A Mesoscale Diffusion Model in Population Genetics with Dynamic Fitness

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The Discrete Model

- Consider a single haploid panmictic population of constant size $N$ with $n$ diallelic loci.
- Suppose that the two alleles at locus $i \in \{1, \ldots, n\}$ are $A_i$ and $a_i$.
- The effect of allele $A_i$ is greater than the effect of allele $a_i$.
- We assume that the difference in phenotype between $A_i$ and $a_i$ is $Q$, and that this is constant across loci.
- We assume strict additivity, so that dominance and epistasis are absent.
The Discrete Model

- Let the fraction of the population with allele $A_i$ at locus $i$ be denoted by $x_i$.

- The population phenotypic mean is then

\[
\mu = \sum_{i=1}^{n} \left[ x_i \left( \frac{1}{2} \right)^Q + (1 - x_i) \left( -\frac{1}{2} \right)^Q \right]
\]

\[
= \sum_{i=1}^{n} \left( x_i - \frac{1}{2} \right)^Q
\]

up to a constant.

- We assume that the environment has a most fit phenotype $r_{opt}$, and that there is a fitness function of the form

\[
f(r) = e^{-\kappa(r-r_{opt})^2}
\]

which gives the relative fitness of a phenotype $r$. 
The Discrete Model

- Given the population in one generation, we want to find the probability \( p_i \) that an individual in the next generation will contain allele \( A_i \).
- Clearly, \( p_i \propto x_i \).
- In addition, \( p_i \) is proportional to the average fitness of the population that carries \( A_i \).
- The average phenotype \( \mu_i \) of the population that carries the allele \( A_i \) is \( \mu_i = \mu + (1 - Q) x_i \).
- The average phenotype \( \nu_i \) of the population that carries the allele \( a_i \) is \( \nu_i = \mu - Q x_i \).
- Now \( p_i \propto x_i \) and \( p_i \propto \mu_i \). On the other hand, because the population size is fixed at \( N \), we also know \( (1 - p_i) \propto (1 - x_i) \) and \( (1 - p_i) \propto \nu_i \). Thus

\[
p_i = \frac{x_i f(\mu + (1 - x_i)Q)}{x_i f(\mu + (1 - x_i)Q) + (1 - x_i) f(\mu - x_i Q)}.
\]
The Discrete Model

- We could try to track each individual locus; this results in a set of \( n \) nonlinear equations (one for each locus), and little useful information can be extracted when \( n \) is large.

- Rather than track each individual locus, we want to look at the limit when \( n \to \infty \), \( N \to \infty \), and time becomes continuous.

- We introduce the variable \( \phi(x, t) \), chosen so that

\[
\int_{a}^{b} \phi(x, t) \, dx
\]

represents the fraction of loci whose allele frequency is between \( a \) and \( b \).

- This yields a mesoscale model that no longer tracks the behavior of each individual locus.
The Meoscale Model

- These models were initially developed by Richard Hamilton, Judith Miller, and Mary Pugh.
  - They have studied these models from a numerical and from a formal asymptotic point of view.
  - Model development continues.

- These models can be used to answer biologically relevant questions:
  - How fast does the trait mean approach optimal?
  - At what rate are alleles fixed in the population?

- The problem is that basic mathematical questions-like whether or not the model has a solution- have not yet been answered.
The Continuous Model

• We analyze the general system of equations of the form

\[ \phi_t = -(M\phi)_x + \frac{1}{2}(V\phi)_{xx} \]

where

\[ M = M(x, t, R) = x(1-x)m(x, t, R), \]
\[ V = V(x, t, R) = x(1-x)v(x, t, R). \]

• The function \( R(t) \) is defined by

\[ R(t) = \int_0^1 (x - \frac{1}{2})\phi(x, t) \, dx + R_0(t) + R_1(t) \]

where

\[ R_0(t) = -\frac{1}{4} \int_0^t (V\phi)_x(0, s) \, ds + R_0(0) \]
\[ R_1(t) = -\frac{1}{4} \int_0^t (V\phi)_x(1, s) \, ds + R_1(0). \]
Features of the Problem

• The problem is highly nonlinear.
  – The coefficients of the equation $M$ and $V$ both depend on $R$, which depends on the solution $\phi$.
  – Moreover, $R$ also depends on the coefficient $V$ and so even if $\phi$ were known, there is still no closed form expression for $M$ or $V$.

• The problem is also non-local, as the coefficients $M$ and $V$ depend on an integral of $\phi$.

• $R(t)$ represents the (suitably scaled) trait mean of the population.

