9-1993

Approximation Methods for Singular Diffusions Arising in Genetics

Nacer E. Abrouk
Rose-Hulman Institute of Technology

APPROXIMATION METHODS FOR SINGULAR DIFFUSIONS ARISING IN GENETICS

Nacer Abrouk

MS TR 93-06

September 1993

Department of Mathematics
Rose-Hulman Institute of Technology
Terre Haute, IN 47803

FAX(812) 877-3198 Phone: (812) 877-8391

APPROXIMATION METHODS FOR SINGULAR DIFFUSIONS ARISING IN GENETICS

N. Abrouk
Department of Mathematics
Rose-Hulman Institute of Technology
Terre Haute, IN 47803

Key Words and Phrases: Stochastic Process; Martingale Property; Transition Probability Function; Gauss Galerkin; Fokker Planck; Moments; Hankel Determinants, Weak Convergence; Steady State.

ABSTRACT

Stochastic models in population genetics leading to diffusion Equations are considered. When the drift and the square of the diffusion coefficients are polynomials, an infinite system of ordinary differential Equations for the moments of the diffusion process can be derived using the martingale property. An example is provided to show how the classical Fokker Planck Equation approach may not be appropriate for this derivation. A Gauss Galerkin method for approximating the laws of the diffusion which originally proposed by Dawson (1980) is examined. In the few special cases for which exact solutions are known, comparison shows that the method is accurate and the new algorithm is efficient. numerical results relating to population genetics models are presented and discussed. An example where the Gauss Galerkin method fails is provied.

1. Introduction

In stochastic population genetics the fundamental quantity used for describing the genetic composition of a Mendelian population is the gene frequency. The process of change in the gene frequency is generally modeled as a stochastic process (see Kimura and Crow (1970)) satisfying the stochastic differential Equation $dY_t = a(Y_t)dt + \sigma(Y_t)dB_t$. The coefficients involved in this Equation (the drift a and the diffusion σ) reflect the mechanisms affecting the population, such as mutation, selection, migration, etc. Since, in general the probability law of the stochastic process of change in gene frequency Y_t, for $t > 0$, is difficult to determine except in very simple cases, an important task is the problem of numerically approximating the probability law of Y_t, for $t > 0$. Because most population genetic models have singularities at the boundaries of the state space of the process $Y = \langle Y_t, t \geq 0 \rangle$, it is even more difficult to approximate the probability law of Y_t through the Fokker Planck Equation. We shall present a method for solving the problem, which enables us to approximate more realistic models than those treated previously. The method was originally proposed by Dawson (1980). This method is called the Gauss

Galerkin method since it combines elements of the method of Gauss quadratures and the Galerkin approximation. The method involves the construction of a sequence of discrete probability measures by solving a non linear system of differential Equations. These concepts will be introduced and explained in Sections 2 through 5. In Section 6 the theory will be applied to particular genetic models, and numerical computations will be shown. They will be compared with those exact results which have been found in special cases by Kimura and Crow (1970).

2. Formulation

Let us assume that a pair of alleles A and a are segregating in a population of large size. We shall assume that the process of change in gene frequency satisfies a stochastic differential Equation of the following form

$$dY_t = a(Y_t)dt + \sigma(Y_t)dB_t, \tag{2.1}$$
$$Y_0 = X, \tag{2.2}$$

where X is a given random variable, B_t is the standard Brownian motion and the coefficients a and σ satisfy the standard conditions for the existence and uniqueness of the solution. Under the following assumption, it is known that the solution of Equations (2.1) and (2.2) is a Markov process with state space $[0,1]$, for more details see Ethier and Kurtz (1986).

A1. $a \in C^1[0,1]$, $\sigma^2 \in C^2[0,1]$,
A2. $\sigma(x) > 0$, $\forall x \in (0,1)$,
A3. X is independent of the σ-fields $\sigma\{B_t; t \geq 0\}$,
A4. $a(0) \geq 0$, $a(1) \leq 0$ and $\sigma(0) = \sigma(1) = 0$.

Let $P(t,x,y)$ denote the probability transition function associated with the process Y. Since for each $t \geq 0$, $x \in [0,1]$, $P(t,x,.)$ is a non negative measure on $[0,1]$, the Lebesgue decomposition implies

$$P(t,x,.) = P_A(t,x,.) + P_S(t,x,.),$$

where $P_A(t,x,.) \ll \lambda$ and $P_S(t,x,.) \perp \lambda$, and λ is the Lebesgue measure on [0,1]. It is well known that the Radon Nikodym derivative $p(t,x,y)=\frac{dP_A(t,x,y)}{d\lambda}$ satisfies, $\forall x,y \in (0,1)$, the Fokker Planck Equation

$$\frac{\partial p(t,x,y)}{\partial t} = L^*p = -\frac{\partial[a(y)p(t,x,y)}{\partial y} + \frac{\partial^2[b(y)p(t,x,y)]}{\partial y^2}, \tag{2.3}$$
$$p(0,x,y) = \delta(y-x), \tag{2.4}$$

where $2b = \sigma^2$ and with the following boundary conditions at $y = 0$ and $y = 1$,

$$\lim_{y\to 0}\{\frac{\partial[2b(y)p(t,x,y)]}{\partial y} - a(y)p(t,x,y)\} = 0, \; if \; a(0) \neq 0, \tag{2.5}$$

$$\lim_{y\to 0}[b(y)p(t,x,y)] = 0,\ if\ a(0) = 0, \tag{2.6}$$

$$\lim_{y\to 1}\{\frac{\partial[2b(y)p(t,x,y)]}{\partial y} - a(y)p(t,x,y)\} = 0,\ if\ a(1) \neq 0, \tag{2.7}$$

$$\lim_{y\to 1}[b(y)p(t,x,y)] = 0,\ if\ a(1) = 0. \tag{2.8}$$

The classification of boundary behavior of the stochastic process Y (based on the definition given in Karlin and Taylor (1981)) which is in agreement with the classification given by Feller (1954) is summarized as follows

- 0 is an exit boundary if a(0)=0,
- 1 is an exit boundary if a(1)=0,
- 0 is a regular boundary if $0 < a(0) < b'(0)$,
- 1 is a regular boundary if $b(1)b'(1) < a(1) < 0$,
- 0 is an entrance boundary if $a(0) \geq b'(0)$,
- 1 is an entrance boundary if $a(1) \leq b'(1)$.

Note that the Fokker Planck Equation is valid only for gene frequencies in the interval $0 < y < 1$ (unfixed classes). Separate treatments are required to obtain the probability that the gene frequency is 0 or 1 at time t (terminal classes). When the boundaries $\{0\}$ and $\{1\}$ act as absorbing boundaries it can be shown, see Ethier and Kurtz (1986), that we have

$$\frac{dP_S(t,x,0)}{dt} = \Phi(t,x,0),\ P(0,x,0) = 0, \tag{2.9}$$

$$\frac{dP_S(t,x,1)}{dt} = \Phi(t,x,1),\ P(0,x,1) = 0, \tag{2.10}$$

where

$$\Phi(t,x,i) = \{a(y)P(t,x,y) - \frac{1}{2}\frac{\partial[b^2(y)P(t,x,y)}{\partial y}]\}|_{y=i},\ for\ i = 0,1.$$

Let f be the density of the random variable X. Then through a simple integration with respect to the backward variable x of Equations (2.3) and (2.4) the Radon Nikodym derivative $\phi(.,t)$ of the absolutely continuous part of the law of Y_t satisfies

$$\frac{\partial\phi(y,t)}{\partial t} = L^*\phi(y,t), \tag{2.11}$$

$$\phi(y,0) = f(y), \tag{2.12}$$

plus possibly boundary conditions depending on the behavior of the process at the boundaries of the state space [0,1]. Since in general, the law of Y_t, for $t > 0$, is difficult to determine, an important task is the problem of numerically approximating this probability law. Because most population genetics models have singularities at the boundary of the state space of the process Y, it is even more difficult to approximate the law of Y_t, for $t > 0$, through the Fokker Planck Equation. The traditional deterministic approach

has been to attempt a numerical approximation of the Fokker Planck Equation. This Equation is usually very difficult to solve, if not impossible.

