A SEQUENTIAL CLINICAL TRIALS MODEL FOR DETERMINING THE BEST AMONG THREE TREATMENTS WITH NORMAL RESPONSES

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A SEQUENTIAL CLINICAL TRIALS MODEL
FOR DETERMINING THE BEST AMONG THREE TREATMENTS
WITH NORMAL RESPONSES

by

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(Under the direction of GORDON D. SIMONS)

ABSTRACT

Patients are frequently involved with clinical trials which are designed to compare two or more treatments. For ethical reasons, any unnecessary use of inferior treatments should be avoided. This concern invites the use of a sequential clinical trial. The focus of attention here is upon the case of three treatments, and the approach is Bayesian with the adaptation of a decision-theoretic model proposed by Anscombe (1963). The main feature of his approach is the use of a testing stage within which patients are assigned three at a time to the three treatments followed by a post testing stage within which all remaining patients are assigned to what (by this time) appears to be the best of the three treatments. The main statistical problem is to find an optimal stopping rule for stopping the testing stage.

It is assumed that both the treatment responses and prior parameters are normally distributed. As with earlier work by Chernoff and Petkau (1981) for two treatments, a "continuous time" approximation is introduced, which, in the present case, leads to the consideration of two independent Brownian motions, and a heat equation in two spatial variables. The problem of finding an optimal stopping time becomes that of finding the solution of a free boundary problem.

The emphasis here is on finding this free boundary numerically by approximating the two Brownian motions by a two-dimensional simple
random walk. The approach mirrors an approach developed by Chernoff and Petkau for statistical problems involving a single spatial variable. Their approach requires an approximating one-dimensional random walk. Its implementation in two dimensions is much more demanding.
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CHAPTER I
INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction

This dissertation develops a sequential clinical trials model to select the best among two new treatments, called A and B, and a standard treatment by treating a specified number \( N \) of patients. Of particular interest are treatments with normal responses and with normally distributed prior parameters.

Patients are frequently involved in clinical trials which are designed to compare two or more treatments. For ethical reasons, any unnecessary use of inferior treatments should be avoided. This concern motivates the use of a sequential clinical trial. Armitage (1961) discusses some sequential stopping rules for trials comparing two treatments. Compared to any fixed sample size design, these rules reduce the expected sample size while maintaining the same error probabilities.

Many studies in the literature address trials having two treatments. Some of them are discussed in Sections 1.2.2 and 1.2.3. However, for any illness, there might be numerous potential new treatments. Pocock (1977) describes some methods for the three treatments as three pairwise ongoing trials analyzed by so-called
"group sequential" methods. This is further discussed by McPherson (1984).

The trial, that the dissertation research concerns, consists of allocation of treatments to n triplets of patients. A conclusion is made as to which treatment appears to be best, so that the remaining N-3n patients will be given the apparently best treatment based on the results of the first n triplets. The main feature of this model is the use of a testing stage followed by a post-testing stage. The statistical problem is to determine the number of triplets to be considered for the testing phase.

The strategy, from three treatments to one, is not a satisfactory model for ethical reasons. It is difficult to justify a clinical trial which continues sampling by triplets while a treatment is performing relatively very poorly. This, however, can occur since the model is constrained to make a single switch to a unique treatment. Our work is useful for developing the more complicate model in the future. Palmer (1988) discusses a model for a clinical trial involving three treatments with dichotomous responses. The computations involving treatments with continuous responses are much more difficult. The model discussed by Palmer begins with an initial testing stage, called stage I. This continues until a decision is reached to eliminate the single worst-appearing treatment leaving two treatments in contention. Secondly, one decides after stage II, when to switch all remaining patients to the better of these two treatments. He demonstrates that the model is more applicable and useful than two pairwise trials, likewise better than the model which jumps directly from three treatments to one.
Chapter II discusses how the model is developed and introduces a risk function when a total of $N$ patients are to be treated with one of three medical treatments. The risk function is constructed with but one risk, the consequence of treating a patient with the best, second best or the worst of the three treatments. A Bayesian approach is described which is based on a decision-theoretic model proposed by Anscombe (1963). In the approach, triplets of patients are assigned to the three treatments sequentially in the testing stage. When to stop allocating patients depends on the stopping risk. Let the optimal stopping risk be the expected stopping risk associated with the optimal stopping rule. If the stopping risk is smaller than the optimal stopping risk, the testing stage is stopped; otherwise, the testing stage continues. Deciding the best treatment after the testing stage is terminated should be based on the information from the treated patients. This concern leads to the consideration of two independent Gaussian processes. The optimal stopping risk can then be solved by a backward induction. Each stopping rule can be represented by a continuation region and its complement, a stopping region. The problem of finding an optimal stopping rule becomes that of finding the solution of a free boundary problem. A simple 2-dimensional random walk is introduced to solve the boundary of the optimal continuation region numerically.

Chapter III focuses on the solution of the optimal continuation region for the 2-dimensional random walk. Several properties of the optimal continuation region are described in this chapter. With these results, the problem can be solved efficiently. Programming techniques using the properties are discussed. A numerical method, interpolation,
is presented which can be employed to obtain smooth estimates of the boundary of the continuation region and using less computer time.

Chapter IV discusses the asymptotically expected excess over the boundary by a 2-dimensional random walk. The boundary is formed by two parallel lines. The results here is useful in investigating the relation between the solution of the optimal stopping rule for the 2-dimensional random walk and that of the continuous version of our problem.

The remainder of this chapter is a literature review of previous research on the sequential clinical trials.

1.2 Literature Review

The literature review may be roughly divided into five parts. The first section describes two opposing viewpoints among theoreticians of sequential clinical trials. The second section discusses sequential clinical trials models for treatments with dichotomous responses. The third section is devoted to the description of a sequential clinical trial model for two treatment with normal responses. A Bayesian strategy for the testing of a normal mean is discussed in Section 1.2.4. Lastly, numerical methods for obtaining the optimal stopping rule for the problem, which is described in Section 1.2.4, are discussed in Section 1.2.5. Sections 1.2.4 and 1.2.5 do not seem directly related to our topic. But, their work will be referred to in our research.

1.2.1 Sequential Clinical Trials

For the comparison of two treatments, Armitage(1960) considers
three hypothesis — that treatment A is preferable to treatment B, or vice versa, or that A and B show no difference in their effects. His approach is to control the error probabilities of reaching an incorrect conclusion. This is accomplished by determining stopping boundaries for a sequential trial. Colton (1963) asserts that in many cases it is indeed difficult for the medical experimenter to select a difference and to state with what probability he wants to detect this difference.

On the other hand, Anscombe (1963) in his paper, reviewing Armitage’s book, suggests having only two possible conclusions (not the third), and uses a two-stage, decision-theoretic approach. The suggested approach begins with the use of both treatments and finishes with all remaining patients assigned to the most promising treatment. The reason for adopting a two-decision formulation is that a better basis is provided for determining the sequential stopping rule. His suggested two-stage approach is motivated by the fact that in the improvement of knowledge some patients will be ill-treated, but if knowledge is not improved all patients may be ill-treated. He assumes that there is a fixed number of patients, N, and the difference between the effects of treatment A and B is \( \theta \) (the effect of A minus the effect of B). If \( n \) pairs of patients have been tested in the first stage, let \( y \) be the sum of the \( n \) response differences (the response of the patient treated by A minus the response of patient treated by B). The remaining \( N-2n \) patients will be given A or B according to whether \( y \) is positive or negative. Let \( |\theta| \) be the cost attributed to each patient receiving the inferior treatment. Then, a total regret at the end of the trial, which is based on the cost of treating patients
suffering from a serious illness by what appears to be an inferior treatment, can be assessed by

\[ nE(|\theta|) + (N-2n)E[\max(0, -\theta \text{sgn}(y))] \].

Anscombe also finds an intuitively reasonable sequential stopping rule such that the first stage is stopped as soon as further continuance is expected to lead to an increase in the total regret.

Further, Anscombe attempts to argue against the formal methodology of hypotheses testing which focuses attentions on significance level and power function and ignores the cumulative benefits of patients.

Colton (1963) uses Anscombe's approach in the continuous variable case.

1.2.2 Treatments with Dichotomous Responses

For some trials, the treatments display dichotomous responses; a treatment either works, or it does not. One sometimes speaks of Bernoulli responses of "successes" and "failures" instead of working or not. In such cases, the primary question becomes a matter of identifying the treatment with the maximal success probability.

Hoel, Sobel and Weiss (1972) investigate a two-stage procedure for choosing the better of two binomial populations. They show that a two-stage procedure can take advantage of the difference between Vector-at-a-Time rule (Bechhofer, Kiefer and Sobel, 1968) and Play-the-Winner rule (Robbins, 1956; Zelen, 1969) for assigning treatments. The first of these assigns two treatments in alternation. In the second, a success on a treatment generates a further test with
that treatment while a failure generates a test on the other
treatment.

Bather & Simons (1985) and Simons (1986) are concerned with two
treatments which successfully treat the illness with unknown
probabilities $p_1$ and $p_2$, respectively. Both papers seek to find
suitable stopping rules for terminating the first stage under
Anscombe's clinical trials design. Bather & Simons (1985) find a
stopping rule which is minimax within the class of two-stage
procedures. Simons (1986) considers Bayes rules and obtains a stopping
rule which is best amongst admissible rules for symmetric priors. A
clinical trials model for deciding the best of three treatments with
dichotomous responses is discussed in Palmer (1988). He extends the
work of Simons (1986) to three treatments and develops the methodology
for a simple, well-performing, ethical, pragmatic and potentially
useful model.

1.2.3 Treatments with Normal Responses

Some work about comparing two treatments with normal responses
has been done under Anscombe's formulation. The Bayes rule for
deciding when to stop the first stage is discussed in Chernoff and
Petkau (1981) in the context of a normal prior. They use many of the
techniques which are described in Chernoff (1972). Let $Z_i$ denote the
difference in response between the patient receiving treatment A and
the patient receiving treatment B in the $i$-th trial pair. Assume $Z_i$, $Z_2$, ...
are independent $\mathcal{N}(\mu, \sigma^2)$ variables, with $\sigma^2$ known. Further,
suppose the parameter $\mu$ has a normal prior distribution: $\mathcal{N}(\mu_0, \sigma_0^2)$. 

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The posterior distribution of $\mu$ given $Z_1, Z_2, \ldots, Z_n$ is $\mathcal{N}(\bar{Y}_n^*, s_n^*)$, where

$$
\bar{Y}_n^* = (\sigma_0^{-2} \mu_0 + \sigma^{-2} \sum_{i=1}^{n} Z_i) / (\sigma_0^{-2} + n\sigma^{-2}).
$$

and

$$
s_n^* = (\sigma_0^{-2} + n\sigma^{-2})^{-1}.
$$

Since the treatment for the remaining $(N-2n)$ patients is indicated by the sign of $Y_n^*$, the posterior risk and the expected risk associated with stopping after treating $n$ pairs of patients is

$$
nE(|\mu|) + (N-2n)E[\max(0, -\text{sgn}(Y_n^*)\mu)].
$$

Simple calculations can convert this posterior risk into $d_1(Y_n^*, s_n^*)$:

$$
d_1(y,s) = N s_1^{1/2} \psi(y s^{-1/2}) - 2 (\sigma_0^{-2} + (1/2) N \sigma^{-2} - s^{-1}) |y|.
$$

where $\psi(u) = \phi(u) + u(\phi(u) - 1/2)$ and $\phi$ and $\Phi$ are the standard normal density and cumulative respectively.

The distribution of $Y_n^*-Y_m^*$, where $n \geq m \geq 0$, is $\mathcal{N}(0, s_m^*-s_n^*)$ and $Y_n^*-Y_m^*$ is independent of $Y_m^*$. The distribution of $Y_m^*$ is $\mathcal{N}(0, \sigma_0^{-2} - s_m^*)$.

Denote by $T$ the set of integers between $0$ and $N/2$. Then, the process $(Y_n^*, s_n^*, n \in T)$ is a Gaussian stochastic process with independent increments, starting from $(Y_0^*, s_0^*)$.

Chernoff and Petkau (1981) solve the problem of selecting the best sequential procedure for terminating the experimental phase by finding the stopping time $N$ which minimizes the expected risk, i.e., the expectation of $d_1(Y_N^*, s_N^*)$. Since $s_n^*$ is decreasing in $n$, it is
equivalent to find a stopping time $s^*_M$ to minimize $E[d_1(Y^M_N, s^*_M)]$. The possible stopping times are \{s^*_0, s^*_1, \ldots, s^*_m\}, where $s^*_m = s^*_M$ and $m = \lceil N/2 \rceil$. Since $s^*_0 \geq s^*_1 \geq \ldots \geq s^*_M$, i.e., $s^*_n$ goes backward in time, Chernoff says this process is in the $-s$ scale. The continuous version of this process is that the stopping may be taken to be any value between $s^*_0$ and $s^*_M$. The process $Y^*_n$ is replaced by $Y^*_n(s)$ starting at $Y^*_n(s_0^*)$, where $Y^*_n(s)$ has the $N(0, \sigma^2_0 - s)$ distribution for $s^*_0 \geq s \geq s^*_M$ and $Y^*_n(s_0^*) - Y^*_n(s_p^*)$ has the $N(0, s_p^* - s_q^*)$ distribution for $s^*_0 \geq s_p^* \geq s_q^* \geq s^*_M$. Thus, $Y^*_n(s)$ is a Wiener process in the $-s$ scale for $s^*_0 \geq s \geq s^*_M$ starting at $Y^*_n(s_0^*)$ with

$$E(dY^*_n(s)) = 0 \text{ and } \text{Var}(dY^*_n(s)) = -ds.$$ 

Here, $s$ is decreasing in time, so $-ds$ may be thought of as positive.

The results of Chernoff and Petkau on the Bayes risk show that Anscombe's (1963) rule is remarkably close to optimal, but the procedure obtained by Begg and Mehta (1979) is a relative poor competitor. Begg and Mehta propose stopping the first stage as soon as no fixed size continuation of that stage does as well as stopping. Colton (1963) proposes to use horizontal stopping boundaries based on a truncated sequential probability ratio test. Lai, Robbins and Siegmund (1983) study the asymptotic properties of these rules.

1.2.4. Testing for the Sign of a Normal Mean

The Bayes sequential test for the sign of a normal mean is discussed in Chernoff (1972). Assume $X_1, X_2, \ldots$ are independently
identically normal distributed with unknown mean \( \mu \) and known variance \( \sigma^2 \). If the parameter \( \mu \) has the \( \mathcal{N}(\mu_0, \sigma_0^2) \) distribution, denote by \( Y_n \) and \( s_n \) the posterior mean and variance of \( \mu \), respectively. Then, the process \((Y_n, s_n)\) is a Gaussian process like the process \((Y^*_n, s^*_n)\) in the last section.

Chernoff considers that the cost of a wrong decision is \( r(\mu) = k|\mu| \) and the cost of observing \( n \) X's is \( cn \), \( k > 0 \) and \( c > 0 \). Then, the posterior risk (including the risk of accepting the hypothesis \( H_1 \) or \( H_2 \) and the cost of sampling) associated with stopping at the \( n \)-th observation in the sequential analysis problem is \( d(Y_n, s_n) \), where

\[
d(y, s) = ks^{1/2}\psi(ys^{-1/2}) + c\sigma_2 s^{-1} - c\sigma_0^{-2}\sigma^2
\]

and

\[
\psi(u) = \begin{cases} 
\varphi(\mu) - \mu[1 - \Phi(u)], & \mu \geq 0, \\
\varphi(\mu) + \mu\Phi(\mu), & \mu \leq 0,
\end{cases}
\]

with \( \varphi \) the standard normal density and \( \Phi \) the standard normal c.d.f. He attempts to find a stopping rule (a random variable \( N \)) to minimize

\[E[d(Y_N, s_N)].\]

Discrete time stopping problems with infinitely many possible stopping times lead to substantial difficulties which have been discussed in Chow, Robbins and Siegmund (1971). Chernoff asserts that the resulting problem could be attacked by the backward induction method if one truncates the problem so that stopping must happen by
the $n_{1}$ st observation for some $n_{1}$. The nontruncated sequential problem can be treated as a limit of truncated problem.