• $R_0(t)$ and $R_1(t)$ represent the effect of fixed loci on the trait mean.
The Results

- This problem has a solution.
- The solution is unique.
- The system is stable under perturbations of the initial data.
The Spaces $B_i$

- $B_0 = \{ \psi \text{ measurable on } [0, 1] : \langle \psi, \psi \rangle_{B_0}^2 < \infty \}$ where
  \[
  \langle \phi, \psi \rangle_{B_0} = \int_0^1 x(1-x)\phi\psi \, dx.
  \]

- $B_1 = \{ \psi \in B_0 : \langle \psi, \psi \rangle_{B_1}^2 < \infty \}$ where
  \[
  \langle \phi, \psi \rangle_{B_1} = \langle \phi, \psi \rangle_{B_0} + \int_0^1 [x(1-x)\phi]_x [x(1-x)\psi]_x \, dx.
  \]

- $B_2 = \{ \psi \in B_1 : \langle \psi, \psi \rangle_{B_2}^2 < \infty \}$ where
  \[
  \langle \phi, \psi \rangle_{B_2} = \langle \phi, \psi \rangle_{B_1} + \int_0^1 x(1-x)[x(1-x)\phi]_{xx} \cdot [x(1-x)\psi]_{xx} \, dx.
  \]
Hypotheses: Coefficients

(H1) The functions

\[ (x, t, R) \mapsto m(x, t, R) \]
\[ (x, t, R) \mapsto v(x, r, R) \]

are continuous.

(H2) For any \( \gamma > 0 \), there exist constants \( C'(\gamma), C''(\gamma) > 0 \) so that for \( |R| \leq \gamma \) and for any \( 0 \leq x \leq 1 \) and \( t \geq 0 \)

\[ v(x, t, R) \geq C''(\gamma), \]
\[ |v| + |v_x| + |v_{xx}| + |m| + |m_x| \leq C(\gamma), \]
\[ |m_R| + |v_R| + |v_{Rx}| \leq C(\gamma). \]

(H3) There are nonnegative integrable functions \( M_1(t) \) and \( M_2(t) \) so that

\[ \sup_{0 \leq x \leq 1} |M(x, t, R)| \leq M_1(t) + M_2(t)|R|. \]
Hypotheses: Initial Data

- \( \phi_0 \in B_1 \),
- \( \phi_0(x) \geq 0 \) for almost every \( x \),
- \( R_0(0) \) and \( R_1(0) \) are given, and
- \( T > 0 \) is given.
Theorem 1: Existence

- Then there exists a function $\phi(x, t)$, so that
  
  $$\phi \in C([0, T); B_1) \cap L_2(0, T; B_2) \cap C^{\alpha}([0, T); L_p(0, 1)) \cap C((0, 1) \times [0, T))$$

  for any $1 \leq p < 2$, for any $0 < \alpha < \frac{1}{p} - \frac{1}{2}$.

- There exist functions $R_0(t), R_1(t)$ so that
  
  $$R_0, R_1 \in C^{\beta}[0, T)$$

  for any $0 < \beta < \frac{1}{2}$.

- Define
  
  $$R(t) = \int_0^1 (x - \frac{1}{2})\phi(x, t) \, dx + R_0(t) + R_1(t).$$

  Then $R \in C^1[0, T)$. 
Theorem 1: Existence

• Then

\[ \phi_t = - (M \phi)_x + \frac{1}{2} (V \phi)_{xx} \]

as elements of \( L_2(0, T; B_0) \).

• Further,

\[ \lim_{t \downarrow 0} \phi(x, t) = \phi_0(x) \]

with the limit taken strongly in \( B_1 \).

• Set

\[ \nu(x, t) = \int_0^t (V \phi)_x(x, s) \, ds. \]

Then \( \nu \in C^\alpha([0, T); C^{1-\frac{1}{p}}[0, 1]) \) for any \( 1 \leq p < 2 \) and any \( 0 < \alpha < \frac{1}{p} - \frac{1}{2} \). Further

\[ R_0(t) = R_0(0) - \frac{1}{4} \nu(0, t), \]

\[ R_1(t) = R_1(0) - \frac{1}{4} \nu(1, t). \]
Theorem 1: Existence

- There is a constant $C$ depending only on $T$ and initial data so that

$$
\sup_{0 \leq t < T} \| \phi(\cdot, t) \|_{B_0} + \| \phi \|_{L^2(0,T;B_1)} \leq C \| \phi_0 \|_{B_0},
$$
$$
\| \phi \|_{C^{\frac{1}{2}}([0,T];B_0)} \leq C \| \phi_0 \|_{B_1},
$$
$$
\sup_{0 \leq t < T} \| \phi(\cdot, t) \|_{B_1} + \| \phi \|_{L^2(0,T;B_2)} \leq C \| \phi_0 \|_{B_1}.
$$

- For all $x \in (0, 1)$ and for all $0 \leq t < T$ we have

$$
|\phi(x, t)| \leq C \max \left( \frac{1}{\sqrt{x}}, \frac{1}{\sqrt{1-x}} \right) \| \phi_0 \|_{B_1}.
$$