Lemma 2.1 *Suppose the semigroup $\langle T_t, t \geq 0\rangle$ associated with the diffusion Y is strongly continuous, and let $h \in C^2[0,1] \cap D(L)$, then*

$$\frac{dE[h(Y_t)]}{dt} = E[(Lh)(Y_t)], \tag{2.13}$$

$$Y_0 = X, \tag{2.14}$$

where L is the formal adjoint of L^*, and is defined by

$$Lh = a\frac{\partial h}{\partial x} + b\frac{\partial^2 h}{\partial x^2}, \ \forall h \in D(L).$$

Proof: Equation 2.14 is obvious. To prove Equation 2.13 let $t \in (0,\infty)$ and $h \in C^2[0,1] \cap D(L)$, then by applying Ito's lemma to Equation (2.1), we have for all $0 \leq s \leq t < \infty$

$$h(Y_t) - h(Y_s) = \int_s^t [a(Y_u)h'(Y_u) + b(Y_u)h''(Y_u)]du + \int_s^t b(Y_u)dB_u,$$

by taking the expectation of both sides of the above Equation and then by applying Fubini's theorem we obtain

$$E[h(Y_t)] - E[h(Y_s)] = \int_s^t E[(Lh)(Y_u)]du. \tag{2.15}$$

We note that an alternative way for deriving (2.15) is through the martingale $\langle h(Y_t) - \int_0^t (Lh)(X_u)du, t \geq 0, \sigma B_t, t \geq 0\rangle$. Using the strong continuity of $\langle T_t, t \geq 0\rangle$, the function $t \to E[(Lh)(Y_t)]$ can be shown to be continuous as follows

$$\begin{aligned} E[(Lh)(Y_t)] &= \int_\Omega (Lh)(Y_t)(\omega)dP(\omega) = \int_0^1 (Lh)(y)d\mu_t(y) \\ &= \int_0^1 (Lh)(y)[\int_0^1 P(t,x,dy)d\mu_0(x)] \\ &= \int_0^1 [\int_0^1 (Lh)(y)P(t,x,dy)]d\mu_0(x) \quad \text{(by Fubini's theorem)} \end{aligned}$$

by the strong continuity of the semigroup $\langle T_t, t \geq 0\rangle$, we have

$$\begin{aligned} \lim_{t\to u}\int_0^1 [\int_0^1 (Lh)(y)P(t,x,dy)]d\mu_0(x) &= \int_0^1 \lim_{t\to u}[\int_0^1 (Lh)(y)P(t,x,dy)]d\mu_0(x) = \\ \int_0^1 [\int_0^1 (Lh)(y)P(u,x,dy)]d\mu_0(x) &= E[(Lh)(Y_u)]. \end{aligned}$$

Therefore, using (2.15) and the continuity of the map $t \to E[(Lh)(Y_t)]$ we have

$$\frac{dE[h(Y_t)]}{dt} = E[(Lh)(Y_t)], \tag{2.16}$$

which completes the proof.

3. Moments System of Differential Equation

In this section (and in the remainder of the paper) we shall assume that a and b are both polynomials, i.e.: $a(x) = \sum_{j=0}^{\alpha} A_j x^j$,and $b(x) = \sum_{j=0}^{\beta} B_j x^j$, where α, $\beta \in \mathbf{N}$. In order to obtain Equations for the moments of the process the following assumption is needed

A5. $D(L)$ contains all the monomials, where $D(L)$ represents the domain of the operator L.

By specializing Equation (2.13) to $h_k(x) = x^k$, where $k \in \mathbf{N} \cup \{0\}$, the following initial value problem is obtained

$$\frac{dM_k(t)}{dt} = k[\sum_{j=0}^{\alpha} A_j M_{k+j-1}(t)] + \theta_k[\sum_{j=1}^{\beta} B_j M_{k+j-2}(t)] \tag{3.1}$$

$$M_k(0) = E(X^k), \forall k \in \mathbf{N} \cup \{0\}. \tag{3.2}$$

where $\theta_k = \frac{k(k-1)}{4}$, and $M_k(t) = E(Y_t^k)$.

When either $\alpha \geq 2$ or $\beta \geq 3$ system (3.1) forms an "open hierarchy" in which the differential Equation for the k-th moment may contain terms involving the (k+1)-th or higher moments. Various truncation schemes have been proposed to approximate the solution of system (3.1). The simplest and most frequently used is the cumulant neglect method in which the (k+1)-th and higher cumulants are set Equationl to zero. In this way the system of moment Equations reduces to a closed system of differential Equations. Unfortunately, the use of the cumulant neglect (or any of its variants) can give misleading results.

Remark:
Previous derivations of the Gauss Galerkin method (see HajJafar (1986)) used Equation 2.11 as a starting point and then multiplied both sides of this Equation by y^k, and integrated by parts to obtain

$$\frac{d\int_0^1 y^k \phi(y,t)}{dt} = \int_0^1 \phi(y,t) L(y^k) + [a\phi y^k + y^k \frac{\partial b\phi}{\partial y} - k y^{k-1} b\phi]|_{y=0,1}. \tag{3.3}$$

It is only when the boundary term $[a\phi y^k + y^k \frac{\partial b\phi}{\partial y} - k y^{k-1} b\phi]|_{y=0,1} = 0$ that Equation 2.16 and Equation 3.3 are the same (this correspond to the case where $P_S \equiv 0$). Therefore, system 3.1 cannot be derived using the Fokker Planck Equation whenever P_S is not identically 0. In fact, as the following example shows, the behavior of the distribution

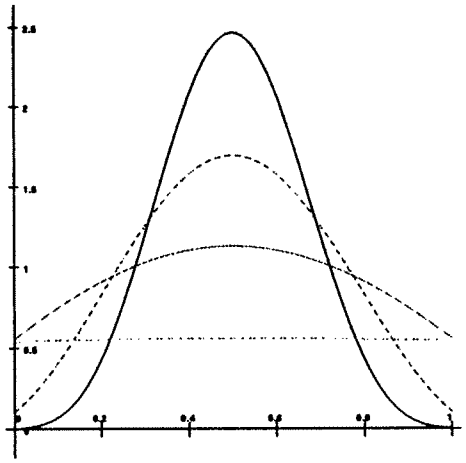


Figure 3.1: Behavior of the Solution of the Fokker Planck Equation

of the process is not totally accounted for (for all $t > 0$ and also at ∞) if Equation 3.3 is used to derive a system similar to 3.1 (ie: the dropping of the boundary term may not be appropriate).

Example:
Consider the model where $a(x) \equiv 0$ and $b(x) = 0.25x(1-x)$. Both 0 and 1 are exit boundaries. The boundary term $[a\phi y^k + y^k \frac{\partial b\phi}{\partial y} - ky^{k-1}b\phi]|_{y=0,1} \neq 0$, $\forall t > 0$. The exact solution of the Fokker Planck Equation (i.e: the Radon Nikodym derivative of the absolutely continuous part of the distribution) was first derived by Kimura and Crow (1970) and is given by

$$p(t,x,y) = \sum_{i=1}^{\infty} x(1-x)i(i+1)(2i+1)F(1-i,i+2,2,x) \times F(1-i,i+2,2,y)e^{-i(i+1)t}, \quad (3.4)$$

where F is the hypergeometric function. We have evaluated the above series using up to 100 terms. Figure 3.1 shows the behavior of the solution for t=0.05, 0.10, 0.20, 0.50, and 10. As t increases from 0 to 10, the solution goes from a unimodal curve to become identically zero. This behavior is due to the fact that the mass is leaking towards the boundaries 0 and 1 (exit boundaries). This is an illustration of a case where the transition is not absolutely continuous with respect to the Lebesgue measure on the state space $[0,1]$.