The continuous version of this problem is related to the Wiener Process. Chernoff (1972) points out that the solution of the continuous time stopping problem involving a Wiener process is related to the heat equation defined later. There is a continuation region, which is an open set, and a stopping region, which is the complement of this open set, corresponding to a particular stopping rule for a continuous time stopping problem. So, the solution of the problem can be expressed in term of a stopping set and a continuation set in the $(y,s)$ plane if the process $Y(s)$ is considered. Suppose $Y(s)$ is a Wiener Process in the $-s$ scale. Let $d(y,s)$ be the stopping cost. If $\mathcal{C}$ and $\mathcal{F}$ are an open continuation set and the stopping set corresponding to a particular stopping rule, and $b(y,s)$ is the expected cost associated with this stopping rule, the following equations are true:

$$\frac{1}{2} b_{yy}(y,s) = b_s(y,s) \quad (y,s) \in \mathcal{C}$$

(heat equation)

$$b(y,s) = d(y,s) \quad (y,s) \in \mathcal{F}.$$  

The heat equation, here, can be justified by expanding $E[b(y+W\sqrt{\delta},s)]$ in a Taylor series:

$$b(y,s+\delta) = E[b(Y(s),s)|Y(s+\delta) = y] + o(\delta)$$

$$= E[b(y+W\sqrt{\delta},s)] + o(\delta), \quad \text{for } (y,s) \in \mathcal{C}.$$  

Here, $W$ is a generic $N(0,1)$ random variable. More detail is provided by Chernoff (1972).
Denote by \( S \) the set of all stopping rules. Let

\[
\rho(y_0, s_0) = \inf_{\mathcal{S}} r(y_0, s_0),
\]

where \( r(y_0, s_0) \) is the expected cost associated with a particular stopping rule in \( S \). The procedure: Stop as soon as \( \rho(y, s) = d(y, s) \), is an optimal procedure (under regularity conditions sufficient to imply the existence of an optimal procedures). Denote by \( \mathcal{C}_0 \) the optimal continuation region and by \( \mathcal{I}_0 \) the optimal stopping region. Then, \( \mathcal{C}_0 \) is the set: \( \{(y, s) : \rho(y, s) < d(y, s)\} \) and \( \mathcal{I}_0 \) is the set: \( \{(y, s) : \rho(y, s) = d(y, s)\} \). Chernoff obtains:

\[
\begin{align*}
\frac{1}{2} \rho_{yy}(y, s) &= \rho_s(y, s), & (y, s) \in \mathcal{C}_0, \\
\rho(y, s) &= d(y, s), & (y, s) \in \mathcal{I}_0, \\
\rho_y(y, s) &= d_y(y, s) & \text{on the boundary of } \mathcal{C}_0.
\end{align*}
\]

The optimal stopping rule is characterized by the optimal continuation region and its complement, the stopping region. In the preface of "Free Boundary Problems: Theory and Applications", Hoffmann (1990) say, "Free boundaries, that is, singular surfaces with a priori unknown location in space that separate spatial regions with different physical characteristics, occur as a natural feature in the evolution of a great variety of very important scientific and technological processes; ...". So, the problem of find the optimal stopping rule for the continuous time problem becomes a free boundary problem.

Bather (1962) exploits very effective techniques to decide whether a specified point \((y_0, s_0)\) is a continuation point for the optimal procedure. Chernoff (1972) also provides methods to yield
inner and outer bounds of $\Phi_0$. All of these techniques require the
ability to generate convenient solutions of the heat equation.

1.2.5 Numerical Methods

Denote by $\tilde{\gamma}$ the upper boundary of the optimal continuation region
for the continuous time problem described in the last section. Let $\tilde{\gamma}_0$
be the upper boundary for a discrete version of the problem that
results when stopping is restricted to a lattice with adjacent points
a distance $\delta$ apart. According to Chernoff (1965) the relation between
$\tilde{\gamma}$ and $\tilde{\gamma}_0$ is expressed by

$$\tilde{\gamma} - \tilde{\gamma}_0 \approx \tilde{Z} \sqrt{\delta}.$$

$\tilde{Z} = 0.582$. The key step in the proof of this is to introduce an
auxiliary problem in which a Wiener process is started at a point
$(z,t)$, $t < 0$, no payoff is made if stopping occurs before time 0, and
at $t = 0$ stopping is enforced and a payoff $Z^2 I_{(z<0)}$ is received,
stopping is permitted only at times $t = 0, -1, \ldots$, and each
observation costs a dollar. For this problem the optimal stopping
boundary can be shown to be increasing and contained in $[-1,0]$, and
therefore it has a limit as $t \to -\infty$ which turns out to be $\tilde{Z}$.

Let $S_n = \sum_{i=1}^{n} X_i$ be a random walk with $E S_1 = 0$, $E S_1^2 = 1$, and
$E|S_1|^4 < \infty$. Let $\tau_a = \inf \{n : S_n > a\}$, $\tau_+ = \tau_0$. For the normal random
walk, Siegmund (1985) remarks that

$$ER = -E S_{\tau+}^2 / 2E S_{\tau+},$$

where $R$ is a random variable whose distribution is the same as that of
the asymptotic excess over the boundary as $a \to \infty$. Following the work of Siegmund, Hogan (1986) uses another method to get the amount $\hat{Z}$. He proves

$$\hat{Z} = -ES_{\tau^+}^2 / 2ES_{\tau^+}.$$  

Chernoff & Petkau (1986) attack the problem described in the last section, which is about finding the boundary of the optimal continuation region for the testing of a normal mean, numerically. The numerical methods are investigated in great detail in Chernoff & Petkau (1984). The basic idea is: the process $Y(s)$, which is a Wiener process in the $-s$ scale, is approximated by a discrete time process; backward induction is used to solve the optimal stopping problem for this new process. Consider the discrete time problem where one is permitted to stop only on the discrete set of possible values of $s$, \( \{s_0 + i\Delta, 1 = 0, 1, 2, \ldots \} \) to have the backward induction easier to carry out. While the value of $s$ decreases by $\Delta$ between these successive possible stopping times, the process $Y(s)$ changes by a normal deviate with mean 0 and variance $\Delta$. The optimal risk $\hat{d}$ is defined recursively by

$$\hat{d}(y, s) = \min (d(y, s), E(\hat{d}(Y(s-\Delta), s-\Delta) | Y(s)=y))$$

$$= \min (d(y, s), E(\hat{d}(y+z\sqrt{\Delta}, s-\Delta)) \quad \text{for } s > s_0,$$

where $z$ represents a standard normal deviate.

If stopping is enforced when $s = s_0$, then

$$\hat{d}(y, s_0) = d(y, s_0).$$
The optimal risk can be solved by using the backward induction algorithm. The boundary of the optimal continuation region for this discrete time problem is determined by the "break-even" points \( \tilde{Y}_\alpha(s) \) at which

\[
d(y,s) = E(\hat{d}(y+z\sqrt{\Delta}.s-\Delta)).
\]

The numerical integration to evaluate the risk at each point \((y,s+\Delta)\) could be quite time consuming. Consequently, the discrete time process with normal increment is replaced by the simple random walk process where

\[
Y(s+\Delta) = Y(s) \pm \sqrt{\Delta}
\]

each with probability 1/2.

The first two moments of the Bernoulli random variable are chosen to match those of the increment it is replacing; the higher even moments do not match. Chernoff & Petkau (1976) have investigated the following relation of this discrete time simple random walk problem to the original continuous time problem:

\[
(1.2.5.1) \quad \tilde{Y}(s) = \tilde{Y}_\alpha(s) \pm 0.5\sqrt{\Delta} + o(\sqrt{\Delta}).
\]

It is not easy to calculate \( \tilde{Y}_\alpha(s) \) directly, so another approximation is proposed by Chernoff and Petkau (1984). Derive \( Y_0(s) \) and \( Y_1(s) \), the continuation points on the grid which are closest and second closest to the stopping region at the stopping time \( s \). Let

\[
D_0 = \hat{d}(Y_0(s),s) - d(Y_0(s),s)
\]

\[
D_1 = \hat{d}(Y_1(s),s) - d(Y_1(s),s).
\]
Then, the following continuation correction can be applied to get the optimal stopping boundary, $\tilde{Y}(s)$, for the original problem:

$$\tilde{Y}(s) = Y_0(s) + \left\{ \frac{D_1}{4D_0 - 2D_1} \right\} \sqrt{A}.$$  

(1.2.5.2)

Considering the boundary of the optimal continuation region for nonnegative $s$ is enough, since $d(y,s)$ is symmetric. Also, given that $y_0$ and $y_0 + \sqrt{A}$ are stopping points at $s = s_\pi - A$, then it can be shown that $y_0 + \sqrt{A}$ will be a stopping point at $s = s_\pi$ (at least for small values of $A$). Based on the above results, Chernoff & Petkau (1984) write a Fortran program which solves the optimal stopping time problem very efficiently. Two approximations of $\tilde{Y}(s)$ can be calculated directly from the program. The first one, simply uses the continuity correction to $Y_0(s)$, shown in (1.2.5.1), i.e.,

$$\tilde{Y}(s) = Y_0(s) + 0.5 \sqrt{A}.$$  

The second one uses the continuity correction, shown in (1.2.5.2). This approach is not well adapted for very precise results but is surprisingly effective for rough approximation.
CHAPTER II
ESTABLISHING THE MODEL

2.1 Introduction

This chapter presents a model to test two new treatments against a standard treatment with a two-stage approach described by Anscombe (1963). The treatments considered are with continuous responses which are normally distributed. The number of patients available for the trial is fixed and denoted by N. A stopping rule is discussed which indicates when to discontinue allocating triplets of patients and begin giving the apparently best treatment to all remaining patients. The decision rule for determining the best treatment when the testing stage is stopped is also discussed. The following is an example of the problem that we are interested in:

Suppose Bactrim, Pentamidine and Pentamidine with Steroids are the treatments for Pneumocystis Carinii Pneumonia (PCP) and 297 patients are suffering from PCP. We would like to know which treatment is best on this disease for treating the 297 patients. PaO₂ means the partial pressure of oxygen in the blood. A patient with higher PaO₂ is recovering better from PCP. So, PaO₂ can be a quantitative measure of response to indicate the effect of a treatment. By Anscombe's approach, triplets of patients are assigned sequentially to the three
treatments until the testing stage is terminated, and then the remaining patients are assigned to the apparently best treatment. When to stop the testing stage and how to decide the best treatment by the PaO\textsubscript{2}’s of treated patients will be discussed in Section 3.4 of the next chapter.

Section 2.2 relates the problem of finding the stopping rule to two independent Gaussian processes. Section 2.3 defines the stopping risk if the first stage is stopped after n triplets of patients have been allocated.

In Section 2.4, we discuss a continuous time version of the problem described in Section 2.2 and 2.3. The continuous time problem becomes a free boundary problem. Section 2.5 is devoted to the transformation of the problem of finding an optimal stopping rule to a parameter-free problem.

Section 2.6 describes an approach for solving the boundary of the optimal continuation region, which characterizes the optimal stopping rule, by means of a 2-dimensional random walk.

2.2 Two Independent Gaussian Processes

We shall assume that the treatment responses are independently normally distributed. Let \( X_{j1}, X_{j2}, \ldots \) denote the responses to the \( j \)-th treatment, where \( j = 0 \) refers to the standard treatment, and \( j = 1 \) and 2, respectively, refer to new treatments A and B. The assumption is that the \( X_{j1} \)'s (\( j = 0, 1, 2, i = 1, 2, 3, \ldots \) ) are independent and \( \mathcal{N}(\Theta_j, \sigma^2) \) variables, where \( \sigma^2 \) is known. For the convenience in considering the time variable later, the variances of the responses of the treatments are set to be equal. Further, suppose
that the $\theta_j$'s are independent and have prior density $N(\mu_j, \sigma^2_j)$. If $n$ triplets of patients have been assigned to the three treatments, the posterior distribution is given by the following lemma:

**Lemma 2.2.1.** The posterior distribution of $\theta = (\theta_0, \theta_1, \theta_2)$, given $x_{j_1}, j = 0, 1, 2, i = 1, 2, \ldots, n$, is

$$
\mathcal{N}(\begin{bmatrix}
    (n\sigma^{-2}_{\bar{x}_{n0}} + \sigma^{-2}_{\bar{x}_{n1}} - \mu_0)/(n\sigma^{-2}_{\bar{x}_{n0}} + \sigma^{-2}_{\bar{x}_{n1}})
    \\
    (n\sigma^{-2}_{\bar{x}_{n1}} + \sigma^{-2}_{\bar{x}_{n2}} - \mu_1)/(n\sigma^{-2}_{\bar{x}_{n1}} + \sigma^{-2}_{\bar{x}_{n2}})
    \\
    (n\sigma^{-2}_{\bar{x}_{n2}} + \sigma^{-2}_{\bar{x}_{n3}} - \mu_2)/(n\sigma^{-2}_{\bar{x}_{n2}} + \sigma^{-2}_{\bar{x}_{n3}})
\end{bmatrix}, \begin{bmatrix}
    (n\sigma^{-2}_{\bar{x}_{n0}} + \sigma^{-2}_{\bar{x}_{n1}})^{-1} & 0 & 0 \\
    0 & (n\sigma^{-2}_{\bar{x}_{n1}} + \sigma^{-2}_{\bar{x}_{n2}})^{-1} & 0 \\
    0 & 0 & (n\sigma^{-2}_{\bar{x}_{n2}} + \sigma^{-2}_{\bar{x}_{n3}})^{-1}
\end{bmatrix})
$$

where $\bar{x}_{n0} = \frac{1}{n} \sum_{i=1}^{n} x_{0i}$, $\bar{x}_{n1} = \frac{1}{n} \sum_{i=1}^{n} x_{1i}$, $\bar{x}_{n2} = \frac{1}{n} \sum_{i=1}^{n} x_{2i}$.

**Proof:** Let $\bar{x}_{nj} = \frac{1}{n} \sum_{j=1}^{n} x_{j1}$, $j = 0, 1, 2$. Then, the $\bar{x}_{nj}$'s are independently normally distributed with mean $\theta_j$ and variance $\sigma^2/n$.

Consider

$$
\begin{align*}
\theta_0 &= \mu_0 + Z_{01}\sigma_{\mu}, & \bar{x}_{n0} &= \mu_0 + Z_{01}\sigma_{\mu} + Z_{01}\sigma/\sqrt{n}, \\
\theta_1 &= \mu_1 + Z_{11}\sigma_{\mu}, & \bar{x}_{n1} &= \mu_1 + Z_{11}\sigma_{\mu} + Z_{11}\sigma/\sqrt{n}, \\
\theta_2 &= \mu_2 + Z_{22}\sigma_{\mu}, & \bar{x}_{n2} &= \mu_2 + Z_{22}\sigma_{\mu} + Z_{22}\sigma/\sqrt{n},
\end{align*}
$$

where $Z_{ij}$'s are independent standard normal random variables. Then, the joint distribution of $(\theta_0, \theta_1, \theta_2, \bar{x}_{n0}, \bar{x}_{n1}, \bar{x}_{n2})$ is easily
computed to be

\[ \mathcal{N}(\begin{bmatrix} \mu \\
\end{bmatrix}, \begin{bmatrix} \sigma^2_{\theta_0} I_3 & \sigma^2_{\theta_1} I_3 \\
\sigma^2_{\theta_1} I_3 & (\sigma^2 + \sigma^2 / \sqrt{n}) I_3 \\
\end{bmatrix}) \]

where \( \mu = (\mu_0, \mu_1, \mu_2)' \) and \( I_3 \) is an identity matrix of order \( 3 \times 3 \).