- For any $1 \leq p < 2$ and any $0 < \alpha < \frac{1}{p} - \frac{1}{2}$

$$
\| \phi \|_{C^{\alpha}([0,T];L^p(0,1))} \leq C \| \phi_0 \|_{B_1},
$$
$$
\| \nu \|_{C^{\alpha}([0,T];C^{1-\frac{1}{p}}[0,1])} \leq C \| \phi_0 \|_{B_1};
$$

where $C'$ also depends on $p$ and $\alpha$. 
Theorem 1: Existence

- Further, for any $0 < \beta < \frac{1}{2}$,
  \[
  \|R_0\|_{C^{\beta}[0,1]} + \|R_1\|_{C^{\beta}[0,1]} \leq C \|\phi_0\|_{B_1}
  \]
  where $C$ also depends on $\beta$.

- Moreover, $\phi \geq 0$, and for any $0 \leq t_1 < t_2 < T$
  \[
  \int_0^1 \phi(x, t_2) \, dx \leq \int_0^1 \phi(x, t_1) \, dx.
  \]

- Finally
  \[
  |R(t)| \leq \left[ |R(0)| + \|\phi_0\|_{L^1(0,1)} \int_0^t \mathcal{M}_1(s) \, ds \right] \\
  \exp \left[ \|\phi_0\|_{L^1(0,1)} \int_0^t \mathcal{M}_2(s) \, ds \right]
  \]
  and
  \[
  R(t_2) - R(t_1) = \int_{t_1}^{t_2} \int_0^1 M\phi \, dx \, dt.
  \]
Theorem 2: Uniqueness and Stability

- Let $\phi, \phi^* \in C([0, T]; B_1) \cap L_2(0, T; B_2)$.
- Let $R_0, R_0^*, R_1, R_1^* \in C[0, T]$.
- Define
  \[ R(t) = \int_0^1 \left( x - \frac{1}{2} \right) \phi(x, t) + R_0(t) + R_1(t), \]
  \[ R^*(t) = \int_0^1 \left( x - \frac{1}{2} \right) \phi^*(x, t) + R_0^*(t) + R_1^*(t). \]
- Define
  \[ M = M(x, t, R(t)), \]
  \[ M^* = M(x, t, R^*(t)), \]
  \[ V = V(x, t, R(t)), \]
  \[ V^* = V(x, t, R^*(t)). \]
Theorem 2: Uniqueness and Stability

Suppose that

\[
\begin{align*}
\phi_t &= -(M\phi)_x + \frac{1}{2}(V\phi)_{xx}, \\
\phi\bigg|_{t=0} &= \phi_0 \in B_1,
\end{align*}
\]

and

\[
\begin{align*}
\phi^*_t &= -(M^*\phi^*)_x + \frac{1}{2}(V^*\phi^*)_{xx}, \\
\phi^*_0 \bigg|_{t=0} &= \phi_0^* \in B_1,
\end{align*}
\]

If

\[
R_0(0) - R_1(0) = R_0^*(0) - R_1^*(0)
\]

\[
\phi_0 = \phi_0^*
\]

then \( \phi^* = \phi \).
Theorem 2: Uniqueness and Stability

- There is a constant $C$ depending only on initial data and $T$ so that

$$\sup_{0 \leq t \leq T} \int_{0}^{1} x(1-x)(\phi - \phi^*)^2 \, dx \bigg|_t$$

$$+ \int_{0}^{T} \int_{0}^{1} [x(1-x)(\phi - \phi^*)]^2 \, dx \, dt$$

$$\leq C \int_{0}^{1} x(1-x)(\phi_0 - \phi_0^*)^2 \, dx$$

$$+ \int_{0}^{1} [x(1-x)(\phi_0 - \phi_0^*)]^2 \, dx$$

$$+ C |R_0(0) - R_0^*(0)|^2$$

$$+ C |R_1(0) - R_1^*(0)|^2.$$
**Theorem 1: Sketch of Proof**

Theory of the spaces $B_0$, $B_1$, and $B_2$.

- $C_0^\infty(0, 1)$ is dense in $B_0$.
- If $\phi \in B_1$, then

\[ x(1 - x)\phi \in \tilde{W}^1_2(0, 1). \]

Further $\phi$ has a continuous representative with

\[ x(1 - x)\phi \in C^{\frac{1}{2}}[0, 1] \]

so that

\[
|x_1(1 - x_1)\phi(x_1) - x_2(1 - x_2)\phi(x_2)| \\
\leq |x_2 - x_1|^{\frac{1}{2}} \left( \int_0^1 [x(1 - x)\phi(x)]^2 dx \right)^{\frac{1}{2}}.
\]
Theorem 1: Sketch of Proof

Theory of $B_1$.

