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

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

  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

$$f(r) = e^{-\kappa(r - r_{\text{opt}})^2}$$

  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 μ_i of the population that carries the allele A_i is $\mu_i = \mu + (1 - Q)x_i$.
- The average phenotype ν_i of the population that carries the allele a_i is $\nu_i = \mu - Qx_i$.
- 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

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

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 ϕ.
  - Moreover, R also depends on the coefficient V and so even if ϕ 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 ϕ.
- $R(t)$ 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

- $B_0 = \left\{\psi \text{ measurable on } [0,1] : \langle\psi,\psi\rangle_{B_0}^2 < \infty\right\}$ where

$$\langle\phi,\psi\rangle_{B_0} = \int_0^1 x(1-x)\phi\psi\,dx.$$

- $B_1 = \left\{\psi \in B_0 : \langle\psi,\psi\rangle_{B_1}^2 < \infty\right\}$ where

$$\begin{aligned}\langle\phi,\psi\rangle_{B_1} &= \langle\phi,\psi\rangle_{B_0} \\ &\quad + \int_0^1 [x(1-x)\phi]_x[x(1-x)\psi]_x\,dx.\end{aligned}$$

- $B_2 = \left\{\psi \in B_1 : \langle\psi,\psi\rangle_{B_2}^2 < \infty\right\}$ where

$$\begin{aligned}\langle\phi,\psi\rangle_{B_2} &= \langle\phi,\psi\rangle_{B_1} \\ &\quad + \int_0^1 x(1-x)[x(1-x)\phi]_{xx} \\ &\qquad\qquad \cdot [x(1-x)\psi]_{xx}\,dx.\end{aligned}$$

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 $\mathcal{M}_1(t)$ and $\mathcal{M}_2(t)$ so that

$$\sup_{0 \leq x \leq 1} |M(x,t,R)| \leq \mathcal{M}_1(t) + \mathcal{M}_2(t)|R|.$$

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

$$\begin{aligned}\phi \in & C([0,T);B_1) \\ & \cap L_2(0,T;B_2) \\ & \cap C^{\alpha}([0,T);L_p(0,1)) \\ & \cap C((0,1)\times[0,T))\end{aligned}$$

  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

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

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

Theorem 1: Existence

- Then
$$\phi_t = -(M\phi)_x + \tfrac{1}{2}(V\phi)_{xx}$$
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 $1 \le p < 2$ and any $0 < \alpha < \frac{1}{p} - \frac{1}{2}$. Further
$$R_0(t) = R_0(0) - \tfrac{1}{4}\nu(0,t),$$
$$R_1(t) = R_1(0) - \tfrac{1}{4}\nu(1,t).$$

Theorem 1: Existence

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

$$\sup_{0\le t<T} \|\phi(\cdot,t)\|_{B_0} + \|\phi\|_{L_2(0,T;B_1)} \le C\,\|\phi_0\|_{B_0}\,,$$
$$\|\phi\|_{C^{\frac{1}{2}}([0,T);B_0)} \le C\,\|\phi_0\|_{B_1}\,,$$
$$\sup_{0\le t<T} \|\phi(\cdot,t)\|_{B_1} + \|\phi\|_{L_2(0,T;B_2)} \le C\,\|\phi_0\|_{B_1}\,.$$

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

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

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

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

where C also depends on p and α.

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 β.

- 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

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

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

- Define

$$\begin{aligned} M &= M(x,t,R(t)), \\ M^* &= M(x,t,R^*(t)), \\ V &= V(x,t,R(t)), \\ V^* &= V(x,t,R^*(t)). \end{aligned}$$

Theorem 2: Uniqueness and Stability

- Suppose that

$$\begin{cases} \phi_t = -(M\phi)_x + \frac{1}{2}(V\phi)_{xx}, \\ \phi\Big|_{t=0} = \phi_0 \in B_1, \\ R(t) - R(0) = \int_0^t \int_0^1 M\phi \, dx \, dt, \end{cases}$$

and

$$\begin{cases} \phi_t^* = -(M^*\phi^*)_x + \frac{1}{2}(V^*\phi^*)_{xx}, \\ \phi^*\Big|_{t=0} = \phi_0^* \in B_1, \\ R^*(t) - R^*(0) = \int_0^t \int_0^1 M^*\phi^* \, dx \, dt, \end{cases}$$