By Theorem 2.5.1 of Anderson (1958), the posterior distribution of \( \theta \) given the \( \bar{x}_{nj} \)'s is

\[ \mathcal{N}(\begin{bmatrix}
(n\sigma^2 - \overline{x}_{n0} + \sigma^2 \mu_0)/(n\sigma^2 + \sigma^2) \\
(n\sigma^2 - \overline{x}_{n1} + \sigma^2 \mu_1)/(n\sigma^2 + \sigma^2) \\
(n\sigma^2 - \overline{x}_{n2} + \sigma^2 \mu_2)/(n\sigma^2 + \sigma^2)
\end{bmatrix}, \begin{bmatrix}
(n\sigma^2 + \sigma^2)^{-1} & 0 & 0 \\
0 & (n\sigma^2 + \sigma^2)^{-1} & 0 \\
0 & 0 & (n\sigma^2 + \sigma^2)^{-1}
\end{bmatrix}) \]

Since \( (\overline{x}_{n0}, \overline{x}_{n1}, \overline{x}_{n2}) \) is sufficient for \( (\theta_0, \theta_1, \theta_2) \) (Anderson (1958), p. 56), the posterior distribution of \( \theta \) given \( x_{ji} \), \( j = 0, 1, 2, \)

\( i = 1, 2, \ldots, n \), is equivalent to the posterior distribution of \( \theta \)

given \( \bar{x}_{nj} \), \( j = 0, 1, 2 \). This proves the Lemma. \( \square \)

If \( n \) triplets of patients have been observed, the best appearing

treatment can be decided by comparing the posterior mean of \( \theta \). The

posterior means of the difference of the response parameters \( \theta_1 - \theta_0 \) and

\( \theta_2 - \theta_0 \) seem to be the obvious contrasts for selecting the best

treatment. It will prove more convenient, however, to study the

posterior mean of the contrasts \( (\theta_2 - \theta_1) / \sqrt{2} \) and \( (\theta_1 + \theta_2 - 2\theta_0) / \sqrt{6} \).
Specifically, let

$$W_n = \begin{bmatrix} W_{n1} \\ W_{n2} \end{bmatrix}$$

(2.2.1)  

$$E\left(\frac{(\theta_2 - \theta_1)\sqrt{2}}{(\theta_1 + \theta_2 - \theta_0)/\sqrt{6}}\right) X_{j_1}, \text{ } j = 0, 1, 2, i = 1, 2, \ldots, n$$

$$= \begin{bmatrix} s_n (n^{-2}(\bar{x}_{n2} - \bar{x}_{n1}) + \sigma^{-2}_n (\mu_2 - \mu_1)) / \sqrt{2} \\ s_n (n^{-2}(\bar{x}_{n1} + \bar{x}_{n2} - 2\bar{x}_{n0}) + \sigma^{-2}_n (\mu_1 + \mu_2 - 2\mu_0)) / \sqrt{6} \end{bmatrix}.$$

and

(2.2.2)  

$$s_n = (n^{-2} + \sigma^{-2}_n)^{-1}.$$

Following Chernoff (1972), the next step is to consider the distribution of \( \frac{W_m}{W_n} \) for \( n \geq m \geq 0 \), which is obtained in Lemma 2.2.2.

**Lemma 2.2.2.** For \( n \geq m \geq 0 \), the distribution of \( \frac{W_m}{W_n - W_m} \) is

$$N\left( \begin{bmatrix} (\mu_2 - \mu_1) / \sqrt{2} \\ (\mu_1 + \mu_2 - 2\mu_0) / \sqrt{6} \\ 0 \\ 0 \end{bmatrix} \right), \begin{bmatrix} \sigma^2_{m-s} & 0 & 0 & 0 \\ 0 & \sigma^2_{m-s} & 0 & 0 \\ 0 & 0 & s_{m-s-n} & 0 \\ 0 & 0 & 0 & s_{m-s-n} \end{bmatrix}. $$

**Proof:** Let \( a_{n\times n} \) be an \( n \times n \) matrix of constant \( a \) and let \( I_n \) be an identity matrix of order \( n \times n \). By an argument, similar to the argument about the distribution of \((\theta_0, \theta_1, \theta_2, \bar{x}_{n0}, \bar{x}_{n1}, \bar{x}_{n2})\) in Lemma 2.2.1.
the distribution of \((\theta_0, X_{01}, \ldots, X_{0n}, \theta_1, X_{11}, \ldots, X_{1n}, \theta_2, X_{21}, \ldots, X_{2n})'\) is normal with mean \(\mu_1\) and covariance matrix \(\Sigma_1\), where

\[
\mu_1 = \begin{bmatrix}
\mu_0^1_{\text{n x 1}} \\
\mu_1^1_{\text{n x 1}} \\
\mu_2^1_{\text{n x 1}}
\end{bmatrix}, \quad 
\Sigma_1 = \begin{bmatrix}
C & D & D \\
D & C & D \\
D & D & C
\end{bmatrix},
\]

\[D = O_{(n+1)\times(n+1)},\]

and

\[C = \sigma_1^2 \times (n+1)\times(n+1) + \sigma_2^2 \begin{bmatrix}
0_{\text{n x 1}} & 0_{\text{n x 1}} \\
0_{\text{n x 1}} & I_n
\end{bmatrix}.
\]

Let \(U_{n1} = \overline{X}_{n2} - \overline{X}_{n1}\), \(U_{n2} = \overline{X}_{n1} + \overline{X}_{n2} - 2\overline{X}_{n0}\). then

\[\mathbf{U} = [U_{n1}, U_{n2}, U_{m1}, U_{m2}]' = A_1 Q.
\]

where

\[
A_1 = \begin{bmatrix}
0 & 0_{1\times n} & 0 & (-1/n)_{1\times n} & 0 & (1/n)_{1\times n} \\
0 & (-2/n)_{1\times n} & 0 & (1/n)_{1\times n} & 0 & (1/n)_{1\times n} \\
0 & 0_{1\times n} & 0 & (-1/m)_{1\times (n-m)} & 0 & (1/m)_{1\times (n-m)} \\
0 & (-2/m)_{1\times (n-m)} & 0 & (1/m)_{1\times (n-m)} & 0 & (1/m)_{1\times (n-m)}
\end{bmatrix}.
\]
and the distribution of $\underline{U}$ is normal with mean $\underline{M}_2$ and covariance matrix $\Sigma_2$, where

$$\underline{M}_2 = \begin{bmatrix} \mu_2 - \mu_1, \mu_1 + \mu_2 - 2\mu_0, \mu_2 - \mu_1, \mu_1 + \mu_2 - 2\mu_0 \end{bmatrix}'.$$

$$\Sigma_2 = A_1\Sigma_1A_1' = \begin{bmatrix} E & E \\ E & F \end{bmatrix},$$

$$E = \begin{bmatrix} 2(\sigma^2_m + \sigma^2/n) & 0 \\ 0 & 6(\sigma^2_m + \sigma^2/n) \end{bmatrix},$$

and

$$F = \begin{bmatrix} 2(\sigma^2_m + \sigma^2/m) & 0 \\ 0 & 6(\sigma^2_m + \sigma^2/m) \end{bmatrix}.$$

Since $\underline{W}_{n1}$ is a linear function of $\underline{U}_{n1}$, $i = 1, 2$, $\underline{W} = [\underline{W}_{n1}, \underline{W}_{n2}, \underline{W}_{m1}, \underline{W}_{m2}]'$ has a normal distribution with mean $\underline{M}_3$ and covariance matrix $\Sigma_3$, where

$$\underline{M}_3 = [(\mu_2 - \mu_1)/\sqrt{2}, (\mu_1 + \mu_2 - 2\mu_0)/\sqrt{6}, (\mu_2 - \mu_1)/\sqrt{2}, (\mu_1 + \mu_2 - 2\mu_0)/\sqrt{6}],$$

$$\Sigma_3 = \begin{bmatrix} \begin{array}{c} G \\ H \\ H \end{array} \end{bmatrix},$$

$$G = (\sigma^2_m - s_n)I_2$$

and

$$H = (\sigma^2_m - s_m)I_2.$$
Similarly, \( \begin{pmatrix} \frac{W}{n} \\ -\frac{W}{m} \end{pmatrix} \) is normal with mean \( M \) and covariance matrix \( \Sigma \), where

\[
M = A_3 W_3 = \begin{pmatrix} \mu_2 - \mu_1 / \sqrt{2} \\ \mu_1 + \mu_2 - 2\mu_0 / \sqrt{6} \end{pmatrix}, \quad 0, 0. \]

\[
\Sigma = A_3 \Sigma_3 A_3' = \begin{bmatrix}
\sigma_m^2 & 0 & 0 & 0 \\
0 & \sigma_m^2 & 0 & 0 \\
0 & 0 & s_n - s_m & 0 \\
0 & 0 & 0 & s_n - s_m
\end{bmatrix}, \text{ and}
\]

\[
A_3 = \begin{bmatrix}
0 & 0 & 1 & 0 \\
0 & 0 & 0 & 1 \\
1 & 0 & -1 & 0 \\
0 & 1 & 0 & -1
\end{bmatrix}, \text{ since } \begin{pmatrix} \frac{W}{n} \\ -\frac{W}{m} \end{pmatrix} = A_3 W.
\]

\[\square\]

Lemmas 2.2.1 and 2.2.2 indicate that as evidence accumulates, the posterior means of the chosen contrasts (referred to above) of \( \theta = (\theta_0, \theta_1, \theta_2)' \) behave like two independent Gaussian stochastic processes, each with independent increments. The vectors \( W_0, W_1, \ldots \) form a Markov process starting from

\[
W_0 = (w_{01}', w_{02}')' = (\mu_2 - \mu_1 / \sqrt{2}, \mu_1 + \mu_2 - 2\mu_0 / \sqrt{6})'.
\]

Note here that the obvious contrasts give posterior means that behave like dependent processes.

The following lemma is used in the proof of Proposition 2.2.1.

Lemma 2.2.3. Let \( X \) and \( Y \) be two independent random variables. If \( G_1(X) \) and \( G_2(Y) \) are sufficient statistics for \( \gamma_1 \) and \( \gamma_2 \), respectively, then \( (G_1(X), G_2(Y)) \) is sufficient for \( (\gamma_1, \gamma_2) \).
Proof: By Theorem 2.2.1 of Bickel and Doksum (1977), the distribution of \( X \) is
\[
g_1(G_1(x), \tau_1)h_1(x)
\]
for some functions \( g_1 \) and \( h_1 \). And the distribution of \( Y \) is
\[
g_2(G_2(y), \tau_2)h_2(y)
\]
for some functions \( g_2 \) and \( h_2 \). Since \( X \) and \( Y \) are independent, the joint distribution of \( X \) and \( Y \) is
\[
[g_1(G_1(x), \tau_1)h_1(x)][g_2(G_2(y), \tau_2)h_2(y)]
\]
\[
= [g_1(G_1(x), \tau_1)g_2(G_2(x), \tau_2)][h_1(x)h_2(x)].
\]
Hence, \((G_1(X), G_2(Y))\) is sufficient for \((\tau_1, \tau_2)\).

The next result shows the property of the statistic
\[
[\sqrt{2}, (\bar{X}_{n1} + \bar{X}_{n2} - 2\bar{X}_{n0})/\sqrt{6}]
\]
where
\[
\bar{X}_{n0} = \sum_{i=1}^{n} X_{0i}/n, \quad \bar{X}_{n1} = \sum_{i=1}^{n} X_{1i}/n, \quad \bar{X}_{n2} = \sum_{i=1}^{n} X_{2i}/n.
\]

**Proposition 2.2.1.** The statistic
\[
[(\bar{X}_{n2} - \bar{X}_{n1})/\sqrt{2}; (\bar{X}_{n1} + \bar{X}_{n2} - 2\bar{X}_{n0})/\sqrt{6}]
\]
is sufficient for \[(\theta_2 - \theta_1)/\sqrt{2} \ notices (\theta_1 + \theta_2 - 2\theta_0)/\sqrt{6} \], where \( \bar{X}_{n0}, \bar{X}_{n1} \) and \( \bar{X}_{n2} \) are as defined above.
Proof: It is known that \((\bar{x}_{n0}, \bar{x}_{n1}, \bar{x}_{n2})'\) is normally distributed with mean \(\theta\) and variance \(M\), where

\[
\theta = (\theta_0, \theta_1, \theta_2)'
\]

and

\[
M = \begin{bmatrix}
\sigma^2/n & 0 & 0 \\
0 & \sigma^2/n & 0 \\
0 & 0 & \sigma^2/n
\end{bmatrix}
\]

Let \(B_1 = (0, -1/\sqrt{2}, 1/\sqrt{2})'\) and \(B_2 = (-2/\sqrt{6}, 1/\sqrt{6}, 1/\sqrt{6})'\). Then \((\bar{x}_{n2} - \bar{x}_{n1})/\sqrt{2} = B_1'(\bar{x}_{n0}, \bar{x}_{n1}, \bar{x}_{n2})'\) is normally distributed with mean

\[
B_1' \theta = (\theta_2 - \theta_1)/\sqrt{2}
\]

and variance

\[
B_1'MB_1 = \sigma^2/n.
\]

and \((\bar{x}_{n1} + \bar{x}_{n2} - 2\bar{x}_{n0})/\sqrt{6} = B_2'(\bar{x}_{n0}, \bar{x}_{n1}, \bar{x}_{n2})'\) is normally distributed with mean

\[
B_2' \theta = (\theta_1 + \theta_2 - 2\theta_0)/\sqrt{6}
\]

and variance

\[
B_2'MB_2 = \sigma^2/n.
\]

Hence, \((\bar{x}_{n2} - \bar{x}_{n1})/\sqrt{2}\) is a sufficient statistic for \((\theta_2 - \theta_1)/\sqrt{2}\) and \((\bar{x}_{n1} + \bar{x}_{n2} - 2\bar{x}_{n0})/\sqrt{6}\) is a sufficient statistic for \((\theta_1 + \theta_2 - 2\theta_0)/\sqrt{6}\).

Since \(B_1\) and \(B_2\) are orthogonal, by Theorem 3.3.1 of Anderson (1958) \(B_1'(\bar{x}_{n0}, \bar{x}_{n1}, \bar{x}_{n2})\) and \(B_2'(\bar{x}_{n0}, \bar{x}_{n1}, \bar{x}_{n2})\) are independent. The result then follows from Lemma 2.2.3. \(\square\)
2.3 The Stopping Risk

Suppose the number of patients available is $N$, where $N$ is a multiple of 3. Let

$$T_0 = \{(w_1, w_2) : w_1 + \sqrt{3}w_2 \leq 0 \text{ and } w_1 - \sqrt{3}w_2 \geq 0\},$$

(2.3.1)  \[ T_1 = \{(w_1,w_2) : w_1 \leq 0 \text{ and } w_1 - \sqrt{3}w_2 < 0\}, \]

and  \[ T_2 = \{(w_1,w_2) : w_1 \geq 0 \text{ and } w_1 + \sqrt{3}w_2 > 0\}. \]

Figure 2.3.1 gives the picture of the regions $T_0$, $T_1$ and $T_2$ on $(w_1,w_2)$ plane. That $(W_{n1},W_{n2})$ defined in (2.2.1) is in region $T_0$ is equivalent to the assertion that the posterior mean of $\theta_0$ is larger than the posterior means of $\theta_1$ and $\theta_2$. Thus, after $n$ triplets of patients are allocated, we will select the standard treatment for the remaining $(N-3n)$ patients if the observed $(W_{n1},W_{n2})$ is in $T_0$. Similarly, we will select treatment A if the observed $(W_{n1},W_{n2})$ is in $T_1$, select treatment B if the observed $(W_{n1},W_{n2})$ is in $T_2$, select either treatment A or B if the observed $(W_{n1},W_{n2})$ is on the boundary of $T_1$ and $T_2$, select either standard treatment or treatment A if the observed $(W_{n1},W_{n2})$ is on the boundary of $T_0$ and $T_1$, select either standard treatment or treatment B if the observed $(W_{n1},W_{n2})$ is on the boundary of $T_0$ and $T_2$, and select either one of standard treatment, treatment A and treatment B if $(W_{n1},W_{n2}) = (0,0)$.

For ethical considerations mentioned in the last chapter, the stopping risk associated with the above decision rule should be considered over the entire patient horizon. Here, "stopping" means switching from all three treatments to the best appearing treatment for the remaining patients in the trial. Of course, the ideal procedure assigns all $N$ patients to the best treatment. The posterior
Bayes risk at "time" $n$ is the expected total difference in response between the ideal procedure and the procedure that stops the testing stage after $n$ triplets of patients have been allocated and gives the remaining $N-3n$ patients the treatment selected by the rule described above. Let $\mathcal{F}_n$ be the $\sigma$-field generated by

$$\{X_{ji} : j = 0, 1, 2, \ i = 1, 2, \ldots, n\},$$

and

$$E_n(\mathcal{F}) = E(\mathcal{F}|\mathcal{F}_n).$$

The risk associated with stopping patient allocation at "time" $n$ is:

$$nE_n(3\theta_{\max} - \theta_0 - \theta_1 - \theta_2) + (N - 3n)E_n(\theta_{\max} - \theta_a),$$

where $\theta_{\max} = \text{Max}(\theta_0, \theta_1, \theta_2)$ and

$$\theta_a = \theta_j \text{ if } \theta_j \text{ is selected, } j = 0, 1, 2.$$

This can be rewritten as

$$nE_n(\theta_{\max} - (\theta_0 + \theta_1 + \theta_2)/3) - (N-3n)E_n(\theta_a - (\theta_0 + \theta_1 + \theta_2)/3).$$

The objective is to find a stopping rule (or a random variable $\mathcal{M}$ that can only assume the values 0, 1, 2, ..., $N/3$) to minimize

$$nE_{\mathcal{M}}(\theta_{\max} - (\theta_0 + \theta_1 + \theta_2)/3) - (N-3\mathcal{M})E_{\mathcal{M}}(\theta_a - (\theta_0 + \theta_1 + \theta_2)/3).$$

Since $\mathcal{F}_n$ is nondecreasing in $n$ and

$$E_n(E_{n+1}(\theta_{\max} - (\theta_0 + \theta_1 + \theta_2)/3)) = E_n(\theta_{\max} - (\theta_0 + \theta_1 + \theta_2)/3)$$

the first term of (2.3.3), $nE_n(\theta_{\max} - (\theta_0 + \theta_1 + \theta_2)/3)$, is a martingale in
n. By combining this and the fact that stopping is enforced when
n = N/3, it can be proven that

\[ E(M(\theta_{\max}-(\theta_0+\theta_1+\theta_2)/3)) = E(\theta_{\max}-(\theta_0+\theta_1+\theta_2)/3) \]

where \( M \) is a random number to define the stopping rule and
n \( \in \{0, 1, 2, \ldots, N/3\} \). Hence, the first term of (2.3.3) has no
bearing on our optimal stopping problem.