- Let $\phi \in B_1$; then

\[
\sup_{x \in [0,1]} x(1-x)\phi^2(x) \leq 2 \int_0^1 [x(1-x)\phi']^2 x \, dy
\]

- Let $\phi \in B_1$; then for any $0 < x < 1$

\[
|\phi(x)| \leq 2 \max\left(\frac{1}{\sqrt{x}}, \frac{1}{\sqrt{1-x}}\right) \|\phi\|_{B_1}.
\]

- For any $1 \leq p < 2$,

\[
B_1 \hookrightarrow L_p
\]

and there exists a constant $C = C(p)$ so that if $\phi \in B_1$ then

\[
\|\phi\|_{L_p} \leq C \|\phi\|_{B_1}.
\]

- $C_0^\infty(0,1)$ is dense in $B_1$. 
**Theorem 1: Sketch of Proof**

*Representation Theorem for $B_2$.*

- Suppose that $\phi \in B_2$. Then

\[
\phi(x) = \frac{1}{x(1-x)} \int_0^1 G(x, y)[y(1-y)\phi]_{yy} \, dy.
\]

where

\[
G(x, y) = \begin{cases} 
  x(y - 1) & x \leq y \\
  (x - 1)y & x \geq y 
\end{cases}
\]

is the Green’s function for the problem $\psi'' = 0$, $\psi(0) = \psi(1) = 0$. 

![Graph of $G(x, \frac{1}{3})$](image)
Theorem 1: Sketch of Proof

Theory of $B_2$.

- We have the embedding

$$B_2 \hookrightarrow C_{\text{loc}}^{3/2}(0, 1).$$

- Let $\phi \in B_2$; then

$$\int_0^1 x(1-x)\phi^2 \, dx$$

$$\leq 2 \int_0^1 x(1-x)[x(1-x)\phi]_{xx}^2 \, dx,$$

and

$$\int_0^1 [x(1-x)\phi]^2_x$$

$$\leq 8 \int_0^1 x(1-x)[x(1-x)\phi]_{xx}^2 \, dx.$$

- $C^\infty[0, 1]$ is dense in $B_2$. 
Theorem 1: Sketch of Proof

The Elements of $B_0$, $B_1$, and $B_2$.

- It is easy to check that, for monomials $f(x) = x^p$
  - $x^p \in B_0$ iff $p > -1$,
  - $x^p \in B_1$ iff $p > -1/2$, and
  - $x^p \in B_2$ iff $p > 0$.

- As a consequence you might expect that if $\phi \in B_2$, then $[x(1 - x)\phi(x)]_x \to 0$ as $x \to 0$ or $x \to 1$.

- This is important because $V = x(1 - x)v(x, t, R)$ and

$$R_0(t) = -\frac{1}{4} \int_0^t (V\phi)_x(0, s) \, ds + R_0(0)$$

$$= -\frac{1}{4} \int_0^t (v \, x(1 - x)\phi)_x(0, s) \, ds + R_0(0).$$
Theorem 1: Sketch of Proof
The Elements of $B_0$, $B_1$, and $B_2$.

- Let $\zeta \in C^\infty[0, 1]$ be a smooth cutoff function

\[
\zeta(x) = \frac{\zeta(x)}{x(1-x)} \Gamma(p+1, -\ln x)
\]

is an element of $B_2$, but

\[
\lim_{x \downarrow 0} [x(1-x)f(x)]_x = +\infty.
\]

- Here $\Gamma(a, x) = \int_x^\infty t^{a-1} e^{-t} \, dt$ is the incomplete gamma function.
Theorem 1: Sketch of Proof

Compact Embeddings of $B_1$.

• The embedding $B_1 \hookrightarrow B_0$ is compact.

• The embedding $B_1 \hookrightarrow L_p(0, 1)$ is compact.
Theorem 1: Sketch of Proof

Eigenfunction Decomposition of $B_0$ and $B_1$.

There exists a sequence of eigenvalues $\lambda_k$ and eigenfunctions $\phi_k$ so that:

- The sequence $\lambda_k$ is increasing with $\lambda_k \to \infty$,
- $\phi_k \in B_2$,
- $-[x(1-x)\phi_k]'' = \lambda_k \phi_k$,
- The set $\{\phi_k\}_{k=1}^{\infty}$ is an orthonormal basis for $B_0$, and
- The set $\{\phi_k\}_{k=1}^{\infty}$ forms a basis for $B_1$. 
Theorem 1: Sketch of Proof

The Approximating Problem.

- Let $T > 0$, and choose
  \[
  \tilde{\phi} \in C([0, T); L_1(0, 1)),
  \]
  \[
  \tilde{R}_0, \tilde{R}_1 \in C[0, T). \]

- Define
  \[
  \tilde{R}(t) = \int_0^1 (x - \frac{1}{2}) \tilde{\phi}(x, t) \, dx + \tilde{R}_0(t) + \tilde{R}_1(t)
  \]

- There is a constant
  \[
  \gamma = \gamma \left( \| \tilde{\phi} \|_{C([0, T); L_1)}, \| \tilde{R}_0, \tilde{R}_1 \|_{C^0} \right)
  \]
  so that $|\tilde{R}(t)| \leq \gamma$. 