4. Gauss Galerkin Method

Gauss Galerkin methods for approximating the law of Y_t were originally proposed by Dawson (1980). Attempts have been made subsequently by HajJafar (1986) to improve the efficiency of such methods. We shall provide the details of the proofs of some

results and suggest a new numerical algorithm which reduces the ill-conditioning considerably. We also provide an example of a model from population gebetics where the Gauss Galerkin method is not applicable. We start by reviewing the Gauss Galerkin method.

The following preparatory lemmas will be needed

Lemma 4.2 *Let μ be a probability measure on [0,1] such that its support does not reduce to a finite set. Then $\forall n \in \mathbf{N}$, $\forall g \in C^{2n}[0,1], \exists \xi \in (0,1)$ such that*

$$\int_0^1 g(x)d\mu(x) = \int_0^1 g(x)d\mu_n(x) + \frac{g^{(2n)}(\xi)}{(2n)!}\int_0^1 p_n^2(x,t)d\mu(x), \tag{4.1}$$

where $p_n(.,t)$ is the n-th member of the family $\{p_i(.,t), i \geq 0\}$ of orthogonal polynomials generated by the measure μ_t and where μ_n is a discrete probability measure with n distinct nodes lying in $(0,1)$ and is usually referred to as the Gauss Christoffel measure.

The proof of Lemma 4.2 can be found in Stoer and Bulirsch (1980).

Lemma 4.3 *Given a sequence of numbers $\{m_i, i \geq 0\}$ there exist a unique atomic measure whose support consists of exactly n nodes in (0,1) if and only if*

1. $\Delta_r > 0, \forall r \in 0, 1, ..., n-1$,
2. $\Gamma_r > 0, \forall r \in 0, 1, ..., n-1$, *and*
3. $\Delta_r = \Gamma_r = 0, \forall r \geq n$,

where the Hankel determinants Δ_r and Γ_r are defined as follows, for each $r \in \mathbf{N} \cup 0$,

$$\Delta_r = \begin{vmatrix} m_0 & m_1 & \dots & m_r \\ m_1 & m_2 & \dots & m_{r+1} \\ \vdots & \vdots & & \vdots \\ m_r & m_{r+1} & \dots & m_{2r} \end{vmatrix},$$

$$\Gamma_r = \begin{vmatrix} m_1 & m_2 & \dots & m_{r+1} \\ m_2 & m_3 & \dots & m_{r+2} \\ \vdots & \vdots & & \vdots \\ m_{r+1} & m_{r+2} & \dots & m_{2r+1} \end{vmatrix}.$$

The proof of Lemma 4.3 can be found in Shohat and Tamarkin (1943).

Now we turn to the solution of system 3.1. Using Equation 4.1, system 3.1 can be written in the form, $\forall k \in \mathbf{N} \cup \{0\}$

$$\frac{d[m_k(t,n)+e_k(t,n)]}{dt} = k\{\sum_{j=0}^{\alpha} A_j[m_{k+j-1}(t,n)+e_{k+j-1}(t,n)] + \tag{4.2}$$

$$\theta_k[\sum_{j=1}^{\beta} B_j[m_{k+j-2}(t,n)+e_{k+j-2}(t,n)]\}, \tag{4.3}$$

where $m_j(t,n) = \int_0^1 x^j d\mu_{t,n}(x)$. The Gauss Galerkin method consists in dropping the error terms involved in system 4.2 and retaining its first $2n$ Equations, which leads to the following initial value problem, for $0 \leq k \leq 2n-1$

$$\frac{du_k(t,n)}{dt} = k[\sum_{j=0}^{\alpha} A_j u_{k+j-1}(t,n)] + \tag{4.4}$$

$$\theta_k[\sum_{j=1}^{\beta} B_j[u_{k+j-2}(t,n)],$$

$$u_k(0,n) = E(X^k). \tag{4.5}$$

Lemma 4.4 *Assume the support of the law of X does not reduce to a finite set, then for each $n \in \mathbf{N}$, the initial value problem 4.4 and 4.5 has a unique solution $\langle u_k(t,n), 0 \leq k \leq 2n-1\rangle$ defined on some interval $[0,\tau_n]$ with the property,*

$$u_k(t,n) = \int_0^1 x^k d\nu_{t,n}(x), \quad 0 \leq k \leq 2n-1, \forall t \in [0,\tau_n],$$

where $\nu_{t,n}$ is a probability measure defined on $[0,1]$ and having n distinct nodes.

Proof: Fix $n \in \mathbf{N}$, and let $\nu_{0,n}$ be the Gauss Christoffel measure associated with X. The Hankel determinants are defined as follows

$$H_{n,j}(t) = \begin{vmatrix} u_0(t,n) & u_1(t,n) & \dots & u_j(t,n) \\ u_1(t,n) & u_2(t,n) & \dots & u_{j+1}(t,n) \\ \dots & \dots & \dots & \dots \\ u_j(t,n) & u_{j+1}(t,n) & \dots & u_{2j}(t,n) \end{vmatrix},$$

and

$$G_{n,j}(t) = \begin{vmatrix} u_1(t,n) & u_2(t,n) & \dots & u_{j+1}(t,n) \\ u_2(t,n) & u_3(t,n) & \dots & u_{j+2}(t,n) \\ \dots & \dots & \dots & \dots \\ u_{j+1}(t,n) & u_{j+2}(t,n) & \dots & u_{2j+1}(t,n) \end{vmatrix}.$$

Using Lemma 4.3, we have $H_{n,j}(0), G_{n,j}(0) > 0$, for $0 \leq j \leq n-1$. Thus, by continuity $\exists\ \tau_n > 0$, such that $H_{n,j}(t)$, $G_{n,j}(t) > 0$, for $0 \leq j \leq n-1$, $\forall t \in [0, \tau_n]$, where Let $U = \langle u_0(t,n), u_1(t,n), \ldots, u_{2n-1}(t,n) \rangle$ and consider the initial value problem

$$U' = AU + \Phi(U), \tag{4.6}$$

$$U(0) = M(0), \tag{4.7}$$

where $M(0) = \langle M_0(0), M_1(0), \ldots, M_{2n-1}(0) \rangle$, A is a $(2n \times 2n)$ matrix such that

$$(AU)_{k,j} = \begin{cases} k[\sum_{j=0}^{\alpha} A_j u_{k+j-1}(t,n)] + \\ \theta_k[\sum_{j=1}^{\beta} B_j[u_{k+j-2}(t,n)] & \text{if } 0 \leq k \leq 2n-\alpha \text{ or} 0 \leq k \leq 2n-(\beta-1) \\ 0 & \text{otherwise} \end{cases}$$

and Φ is a rational fraction in terms of $u_0(.,n), u_1(.,n), \ldots, u_0(.,2n-1))$.

Theorem 4.1 *Suppose* $\liminf_{n\to\infty} \tau_n = \tau > 0$. *Then for each* $t \in [0,\tau]$, *the sequence* $\{\nu_{t,n}, n \geq 1\}$ *converges weakly to* μ_t, *as* $n \to \infty$.