The second term of (2.3.3) should be rewritten in term of \( W_{n1} \) and
\( W_{n2} \), since the posterior means of the two chosen contrasts, \((W_{n1}, W_{n2})\),
are considered after n triplets of patients have been allocated. Let
\( I_j \) be the indicator of the set \( T_j \), \( j = 0, 1, 2 \), where \( T_j \)'s are defined
in (2.3.1). Then,

\begin{equation}
E_n[3\theta_0-(\theta_0+\theta_1+\theta_2)] = E_n[(2\theta_0-\theta_1-\theta_2)I_{T_0}(W_{n1}, W_{n2}) + (2\theta_1-\theta_0-\theta_2)I_{T_1}(W_{n1}, W_{n2}) + (2\theta_2-\theta_0-\theta_1)I_{T_2}(W_{n1}, W_{n2})].
\end{equation}

By (2.2.1) \( W_{n1} \) and \( W_{n2} \) are \( \mathcal{F}_n \)-measurable. It follows that \( I_{T_0} \),
\( I_{T_1} \) and \( I_{T_2} \) are \( \mathcal{F}_n \)-measurable, too. Thus, (2.3.5) can be rewritten as
follows:

\begin{equation}
f(W_{n1}, W_{n2}) = -\sqrt{6}W_{n2}I_{T_0}(W_{n1}, W_{n2}) + ((\sqrt{6}W_{n2}-3\sqrt{2}W_{n1})/2)I_{T_1}(W_{n1}, W_{n2}) + ((\sqrt{6}W_{n2}+3\sqrt{2}W_{n1})/2)I_{T_2}(W_{n1}, W_{n2}).
\end{equation}
The next theorem shows that the decision rule, which is discussed in the beginning of this section for determining the best appearing treatment at time "n", is optimal.

**Theorem 2.3.1.** Let $T_0$, $T_1$, and $T_2$ be as defined in (2.3.1). The following decision rule is optimal for deciding the treatment for the patients in the post testing stage if the testing stage is terminated after $n$ triplets of patients have been allocated:

1. Select standard treatment if the observed $(W_{n1}, W_{n2})$ is in $T_0$.
2. Select new treatment $A$ if the observed $(W_{n1}, W_{n2})$ is in $T_1$.
3. Select new treatment $B$ if the observed $(W_{n1}, W_{n2})$ is in $T_2$.

**Proof:** By (2.3.3) and (2.3.5), the stopping risk at time "n" is:

$$-(N-3n)E_n((\theta_0 - (\theta_0^2 + \theta_1^2 + \theta_2^2)/3)$$

$$= \begin{cases} -(N-3n)E_n((2\theta_0 - \theta_1 - \theta_2)/3) & \text{if standard treatment is selected,} \\ -(N-3n)E_n((2\theta_1 - \theta_0 - \theta_2)/3) & \text{if treatment A is selected,} \\ -(N-3n)E_n((2\theta_2 - \theta_0 - \theta_1)/3) & \text{if treatment B is selected.} \end{cases}$$

If the observed $(W_{n1}, W_{n2})$ is in $T_0$, we know that

$$E_n(\theta_0) \geq E_n(\theta_1) \text{ and } E_n(\theta_0) \geq E_n(\theta_2);$$

which imply

$$-E_n((2\theta_0 - \theta_1 - \theta_2)/3) \leq -E_n((2\theta_1 - \theta_0 - \theta_2)/3)$$

and

$$-E_n((2\theta_0 - \theta_1 - \theta_2)/3) \leq -E_n((2\theta_2 - \theta_0 - \theta_1)/3).$$

Hence, it is optimal to select standard treatment if the testing stage is stopped at time "n" and the observed $(W_{n1}, W_{n2}) \in T_0$. 

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Similarly, we can prove it is optimal to select treatment A (B) at time \( n \), if the observed \( (W_{n1}, W_{n2}) \) is in \( T_1 (T_2) \).

From (2.2.1), it can be seen that \( s_n \) is a strictly decreasing function of \( n \). Thus, we consider the process \( (W_{n1}, W_{n2}, s_n) \) instead of the process \( (W_{n1}, W_{n2}, n) \). By Lemma 2.2.2, the decrement of the time variable \( s_n \) is the variances of the increments of the spatial variables \( W_{n1} \) and \( W_{n2} \). To introduce \( s_n \) in the stopping risk, it can be proven that

\[-(N-3n) = \sigma^2 (s_n^{-1} - s_t^{-1}).\]

where \( s_t = (\sigma^2 + (N/3)\sigma^{-2})^{-1} \). Hence, the second term of (2.3.3) can be rewritten as \( r_1(W_{n1}, W_{n2}, s_n) \):

\[ r_1(W_{n1}, W_{n2}, s_n) = \sigma^2 (s_n^{-1} - s_t^{-1}) f(W_{n1}, W_{n2}). \]

The problem of optimal stopping can be recast in terms of a risk sequence \( r(W_{n1}, W_{n2}, s_n) \), where

\[ r(W_{n1}, W_{n2}, s_n) = r_1(W_{n1}, W_{n2}, s_n)/\sigma^2.\]

It is obvious that stopping is enforced when there is no patient available; that is, stopping is enforced when time variable \( s \) is equal to \( s_t \).

Now, the objective is to find a stopping rule (or a random variable \( S \) that can only assume the values \( s_0, s_1, \ldots, s_t \)) to minimize

\[ E[r(W_1(S), W_2(S), S)].\]
Figure 2.3.1: Regions $T_0$, $T_1$, and $T_2$

$W_1 - \sqrt[3]{3} W_2 = 0$

$W_1 + \sqrt[3]{3} W_2 = 0$

$T_0$: Standard treatment is the best appearing treatment

$T_1$: Treatment A is the best appearing treatment

$T_2$: Treatment B is the best appearing treatment
2.4 Continuous Time Version

Consider a continuous time version of our problem, in which stopping may occur at any point in the interval:

\[ [s_t, s_0] \]

The clinical trial model may be regarded as a special case of the continuous time problem with the restriction that stopping may take place only in a limited subset of the \((w_1, w_2, s)\) space, and hence the optimal risks and related stopping sets are larger. Moreover, the discrete time solution converges monotonically to the continuous time solution if the set of possible stopping times \(\{s_0, s_1, s_2, \ldots\}\) increases and \(\sup_t |s_i - s_{i+1}| \to 0\) (Chernoff and Petkau (1986)).

Following Chernoff (1972) discussed in Chapter I, a limiting form of our sequential problem is a special case for \(G = [s_t, s_0]\) of the following stopping problem.

**STopping Problem.** Given two independent Gaussian processes \(\{\mathcal{W}_1(s), s \in G\}\) and \(\{\mathcal{W}_2(s), s \in G\}\) of independent increments in the \(-s\) scale, with

\[
\begin{align*}
E\left[ \begin{bmatrix} d\mathcal{W}_1(s) \\ d\mathcal{W}_2(s) \end{bmatrix} \right] &= \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \quad \text{and} \quad \text{Var}\left[ \begin{bmatrix} d\mathcal{W}_1(s) \\ d\mathcal{W}_2(s) \end{bmatrix} \right] = \begin{bmatrix} -ds & 0 \\ 0 & -ds \end{bmatrix}
\end{align*}
\]

starting at \(\mathcal{W}_1(s_0) = w_{01}, \mathcal{W}_2(s_0) = w_{02}\) where \(s_0 = \sigma^2_w\), find a stopping time \(S\) to minimize

\[ E[r(\mathcal{W}_1(S), \mathcal{W}_2(S), S)]. \]

Stopping is enforced when \(S = s_t\).
Let \( \rho(w_1, w_2, s) \) be the expected stopping risk associated with the optimal stopping rule (under regularity conditions sufficient to imply the existence of an optimal rule). Then, it pays to continue taking observations iff

\[
(2.4.1) \quad \rho(w_1, w_2, s) < r(w_1, w_2, s).
\]

The point which satisfies the above inequality is called an optimal continuation point. The set of all optimal continuation points in the \((w_1, w_2, s)\) space is the optimal continuation region \( \mathcal{Q}_0 \) corresponding (2.4.1). The optimal stopping rule is characterized by the continuation region \( \mathcal{Q}_0 \). We shall see that the continuous time stopping problem can be expressed in terms of a free boundary problem involving the heat equation. The stopping problem can then be attempted using the analytic tools of partial differential equations. The following theorem gives some necessary conditions for the optimal continuation region \( \mathcal{Q}_0 \).

**Theorem 2.4.1.**

(i) For \((w_1, w_2, s) \in \mathcal{Q}_0\), \( \rho(w_1, w_2, s) = r(w_1, w_2, s) \).

(ii) For \((w_1, w_2, s) \in \mathcal{Q}_0\).

\[
(2.4.1) \quad \left(\rho_{w_1} (w_1, w_2, s) + \rho_{w_2} (w_1, w_2, s)\right)/2 = \rho_s (w_1, w_2, s).
\]

(iii) If \((w_1, w_2, s)\) is on the boundary of \( \mathcal{Q}_0 \), then

\[
(2.4.2) \quad \rho_{w_1} (w_1, w_2, s) = r_{w_1} (w_1, w_2, s), \text{ and}
\]

\[
(2.4.3) \quad \rho_{w_2} (w_1, w_2, s) = r_{w_2} (w_1, w_2, s).
\]
Proof: (i) is obvious.

(ii) Suppose \((w_1, w_2, s) \in \mathcal{G}_0\). Then the probability of stopping between \(s+\delta\) and \(s\) is \(o(\delta)\) and \((W_1, W_2)\) change from \((W_1(s+\delta), W_2(s+\delta))\) to \((W_1(s), W_2(s))\). Consequently,

\[
\rho(w_1, w_2, s+\delta) = E(\rho(W_1(s), W_2(s), s) | W_1(s+\delta) = w_1, W_2(s+\delta) = w_2) + o(\delta)
\]

\[
= E(\rho(w_1+Z_1\sqrt{\delta}, w_2+Z_2\sqrt{\delta}, s)) + o(\delta),
\]

where \(Z_1, Z_2\) are independent generic \(N(0,1)\) random variables. By Taylor's formula,

\[
\rho(w_1, w_2, s+\delta)
\]

\[
= E(\rho(w_1, w_2, s) + Z_1\sqrt{\delta}\rho_{w_1}(w_1, w_2, s) + Z_2\sqrt{\delta}\rho_{w_2}(w_1, w_2, s)
\]

\[
+ Z_1^2(\delta/2)\rho_{w_1 w_1}(w_1, w_2, s) + Z_2^2(\delta/2)\rho_{w_2 w_2}(w_1, w_2, s)
\]

\[
+ Z_1 Z_2(\delta)\rho_{w_1 w_2}(w_1, w_2, s)) + o(\delta)
\]

\[
= \rho(w_1, w_2, s) + (\delta/2)\rho_{w_1 w_1}(w_1, w_2, s) + (\delta/2)\rho_{w_2 w_2}(w_1, w_2, s) + o(\delta).
\]

Thus,

\[
(\rho_{w_1 w_1}(w_1, w_2, s) + \rho_{w_2 w_2}(w_1, w_2, s))/2 = \rho_s(w_1, w_2, s).
\]

(iii) At a specified time \(s^*_5\), assume \((w_1^*, w_2^*, s^*_5)\) and \((w_1^*, w_2^*, s^*_5)\) are on the boundary of \(\mathcal{G}_0\), where \(w_1^* < w_1^*\),

\[
\{(W_1, w_2^*, s^*_5): w_1^* < W_1 < w_1^*\} \in \mathcal{G}_0 \quad \text{and} \quad \{(W_1, w_2^*, s^*_5): W_1 > w_1^*\} \in \mathcal{G}_0.
\]

Then, since

\[
\rho(W_1, w_2^*, s^*_5) = r(W_1, w_2^*, s^*_5) \quad \text{for} \quad W_1 > w_1^*.
\]
the right-hand derivative

$$\rho_{w_1}^+ (w_{1\infty}, w_{2\infty}, s_{\infty}) = r_{w_1} (w_{1\infty}, w_{2\infty}, s_{\infty}).$$

For \( w_{1\infty} \leq w_1 \leq w_{1\infty} \), \( \rho(w_{1\infty}, w_{2\infty}, s_{\infty}) \leq r(w_{1\infty}, w_{2\infty}, s_{\infty}) \) and hence,

$$\rho_{w_1}^- (w_{1\infty}, w_{2\infty}, s_{\infty}) \geq r_{w_1} (w_{1\infty}, w_{2\infty}, s_{\infty}).$$

\( E[\rho(w_{1\infty} + Z\sqrt{\delta}, w_{2\infty}, s_{\infty})] \), where \( Z \) is a generic \( N(0,1) \) random variable, corresponds to the risk of the suboptimal procedure in which one insists on not stopping between \( s_{\infty} + \delta \) and \( s_{\infty} \) but proceeding optimally thereafter. So,

$$\rho(w_{1\infty}, w_{2\infty}, s_{\infty} + \delta) \leq E[\rho(w_{1\infty} + Z\sqrt{\delta}, w_{2\infty}, s_{\infty})].$$

But

$$\rho(w_{1\infty} + Z\sqrt{\delta}, w_{2\infty}, s_{\infty})$$

$$= \begin{cases} 
\rho(w_{1\infty}, w_{2\infty}, s_{\infty}) + Z\sqrt{\delta} \rho_{w_1}^+ (w_{1\infty}, w_{2\infty}, s_{\infty}) + o(\delta), & Z > 0, \\
\rho(w_{1\infty}, w_{2\infty}, s_{\infty}) + Z\sqrt{\delta} \rho_{w_1}^- (w_{1\infty}, w_{2\infty}, s_{\infty}) + o(\delta), & Z < 0.
\end{cases}$$

$$E[\rho(w_{1\infty} + Z\sqrt{\delta}, w_{2\infty}, s_{\infty})]$$

$$= \rho(w_{1\infty}, w_{2\infty}, s_{\infty}) + \sqrt{\delta}/2\pi (r_{w_1} (w_{1\infty}, w_{2\infty}, s_{\infty}) - \rho_{w_1}^- (w_{1\infty}, w_{2\infty}, s_{\infty}))$$

$$+ o(\sqrt{\delta}).$$

Thus,

$$\rho(w_{1\infty}, w_{2\infty}, s_{\infty} + \delta) - \rho(w_{1\infty}, w_{2\infty}, s_{\infty})$$

$$\leq \sqrt{\delta}/2\pi (r_{w_1} (w_{1\infty}, w_{2\infty}, s_{\infty}) - \rho_{w_1}^- (w_{1\infty}, w_{2\infty}, s_{\infty}))$$

Assuming that \( (\rho(w_{1\infty}, w_{2\infty}, s_{\infty} + \delta) - \rho(w_{1\infty}, w_{2\infty}, s_{\infty})) / \delta \) is bounded away
from $-\alpha$, it follows that \( r_{w_1, w_2, s_{1\star}, s_{2\star}} - \rho_{w_1, w_2, s_{1\star}, s_{2\star}} \geq 0 \), and then establishes (2.4.2). Similarly, we can verify the expression (2.4.3).  

The partial differential equations in the Theorem 2.4.1 might not have the unique solution. Shepp (1969) discusses a stopping problem and obtains two solutions from the partial differential equations which are the necessary conditions for the optimal rule. He shows that one solution is better than another. Perhaps under some additional conditions, the partial differential equations have the unique solutions. Thus, a solution based on the differential equations in the theorem might not be a solution of our optimal stopping problem. The boundary of the optimal continuation region is calculated in Chapter III numerically without using the result of Theorem 2.4.1.