Theorem 1: Sketch of Proof

The Approximating Problem.

• Consider the approximating problem

\[ \phi_t = - (M(x, t, \tilde{R}(t)) \phi(x, t))_x \]
\[ + \frac{1}{2} (V(x, t, \tilde{R}(t)) \phi(x, t))_{xx} \]
\[ \phi \big|_{t=0} = \phi_0(x). \]

• We need to show that:
  – This problem has a solution \((\phi, R_0, R_1)\), and
  – The resulting map
    \[ \mathcal{F} : (\tilde{\phi}, \tilde{R}_0, \tilde{R}_1) \rightarrow (\phi, R_0, R_1) \]
    has a fixed point.
Theorem 1: Sketch of Proof

The Approximating Problem.

- Choose $\phi_0$ with $\|\phi_0\|_{B_0} < \infty$.

- Then there exists a unique function

$$
\phi \in C([0, T); B_0) \cap L_2(0, T; B_1)
$$

so that

$$
\phi_t = -(M \phi)_x + \frac{1}{2} (V \phi)_{xx}
$$

$$
\phi|_{t=0} = \phi_0(x).
$$

- Moreover there is a constant $C = C(\gamma, T)$ so that

$$
\sup_{0 \leq t \leq T} \int_0^1 x(1-x)\phi^2 \, dx
$$

$$
+ \int_0^T \int_0^1 [x(1-x)\phi]_{xx}^2 \, dx \, dt
$$

$$
\leq C \|\phi_0\|_{B_0}^2.
$$
Theorem 1: Sketch of Proof

The Approximating Problem.

- Further, if $\| \phi_0 \|_{B_1} < \infty$, then

$$\phi \in C([0, T); B_1) \cap L_2(0, T; B_2)$$

and

$$\sup_{0 \leq t \leq T} \int_0^1 [x(1 - x)\phi]^2_x \, dx$$

$$+ \int_0^T \int_0^1 x(1 - x)[x(1 - x)\phi]^2_{xx} \, dx \, dt$$

$$\leq C \| \phi_0 \|^2_{B_1}$$

where again $C$ depends only on $\gamma$ and $T$. 
Theorem 1: Sketch of Proof
Regularity of the Approximating Problem Depending on $\gamma$.

- $x(1 - x)\phi \in C([0, T); C^{1/2}[0, 1])$,
- $\phi \in C_{\text{loc}}((0, 1) \times [0, T))$,
- $\phi_t \in L_2(0, T; B_0)$.
- There is a constant $C$ depending only on $\gamma$ and $T$ so that

$$\sup_{0 \leq t < T} |\phi(x, t)| \leq C \max \left( \frac{1}{\sqrt{x}}, \frac{1}{\sqrt{x - 1}} \right) \|\phi_0\|_{B_1}.$$

- For any $1 \leq p < 2$, there is a constant $C'$ depending only on $\gamma$, $T$ and $p$ so that

$$\sup_{0 \leq t < T} \|\phi(\cdot, t)\|_{L_p(0, 1)} \leq C' \|\phi_0\|_{B_1}.$$
Theorem 1: Sketch of Proof

Regularity of the Approximating Problem in Time

- \( \phi \in C^{1/2}([0, T); B_0) \) and
  \[
  \| \phi(\cdot, t_2) - \phi(\cdot, t_1) \|_{B_0} \leq C |t_2 - t_1|^{\frac{1}{2}} \| \phi_0 \|_{B_1}.
  \]
  for \( C = C(\gamma, T) \).

- \( \phi \in C^\alpha([0, T); L_p) \) and
  \[
  \| \phi(\cdot, t_2) - \phi(\cdot, t_1) \|_{L_p} \leq C |t_2 - t_1|^{\alpha} \| \phi_0 \|_{B_1}
  \]
  for any \( 1 \leq p < 2 \), and any \( 0 < \alpha < \frac{1}{p} - \frac{1}{2} \), where
  \( C = C(\gamma, T, p, \alpha) \).
Theorem 1: Sketch of Proof

Regularity of Boundary Terms for the Approximating Problem

• Define $\nu(x, t) = \int_0^t (V \phi)_x(x, s) \, ds$.

• Then $\nu, \nu_t \in L_\infty(0, T; L_2)$ and

$$\sup_{0 \leq t < T} \left\{ \| \nu(\cdot, t) \|_{L_2(0,1)} + \left\| \frac{\partial \nu}{\partial t}(\cdot, t) \right\|_{L_2(0,1)} \right\} \leq C \| \phi_0 \|_{B_1}$$

for $C = C(\gamma, T)$.