- 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

$$
\begin{aligned}
\sup_{0\le t\le T} \int_0^1 x(1-x)(\phi-\phi^*)^2\,dx\Big|_t \\
+ \int_0^T \int_0^1 [x(1-x)(\phi-\phi^*)]_x^2\,dx\,dt \\
\le C \int_0^1 x(1-x)(\phi_0-\phi_0^*)^2\,dx \\
+ \int_0^1 [x(1-x)(\phi_0-\phi_0^*)]_x^2 \\
+ C|R_0(0)-R_0^*(0)|^2 \\
+ C|R_1(0)-R_1^*(0)|^2.
\end{aligned}
$$

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

$$x(1-x)\phi \in \overset{\circ}{W}{}_2^1(0,1).$$

Further ϕ has a continuous representative with

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

so that

$$|x_1(1-x_1)\phi(x_1) - x_2(1-x_2)\phi(x_2)|$$

$$\leq |x_2 - x_1|^{\frac{1}{2}} \left(\int_0^1 [x(1-x)\phi(x)]_x^2 \, dx \right)^{\frac{1}{2}}.$$

Theorem 1: Sketch of Proof

Theory of B_1.

- Let $\phi \in B_1$; then

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

- 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.

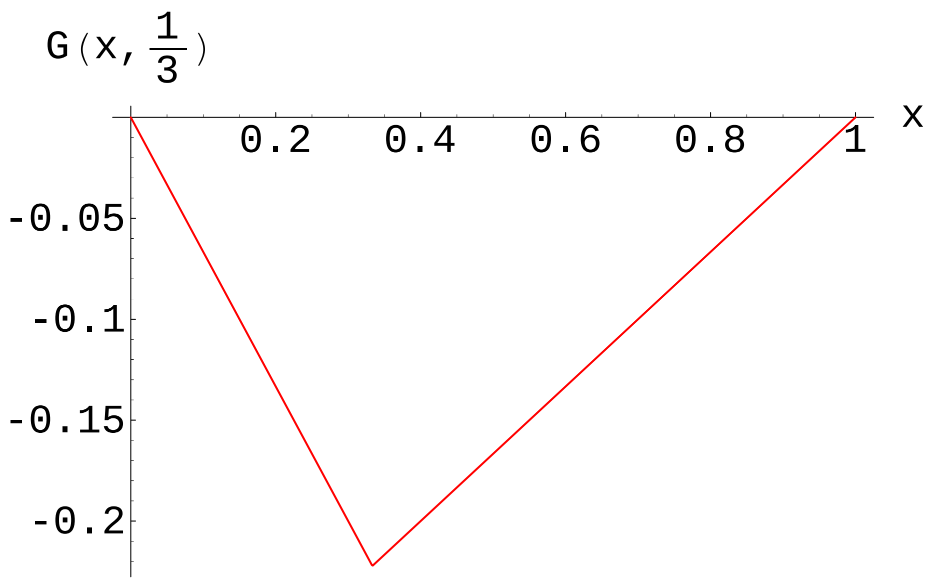
- Suppose that $\phi \in B_2$. Then

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

where

$$G(x,y) = \begin{cases} x(y-1) & x \le y \\ (x-1)y & x \ge y \end{cases}$$

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



Theorem 1: Sketch of Proof

Theory of B_2.

- We have the embedding

$$B_2 \hookrightarrow C^{\frac{3}{2}}_{\text{loc}}(0,1).$$

- Let $\phi \in B_2$; then

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

and

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

- $C^\infty[0,1]$ is dense in B_2.

Theorem 1: Sketch of Proof

The Elements of B_0, B_1, and B_2.