2.5 Parameter-Free Problem

The transformation

\[
W^*(s) = aW_1(s),
\]

\[
W^*(s) = aW_2(s),
\]

and

\[
s^* = \frac{2}{a}s
\]

converts \( W_1(s) \) and \( W_2(s) \) to \( W_1^*(s^*) \) and \( W_2^*(s^*) \) which are also two
independent Wiener processes of independent increments in the \( -s^w \) scale with

\[
E \begin{bmatrix}
   dW^w_1(s^w) \\
   dW^w_2(s^w)
\end{bmatrix} = \begin{bmatrix}
   0 \\
   0
\end{bmatrix},
\]

and

\[
\text{Var} \begin{bmatrix}
   dW^w_1(s^w) \\
   dW^w_2(s^w)
\end{bmatrix} = \begin{bmatrix}
   -a^2ds & 0 \\
   0 & -a^2ds
\end{bmatrix} = \begin{bmatrix}
   -ds^w & 0 \\
   0 & -ds^w
\end{bmatrix}.
\]

Since the function, \( f \), is homogeneous with degree 1, if \( a \) is such that \( a^2s_t = 1 \), the stopping risk, \( r(w_1, w_2, s) \), will be transformed to \( b_1(w_1^w, w_2^w, s^w) \), where

\[
b_1(w_1^w, w_2^w, s^w) = s_t^{-1/2} (1/s^w - 1)f(w_1^w, w_2^w).
\]

Hence, the original problem is equivalent to the parameter-free problem for which the stopping risk corresponding to the stopping at \( (w_1^w, w_2^w, s^w) \) is

\[
b(w_1^w, w_2^w, s^w) = (1/s^w - 1)f(w_1^w, w_2^w).
\]

Note that

\[
(s_n^w)^{-1} = (a^2_s n)^{-1} = (\sigma^2_n^{-2} + n)/(\sigma^2_n^{-2} + n/3)
\]

means the currently available proportion of the total potential information.

The advantages of the parameter-free approach is the enforcement of stopping when \( s^w = 1 \); this point is not affected by the total
number of patients \( N \). Since the risk function \( b(w^1, w^2, s^*) \) only depends on the time variable and two spatial variables, the solution can be applied to any case with specified parameters: \( \sigma, \sigma^* \) and \( N \).

The relationships between the new variables: \( W_n^*, W_n^1, W_n^2, s_n^* \) and the original variables: \( X_{j_1}^* \)'s, \( j = 0, 1, 2; j_1 = 1, 2, 3, \ldots, n \) are summarized as the following:

\[
\begin{align*}
W_{n1}^* &= s_n (n\sigma^* - \frac{2}{n2} (\bar{X}_{n2} - \bar{X}_{n1}) + \frac{3}{2} (\mu_2 - \mu_1)) / \sqrt{2s_n^*}, \\
W_{n2}^* &= s_n (n\sigma^* - \frac{2}{n2} (\bar{X}_{n1} + \bar{X}_{n2} - 2\bar{X}_{n0}) + \frac{3}{2} (\mu_1 + \mu_2 - 2\mu_0)) / \sqrt{6s_n^*}, \\
s_n^* &= (\sigma^2 + (N/3)/\sigma^2 + n)^{-1}.
\end{align*}
\]

where \( \bar{X}_{nj} = \sum_{i=1}^{j} X_{j_1} \), \( j = 0, 1, 2 \),

\[
s_n = (\sigma^* - 2 + n\sigma^{-2})^{-1}, \quad \text{and}
\]

\[
s_t = (\sigma^* - 2 + (N/3)\sigma^{-2})^{-1}.
\]

The second part of the stopping risk at time "n" in (2.3.3):

\[-(N-3n) E_n (\theta - (\theta_0 + \theta_1 + \theta_2)/3),\]

is equal to

\[\sigma^2 b(W_{n1}^*, W_{n2}^*, s_n^*) / \sqrt{s_t}.\]

Since stopping is enforced at \( s^* = 1 \), backward induction can be applied to solve the optimal stopping time of a discrete version of the problem. If a good approximation to the difference between the solution of the continuous time problem and that of discrete version is available, one discrete version could be solved numerically. Its
solution, properly adjusted, can be used to approximate the solution of the continuous problem as well as those of other discrete versions.

In summary, the set of possible stopping times of the original problem is:

\[ \{s^*_0, s^*_1, \ldots, s^*_t=1\} \]

in which \( |s^*_1 - s^*_1| \) decreases in \( i \). For the continuous time problem, the stopping may occur at any point in the interval:

\[ [1,s^*_0] \]

A natural approximation to the results of these problems arises by allowing stopping on a discrete set of possible values of \( s^*_t \):

\[ \{1+i\Delta, i = 0, 1, \ldots\} \]

So that, the backward induction is more forward straight.

Figure 2.5.1 gives an example of the scales of the time variable \( s^*_t \) for all the versions of the problem discussed above.
Figure 2.5.1: The Scales of the Time Variable $S^*$

(a) The original problem

(b) The continuous version

(c) The discrete version with the possible stopping times equally spaced
2.6 **A 2-Dimensional Random Walk**

An important factor in solving a problem numerically is the amount of computing time it will consume. Based on the fact that a simple random walk converges in distribution to a corresponding Brownian motion (Theorem 16.1 of Billingsley (1968)), a 2-dimensional random walk process is used to replace the original two Gaussian processes. This results in a simpler backward induction algorithm. The increments of the random walk are chosen to have the same first two moments as those of the increments they are replacing. If the discrete version of the original problem, in which the spacing of $s^N$ is $\Delta$, is considered then the following is the chosen simple random walk process:

Let $(V_1(s), V_2(s))$ be a random walk in two dimensions starting at $(0,0)$, where 

$$(V_1(s-\Delta), V_2(s-\Delta)) = (V_1(s)+\sqrt{2\Delta}, V_2(s)) \text{ or } (V_1(s), V_2(s)+\sqrt{2\Delta})$$

each with probability $1/4$. Stopping is permitted on the discrete set of possible values of $s$, $\{1+i\Delta, i = 0, 1, 2, \cdots \}$. The risk associated with the stopping on $(v_1, v_2, s)$ is

$$b(v_1, v_2, s) = (1/s - 1)f(v_1, v_2),$$

(2.6.1)

where function $f$ is defined by (2.3.6).
Define

\[(2.6.2) \quad \hat{b}(v_1, v_2, s) = \min\{ b(v_1, v_2, s), [\hat{b}(v_1 - \sqrt{2A} \cdot v_2, s - \Delta) + \hat{b}(v_1 + \sqrt{2A} \cdot v_2, s - \Delta) + \hat{b}(v_1, v_2 - \sqrt{2A} \cdot s - \Delta) + \hat{b}(v_1, v_2 + \sqrt{2A} \cdot s - \Delta)]/4 \}.\]

Then \((v_1, v_2, s)\) is an optimal continuation point if

\[\hat{b}(v_1, v_2, s) < b(v_1, v_2, s);\]

otherwise, it is a stopping point.

Denote by \(C_s\) and \(T_s\) the set of continuation points and stopping points respectively for a fixed time \(s\). Following the definition of the last continuation point in Chernoff and Petkau (1984), we would call \((v_1, v_2, s)\) a last continuation point if \((v_1 - \sqrt{2A} \cdot v_2, s)\) is a continuation (stopping) point and \((v_1 + \sqrt{2A} \cdot v_2, s)\) is a stopping (continuation) point. Let \(L_s\) be the set of last continuation points for a fixed time \(s\). Then, \(L_s\) characterizes \(C_s\) and \(T_s\). The next chapter discusses a numerical method for finding \(L_s\) for a specified value of \(s\).
CHAPTER III
NUMERICAL SOLUTIONS OF A 2-DIMENSIONAL RANDOM WALK

3.1 Introduction

The main result of this chapter is a numerical solution of the set of the last optimal continuation points at a fixed time $s$, denoted by $L_s$, for a simple 2-dimensional random walk. The 2-dimensional random walk considered here, the risk associated with the stopping on $(v_1,v_2,s)$, and the optimal stopping rule are defined in the previous chapter. A grid point $(v_1,v_2,s)$ is called a last continuation point if it is a continuation point and satisfies one of the following conditions:

1. The grid point $(v_1-\sqrt{2\lambda},v_2,s)$ is a continuation point and $(v_1+\sqrt{2\lambda},v_2,s)$ is a stopping point.

2. The grid point $(v_1+\sqrt{2\lambda},v_2,s)$ is a continuation point and $(v_1-\sqrt{2\lambda},v_2,s)$ is a stopping point.

The direct solution involves checking all the grid points in the $(V_1,V_2)$ plane, $\{(v_1,v_2): v_1 = 0 \pm i\sqrt{2\lambda}, v_2 = 0 \pm i\sqrt{2\lambda}, i = 1, 2, \ldots \}$, individually. This is very computationally intensive. If the number of grid points necessary to be considered can be reduced, we can save the computing time. Section 3.2 is devoted to describes the properties of $L_s$ which might be applied to reduce computation time.
The numerical techniques to determine \( L_s \) for a fixed time \( s \) will be discussed in Section 3.3. Section 3.4 gives an example to illustrate the use of this sequential clinical trials model.

### 3.2 The Properties of the Set of the Last Continuation Points

The symmetry of \( L_s \) stated in Proposition 3.2.1 can be derived directly from the symmetry of the stopping risk \( b(v_1, v_2, s) \), which is defined by (2.6.1).

**Proposition 3.2.1.** For a fixed time \( s \), \((v_1, v_2)\) is an optimal continuation point (an optimal stopping point), iff \((-v_1, v_2)\) is an optimal continuation point (an optimal stopping point).

**Proof:** The proof follows directly from:

\[
b(v_1, v_2, s) = b(-v_1, v_2, s),
\]

for all real \( v_1, v_2 \), and \( s > 0 \).

\[\square\]

More symmetry can be obtained for our original problem, in which two independent Gaussian processes are involved. Denote by \( C_\infty \) the optimal continuation region for the problem. Let \((w_1, w_2, s)\) be a specific point of \((W_1(s), W_2(s), s)\). If \((w_1, w_2, s)\) is on the boundary of \( C_\infty \), there are five other points on the boundary of \( C_\infty \) which can be determined by simply switching the roles of the three treatments. The reason is that all three treatments are on the same footing in the established model. In other words, at a fixed time \( s \), there are six possible conclusions. The plane \((W_1, W_2)\) can be divided into six parts, each corresponding to an appropriate (Bayesian) conclusion if the
testing stage is stopped at time $s$. For example, the region

$$G_1 = \{ (w_1, w_2) : w_1 - \sqrt{3} w_2 \leq 0 \text{ and } w_1 \geq 0 \}$$

corresponds to the conclusion treatment $B$ is the best, $A$ is the second best, and the standard treatment is the worst. Therefore, if the boundary of $C_\infty$ in the region $G_1$ is determined, the boundary of $C_\infty$ in the remaining regions can be solved by interchanging the three treatments. The following result describes the symmetry for the original problem.

**Proposition 3.2.2.** Let $(W_1(s), W_2(s))$ be two independent Gaussian processes. The stopping risk associated with stopping at $(w_1, w_2, s)$ is $b(w_1, w_2, s)$. Then, at a fixed time $s$, if $(w_1, w_2)$ is an optimal continuation (stopping) point then so too are $(w_1, w_2)$, $(w_1/2 + \sqrt{3} w_2/2, \sqrt{3} w_1/2 - w_2/2)$, $(-w_1/2 - \sqrt{3} w_2/2, \sqrt{3} w_1/2 - w_2/2)$, $(-w_1/2 + \sqrt{3} w_2/2, -\sqrt{3} w_1/2 - w_2/2)$, and $(w_1/2 - \sqrt{3} w_2/2, -\sqrt{3} w_1/2 - w_2/2)$.

**Proof:** Let

- $G_1 = \{ (w_1, w_2) : w_1 - \sqrt{3} w_2 \leq 0 \text{ and } w_1 \geq 0 \}$;
- $G_2 = \{ (w_1, w_2) : w_1 - \sqrt{3} w_2 \geq 0 \text{ and } w_1 + \sqrt{3} w_2 \geq 0 \}$;
- $G_3 = \{ (w_1, w_2) : w_1 + \sqrt{3} w_2 \leq 0 \text{ and } w_1 \geq 0 \}$;
- $G_4 = \{ (w_1, w_2) : w_1 + \sqrt{3} w_2 \geq 0 \text{ and } w_1 \leq 0 \}$;
- $G_5 = \{ (w_1, w_2) : w_1 - \sqrt{3} w_2 \leq 0 \text{ and } w_1 + \sqrt{3} w_2 \leq 0 \}$;
- $G_6 = \{ (w_1, w_2) : w_1 - \sqrt{3} w_2 \geq 0 \text{ and } w_1 \leq 0 \}$.

At time $s_n$, $(W_1(s_n), W_2(s_n)) \in G_1$ is equivalent to:

$$E_n(\theta_2) \geq E_n(\theta_1) \geq E_n(\theta_0).$$
Similarly, $(W_1(s_n), W_2(s_n)) \in G_2$ is equivalent to:

$$E_n(\theta_2) \geq E_n(\theta_0) \geq E_n(\theta_1).$$

Thus, the role of treatment B in $G_2$ is the same as the role of treatment B in $G_1$; the role of treatment A in $G_2$ is the role of standard treatment in $G_1$; the role of standard treatment in $G_2$ is the role of treatment A in $G_1$.

Assume $(W_1(s_n), W_2(s_n)) = (w_{n_1}, w_{n_1})$ is an optimal continuation (stopping) point in $G_1$. Then, by interchanging standard treatment and treatment A, there is a corresponding optimal continuation (stopping) point in $G_2$ given by

$$E_n[\left(\frac{\theta_2 - \theta_0}{\sqrt{2}}, \frac{\theta_0 + \theta_2 - 2\theta_1}{\sqrt{6}}\right)]$$

$$= (\frac{w_{n_1}}{2 + \sqrt{3}} w_{n_2}/2, \sqrt{3} \frac{w_{n_1}}{2 - w_{n_2}/2}).$$

Note that

$$(w_{n_1}, w_{n_2})$$

$$= E_n[\left(\frac{\theta_2 - \theta_1}{\sqrt{2}}, \frac{\theta_1 + \theta_2 - 2\theta_0}{\sqrt{6}}\right)].$$

Similarly, there is a corresponding optimal continuation (stopping) point in $G_3$ which is

$$E_n[\left(\frac{\theta_1 - \theta_0}{\sqrt{2}}, \frac{\theta_1 + \theta_0 - 2\theta_2}{\sqrt{6}}\right)]$$

$$= (\frac{w_{n_1}}{2 + \sqrt{3}} w_{n_2}/2, -\sqrt{3} \frac{w_{n_1}}{2 - w_{n_2}/2}).$$
a corresponding optimal continuation (stopping) point in $G_4$ which is

$$E_n[(\theta_1 - \theta_2)\sqrt{2}, (\theta_2 + \theta_1 - 2\theta_0)\sqrt{6}]$$

$$= (-w_{n1}, w_{n2});$$

a corresponding optimal continuation (stopping) point in $G_5$ which is

$$E_n[(\theta_0 - \theta_2)\sqrt{2}, (\theta_2 + \theta_0 - 2\theta_1)\sqrt{6}]$$

$$= (-w_{n1}/2 - \sqrt{3} w_{n2}/2, \sqrt{3} w_{n1}/2 - w_{n2}/2);$$

and a corresponding optimal continuation (stopping) point in $G_6$ which is

$$E_n[(\theta_0 - \theta_1)\sqrt{2}, (\theta_1 + \theta_0 - 2\theta_2)\sqrt{6}]$$

$$= (w_{n1}/2 - \sqrt{3} w_{n2}/2, -\sqrt{3} w_{n1}/2 - w_{n2}/2).$$

This result does not apply to the case involving the 2-dimensional random walk, since the grid points considered by the random walk do not reflect the symmetry. The next two results, Proposition 3.2.3 and Proposition 3.2.4, are very useful for computing last continuation points.

The rest of this section concerns only the case involving the 2-dimensional random walk. In Section 2.6, the optimal stopping rule
is defined and \((v_1, v_2, s)\) is defined to be an optimal continuation point if the following inequality is true:

\[
\hat{b}(v_1, v_2, s) < b(v_1, v_2, s),
\]

where \(b(v_1, v_2, s)\) and \(\hat{b}(v_1, v_2, s)\) are defined by (2.6.1) and (2.6.2), respectively.