• Further $\frac{\partial \nu}{\partial x} \in C^\alpha([0, T); L_p)$ and

$$\left\| \frac{\partial \nu}{\partial x}(\cdot, t_2) - \frac{\partial \nu}{\partial x}(\cdot, t_1) \right\|_{L_p} \leq C |t_2 - t_1|^\alpha \| \phi_0 \|_{B_1}.$$

for any $0 < \alpha < \frac{1}{p} - \frac{1}{2}$ where $C = C(\gamma, T, \alpha, p)$. 
Theorem 1: Sketch of Proof

Regularity of Boundary Terms for the Approximating Problem

- \( \nu \in C^\alpha([0, T); C^{1 - \frac{1}{p}}[0, 1]) \) and

\[
|\nu(x_2, t_2) - \nu(x_1, t_1)| \\
\leq C \left\{ |t_2 - t_1|^\alpha + |x_2 - x_1|^{1 - \frac{1}{p}} \right\} \|\phi_0\|_{B_1}
\]

for any \( 1 \leq p < 2 \) and any \( 0 < \alpha < \frac{1}{p} - \frac{1}{2} \) where
\( C = C(\gamma, T, \alpha, p) \).

- Finally, \( \nu(0, t), \nu(1, t) \in C^\beta[0, T) \) with

\[
|\nu(0, t_2) - \nu(0, t_1)| \leq C |t_2 - t_1|^\beta \|\phi_0\|_{B_1} \\
|\nu(1, t_2) - \nu(1, t_1)| \leq C |t_2 - t_1|^\beta \|\phi_0\|_{B_1}
\]

for any \( 0 \leq t_1 < t_2 < T \) and any \( 0 < \beta < \frac{1}{2} \) where
\( C = C(\gamma, T, \beta) \).
Theorem 1: Sketch of Proof

The Maximum Principle

- For any \(0 \leq t_1 < t_2 < T\).

\[
\int_0^1 \phi^\pm(x, t_2) \, dx \leq \int_0^1 \phi^\pm(x, t_1) \, dx.
\]

Proof Sketch: Use the test function

\[
\psi = \pm \frac{x(1 - x)\phi^\pm}{x(1 - x)\phi^\pm + \epsilon}
\]

on an interval \([a, b] \subset [0, 1]\). Then the last term is estimated

\[
\pm \int_{t_1}^{t_2} \int_a^b (V\phi)_{xx} \frac{x(1 - x)\phi^\pm}{x(1 - x)\phi^\pm + \epsilon} \, dx \, dt
\]

\[
= \pm \int_{t_1}^{t_2} (V\phi)_x \frac{x(1 - x)\phi^\pm}{x(1 - x)\phi^\pm + \epsilon} \bigg|_{x=a}^{x=b} \, dt
\]

\[
- \int_{t_1}^{t_2} \int_a^b (V\phi^\pm)_x \frac{\epsilon [x(1 - x)\phi^\pm]_x}{(x(1 - x)\phi^\pm + \epsilon)^2} \, dx \, dt.
\]
Theorem 1: Sketch of Proof

The Maximum Principle

However $V = x(1 - x)v$, so

$$
\begin{align*}
\int_{t_1}^{t_2} \int_a^b (V \phi^\pm)_x \frac{\epsilon [x(1 - x)\phi^\pm]_x}{(x(1 - x)\phi^\pm + \epsilon)^2} \, dx \, dt \\
= \int_{t_1}^{t_2} \int_a^b v \frac{\epsilon [x(1 - x)\phi^\pm]_x^2}{(x(1 - x)\phi^\pm + \epsilon)^2} \, dx \, dt \\
+ \int_{t_1}^{t_2} \int_a^b v_x \frac{\epsilon x(1 - x)\phi^\pm [x(1 - x)\phi^\pm]_x}{(x(1 - x)\phi^\pm + \epsilon)^2} \, dx \, dt
\end{align*}
$$

Thus for almost every $0 < a < b < 1$

$$
\left. \int_a^b \phi^\pm \, dx \right|_{t=t_2} \leq \int_{t_1}^{t_2} \int_a^b (M \phi^\pm)_x \, dx \, dt \\
\pm \int_{t_1}^{t_2} (V \phi)_x \chi[\phi^\pm > 0] \, dt \bigg|_{x=a} \bigg|_{x=b}.$$

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Mike O’Leary and Judith Miller
Slide 37
Theorem 1: Sketch of Proof

The Maximum Principle

- \( \phi \in L_2(0, T; B_2) \hookrightarrow L_2(0, T; C^3_{\text{loc}}(0, 1)) \), so \( \pm (V \phi)_x \chi[\phi^\pm > 0] \) is defined for all \( x \), but it need not be continuous.

- Define \( \mu^\pm(x) = \int_{t_1}^{t_2} (V \phi^\pm)(x, t) \, dt \).