Proof: Using system 4.4, we have

$$\|\frac{du_k(t,n)}{dt}\| \leq k\sum_{j=0}^{\alpha}|A_j| + \theta_k\sum_{j=1}^{\beta}|B_j| = C(k,\alpha,\beta),$$

moreover, by the mean value theorem

$$\|u_k(t,n)\| \leq 1 + C(k,\alpha,\beta)\tau, \forall t \in [0,\tau].$$

Therefore, by Arzela Ascolli a subsequence of $\{u_k(t,n), n \geq \frac{k+1}{2}\}$ will converge uniformly on $[0,\tau]$ to some limit $v_k(t)$, as $n \to \infty$. By taking the intersection of theses subsequences successively it follows that a subsequence $\{u_k(t,i_n), i_n \geq 1\}$ satisfies

$$\lim_{i_n\to\infty} \|u_k(t,i_n) - v_k(t)\|_\infty = 0, \forall k \in \mathbf{N} \cup \{0\}.$$

Now since $\{\nu_{t,n}, n \geq 1\}$ is relatively compact (by tightness) it follows that for some subsequence $\{i_n\}$, we have $\forall g \in C[0,1]$,

$$\int_0^1 g(x)d\nu_{t,i_n}(x) \to \int_0^1 g(x)d\nu_t(x), \quad as \quad i_n \to \infty,$$

which implies

$$v_k(t) = \int_0^1 x^k d\nu_t(x), \forall k \in \mathbf{N} \cup \{0\}.$$

Moreover, Equation 4.4 implies

$$\begin{aligned} u_k(t,i_n) - u_k(0,i_n) &= k\sum_{j=0}^{\alpha} A_j \int_0^t u_{k+j-1}(s,i_n)ds + \theta_k \sum_{j=1}^{\beta} B_j \int_0^t u_{k+j-2}(s,i_n)ds, \\ &= \int_0^t [\int_0^1 L(x^k)d\nu_{s,i_n}(x)]ds. \end{aligned}$$

We let $i_n \to \infty$, to get

$$v_k(t) - v_k(0) = \int_0^t [\int_0^1 L(x^k) d\nu_s(x)] ds, \forall k \in \mathbf{N} \cup \{0\}. \tag{4.8}$$

Using a result from differential inEquationlities (see [?], Chapter 1), it follows that $v_k(t) \equiv M_k(t)$, $\forall k \in \mathbf{N} \cup \{0\}$, and since

$$0 < \sum_{k=0}^{\infty} \frac{M_k r^k}{k!} \leq e^r, \forall r > 0.$$

It follows that Y_t and Z_t have the same law for all $t \in [0, T]$. This completes the proof of the theorem.

Remark 1:
Dawson (1980) and HajJafar (1986) assumed conditions 1, 2 and 3 of Lemma 4.3. They then verified these assumptions numerically (a theoretical proof is not available) for the models they considered. We shall provide two models where these assumptions are satisfied theoretically (see models 1 and 2 below), one model where they are satisfied numerically (see model 3 below), and one model where these assumptions do not hold (see model 4 below) and therefore the Gauss Galerkin method may not be applicable.

Remark 2:
The nodes and weights of the discrete measure $\mu(n, t)$ resulting from the Gauss Galerkin method can be found through the usual inversion of the well known Vandermonde matrix, see Dawson (1980) and HajJafar (1986). However, the determinant of this matrix is directly proportional to the quantity

$$\prod_{i,j=1, i \neq j}^{n} [(x_{n,i}(t) - x_{n,j}(t)]^2,$$

where $\{x_{n,i}(t), 1 \leq i \leq n\}$ are the nodes corresponding to the discrete measure $\mu(n, t)$. This quantity may become negligible as n increases. As a consequence the involved Vandermonde matrices may become nearly singular, causing the problem of solving for the nodes and weights of the measure $\mu(n, t)$ to become ill-conditioned. An alternative method which considerably reduces the ill-conditioning when computing the nodes and weights is the content of the numerical algorithm below.

5. An Improved Numerical Algorithm

Our numerical algorithm for finding the nodes and the weights of the Gauss Galerkin measure $\mu(n, t)$ is based on the relationship between the orthogonal polynomials associated with $\mu(n, t)$ and its moments. The nodes $\{x_{n,i}(t), 1 \leq i \leq n\}$ and the weights $\{w_{n,i}(t), 1 \leq i \leq n\}$ of the measure $\mu(n, t)$ are related to the following real symmetric tridiagonal matrix

$$J_n(t) = \begin{pmatrix} \delta_1 & \gamma_2 & & \\ \gamma_2 & \delta_2 & \ddots & \\ & \ddots & \ddots & \gamma_n \\ & & \gamma_n & \delta_n \end{pmatrix},$$

in such a way that the nodes $\{x_{n,i}(t), 1 \leq i \leq n\}$ are the eigenvalues of $J_n(t)$ and $\{w_{n,i}(t), 1 \leq i \leq n\}$ are the squares of the first components of the normalized eigenvectors. The coefficients δ_j, and β_j, $for 1 \leq j \leq n$, are determined by the following three-term recurrence for the orthogonal polynomials corresponding to the discrete measure $\mu(n,t)$

$$\begin{aligned} p_0(x,t) &\equiv 1, && (5.1)\\ p_{i+1}(x,t) &= (x - \delta_{i+1}(t))p_i(x,t) - \gamma_{i+1}(t)^2 p_{i-1}(x,t), && (5.2)\\ \delta_{i+1}(t) &= \frac{\langle xp_i, p_i\rangle}{\langle p_i, p_i\rangle}, && (5.3)\\ \gamma_{i+1}^2(t) &= \begin{cases} 0 & \text{if } i = 0, \\ \frac{\langle p_i, p_i\rangle}{\langle p_{i-1}, p_{i-1}\rangle} & \text{if } i \geq 1, \end{cases} && (5.4) \end{aligned}$$

where $p_{-1}(x,t) \equiv 0$, and $\langle , \rangle$ denotes the inner product with respect to μ_t, for more details see Stoer and Bulirsch (1980).

Our numerical algorithm for finding the nodes and weights of the Gauss Galerkin measure $\mu(n,t)$ is based on Equation. 5.1 through 5.4. The relationship between the orthogonal polynomials associated with $\mu(n,t)$ and its first $2n$ moments $\{m_j(t), 0 \leq j \leq 2n-1\}$ is exploited. The moments of $\mu(n,t)$ are used to compute the entries of the tridiagonal matrix $J_n(t)$. We shall now present the detailed derivation of the algorithm.

Given the $2n$ moments $\{u_j(t), 0 \leq j \leq 2n-1\}$, the inner products involved in the construction of the matrix J_n can be expressed in terms of the given moments as follows

$$\langle p_0, p_0\rangle = u_0,$$

$$\langle xp_0, p_0\rangle = u_1,$$

in general, given

$$\langle p_i, p_i\rangle = \sum_{j=0}^{2i} \alpha_j^{(2i)} u_{2i-j}, where 0 \leq i \leq n-1,$$

and the $\alpha_j^{(2i)}$ are known. Then

$$\langle xp_i, p_i \rangle = \sum_{j=0}^{2i} \alpha_j^{(2i)} u_{2i-j+1}.$$

Through the three term recursion formula we also have the following

$\langle xp_i, p_i \rangle - \delta_{i+1}\langle p_i, p_i \rangle = 0 \Rightarrow$

$\langle p_{i+1}, p_{i+1} \rangle = \alpha_0^{(2i)} u_{2i+2} + \ldots + \alpha_{2i}^{(2i)} u_2 - 2\delta_{i+1}(\alpha_0^{(2i)} u_{2i+1} + \ldots + \alpha_{2i}^{(2i)} u_1) +$
$(\delta_{i+1})^2(\alpha_0^{(2i)} u_{2i} + \ldots + \alpha_{2i}^{(2i)} u_0) -$
$\langle p_i, xp_{i-1} \rangle + (\gamma_{i+1})^4 \langle p_{i-1}, p_{i-1} \rangle.$

We now describe a one step computational algorithm from $t = 0$ to Δt. This computational algorithm is used to compute the approximate values of the first $2n$ moments of the process at time Δt using the initial conditions $\{M_k(0), 0 \leq k \leq 2n-1\}$.