To verify Proposition 3.2.3, we make the following transformation on \(\hat{b}(v_1, v_2, s)\):

\[
\hat{e}(v_1, v_2, s_n) = \begin{cases} 
0 & \text{if } n = 0, \\
\frac{\hat{b}(v_1, v_2, s_n)}{g(s_n)} & \text{otherwise}.
\end{cases}
\]

Note that

\[
\frac{\hat{b}(v_1, v_2, s_n)}{g(s_n)} = \min(-f(v_1, v_2), a_n[\hat{e}(v_1^-\sqrt{2A}, v_2, s_{n-1}) + \hat{e}(v_1^+\sqrt{2A}, v_2, s_{n-1}) \\
+ \hat{e}(v_1, v_2^-\sqrt{2A}, s_{n-1}) + \hat{e}(v_1, v_2^+\sqrt{2A}, s_{n-1})])/4 \}
\]

where \(s_n = 1 + n\Delta\) and \(a_n = g(s_{n-1})/g(s_n)\).

This transformation converts the stopping rule to: stop as soon as

\[
\hat{e}(V_1(s), V_2(s), s) = -f(V_1(s), V_2(s)).
\]

The next lemma leads to the result of Proposition 3.2.3.

**Lemma 3.2.1.**

\[a_{n+1} \hat{e}(v_1, v_2, s_n)\] is nondecreasing in \(n\), for \(n = 1, 2, \ldots\).
Proof: The proof proceeds by induction on n. First, the following inequality must be proved:

\[(3.2.1) \quad a_3 \hat{e}(v_1, v_2, s_2) \leq a_2 \hat{e}(v_1, v_2, s_1) = a_2[-f(v_1, v_2)].\]

By the definition of \(\hat{e}(v_1, v_2, s_n)\),

\[\hat{e}(v_1, v_2, s_2) \leq -f(v_1, v_2).\]

Since \(a_n\) is nonnegative and nondecreasing in n,

\[(3.2.2) \quad a_3[-f(v_1, v_2)] \leq a_2[-f(v_1, v_2)].\]

So, the lemma is true for \(n = 1\).

For the induction step, the following must be proved:

If

\[a_{n+1} \hat{e}(v_1, v_2, s_{n}) \leq a_n \hat{e}(v_1, v_2, s_{n-1}) \text{ for } n = 3, 4, \ldots, k,\]

then

\[a_{k+1} \hat{e}(v_1, v_2, s_{k}) \leq a_k \hat{e}(v_1, v_2, s_{k-1}).\]

Case 1: \(\hat{e}(v_1, v_2, s_n) = -f(v_1, v_2), n = k-1, k.\)

It is obvious that

\[a_{k+1} \hat{e}(v_1, v_2, s_k) = a_{k+1}[-f(v_1, v_2)] \leq a_k[-f(v_1, v_2)] = a_k \hat{e}(v_1, v_2, s_{k-1})\]

since \(a_n\) is nondecreasing in n.
Case 2: \( \hat{e}(v_1, v_2, s_n) \)

\[
= \frac{1}{4} a_n \left[ \hat{e}(v_1 - \sqrt{2A}, v_2, s_{n-1}) + \hat{e}(v_1 + \sqrt{2A}, v_2, s_{n-1}) + \hat{e}(v_1, v_2 - \sqrt{2A}, s_{n-1}) + \hat{e}(v_1, v_2 + \sqrt{2A}, s_{n-1}) \right], \quad n = k-1, k.
\]

Since

\[
a_k \hat{e}(u_1, u_2, s_{k-1}) \leq a_{k-1} \hat{e}(u_1, u_2, s_{k-2}), \quad \forall \ u_1, u_2,
\]

and \( a_n \) is nondecreasing in \( n \),

\[
a_{k+1} a_k \hat{e}(u_1, u_2, s_{k-1}) \leq a_k a_{k-1} \hat{e}(u_1, u_2, s_{k-2}), \quad \forall \ u_1, u_2.
\]

Thus,

\[
a_{k+1} \hat{e}(v_1, v_2, s_k) \leq a_k \hat{e}(v_1, v_2, s_{k-1}).
\]

Case 3: \( \hat{e}(v_1, v_2, s_{k-1}) = \frac{1}{4} a_{k-1} \left[ \hat{e}(v_1 - \sqrt{2A}, v_2, s_{k-2}) + \hat{e}(v_1 + \sqrt{2A}, v_2, s_{k-2}) + \hat{e}(v_1, v_2 - \sqrt{2A}, s_{k-2}) + \hat{e}(v_1, v_2 + \sqrt{2A}, s_{k-2}) \right], \quad \text{and}
\]

\[
\hat{e}(v_1, v_2, s_k) = -f(v_1, v_2).
\]

By the definition of \( \hat{e}(v_1, v_2, s_n) \), we know

\[
\hat{e}(v_1, v_2, s_k) \leq \frac{1}{4} a_k \left[ \hat{e}(v_1 - \sqrt{2A}, v_2, s_{k-1}) + \hat{e}(v_1 + \sqrt{2A}, v_2, s_{k-1}) + \hat{e}(v_1, v_2 - \sqrt{2A}, s_{k-1}) + \hat{e}(v_1, v_2 + \sqrt{2A}, s_{k-1}) \right].
\]

Together with the arguments in Case 2, we get

\[
a_{k+1} \hat{e}(v_1, v_2, s_k) \leq a_k \hat{e}(v_1, v_2, s_{k-1}).
\]
Case 4: $\hat{e}(v_1, v_2, s_{k-1}) = -f(v_1, v_2)$, and

$$
\hat{e}(v_1, v_2, s_k) = \frac{1}{4} a_k \left[ \hat{e}(v_1 - \sqrt{2A}, v_2, s_{k-1}) + \hat{e}(v_1 + \sqrt{2A}, v_2, s_{k-1}) + \hat{e}(v_1, v_2 - \sqrt{2A}, s_{k-1}) + \hat{e}(v_1, v_2 + \sqrt{2A}, s_{k-1}) \right].
$$

It is obvious that $\hat{e}(v_1, v_2, s_k) \leq -f(v_1, v_2)$. Since $a_{k+1} \geq a_k \geq 0$, we have

$$a_{k+1} \hat{e}(v_1, v_2, s_k) \leq a_{k+1} [-f(v_1, v_2)] \leq a_k [-f(v_1, v_2)] = a_k \hat{e}(v_1, v_2, s_{k-1}).$$

By the optimal stopping rule, $(v_1, v_2, s)$ is an optimal continuation point if

$$\hat{e}(v_1, v_2, s_n) < -f(v_1, v_2).$$

By the result of Lemma 3.2.1, the Bayes risk, $\hat{e}(v_1, v_2, s_n)$ is nonincreasing in $n$. Thus, if

$$\hat{e}(v_1, v_2, s_{n-1}) < -f(v_1, v_2),$$

then

$$\hat{e}(v_1, v_2, s_n) < -f(v_1, v_2).$$

In other words, if $(v_1, v_2)$ is an optimal continuation point at time $s = s_{n-1}$, $(v_1, v_2) \in C_n$ is an optimal continuation point at time $s = s_n$. Hence, we establish the following result.
Proposition 3.2.3.

\( C_n \) is nondecreasing in \( n \), where \( C_n \) is the set of the optimal continuation points when \( s = s_n \).

Proof: The proof follows directly from the above argument.

In general, the above result is true for a sequential stopping problem involving the 2-dimensional random walk process described above, if the stopping risk associated with a grid point, \( (u_1, u_2, t) \) say, can be expressed as \(-h(t)q(u_1, u_2)\) such that:

1. \( h(t) \) is nonnegative and log concave;
2. \( q(u_1, u_2) \) is nonnegative and "informative".

(For example, if \( q(u_1, u_2) \) is a constant function, it is not "informative".)

By Proposition 3.2.3, all the points, \( (v_1, v_2) \)'s, which are continuation points at time \( s_n \), would be continuation points at time \( s_{n+1} \). Thus, the number of points which must be examined to determine whether they are continuation points or stopping points, is reduced.

Recall the decision rule discussed in Section 2.3. The standard treatment will be used on the remaining patients if we decide to stop allocating patients at time \( s_n \) and the observed posterior mean of the chosen contrasts, \((W_1^{*}(s_n), W_2^{*}(s_n))\), is in the region \( T_0 \). Similarly, new treatment A (B) will be selected if the observed \((W_1^{*}(s_n), W_2^{*}(s_n))\) is in the region \( T_1 \) (or \( T_2 \)), where

\[
T_0 = \{(x, y) : x + \sqrt{3}y \leq 0 \text{ and } x - \sqrt{3}y \geq 0\}.
\]

(3.2.3) \[
T_1 = \{(x, y) : x \leq 0 \text{ and } x - \sqrt{3}y \leq 0\}, \quad \text{and}
\]
\[
T_2 = \{(x, y) : x \geq 0 \text{ and } x + \sqrt{3}y \geq 0\}.
\]
Here, the inverse of time $s_n$, $1/s_n$, means the proportion of patients that have been allocated.

The following property tells us that a grid point $(v_1,v_2)$ is a stopping point at time $s_n$, if all its four adjacent grid point are stopping points at the previous step and in the region $T_0$ (or $T_1$ or $T_2$).

**Proposition 3.2.4.** If $(v_1 \pm \sqrt{2A}, v_2)$ and $(v_1, v_2 \pm \sqrt{2A})$ are stopping points at time $s_n-1$ and in the region $T_i$, $i = 0, 1, 2$, then $(v_1, v_2)$ is a stopping point at $s_n$.

**Proof:** The points $(v_1 \pm \sqrt{2A}, v_2)$ and $(v_1, v_2 \pm \sqrt{2A})$ are stopping points at time $s_n-1$. Then,

$$\hat{e}(v_1,v_2,s_n) = \min\{-f(v_1,v_2), -a_n f(v_1,v_2)\}.$$

We know that $0 < a_n < 1$ for all $n$ and $f(v_1,v_2) \geq 0$ for all $v_1, v_2$. Therefore, $-f(v_1,v_2) < -a_n f(v_1,v_2)$ and $(v_1,v_2)$ is a stopping point at time $s_n$.

Suppose by the current information it is known that we will stop at the next step and make a decision. The decision is the same as that we will make at the current step if stopping is chosen. Then we should stop at the current step because there is no need to go one step further. The above is what Proposition 3.2.4 states. The next result is strongly supported by computer-generated numerical evidence, and intuition, but remains unproven.
Conjecture 3.2.1. If at time $s_n$, $n = 0, 1, 2, \ldots$, $(v_1, v_2)$ is an optimal stopping point in the region $T_2$, then the points $(v_1 + \sqrt{2\Lambda}, v_2)$ and $(v_1, v_2 + \sqrt{2\Lambda})$ are stopping points, too.

Proposition 3.2.5. Assume the distance of the time steps $\Delta$ is greater than $(2\sqrt{3} - 3)/6$. Then,

\[ (0, v_2): v_2 \geq a_n \sqrt{2\Delta}, \quad a_n = \sqrt{3} (n-1)(1+n\Delta)/2 \]

are optimal stopping points at time, $s_n$, $n = 2, 3, \ldots$. Proof: At time $s_2$,

\[ (0, v_2): v_2 \geq \sqrt{2\Delta} \]

are optimal stopping points if

\[ b(0, v_2, s_2) \leq E \{ \hat{b}(0 + R_1 \sqrt{2\Delta}, v_2 + R_2 \sqrt{2\Delta}, s_1) \} \]

where $(R_1, R_2) = (0, \pm 1)$ or $(\pm 1, 0)$ each with probability $1/4$. Since

\[ \hat{b}(v_1, v_2, s_1) = b(v_1, v_2, s_1) \vee v_1, v_2 \]

$(0, v_2)$ is an optimal stopping point when

\[ v_2 \geq \sqrt{3}(1+2\Delta)\sqrt{2\Delta}/2 \geq \sqrt{2\Lambda} \]

This is equivalent to saying $(0, v_2)$ is an optimal stopping point when

\[ v_2 \geq a_2 \sqrt{2\Lambda} \]

for $\Lambda \geq (2\sqrt{3} - 3)/6$. 

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Now assume \((0,v_2)\) is an optimal stopping point at \(s_k\), \(k = 3, 4, \ldots, m-1\), if

\[ v_2 \geq a_k \sqrt{2A} \]

where \(A \geq (2\sqrt{3} - 3)/6\). Then, at time \(s_m\),

\[ ((0, v_2): v_2 \geq (a_{m-1} + 1)\sqrt{2A}) \]

are stopping points if

\[ (3.2.3) \quad b(0,v_2,s_m) \geq E \left[ b(0+R_1, \sqrt{2A}, v_2+R_2 \sqrt{2A}, s_{m-1}) \right] \]

\[ = E \left[ b(0+R_1, \sqrt{2A}, v_2+R_2 \sqrt{2A}, s_{m-1}) \right] \]

where \((R_1, R_2) = (0, \pm 1)\) or \((\pm 1, 0)\) each with probability \(1/4\).

The inequality, \(3.2.3\), is equivalent to

\[ v_2 \geq a_m \sqrt{2A} \]

If \(A \geq (2\sqrt{3} - 3)/6\),

\[ a_m \geq a_{m-1} + 1 \]

Hence, the proof is complete.

\[ \square \]

Proposition 3.2.5 provides the growth rate in \(s\) of the continuation region in the \(V_2\) direction when the distance of the time steps \(A\) is large enough. The growth rate is a factor of the square of the number of time steps between \(s=1\) and the current step. Note that

\[ W_{n2} = E_n \left[ (\theta_1 + \theta_2 - 2\theta_0)/\sqrt{6} \right] \]

Thus, the inferiority of the standard treatment to one of the new treatments is quantified by the magnitude of \(W_{n2}\). Specifically, if \(W_{n1}\)
is 0, i.e., if based on the available information the two new treatments have the same effects, then the magnitude of $\mathbb{W}_{n2}$ can tell how much the standard treatment is worse than both of the two new treatments. Because of this, the continuation region grows quickly in $s$ in the $V_2$ direction. Equivalently, the continuation region is reducing very fast in the $V_2$ direction in $1/s$ which means the currently available proportion of total potential information.

The next proposition describes the relationship between the optimal continuation regions which are obtained by using different spacings of the time variable $s$.

**Proposition 3.2.6.** Let $C_{s,1}$ be the set of the optimal continuation point at time $s$ corresponding to the grid spacing (the step size) $\Lambda_1$. Then at any fixed time $s$

$$C_{s,1} \subset C_{s,2} \subset C_{s,3} \subset \ldots;$$

if $\Lambda_i = \Lambda_1/(4^{i-1})$, $i = 1, 2, 3, \ldots$.

**Proof:** The proof is immediate because the optimal stopping rule, corresponding to the grid spacing $\Lambda_1$, is a suboptimal stopping rule, corresponding to the grid spacing $\Lambda_{i+1}$. \(\square\)

Figure 3.2.1 illustrates the result of Proposition 3.2.6 using $\Lambda_1 = 0.125$ and $s = 12$. 

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Figure 3.2.1: The Last Continuation Points at s=3
(Considering Different Time Variable Spacings)
3.3 The Numerical Techniques

This section describes the techniques employed in obtaining numerical descriptions of the last optimal continuation points. The results established in Section 3.2 allow the computational effort to be substantially reduced.

Section 3.3.1 discusses how those results are applied in programming. Section 3.3.2 discusses some programming techniques for handling huge matrices, and an alternative algorithm to what is described in Section 3.3.1. An interpolating method is described in Section 3.3.3 which reduce the computer time required for small grid spacings.

3.3.1 Programming Techniques

First recall the stopping risk and the Bayes risk associated at a specific point \((v_1, v_2, s)\). Let

\[
 f(v_1, v_2) = -\sqrt{6} v_2 I_T(v_1, v_2) + ((\sqrt{6} v_2 - 3\sqrt{2} v_1)/2) I_{T_1}(v_1, v_2) \\
 + ((\sqrt{6} v_2 + 3\sqrt{2} v_1)/2) I_{T_2}(v_1, v_2),
\]

where \(I_T\) is the indicator of the set \(T\), and \(T_0, T_1\) and \(T_2\) are defined by (3.2.3).

Then the stopping risk at \((v_1, v_2, s)\) is

\[
 (3.3.1.1) \quad b(v_1, v_2, s) = (1/s - 1)f(v_1, v_2).
\]
The Bayes risk associated with the optimal stopping rule at \((v_1, v_2, s)\) is:

\[
\hat{b}(v_1, v_2, s) = \min\{ b(v_1, v_2, s), E[\hat{b}(v_1 + R_1 \sqrt{2\Delta}, v_2 + R_2 \sqrt{2\Delta}, s - \Delta)] \}
\]  

where \((R_1, R_2) = (\pm 1, 0)\) or \((0, \pm 1)\) each with probability 1/4, respectively.