- Now \( \mu^\pm \in W^{1}_{2}(0, 1) \hookrightarrow C^{1/2}[0, 1] \); indeed

\[
\| \mu^\pm \|_{W^{1}_{2}(0,1)} \leq C \| \phi \|_{L_2(0,T;B_1)}.
\]

- \( \mu(x) \geq 0 \) and \( \mu(0) = \mu(1) = 0 \); indeed

\[
\mu^\pm(x) = \int_{t_1}^{t_2} vx(1 - x) \phi^\pm \, dt \\
\leq C x (1-x) \max \left( \frac{1}{\sqrt{x}}, \frac{1}{\sqrt{1-x}} \right) \| \phi \|_{L_2(0,T;B_1)}.
\]
Theorem 1: Sketch of Proof
The Maximum Principle

• Then for any $\delta > 0$

$$\text{meas}\{x \in (0, \delta): \mu_x^\pm(x) \geq 0\} > 0 \text{ and}$$

$$\text{meas}\{x \in (1 - \delta, 1): \mu_x^\pm(x) \leq 0\} > 0.$$  

• As a consequence, we can find sequences $a_n \downarrow 0$ and $b_n \uparrow 1$ so that

$$\pm \int_{t_1}^{t_2} (V \phi)_x \chi[\phi^\pm > 0] \, dt \bigg|_{x=a_n} \geq 0$$

$$\pm \int_{t_1}^{t_2} (V \phi)_x \chi[\phi^\pm > 0] \, dt \bigg|_{x=b_n} \leq 0.$$  

• Thus

$$\int_{t=t_1}^{t=t_2} \phi^\pm(x, t) \, dx \leq 0. \quad \blacksquare$$
Theorem 1: Sketch of Proof
Estimates of $R(t)$

- Make the definitions

$$R_0(t) = R_0(0) - \frac{1}{4} \nu(0, t)$$

$$R_1(t) = R_1(0) - \frac{1}{4} \nu(1, t)$$

so that

$$R(t) = \int_0^1 (x - \frac{1}{2}) \phi(x, t) \, dx + R_0(t) + R_1(t).$$

- Use $(x - 1/2)$ as a test function to find that

$$R(t_2) - R(t_1) = \int_{t_1}^{t_2} \int_0^1 M \phi \, dx \, dt.$$
Theorem 1: Sketch of Proof

Estimates of $R(t)$

- Applying (H3) and the fact that

$$\| \phi(\cdot, t) \|_{L^1(0,1)} \leq \| \phi_0 \|_{L^1(0,1)} ,$$

we find

$$|R(t)| \leq \left[ |R(0)| + \| \phi_0 \|_{L^1(0,1)} \int_0^t \mathcal{M}_1(s) \, ds \right]$$

$$+ \| \phi_0 \|_{L^1(0,1)} \int_0^t \mathcal{M}_2(s) |R(s)| \, ds .$$

- Thus

$$|R(t)| \leq \left[ |R(0)| + \| \phi_0 \|_{L^1(0,1)} \int_0^t \mathcal{M}_1(s) \, ds \right]$$

$$\exp \left[ \| \phi_0 \|_{L^1(0,1)} \int_0^t \mathcal{M}_2(s) \, ds \right] .$$
Theorem 1: Sketch of Proof

Compactness of the Solutions

• Suppose that

\[ \{ \phi_n \}_{n=1}^{\infty} \subset C([0, T); B_1) \cap C^\alpha([0, T); L_1) \]

\[ \sup_{0 \leq t < T} \| \phi_n(\cdot, t) \|_{B_1} \leq C \]

\[ \| \phi_n(\cdot, t_2) - \phi_n(\cdot, t_1) \|_{L_1} \leq C |t_2 - t_1|^\alpha \]

for \( 0 < \alpha < \frac{1}{2} \) and a constant \( C \) independent of \( n \).

• Then there is a subsequence \( \{ \phi_{n_j} \}_{j=1}^{\infty} \) and a function \( \phi \in C^\alpha([0, T); L_1) \) so that

\[ \| \phi_{n_j}(\cdot, t) - \phi(\cdot, t) \|_{L_1} \rightarrow 0 \]

uniformly for \( t \in [0, T) \).

• If \( \alpha = \frac{1}{2} \), then the conclusion holds true with \( B_0 \) in place of \( L_1 \).
Theorem 1: Sketch of Proof

The Fixed Point

- Define
  \[ \mathcal{U} = C([0, T]; L_1(0, 1)) \times C[0, T) \times C[0, T). \]