1. Using $\{M_k(0), 0 \leq k \leq 2n-1\}$ as initial conditions we solved system 4.4 by using a Runge Kutta method (through the computer algebra system Maple) to obtain $\{u_k(\Delta t), 0 \leq k \leq 2n-1\}$.

2. With the new $\{u_k(\Delta t), 0 \leq k \leq 2n-1\}$ we compute $\delta_k(\Delta t)$ and $\gamma_k(\Delta)$ for $1 \leq k \leq n$ by using Equation 5.3 and 5.4. Then we form the matrix $J_n(\Delta t)$. The eigenvalues of $J_n(\Delta t)$ and their corresponding eigenvectors are then found (using Maple). This yields the nodes $\{x_{n,i}(\Delta t), i = 1, 2, \ldots, n\}$ and the weights $\{w_{n,i}(\Delta t), i = 1, 2, \ldots, n\}$.

3. Using the first iterates, we obtain the second and higher iterates from $\{u_k(\Delta t), 0 \leq k \leq 2n-1\}$ by repeating step 1.

This numerical algorithm has proved to perform better than the algorithm proposed by HajJafar (1986) and Dawson (1980) in which several matrix inversions are required causing the problem of finding the weights and nodes to become ill-conditioned (see Remark 2 above). Our algorithm does not require any matrix inversion. Therefore, our numerical algorithm is more suitable when higher values of n need to be considered.

6. Application to Genetic Models

In this section (and in the remainder of the paper) we shall assume the following form for the drift and the diffusion coefficients, respectively

$$\begin{aligned} a(x) &= sx(1-x)[h + (1-2h)x] - ux + v(1-x), \\ \sigma(x) &= \sqrt{\frac{x(1-x)}{2}}. \end{aligned}$$

where s, u, v, and h are given parameters.

$$\begin{aligned} \frac{dM_k(t)}{dt} &= (vk+\theta_k)M_{k-1}(t) + (k(sh-u-v)-\theta_k)M_k(t) + \\ &\quad s(1-3h)kM_{k+1}(t) - s(1-2h)kM_{k+2}(t) \qquad (6.1) \\ M_k(0) &= E(\xi)^k. \qquad (6.2) \end{aligned}$$

When $s = 0$, Equations (6.1) and (6.2) admit a unique solution given by

$$M_k(t) = [M_k(0) + k(\frac{1}{2}+v)\int_0^t M_{k-1}(s)e^{-k(-\frac{1}{2}(k-1)-v-u+sh)s}ds]e^{k(-\frac{1}{2}(k-1)-v-u+sh)t}.$$

To test the accuracy of our computations, we shall compare them with the exact solution, whenever possible.

Model 1 (s=u=v=0): This model represents the case of no selection (s=0), no mutation and no migration (u=v=0). Both 0 and 1 are exit boundaries and the exact solution representing the Radon Nikodym derivative of the transition was derived by Kimura and Crow (1970) and is given by

$$\begin{aligned} p(t,x,y) = \sum_{i=1}^{\infty} x(1-x)i(i+1)(2i+1)F(1-i,i+2,2,x) \\ \times F(1-i,i+2,2,y)e^{-i(i+1)t}, \qquad (6.3) \end{aligned}$$

where F is the hypergeometric function. We have evaluated the above series for x=0.5 and for several values of t using up to 100 terms. Table 6.1 gives the moments $\{M_k, 1 \leq k \leq 7\}$ evaluated at the t values 0, 0.5, 1, ..., 10. Our computations show that the steady state solution is reached when t is approximately 10. Figure 6.2 is a display of the moments M_k, $1 \leq k \leq 7$ as functions of t. It can be seen from Table 6.1 that the steady state value for the k-th moment ($k \geq 1$) is $\frac{1}{2}$. Figure 6.3 shows the Gauss Galerkin measures (with 5 nodes) plotted for several values of t (t=0, 1, 2, 3, 6 and 10). The Gauss Galerkin measures in this case coincide with the Gauss Christoffel measures and the solution of system 4.4 and 4.5 is valid on any compact interval $[0,T]$, $T > 0$. Convergence is very fast (n=5) in this case. Table 6.1 shows that the steady state values of the moments are exactly Equationl to $\frac{1}{2}$. This implies that the steady state distribution measure for the process Y is the atomic measure $\frac{1}{2}(\delta_0 + \delta_1)$. This is in agreement with the graph corresponding to $t = 10$ in Figure 6.3 which shows the steady state discrete measure.

Table 6.1: Approximate Moments, Model 1

Model 1, s=u=v=0							
t	m_1	m_2	m_3	m_4	m_5	m_6	m_7
0.0	0.5	0.333333	0.250000	0.200000	0.166667	0.142857	0.125000
0.5	0.5	0.370199	0.305299	0.266359	0.240398	0.221855	0.207948
1.0	0.5	0.398911	0.348367	0.318040	0.297823	0.283381	0.272550
1.5	0.5	0.421272	0.381908	0.358290	0.342544	0.331297	0.322862
2.0	0.5	0.438687	0.408030	0.389636	0.377374	0.368615	0.362045
2.5	0.5	0.452249	0.428373	0.414048	0.404498	0.397676	0.392560
3.0	0.5	0.462811	0.444217	0.433060	0.425623	0.420310	0.416326
3.5	0.5	0.471037	0.456556	0.447867	0.442075	0.437937	0.434834
4.0	0.5	0.477444	0.466166	0.459399	0.454888	0.451665	0.449248
4.5	0.5	0.482433	0.473650	0.468380	0.464867	0.462357	0.460475
5.0	0.5	0.486319	0.479478	0.475374	0.472637	0.470683	0.469217
5.5	0.5	0.489345	0.484017	0.480821	0.478690	0.477167	0.476025
6.0	0.5	0.491702	0.487553	0.485063	0.483404	0.482218	0.481329
6.5	0.5	0.493537	0.490306	0.488367	0.487074	0.486151	0.485459
7.0	0.5	0.494967	0.492450	0.490940	0.489933	0.489214	0.488675
7.5	0.5	0.496080	0.494120	0.492944	0.492160	0.491600	0.491180
8.0	0.5	0.496947	0.495421	0.494505	0.493894	0.493458	0.493131
8.5	0.5	0.497622	0.496433	0.495720	0.495244	0.494905	0.494650
9.0	0.5	0.498148	0.497222	0.496667	0.496296	0.496032	0.495833
9.5	0.5	0.498558	0.497836	0.497404	0.497115	0.496909	0.496755
10	0.5	0.498877	0.498315	0.497978	0.497753	0.497593	0.497472