As discussed in Section 2.6, \((v_1, v_2, s)\) is an optimal continuation point if

\[
\hat{b}(v_1, v_2, s) < b(v_1, v_2, s);
\]

otherwise, it is an optimal stopping point.

The backward induction algorithm yields the optimal solution to the stopping problem, since stopping is enforced when \(s = 1\). Actually, the testing stage will not continue after \(s = 1 + \Delta\), since

\[
b(v_1, v_2, 1 + \Delta) < 0 = \hat{b}(v_1, v_2, 1 + \Delta).
\]

Two programs, say D (direct) and F (fast), are coded in the computer language C with the backward induction algorithm to solve the last continuation points numerically. Conjecture 3.2.1 is applied in both programs. A direct algorithm, i.e., checking every grid point until Conjecture 3.2.1 can be applied, is used in program D. Program F is more efficient by applying Propositions 3.2.3 and 3.2.4.

The basic features of the programs D and F are:

(a) Two matrices store the risk, one for the previous step, and one for the current step.
(b) updating the risk occurs only at the grid points which are in the optimal continuation region;

(c) grid points are chosen symmetrically with respect to the line \( V_1 = 0 \);

(d) deciding the number of the grid points, which need to complete the computation to justify whether the inequality (3.3.1.3) is satisfied before they can be classified as continuation points or stopping points at each time step.

By (3.3.1.2), the Bayes risk at a specified point can be computed directly by recursive method, but it requires heavy expenditures of memory and time. To calculate \( \hat{b}(v_1, v_2, 1+i\Delta) \), it is necessary to know \( \hat{b}(v_1+\sqrt{2\Delta}, v_2, 1+(1-1)i\Delta) \), \( \hat{b}(v_1, v_2+\sqrt{2\Delta}, 1+(1-1)i\Delta) \) and \( b(v_1, v_2, 1+i\Delta) \).

Thus, in order to compute \( \hat{b}(v_1, v_2, 1+n\Delta) \), one must first calculate and store

\[
\sum_{i=0}^{n-1} 5(4^i)
\]

numerical values.

To avoid the demands in computer space and time of using recursion, two matrices are used in both programs. The matrices are used to store the risk for the previous step and the current step, respectively. The risk corresponding to a specific grid point at a specific time step can be calculated using the two matrices, because the risk at the current step depends only on the risk at the previous step. To calculate \( \hat{b}(v_1, v_2, 1+i\Delta) \), it is only necessary to compute \( b(v_1, v_2, 1+i\Delta) \). The numerical values of \( \hat{b}(v_1+\sqrt{2\Delta}, v_2, 1+(1-1)i\Delta) \), \( \hat{b}(v_1, v_2+\sqrt{2\Delta}, 1+(1-1)i\Delta) \) are stored in the matrix. Therefore, compared
to recursive method, the use of two matrices saves computer time and memory.

It is obvious, when s = 1, that all the grid points are stopping points and the stopping risk at each grid point is 0. For convenience, let \( s_1 = 1 + i \Delta \). Then, (3.3.1.4) implies that at \( s = s_1 \),

\[
\hat{b}(v_1, v_2, s_1) = b(v_1, v_2, 1 + \Delta), \quad \forall v_1, v_2.
\]

In other words, when \( s = s_1 \), all the grid points are stopping points, too.

Denote by PS and CS the matrices for storing the risks of the previous step and the current step, respectively. At time \( s = s_2 \) each cell of the matrix PS is determined by the function \( b(v_1, v_2, 1 + \Delta) \). Naturally, the matrix CS should be determined by:

\[
\hat{b}(v_1, v_2, s_2)
\]

\[
= \min \{ b(v_1, v_2, 1 + 2\Delta), \, E[\hat{b}(v_1 + R_1 \sqrt{2\Delta}, v_2 + R_2 \sqrt{2\Delta}, 1 + \Delta)] \}.
\]

\[
= \min \{ b(v_1, v_2, 1 + 2\Delta), \, E[b(v_1 + R_1 \sqrt{2\Delta}, v_2 + R_2 \sqrt{2\Delta}, 1 + \Delta)] \}.
\]

where \((R_1, R_2) = (\pm1, 0)\) or \((0, \pm1)\) each with probability 1/4.

Instead, the matrix CS is determined by:

\[
\hat{b}_{a_2}(v_1, v_2, s_2)
\]

\[
= a_2 \hat{b}(v_1, v_2, s_2)
\]

\[
= \min \{ b(v_1, v_2, 1 + \Delta), \, a_2 E[\hat{b}(v_1 + R_1 \sqrt{2\Delta}, v_2 + R_2 \sqrt{2\Delta}, 1 + \Delta)] \}.
\]

where \( a_2 = (1/s_1 - 1)/(1/s_2 - 1) \) and \((R_1, R_2) = (\pm1, 0)\) or \((0, \pm1)\) each with
probability 1/4. Hence, to update the risk stored in the matrix PS for
deciding the continuation region at \( s = s_3 \), we need to only update the
risk corresponding to the grid points which are continuation points at
time \( s_2 \). If \((v_1, v_2)\) is a stopping point at time \( s_2 \),

\[
\hat{b}_{a_2}(v_1, v_2, s_2) = b(v_1, v_2, 1+\Delta).
\]

So \( b(v_1, v_2, 1+\Delta) \) is stored in the matrix PS corresponding to the grid
point \((v_1, v_2)\). Thus, it is not necessary to update the risk in the
stopping region. Similar settings can be applied to the other time
steps.

In Summary, with this setting at time \( s = s_1 \), if \((v_1, v_2)\) is a
continuation point, the risk stored in the corresponding cell of the
matrix CS would be determined by:

\[
\hat{b}_{a_1}(v_1, v_2, s_1) = a_1 \hat{b}(v_1, v_2, s_1).
\]

where \( a_1 = (1/s_1 - 1)/(1/s_1 - 1) \). Otherwise, if \((v_1, v_2)\) is a stopping
point, the risk stored is

\[
b(v_1, v_2, 1+\Delta).
\]

Note that

\[
\hat{b}_{a_1}(v_1, v_2, s_1) = (a_1/a_{i-1})E[\hat{b}_{a_{i-1}}(v_1+R_1\sqrt{2\Delta},v_2+R_2\sqrt{2\Delta},s_{i-1})],
\]

where \( a_1 = (1/s_1 - 1)/(1/s_1 - 1) \) and \((R_1, R_2) = (\pm 1, 0)\) or \((0, \pm 1)\) each with
probability 1/4. This setting does not change the fact that the risk
at the current step only depends on the risks at the previous step.
However, it is unnecessary to update the risk from one time step to the next for the stopping points with the setting. Hence, the program can be made more efficient with this result.

Due to the symmetry of the function $b(v_1, v_2, s)$,

$$\hat{b}(v_1, v_2, s) = \hat{b}(-v_1, v_2, s).$$

Hence, using a grid which is symmetric about $V = 0$, the continuation region on the negative half plane is known if it is known on the positive half-plane. In programs D and F, we use the grid:

\[(v_1, v_2, s): s = 1+\Delta, \quad v_1 = (-1+j)\sqrt{2\Delta}, \quad v_2 = k\sqrt{2\Delta}, \quad i = 0, 1, \ldots, ns, \quad j = 0, 1, \ldots, nvl, \quad k = 0, \pm 1, \ldots, nv2\],

where ns, nvl and nv2 are specified by the input of the programs.

Figures 3.3.1.1 and 3.3.1.2 give the picture of the last continuation points for several possible values of the time variable $s$. The data for the figures is a computational result of program F. The spacing of the time variable $\Delta$ used is 0.125. Figure 3.3.1.3 shows the optimal continuation region at $s = 100$.

The main difference between programs D (direct) and F (fast) is that we utilize the results of Propositions 3.2.3 and 3.2.4, in addition to Conjecture 3.2.1, in program F. To apply Propositions 3.2.3 and 3.2.4, the algorithm for program F is more complicated than the algorithm for program D. The programming to get the solution of last continuation points, with the application of Propositions 3.2.3 and 3.2.4, is relatively difficult. With the help of the results produced by program D, we are able to code the program F correctly.
For each grid level in $V_2$, program D examines every grid level in $V_1$ until Conjecture 3.2.1 is applicable. To locate the last continuation point corresponding to a grid level in $V_2$, $v_{2n}$ say, program D will sequentially test the grid points:
\[{(iv\sqrt{2A}, v_{2n}): i = 0, 1, 2, \ldots, nvl}\].

where nvl is the number of grid levels considered in $V_1$ (specified in the program). The testing will be terminated if one of the following conditions is true:

(i) All grid levels in $V_1$ have been tested;

(ii) a grid point, $(v_{1n}, v_{2n})$ say, is determined as a stopping point such that $(v_{1n} - \sqrt{2A}, v_{2n})$ is a continuation point.

The computing is very time consuming if a large number of grid levels are considered.

By Proposition 3.2.3, if a grid point is a continuation point at time $s_i$, it is a continuation point at time $s_{i+1}$. Thus, at the current step it is not necessary to examine the grid points which are continuation points at the previous step. Also, by proposition 3.2.4, a grid point is a stopping point at time $s_i$ if all the four adjacent grid points are stopping points at time $s_{i-1}$ and are in the region $T_2$ (or $T_1$ or $T_0$). These results allow the consideration of many fewer grid points than when Conjecture 3.2.1 is applied alone.

Using Propositions 3.2.3, 3.2.4 and Conjecture 3.2.1, some grid points can be determined to be continuation points (or stopping points) with just the information about the continuation region of the
previous step and with no computation. In program F, vectors are used to store the locations of the last continuation points at the previous step. Based on the locations of these continuation points, program F determines whether a computation is necessary to classify a grid point as a continuation point or a stopping point. The number of computations necessary is, therefore, much smaller than the total number of the grid points.

The following is a simple example to illustrate tracking the locations of the last continuation points and determining whether a grid point must be examined in program F. Let

\[
\begin{align*}
V1 & \quad \text{store levels of the grid in } V_1:\ V1[1] = -\sqrt{2A}, \ V1[2] = 0, \\
& \quad V1[3] = \sqrt{2A}, \ etc; \\
V2 & \quad \text{store levels of the grid in } V_2:\ V2[1] = 0, \ V2[2] = \sqrt{2A}, \\
& \quad V2[2] = 2\sqrt{2A}, \ etc; \\
\text{INDP} & \quad \text{store the locations of the last continuation points at the previous step: } \text{INDP}[2] = 3 \text{ means that } (V1[3], V2[2]) \text{ is a last continuation point at the previous step.}
\end{align*}
\]

Suppose currently \text{INDP}[2] = 6, \text{INDP}[3] = 6 and \text{INDP}[4] = 8. For this example, fewer grid points must be examined to solve the last continuation point corresponding to the grid level in \(V_2\). \(V2[3]\), using program F than program D.

Program D will sequentially examine the grid points:

\[\{V1[i], V2[3], i = 2, 3, 4, \ldots, nvl\}\]

where \(nvl\) is the number of grid levels considered in \(V_1\), until a grid point, \((V1[q], V2[3])\) say, is determined to be a stopping point such that \((V1[q-1], V2[3])\) is a continuation point. By Proposition 3.2.3,
\{V1[1], V2[3], i = 2, 3, 4, 5, 6\} are continuation points since they are continuation points at the previous step. Thus, currently the first possible stopping point is \(V1[7]\) corresponding to the grid level in \(V2[3]\). So, with the algorithm of program D, at least 6 grid points must be examined.

Using the algorithm of program F, the maximum number of the grid points which must be examined is only 3. By Proposition 3.2.3 it is not necessary to consider the grid points
\[\{(V1[i], V2[3]): i = 2, 3, 4, 5, 6\}\]. By Proposition 3.2.4, \(\{(V1[i], V2[3]): i \geq 9\}\) are stopping points at the current step. So, it is not necessary to consider them, either. Therefore, program F will examine only the grid points \(\{(V1[i], V2[3]): i = 6, 7, 8\}\), by the increasing order of \(i\). If one of these grid points is determined to be a stopping point, say \((V1[k], V2[3])\), the examination is terminated and \((V1[k-1], V2[3])\) becomes the last continuation point. If none of them is a stopping point, \((V1[8], V2[3])\) is the last continuation point.

In the above example, the only grid points considered have the grid level in \(V_1\), which is \(-\sqrt{24}\) or 0, or have all adjacent grid points in the region \(T_2\). It is simpler to decide how many grid points should be examined in this case. In the case with the grid points which are not all in the region \(T_2\) or with some of the four adjacent points not in \(T_2\), it is very difficult.

For example, solving the last continuation point, corresponding to a negative grid level in \(V_2\), is more complicated. Because of the shape of the continuation region (refer to Figure 3.3.1.1), corresponding to a positive grid level in \(V_2\), we need only solve for one last continuation point, called the "right-last continuation
point", from the positive grid levels in $V_1$. But, corresponding to a negative grid level in $V_2$, there might be two last continuation points, called the "left-last continuation point" and the "right-last continuation point" in the positive grid levels in $V_1$.

To solve the last continuation point corresponding to a positive grid level in $V_2$, the first grid level in $V_1$, which must be examined, is the grid point right next to the last continuation point at the previous step. This is by the result of Proposition 3.2.3. But, it is not always true in solving last continuation points for negative $V_2$ grid levels because of the reason discussed above.

Program F handles the case with a negative grid level in $V_2$ involved by the following procedure:

1. Decide the number of the last continuation points in positive $V_1$ grid levels, corresponding to the considered $V_2$ grid level, based on the continuation region at the previous step. (The answer can be obtained by Proposition 3.2.3.)

2. If the answer of step 1 is "one", the examining procedure is the same as that of the case with a positive $V_2$ grid level involved. If the answer of step 1 is possibly "two", go to next step.

3. By the locations of the "left-last (right-last) continuation points" at the previous steps, decide the grid levels in $V_1$, which must be examined for determining the "left-last (right-last) continuation points". (The answer of step 3 can be obtained by Conjecture 3.2.1, Proposition 3.2.3 and Proposition 3.2.4).

Hence, program F uses another vector to store the locations of "left-last continuation points", corresponding to negative grid levels in $V_2$.
The above case is only one of many cases which needs more detailed consideration. All the required considerations that should be done are given in program F, which is listed in Appendix A. The program illustrates how Propositions 3.2.3, 3.2.4 and Conjecture 3.2.1 can be utilized to decide how many grid points should be examined to determine the last continuation points.

Both programs D and F are compiled on the CONVEX C240 supercomputer at the University of North Carolina at Chapel Hill. In the case that 2000 grid levels are considered both in \( V_1 \) and \( V_2 \), Table 3.3.1.1 gives the CPU time required to compute the last continuation points at \( 1+(641)\Lambda \). Here \( \Lambda \) is the spacing of the time variable \( s \).

Table 3.3.1.1 The CPU Time Required for the Solution
at Time \( 1+(641)\Lambda \), with \( \Lambda = 0.125 \)

<table>
<thead>
<tr>
<th>Program used</th>
<th>CPU time required</th>
</tr>
</thead>
<tbody>
<tr>
<td>D</td>
<td>11095.14 seconds</td>
</tr>
<tr>
<td>F</td>
<td>1777.74 seconds</td>
</tr>
</tbody>
</table>

As shown in Table 3.3.1.1, program F is much more efficient than program D. The techniques, we have discussed, do reduce the labor involved in carrying out the backward induction algorithm to solve our problem.
Figure 3.3.1.1: The Last Continuation Points at s = (2, 5, 10, 20, 35, 50, 65, 80, 100) \((\Delta = 0.125)\)

Note: The area inside the two lines marked 100 is the optimal continuation region at s=100, etc.
Figure 3.3.1.2: The Last Continuation Points
at $s = \{40, 50, 65, 80, 100\}$
($\Delta = 0.125$)

Note: The area inside the two lines marked 100 is
the optimal continuation region at $s=100$, etc.
Figure 3.3.1.3: The Continuation Region
at $s = 100$ ($\Delta = 0.125$)
3.3.2 Programming with Huge Matrices in C

The computer language C was devised originally for systems programming work, not for scientific computing. Relative to other high-level programming languages, C puts the programmers "very close to the machine". Therefore, declaring a huge matrix in C is not so simple as it is in Pascal or Fortran.