- Consider the function \( \mathcal{F} : \mathcal{U} \rightarrow \mathcal{U} \) defined by the rule
  \[ \mathcal{F}(\tilde{\phi}, \tilde{R}_0, \tilde{R}_1) = (\phi, R_0, R_1) \]
  where \( \phi, R_0, \) and \( R_1 \) are the solutions to the problem

  \[
  \tilde{R}(t) = \int_0^1 (x - \frac{1}{2}) \tilde{\phi}(x, t) \, dx + \tilde{R}_0(t) + \tilde{R}_1(t)
  \]

  \[
  \phi_t = - (M(x, t, \tilde{R}(t)) \phi(x, t))_x
  \]

  \[
  + \frac{1}{2} (V(x, t, \tilde{R}(t)) \phi(x, t))_{xx}
  \]

  \[
  \phi \bigg|_{t=0} = \phi_0(x).
  \]
Theorem 1: Sketch of Proof

The Fixed Point

- The function \( \mathcal{F} : \mathcal{U} \rightarrow \mathcal{U} \) is continuous.
- The function \( \mathcal{F} : \mathcal{U} \rightarrow \mathcal{U} \) is compact.
- The set

\[
\left\{ (\phi, R_0, R_1) \in \mathcal{U} \mid (\phi, R_0, R_1) = \sigma \mathcal{F}(\phi, R_0, R_1) \right\}
\]

for some \( 0 \leq \sigma \leq 1 \)

is bounded in \( \mathcal{U} \).

As a consequence, \( \mathcal{F} \) has a fixed point, which is our solution.
Theorem 2: Sketch of Proof

- Let $\bar{\phi}(x, t) = \phi(x, t) - \phi^*(x, t)$; define $\bar{M}, \bar{V}$, and $\bar{R}$ similarly.

- Then

$$\bar{M} = M(x, t, R(t)) - M(x, t, R^*(t)).$$

- Thus, there is some $0 \leq \lambda \leq 1$ so that

$$|\bar{M}| \leq \left| \frac{\partial M}{\partial R}(x, t, \lambda R(t) + (1 - \lambda) R^*(t)) \right| |\bar{R}(t)|$$

and so

$$|\bar{M}(x, t)| \leq C|\bar{R}(t)|.$$

- Because $R(t) - R(0) = \int_0^t \int_0^1 M\phi \, dx \, dt$,

$$|\bar{M}(x, t)| \leq C \int_0^t \int_0^1 (|\bar{M}\phi| + |M^*\phi|) \, dx \, ds + C|\bar{R}(0)|.$$
Theorem 2: Sketch of Proof

• Thus

$$|\bar{M}(x, t)| \leq C \int_0^t \int_0^1 |M^* \phi| \, dx \, ds + C|\bar{R}(0)|.$$ 

• Now $$R(t) - R(0) = \int_0^t \int_0^1 M \phi \, dx \, dt,$$ so

$$|\bar{R}(t)| \leq \int_0^t \int_0^1 |\bar{M} \phi| \, dy \, ds$$

$$+ \int_0^t \int_0^1 |M^* \bar{\phi}| \, dy \, ds + |\bar{R}(0)|$$

• Thus

$$|\bar{R}(t)| \leq C \int_0^t \int_0^1 |M^* \bar{\phi}| \, dx \, ds + C|\bar{R}(0)|$$

$$\leq C \int_0^t \int_0^1 x(1 - x)|\bar{\phi}| \, dx \, ds + C|\bar{R}(0)|.$$ 

where $$C = C\left(\|R_0^*, R_1^*\|_{C^0[0,T]}, \|\phi^*\|_{C([0,T];B_1)}\right).$$
Theorem 2: Sketch of Proof

- Subtracting the equation for $\phi^*$ from the equation for $\phi$, taking inner products with $\bar{\phi}$ and integrating, we find

$$\int_0^1 x(1 - x)\bar{\phi}^2 dx \bigg|_{t} + \int_0^t \int_0^1 [x(1 - x)\bar{\phi}]_x^2 dx \, ds$$

$$\leq C \int_0^1 x(1 - x)\bar{\phi}_0^2 dx$$

$$+ C \int_0^t \int_0^1 x(1 - x)\bar{\phi}^2 dx \, ds$$

$$+ C \int_0^t \int_0^1 (x(1 - x)\bar{m}\phi)^2 dx \, ds$$

$$+ C \int_0^t \int_0^1 (x(1 - x)\bar{v}\phi)_x^2 dx \, ds.$$
Theorem 2: Sketch of Proof

• We know

\[ |\bar{m}| \leq \left| \frac{\partial m}{\partial \bar{R}}(x, t, \lambda R(t) + (1 - \lambda) R^*(t)) \right| |\bar{R}| \leq C|\bar{R}|; \]

similarly

\[ |\bar{v}| + |\bar{v}_x| \leq C|\bar{R}|. \]

• Thus we can use our estimate of $|\bar{R}|$ to find

\[
\int_0^1 x(1-x)\phi^2 \, dx \bigg|_t + \int_0^t \int_0^1 [x(1-x)\phi]^2 \, dx \, ds \\
\leq C \int_0^1 x(1-x)\phi_0^2 \, dx + C|\bar{R}(0)|^2 \\
+ C \int_0^t \int_0^1 x(1-x)\phi^2 \, dx \, ds.
\]

• Gronwall’s inequality completes the proof.