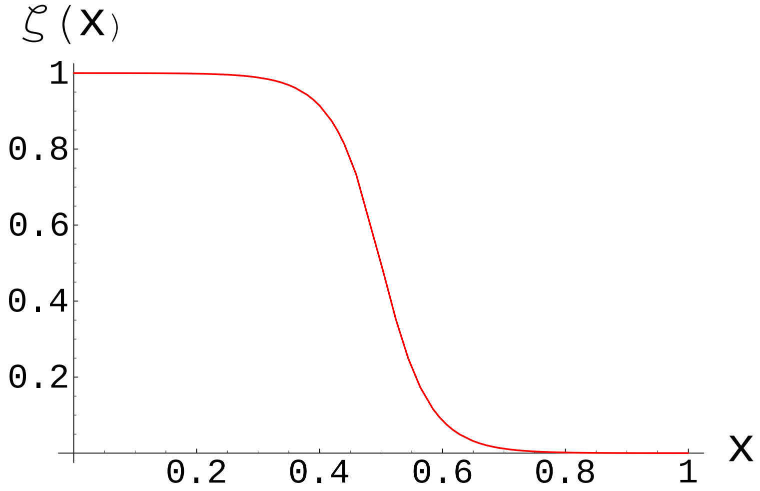
- It is easy to check that, for monomials $f(x) = x^p$
  - $x^p \in B_0$ iff $p > -1$,
  - $x^p \in B_1$ iff $p > -1/2$, and
  - $x^p \in B_2$ iff $p > 0$.
- As a consequence you might expect that if $\phi \in B_2$, then $[x(1-x)\phi(x)]_x \to 0$ as $x \to 0$ or $x \to 1$.
- This is important because $V = x(1-x)v(x,t,R)$ 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



- Then

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

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 λ_k and eigenfunctions ϕ_k so that:

- The sequence λ_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

$$\tilde{R}(t) = \int_0^1 \left(x - \tfrac{1}{2}\right) \tilde{\phi}(x,t)\, dx + \tilde{R}_0(t) + \tilde{R}_1(t)$$

- There is a constant

$$\gamma = \gamma\left(\left\| \tilde{\phi} \right\|_{C([0,T);L_1)}, \left\| \tilde{R}_0, \tilde{R}_1 \right\|_{C^0} \right)$$

so that $|\tilde{R}(t)| \le \gamma$.

Theorem 1: Sketch of Proof

The Approximating Problem.

- Consider the approximating problem

$$\phi_t = -(M(x,t,\tilde{R}(t))\phi(x,t))_x + \tfrac{1}{2}(V(x,t,\tilde{R}(t))\phi(x,t))_{xx}$$

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

- We need to show that:
  - This problem has a solution (ϕ, R_0, R_1), and
  - The resulting map

$$\mathfrak{F} : (\tilde{\phi}, \tilde{R}_0, \tilde{R}_1) \to (\phi, R_0, R_1)$$

    has a fixed point.

Theorem 1: Sketch of Proof

The Approximating Problem.

- Choose ϕ_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

$$\phi_t = -(M\phi)_x + \tfrac{1}{2}(V\phi)_{xx}$$
$$\phi\Big|_{t=0} = \phi_0(x).$$

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

$$\sup_{0\le t\le T} \int_0^1 x(1-x)\phi^2\,dx + \int_0^T \int_0^1 [x(1-x)\phi]_x^2\,dx\,dt \le C\,\|\phi_0\|_{B_0}^2.$$

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

$$\sup_{0\le t\le T} \int_0^1 [x(1-x)\phi]_x^2 \, dx + \int_0^T \int_0^1 x(1-x)[x(1-x)\phi]_{xx}^2 \, dx \, dt \le C \|\phi_0\|_{B_1}^2$$

where again C depends only on γ and T.

Theorem 1: Sketch of Proof

Regularity of the Approximating Problem Depending on γ.

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

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

- For any $1 \le p < 2$, there is a constant C depending only on γ, T and p so that

$$\sup_{0 \le t < T} \|\phi(\cdot,t)\|_{L_p(0,1)} \le C \|\phi_0\|_{B_1}.$$

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

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

  for $C = C(\gamma, T)$.
- Further $\dfrac{\partial \nu}{\partial x} \in C^\alpha([0,T);L_p)$ and

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

  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

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

  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 $0 \le t_1 < t_2 < T$.

$$\int_0^1 \phi^{\pm}(x,t_2)\,dx \le \int_0^1 \phi^{\pm}(x,t_1)\,dx.$$

Proof Sketch: Use the test function

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

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

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

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

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

Theorem 1: Sketch of Proof

The Maximum Principle

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

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

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

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

Theorem 1: Sketch of Proof

The Maximum Principle

- $\phi \in L_2(0,T;B_2) \hookrightarrow L_2(0,T;C^{\frac{3}{2}}_{\text{loc}}(0,1))$, so $\pm(V\phi)_x\chi[\phi^\pm > 0]$ is defined for all x, but it need not be continuous.
- Define $\mu^\pm(x) = \displaystyle\int_{t_1}^{t_2} (V\phi^\pm)(x,t)\,dt$.
- Now $\mu^\pm \in W_2^1(0,1) \hookrightarrow C^{\frac{1}{2}}[0,1]$; indeed $\|\mu^\pm\|_{W_2^1(0,1)} \le C\,\|\phi\|_{L_2(0,T;B_1)}$.
- $\mu(x) \ge 0$ and $\mu(0) = \mu(1) = 0$; indeed

$$\mu^\pm(x) = \int_{t_1}^{t_2} vx(1-x)\phi^\pm\,dt$$

$$\le Cx(1-x)\max\left(\frac{1}{\sqrt{x}}, \frac{1}{\sqrt{1-x}}\right)\|\phi\|_{L_2(0,T;B_1)}.$$

