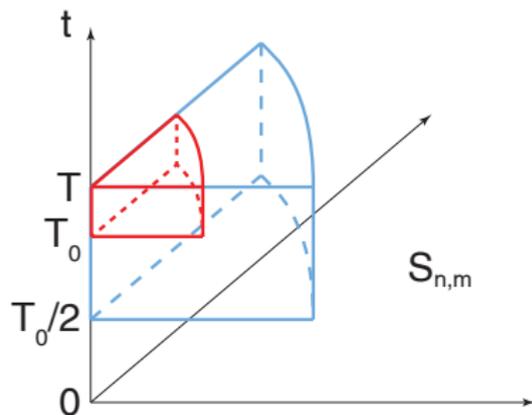
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2. A priori Schauder estimates: for all $0 < T_0 < T$ and $r \in (0, 1)$, there is a universal constant, C , such that

$$\begin{aligned}\|u\|_{C_{WF}^{k,2+\alpha}([T_0, T] \times \bar{B}_r)} \\ \leq C \|u\|_{C([T_0/2, T] \times \bar{B}_{2r})}\end{aligned}$$



Our research – cont'd

3. **Harnack inequality** for nonnegative solutions: there is a positive constant, K , such that for all $(t, z) \in (0, \infty) \times \bar{S}_{n,m}$ and $r \in (0, \sqrt{t}/4)$, we have that

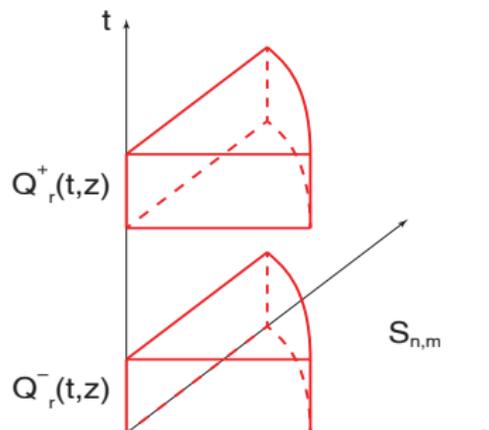
$$\sup_{Q_r^-(t,z)} u \leq K \inf_{Q_r^+(t,z)} u,$$

where we denote

$$B_r(z) := \{w \in \bar{S}_{n,m} : d_{WF}(z, w) < r\},$$

$$Q_r^+(t, z) := (t - r^2, t) \times B_r(z),$$

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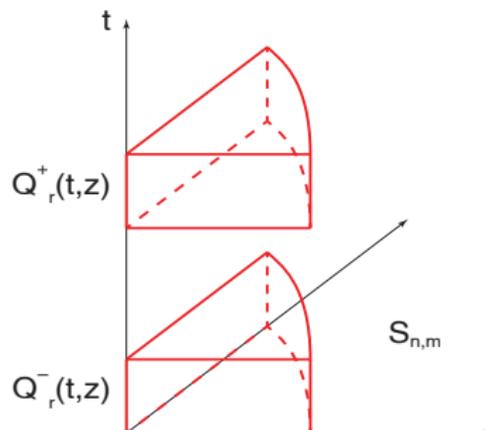
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4. A **stochastic representation** formula for weak solutions to degenerate parabolic equations with unbounded coefficients.

Harnack inequality

Potential applications of the Harnack inequality

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

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- 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).

Ways to prove the Harnack inequality

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

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- 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.

How to choose the perturbation operator \widehat{L} ?

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

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

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$$Q(u, v) := \int_{S_{n,m}} \left(\sum_{i=1}^n x_i u_{x_i} v_{x_i} + \sum_{l=1}^m u_{y_l} v_{y_l} \right) d\mu(z),$$

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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

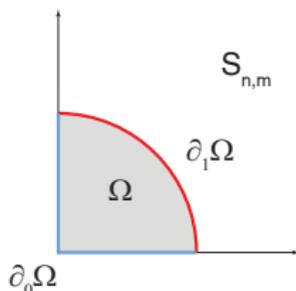
$$\partial_1 \Omega := \partial \Omega \cap S_{n,m} \quad \text{non-degenerate boundary}$$

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

$$\underline{\Omega} := \Omega \cup \partial_0 \Omega.$$

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

$$\begin{aligned} u_t - \widehat{L}u &= 0 && \text{on } (0, \infty) \times \Omega, \\ u &= 0 && \text{on } (0, \infty) \times \partial_1 \Omega, \\ u &= f && \text{on } \{0\} \times \Omega, \end{aligned}$$



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.

Stochastic representation of weak solutions

Theorem (Stochastic representation – Epstein-P. (2014))

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

$$\begin{aligned}u_t - \widehat{L}u &= 0 && \text{on } (0, \infty) \times \Omega, \\u &= 0 && \text{on } (0, \infty) \times \partial_1 \Omega, \\u &= f && \text{on } \{0\} \times \Omega,\end{aligned}$$

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

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

where

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

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

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,

$$\begin{aligned}d\hat{X}_i(t) &= \left(b_i(\hat{Z}(t)) + \sum_{j=1}^n f_{ij}(\hat{Z}(t)) \sqrt{\hat{X}_i(t)} \ln \hat{X}_j(t) \right) dt \\ &\quad + \sqrt{\hat{X}_i(t)} \sum_{k=1}^{n+m} \sigma_{ik}(\hat{Z}(t)) d\widehat{W}_k(t), \quad \forall i = 1, \dots, n, \\ d\hat{Y}_l(t) &= \left(e_l(\hat{Z}(t)) + \sum_{j=1}^n f_{n+l,j}(\hat{Z}(t)) \ln \hat{X}_j(t) \right) dt, \\ &\quad + \sum_{k=1}^{n+m} \sigma_{n+l,k}(\hat{Z}(t)) d\widehat{W}_k(t), \quad \forall l = 1, \dots, m,\end{aligned}$$

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:

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- 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.

THANK YOU!

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