Figure 6.2: Exact Moments, Model 1

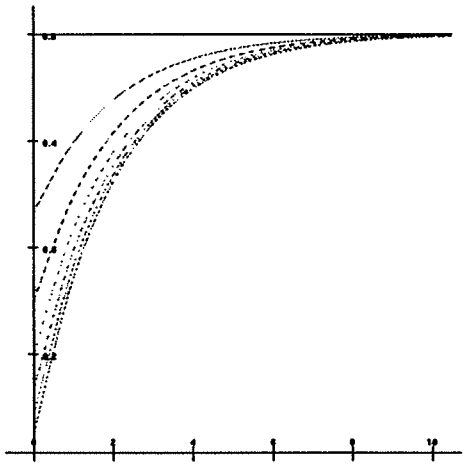


Figure 6.3: Atomic Measures, Model 1

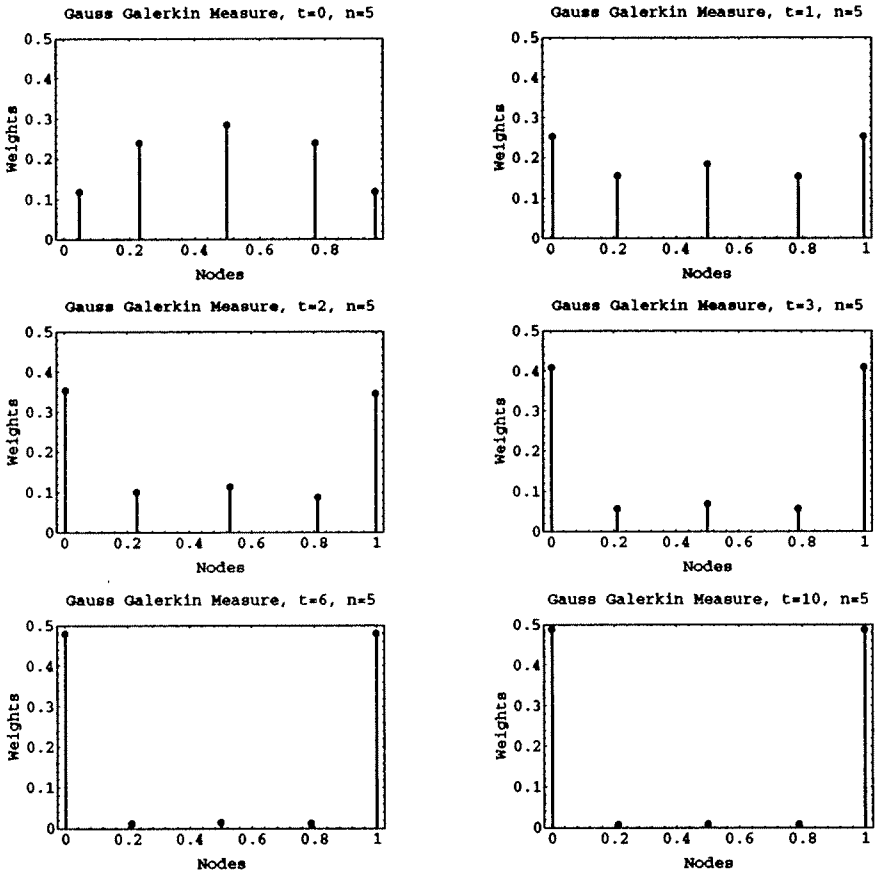


Table 6.2: Approximate Moments, Model 2

Model 2, s=0, u=v=0.125							
t	m_1	m_2	m_3	m_4	m_5	m_6	m_7
0.0	0.5	0.333333	0.250000	0.200000	0.166667	0.142857	0.125000
0.5	0.5	0.349728	0.274591	0.229140	0.198532	0.176428	0.159661
1.0	0.5	0.359672	0.289507	0.246603	0.217329	0.195907	0.179450
1.5	0.5	0.365703	0.298554	0.257166	0.228658	0.207603	0.191288
2.0	0.5	0.369361	0.304041	0.263569	0.235520	0.214682	0.198447
2.5	0.5	0.371580	0.307370	0.267452	0.239681	0.218973	0.202786
3.0	0.5	0.372926	0.309388	0.269807	0.242204	0.221575	0.205417
3.5	0.5	0.373742	0.310613	0.271235	0.243734	0.223153	0.207013
4.0	0.5	0.374237	0.311355	0.272102	0.244663	0.224110	0.207980
4.5	0.5	0.374537	0.311806	0.272627	0.245226	0.224691	0.208568
5.0	0.5	0.374719	0.312079	0.272946	0.245567	0.225043	0.208924
5.5	0.5	0.374830	0.312244	0.273139	0.245774	0.225256	0.209140
6.0	0.5	0.374897	0.312345	0.273257	0.245900	0.225386	0.209271
6.5	0.5	0.374937	0.312406	0.273328	0.245976	0.225465	0.209350
7.0	0.5	0.374962	0.312443	0.273370	0.246022	0.225512	0.209398
7.5	0.5	0.374976	0.312464	0.273396	0.246049	0.225540	0.209426
8.0	0.5	0.374985	0.312478	0.273412	0.246066	0.225558	0.209444
8.5	0.5	0.374991	0.312487	0.273422	0.246077	0.225569	0.209455
9.0	0.5	0.374995	0.312492	0.273428	0.246084	0.225576	0.209462
9.5	0.5	0.374997	0.312495	0.273432	0.246087	0.225579	0.209466
10	0.5	0.374998	0.312497	0.273434	0.246090	0.225582	0.209468

Model 2 (s=0, u=v=0.125): This model represents the case in which migration and mutation occur ($u, v \neq 0$), but no selection (s=0). The exact solution for this model, which was obtained by Kimura and Crow (1970) and by Goldberg (1950), has the same eigenfunction expansion form as 6.3. The theoretical steady state solution is

$$p(\infty, 0.5, y) = \frac{y^{4\times 0.125-1}(1-y)^{4\times 0.125-1}}{B(4\times 0.125, 4\times 0.125)},$$

where $B(.,.)$ is the beta function. Our computation in Table 6.2 show the moments M_k, $1 \leq k \leq 7$ evaluated at the t values 0, 0.5, 1, ..., 10. It can be seen from Table 6.2 that the steady state solution is reached when t is approximately 10. Figure 6.4 is a display of the Gauss Galerkin measures (which coincide with the Gauss Christoffel measures, in this case) and the solution of system ?? is valid on any compact interval $[0, T]$, $T > 0$. For the construction of the Gauss Galerkin measures we took n=5 and again convergence is very fast in this case. According to Figure 6.4 the approximate steady state solution for the distribution of the process is illustrated in the graph corresponding to t=10. This is in agreement with the theoretical calculations.