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

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

- Thus

$$\int_0^1 \phi^{\pm}(x,t)\, dx \Big|_{t=t_1}^{t=t_2} \leq 0. \quad \blacksquare$$

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

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

- 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
  - $\{\phi_n\}_{n=1}^{\infty} \subset C([0,T);B_1) \cap C^{\alpha}([0,T);L_1)$
  - $\sup\limits_{0 \le t < T} \|\phi_n(\cdot,t)\|_{B_1} \le C$
  - $\|\phi_n(\cdot,t_2) - \phi_n(\cdot,t_1)\|_{L_1} \le C|t_2 - t_1|^{\alpha}$

  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

$$\left\|\phi_{n_j}(\cdot,t) - \phi(\cdot,t)\right\|_{L_1} \longrightarrow 0$$

  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 $\mathfrak{F} : \mathcal{U} \longrightarrow \mathcal{U}$ defined by the rule

$$\mathfrak{F}(\tilde{\phi}, \tilde{R}_0, \tilde{R}_1) = (\phi, R_0, R_1)$$

where ϕ, R_0, and R_1 are the solutions to the problem

$$\tilde{R}(t) = \int_0^1 \left(x - \tfrac{1}{2}\right) \tilde{\phi}(x,t)\, dx + \tilde{R}_0(t) + \tilde{R}_1(t)$$

$$\phi_t = -(M(x,t,\tilde{R}(t))\phi(x,t))_x + \tfrac{1}{2}(V(x,t,\tilde{R}(t))\phi(x,t))_{xx}$$

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

Theorem 1: Sketch of Proof

The Fixed Point

- The function $\mathfrak{F} : \mathcal{U} \to \mathcal{U}$ is continuous.
- The function $\mathfrak{F} : \mathcal{U} \to \mathcal{U}$ is compact.
- The set

$$\left\{ (\phi, R_0, R_1) \in \mathcal{U} \,\middle|\, \begin{array}{l} (\phi, R_0, R_1) = \sigma \mathfrak{F}(\phi, R_0, R_1) \\ \text{for some } 0 \leq \sigma \leq 1 \end{array} \right\}$$

is bounded in $\mathcal{U}$.

- As a consequence, $\mathfrak{F}$ 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 $0 \le \lambda \le 1$ so that
$$|\bar{M}| \le \left| \frac{\partial M}{\partial R}(x,t,\lambda R(t) + (1-\lambda)R^*(t)) \right| |\bar{R}(t)|$$
and so
$$|\bar{M}(x,t)| \le C|\bar{R}(t)|.$$
- Because $R(t) - R(0) = \int_0^t \int_0^1 M\phi \, dx \, dt$,
$$|\bar{M}(x,t)| \le C \int_0^t \int_0^1 (|\bar{M}\phi| + |M^*\bar{\phi}|) \, dx \, ds + C|\bar{R}(0)|.$$

Theorem 2: Sketch of Proof

- Thus

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

- 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 $C = C(\|R_0^*, R_1^*\|_{C^0[0,T]}, \|\phi^*\|_{C([0,T];B_1)})$.

Theorem 2: Sketch of Proof

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

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

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

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

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

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

Theorem 2: Sketch of Proof

- We know

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

similarly

$$|\bar{v}| + |\bar{v}_x| \le C|\bar{R}|.$$

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

$$\int_0^1 x(1-x)\bar{\phi}^2 dx\Big|_t + \int_0^t \int_0^1 [x(1-x)\bar{\phi}]_x^2 dx\,ds$$
$$\le C\int_0^1 x(1-x)\bar{\phi}_0^2\,dx + C|\bar{R}(0)|^2$$
$$+ C\int_0^t \int_0^1 x(1-x)\bar{\phi}^2\,dx\,ds.$$

- Gronwall's inequality completes the proof.