Figure 6.4: Approximate Atomic Measures, Model 2

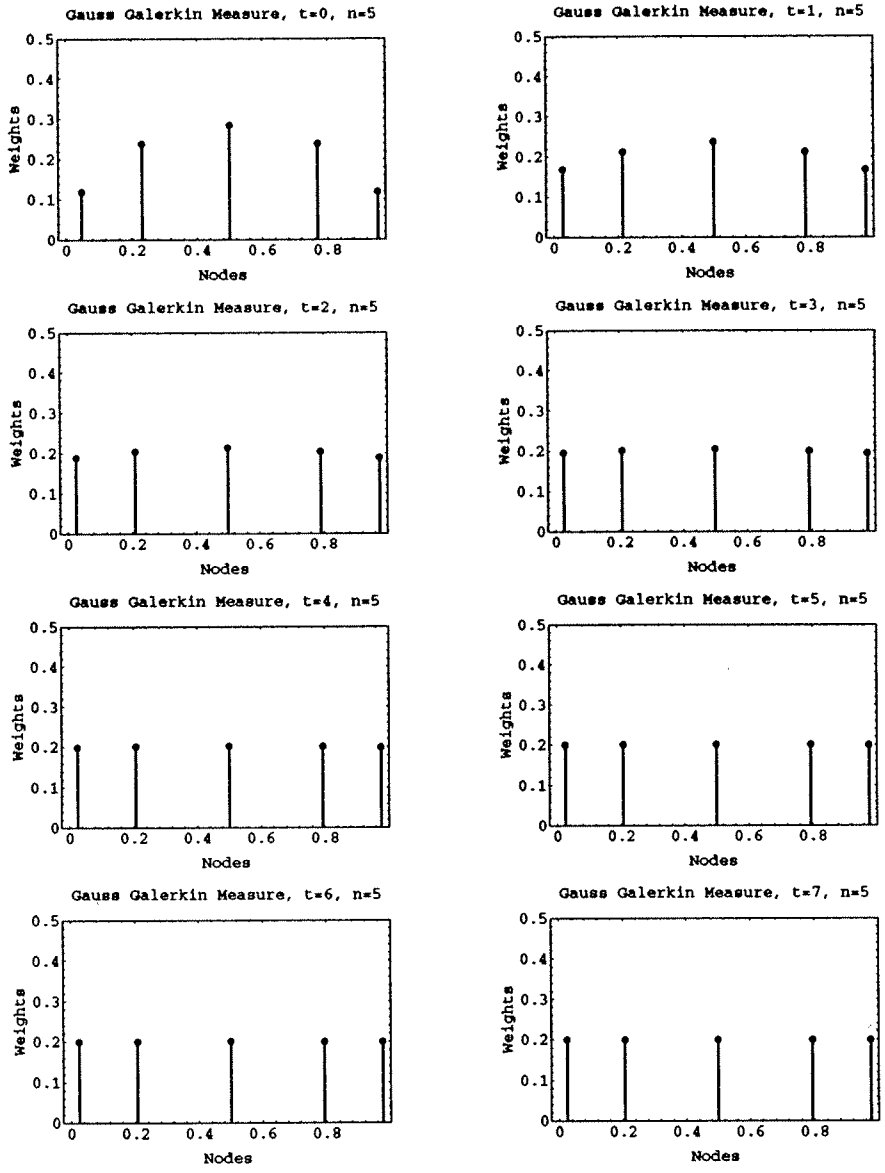
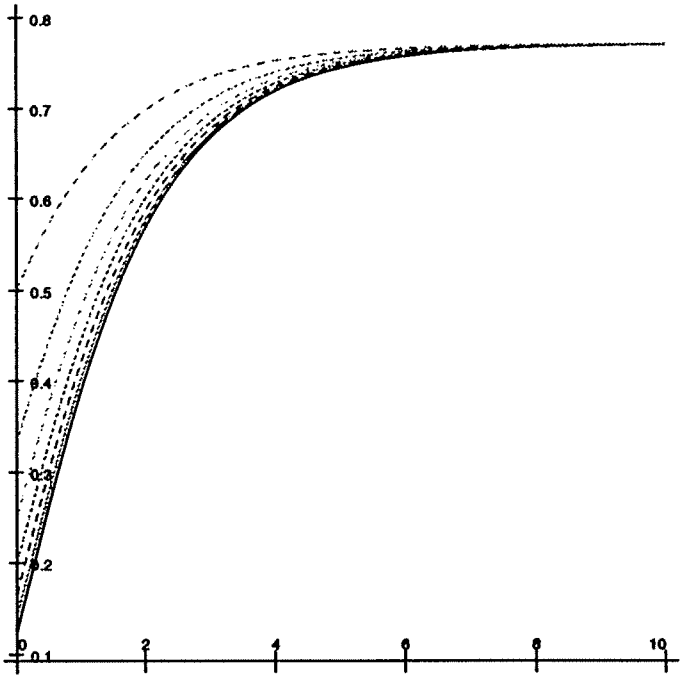


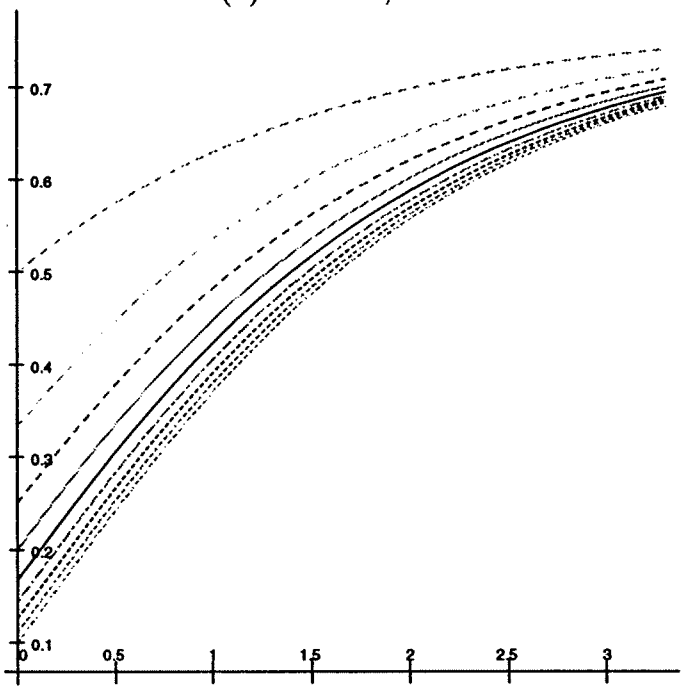
Table 6.3: Exact Steady State Moments, Model 2

Model 2, s=0, u=v=0.125						
$m_{1,\infty}$	$m_{2,\infty}$	$m_{3,\infty}$	$m_{4,\infty}$	$m_{5,\infty}$	$m_{6,\infty}$	$m_{7,\infty}$
.5000000001	.3750000000	.3125000000	.2734375000	.2460937500	.2255859375	.2094726562

Model 3 (s=2, h=0.5, u=v=0): This model represents the case where selection occurs (s=2) but there is no mutation or migration (u=v=0). Our computations show that the system of ode's for the moments of the corresponding process is only local. Therefore, the steady state analysis is not possible through the Gauss Galerkin approach. However, a local approximation of the moments and therefore of the distribution, is possible. Figures (a), (b), (c), and (d) below correspond to different values of n. It is clear from these figures that the solution is valid only locally, approximately in the interval $[0, 2.9]$. A steady state approximation is not possible through the Gauss Galerkin method.



(a) Model 3, n=4



(b) Model 3, n=5

Figure 6.5: Approximate Moments, Model 3.

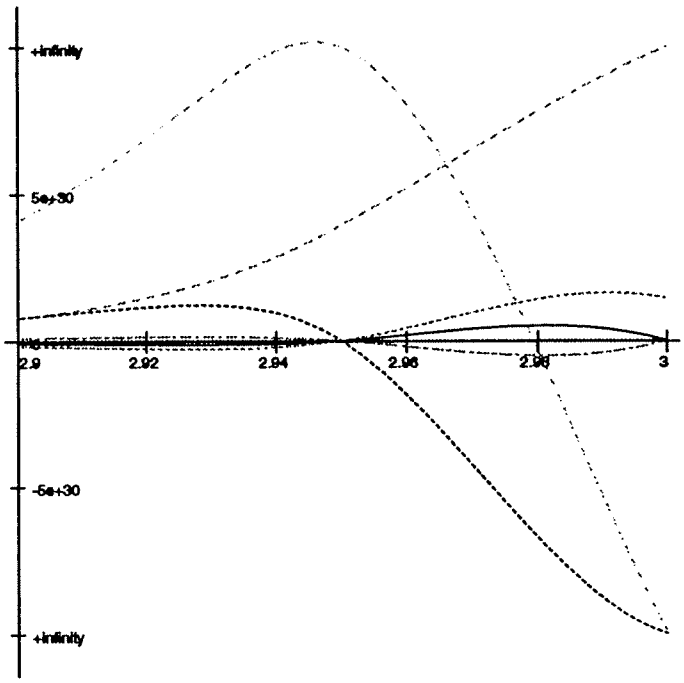
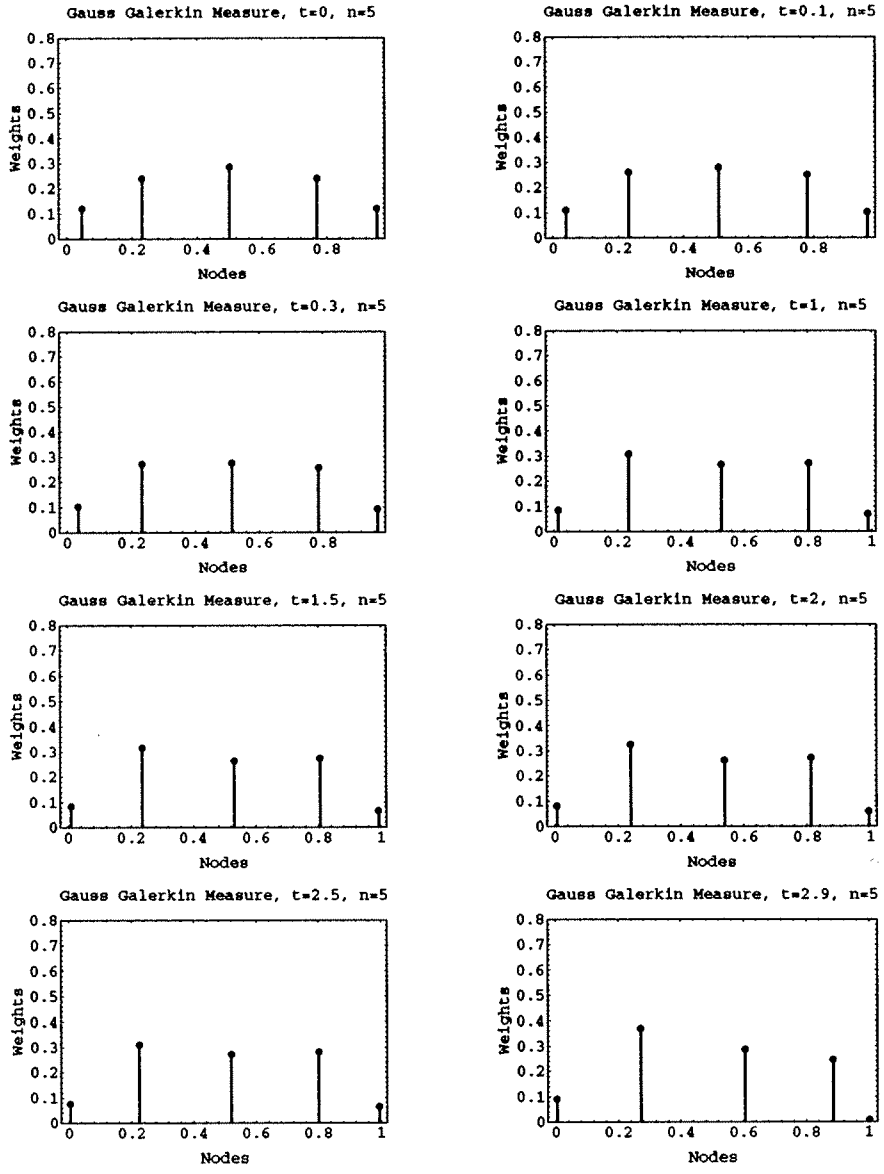
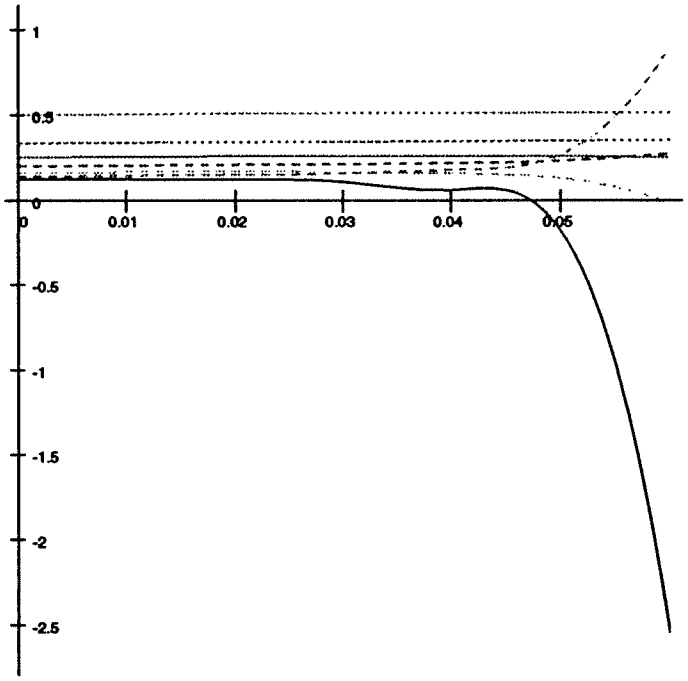


Figure 6.6: Model 3, Local Solution $[0, 2.9]$.

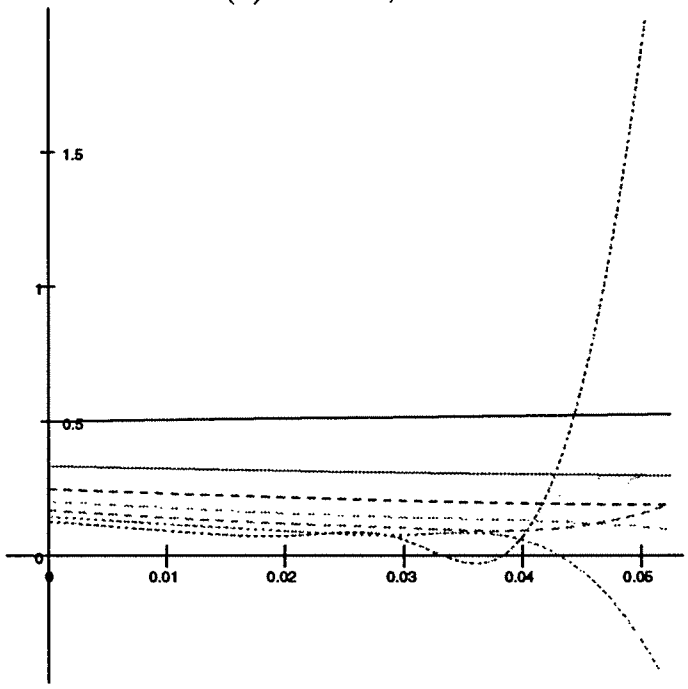
Model 4 (s=2, h=1, u=v=0): This model is an example of a situation where the Gauss Galerkin method does not apply. This is due to the fact that the crucial assumption made in Theorem 4.1 is violated, ie: $\tau_n \downarrow 0$, as $n \uparrow$. Figure 6.8 (a) shows an approximate value $\tau_4 = 0.045$, and Figure 6.8 (b) shows an approximate value of $\tau_5 = 0.03$. τ_n becomes negligible for $n \geq 6$.

Figure 6.7: Atomic Measures, Model 3





(a) Model 4, n=4



(b) Model 4, n=5

Figure 6.8: Model 4, as $n \uparrow$, $\tau_n \downarrow$.

Bibliography

[1] Abrouk, N. (1992). Some Numerical Methods for Singular Diffusions Arising in Genetics. Ph.D. Thesis, Michigan State University.

[2] Dawson, D. A. (1980). Galerkin Approximation of NonLinear Markov Processes, Statistics and Related Topics. Proceedings of the International Symposium on Statistics and Related Topics held in Ottawa, Canada, May 5-7, 1980. North Holland.

[3] Ethier, S. N. and Kurtz, T. J. (1986). Markov Processes, Characterization and Convergence, John Wiley and Sons, New York.

[4] Feller, W (1952). The Parabolic Differential Equations and the Associated Semi-Groups of Transformations, Ann. Math. **55**, 468-519 (1952).

[5] Goldberg, S. (1950). On a Singular Diffusion Equation, Ph.D. Thesis, Cornell University.

[6] Hajjafar, A. (1986). On the Convergence of the Gauss Galerkin Method for the Density of Some Markov Processes. Ph.D. Thesis, Michigan State University.

[7] Karlin, S. and Taylor, H. M. (1981). A second Course in Stochastic Processes. Academic Press.

[8] Kimura, M. and Crow, J. (1970). An Introduction to Population genetics. Harper and Row, New York.

[9] Shohat, J.A. and Tamarkin, J.D. (1964). The Problem of Moments, A.M.S., New York.

[10] Stoer, J. and Bulirsch, R. (1980). Introduction to Numerical Analysis. Springer-Verlag, New York.