A huge matrix, PS say, can be declared in Pascal (on the Vax 6330 at the University of North Carolina at Chapel Hill) with simple "VAR" statement. For example, to declare a 2000×2000 matrix of reals one can simply say:

\[
\text{Var} \quad \text{PS:array}[1..2000,1..2000] \text{ of } \text{"variable-type"}
\]

where "variable-type" can be "real", "single", "double", or "extended". Any similar statement in C (on the Convex 240) would result in a compiler error. Instead, one needs to use something like the following:

1. Define i and PS:
   
   \[
   \text{double: PS[2000]}
   \]
   \[
   \text{int: i}
   \]
   ("Double" is the variable type, it can be "float", too; "int" means integer.)
(2) Run a do loop to make PS a matrix:

    for (i=0; i<2000; i++)
    {
        PS[i] = (double *) malloc((2000*sizeof(double)));
        if (PS[i] == NULL)
        {
            fprintf(stderr, "Memory allocation fails: PS[%d] \n", i);
            exit(-1);
        }
    }

This method, and some other programming conventions in C, are discussed by Press, Flannery, Teukolsky and Vetterling (1988).

Another aspect of computing efficiency concerns how a matrix is allocated memory space in the computer. For example, on the Convex C240, Fortran allocates space by columns while C allocates space by rows.

For most computers, a block of variables stored in adjacent locations are brought into a "quick retrievable state" all at once, as a "page". A program involving a huge matrix, with size larger than a "page", should take advantage of this. The "do loop" related to the computation of the matrix should be set up with the computing sequence in accordance with how the matrix is stored (which can be either by columns or by rows). Failing to do this can cause a heavy burden on memory retrieval. In other words, the computer has to spend more time "swapping pages". This can increase a program's execution time very substantially.

Finally, there is an alternative programming algorithm for this problem which avoids the use of two matrices; only one is needed.
Because two huge matrices demand a large amount of computer memory, the sizes of these matrices are limited.

There is a programming technique called "Sweep" (Knott; personal communication) which permits one to work with a single large matrix and some variables. This can be motivated by considering the formula for the optimal stopping risk defined by (3.3.1.2). Let

\[ V_1[i] = (-2+i)\sqrt{2A}, \ i = 1, 2, \ldots, nv1; \]
\[ V_2[j] = (j-\lfloor nv2/2 \rfloor)\sqrt{2A}, \ j = 1, 2, \ldots, nv2. \]

Then, for a fixed \( p \),

\[ \{\hat{b}(v1[i], v2[p], s_q) : i = 1, 2, \ldots, nv1-1\} \]

can be computed if

\[ \{\hat{b}(v1[i], v2[p-1], s_{q-1}) : i = 1, 2, \ldots, nv1\} \]

and

\[ \{\hat{b}(v1[i], v2[p+1], s_{q-1}) : i = 1, 2, \ldots, nv1\} \]

are known. Therefore, instead of using two matrices to store the risk, "Sweep" uses three long vectors.

Programs D and F consider all the grid levels at a single time step before moving to the next time step. In contrast, "Sweep" works with part of the grid levels for several time steps simultaneously. Naturally, this requires a heavy "bookkeeping burden" so as to
guarantee that information is produced in a timely manner, properly sequenced.

The basis for "Sweep" is that in the backward induction algorithm \( \hat{b}(v_1[i], v_2[p], s_q) \): \( i = 1, 2, ..., nvl \) are useless in the computation of the risk at time \( s_j \), \( j \geq q+1 \), after \( \hat{b}(v_1[i], v_2[p+1], s_{q+1}) \): \( i = 1, 2, ..., nvl-1 \) have been calculated. Assume \( nvl \) is large enough so that

\[
\{(v_1[nvl], v_2[j]), j = 1, 2, ..., nv2\}
\]

are stopping points at all time steps: \( s_k \), \( k \leq 3 \). To get

\[
\hat{b}(v_1[i], v_2[j], s_3) : i = 1, 2, ..., nvl; j = 3, 4\},
\]

the calculation algorithm of "Sweep" is as follows:

Step \( \{1\} \): Calculate and store

\[
\hat{b}(v_1[i], v_2[j], s_1) : i = 1, 2, ..., nvl; j = 1, 2, 3\}.
\]

Step \( \{2\} \): Calculate and store

\[
\hat{b}(v_1[i], v_2[2], s_2) : i = 1, 2, ..., nvl\}.
\]

Step \( \{3\} \): For \( j = 4 \), calculate and store

\[
\hat{b}(v_1[i], v_2[j], s_1) : i = 1, 2, ..., nvl\},
\]

in where

\[
\hat{b}(v_1[i], v_2[j-3], s_1) : i = 1, 2, ..., nvl\}
\]

was stored.
Step (4): For $j = 3$, calculate and store

$$\{\hat{b}(v_1[i], v_2[j], s_2): i = 1, 2, \ldots, n_{v1}\}.$$  

Step (5): Repeat Step (3) with $j = 5$ and then repeat Step (4) with $j = 4$.

Step (6): For $j = 3$ and $k = 3$, calculate and store

$$\{\hat{b}(v_1[i], v_2[j], s_3): i = 1, 2, \ldots, n_{v1}\}.$$  

Step (7): Repeat step (3) with $j = 6$.

Step (8): For $j = 5$, calculate and store

$$\{\hat{b}(v_1[i], v_2[j], s_2): i = 1, 2, \ldots, n_{v1}\},$$  
in where

$$\{\hat{b}(v_1[i], v_2[j-3], s_2): i = 1, 2, \ldots, n_{v1}\}$$  
was stored.

Step (9): Repeat step (6) with $j = 4$.

It can be seen from steps (3), (5) and (8) that the risk which is not needed to estimate the risk for the coming time steps is not stored. Thus, "Sweep" is not as memory-demanding as programs D and F.

Let $n_{v1}$ be the number of grid levels in $V_1$, $n_{v2}$ be the number of grid levels in $V_2$, and $n_s$ be the total number of time steps. Using two matrices requires the memory space to store $2(n_{v1})\times(n_{v2})$ numerical values. "Sweep" needs only the space to store $3(n_{v1})\times(n_s)$ numerical values. The amount of the memory required by "Sweep" is less than three eighths of that required by using two matrices since $n_s$ should be less than $n_{v2}/4$.  

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It is difficult to apply the properties of the last continuation points, described in Section 3.2, with the calculation algorithm of "Sweep". Tracking the locations of the last continuation points is especially hard with the algorithm. Hence, this calculation algorithm was not used in programming.

3.3.3 Interpolation

This section discusses a numerical method which can be employed to obtain smooth estimates of the boundary of the continuation region for the continuous time problem. The use of a large grid spacing produces estimates of the boundary of the continuation region which are not smooth. On the other hand, the use of a small grid spacing in a backward induction, designed to obtain estimates for large values of \( s \), say as large as \( s = 10000 \), would require an exorbitant amount of computer time.

By carrying out a single backward induction that incorporates a changing step size as it proceeds, smooth estimates of the boundary can be obtained without consuming a large amount of computer time. The use of various grid levels may apply to most areas of numerical computation. Briggs and McCormick (1987) introduce some essential principles of multigrid methods designed for partial differential equations. One of the very basic principles of multigrid techniques is the use of various discretization levels to resolve different components of error in the approximation.

The first phase of the backward induction, which incorporates a changing grid spacing as it proceeds, might execute \( N_1 \) steps corresponding to a large grid spacing \( \Delta_1 \), from the initial value \( s = 1 \).
to $s = 1 + \mathcal{M}_1 \Delta_1 = s_1'$ say, and the second phase might execute $\mathcal{M}_2$ steps corresponding to a smaller grid spacing $\Delta_2$, from the initial value for this phase $s_1'$ to $s_1' + \mathcal{M}_2 \Delta_2$ say. The backward induction can be continued for as many phases as desired if

(1) the factor for decreasing $\Delta$ from phase to phase is appropriate;

(2) at the first step of each phase (except the first phase), estimates of the risk at all the new grid levels are precise.

We select a factor of 4 to decrease the $\Delta$ from each phase to the next. To perform the interpolation, the following equality should be true:

$$v2\text{dim} = 4^n \text{ns} + 1,$$

where $v2\text{dim}$ is the number of grid levels in $V_2$ and $\text{ns}$ is the number of steps in each interpolation phase. Each phase executes the same number of time steps. Since the spacing of the spatial variables $V_1$ and $V_2$, is $\sqrt{2} \Delta$, use of the factor 4 from phase to phase implies that the grid at the current phase is a refinement of the grid at the previous phase. Consequently, the estimates of the risk at the new grid levels at the value of $s$ corresponding to the first step of any phase are not provided by the previous phase. Interpolation is necessary. Figures 3.3.3.1 and 3.3.3.2 give pictures of the grid levels of a phase and its next phase on part of the plane $(V_1, V_2)$.

Actually, interpolation is not necessary for the new grid levels which are located in the stopping region at the first step of each phase. The stopping region at the first step of each phase is provided.
by the previous phase since the value of $s$ corresponding to the last step of the previous phase is carried over to the first step of the current phase. Therefore, the function which defines the stopping risk $b(v_1,v_2,s)$ is able to provide the risk for the new grid level located in the stopping region.

The following is the procedures used to compute the estimates of the risk of new grid levels, which are located in the continuation region at the first step of each phase (except the first phase):

Assume the current time step size is $\Delta_x$, and the value of $s$, corresponding to the first step of current phase is $s'$.

Step 1: Compute the estimate of the risk of a new grid level, $(v_1',v_2')$ say, such that $(v_1'-\sqrt{2\Delta_x},v_2')$ and $(v_1'+\sqrt{2\Delta_x},v_2')$ are two grid levels of the previous phase. The estimate of the risk at $(v_1',v_2',s')$ is

$$\left[\hat{b}(v_1'-\sqrt{2\Delta_x},v_2',s') + \hat{b}(v_1'+\sqrt{2\Delta_x},v_2',s')\right]/2,$$

where $\hat{b}(v_1'-\sqrt{2\Delta_x},v_2',s')$ and $\hat{b}(v_1'+\sqrt{2\Delta_x},v_2',s')$ are provided by the previous phase.

Step 2: Compute the estimate of the risk of a new grid level, $(v_1',v_2')$ say, such that $(v_1',v_2'-\sqrt{2\Delta_x})$ and $(v_1',v_2'+\sqrt{2\Delta_x})$ are two grid levels of previous phase. The estimate of the risk at $(v_1',v_2',s')$ is

$$\left[\hat{b}(v_1',v_2'-\sqrt{2\Delta_x},s') + \hat{b}(v_1',v_2'+\sqrt{2\Delta_x},s')\right]/2,$$

where $\hat{b}(v_1',v_2'-\sqrt{2\Delta_x},s')$ and $\hat{b}(v_1',v_2'+\sqrt{2\Delta_x},s')$ are provided by the previous phase.
Step 3: Compute the estimate of the risk of a new grid level, \((v_1', v_2')\) say, such that \((v_1' - \sqrt{2A_{\mu}}, v_2' + \sqrt{2A_{\mu}}), (v_1' + \sqrt{2A_{\mu}}, v_2' + \sqrt{2A_{\mu}})\) \((v_1' + \sqrt{2A_{\mu}}, v_2' - \sqrt{2A_{\mu}}) \text{ and } (v_1' - \sqrt{2A_{\mu}}, v_2' - \sqrt{2A_{\mu}})\) are four grid levels of the previous phase. The estimate of the risk at \((v_1', v_2', s')\) is

\[
\frac{1}{4} \left[ \hat{b}(v_1' - \sqrt{2A_{\mu}}, v_2' + \sqrt{2A_{\mu}}, s') + \hat{b}(v_1' + \sqrt{2A_{\mu}}, v_2' + \sqrt{2A_{\mu}}, s') + \hat{b}(v_1' + \sqrt{2A_{\mu}}, v_2' - \sqrt{2A_{\mu}}, s') + \hat{b}(v_1' - \sqrt{2A_{\mu}}, v_2' - \sqrt{2A_{\mu}}, s') \right],
\]

where \(\hat{b}(v_1' - \sqrt{2A_{\mu}}, v_2' + \sqrt{2A_{\mu}}, s')\), \(\hat{b}(v_1' + \sqrt{2A_{\mu}}, v_2' + \sqrt{2A_{\mu}}, s')\), \(\hat{b}(v_1' + \sqrt{2A_{\mu}}, v_2' - \sqrt{2A_{\mu}}, s')\), and \(\hat{b}(v_1' - \sqrt{2A_{\mu}}, v_2' - \sqrt{2A_{\mu}}, s')\) are provided by the previous phase.

Figures 3.3.3.3–9 present the performance of the above interpolation estimates of the risk by an example. The interpolation used to get the data for the figures is with the starting time variable spacing \(\Delta = 0.125\), and with the time variable spacing \(0.125/4\) in the second phase. By comparing the results obtained by the interpolation and those obtained by starting with the smaller grid spacing \(\Delta = 0.03125\), it can be seen that the approximation is better if the corresponding value of \(s\) is farther away from the first step of the corresponding phase.

Tables 3.3.3.1–6 gives the difference between the estimates of the risk by the above two methods. 10 steps after the step size has been changed, the difference is only one out six digits. The tables and figures suggest that to get a good approximation of the continuation region corresponding to a large value of \(s\), \(s_{1g}\), say, by
interpolation. The interpolation should be set so $s_{ig}$ is an adequate number of steps away from the first step of the corresponding phase.
Figure 3.3.3.1: Sample of Grid Levels

\((\Delta = \Delta_1; \Delta_\nu = \sqrt{2}\Delta_1)\)

\[\text{Figure 3.3.3.2: Sample of Grid Levels}\]

\((\Delta = \Delta' = \Delta_1/4; \Delta_\nu' = \sqrt{2}\Delta' = \Delta_\nu/2)\)
Figure 3.3.3.3: 0 Step after Changing the Step Size

$s = 15$

- --- changing the step size at $s = 15$
- --- starting with the fine grid
Figure 3.3.3.4: 1 Step after Changing the Step Size
\[ s = 15.03125 \]
Figure 3.3.3.5: 2 Steps after Changing the Step Size

\[ s = 15.0625 \]
Figure 3.3.3.6: 5 Steps after Changing the Step Size

s = 15.15625
Figure 3.3.3.7: 10 Steps after Changing the Step Size

\[ s = 15.3125 \]
Figure 3.3.3.8: 20 Steps after Changing the Step Size

\[ s = 15.625 \]
Figure 3.3.3.9: 40 Steps after Changing the Step Size

$s = 16.25$
Table 3.3.3.1 Estimates of the Risk at the Last Continuation Points: 1 Step after Changing the Step Size

Note: (1) starting with $\Delta = 0.03125$; (2) interpolating at $s = 15$.

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Table 3.3.3.2  Estimates of the Risk at the Last Continuation Points: 2 Steps after Changing the Step Size

Note: (1) starting with \( \Delta = 0.03125 \); (2) interpolating at \( s = 15 \).

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Table 3.3.3.4  Estimates of the Risk at the Last Continuation Points: 10 Steps after Changing the Step Size

Note: (1) starting with $A = 0.03125$; (2) interpolating at $s = 15$.

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Table 3.3.3.5  Estimates of the Risk at the Last Continuation Points: 20 Steps after changing the Step Size

Note: (1) starting with $\Delta = 0.03125$; (2) interpolating at $s = 15$.

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Table 3.3.3.6  Estimates of the Risk at the Last Continuation Points: 40 Steps after Changing the Step Size

Note: (1) starting with $\Lambda = 0.03125$; (2) interpolating at $s = 15$.

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</table>
3.4 An Example

This section uses the example about comparing treatments for PCP, which is described in Section 2.1 of last chapter, to illustrate how to apply the solution of the optimal stopping rule. Let $X_{01}$ be the PaO$_2$ of a patient treated by Bactrim, $X_{11}$ be the PaO$_2$ of a patient treated by Pentamidine, and $X_{21}$ be the PaO$_2$ of a patient treated by Pentamidine with Steroid.

Assume $X_{j1}$'s ($j = 0, 1, 2, i = 1, 2, \ldots$) are independently $N(\theta_j, 1)$ random variables. Further, suppose $\theta_j$'s ($j = 0, 1, 2$) are independent and $\theta_0$ has prior density $N(86.8, 1)$, $\theta_1$ has prior density $N(87.1)$ and $\theta_2$ has prior density $N(87.5, 1)$.

If we get $X_{01} = 84.8$, $X_{11} = 85$ and $X_{21} = 86$ from the first three treated patient, then

$$W_{11}^\star = 5.3023$$

and

$$W_{12}^\star = 4.6949$$

by (2.5.1) and (2.5.2).

Also, by (2.5.3)

$$s_1^\star = 50.$$  

Since $(5.3033, 4.6949)$ is in the optimal continuation region in Figure 3.3.1.1, we will continue allocating the other three patients.

Suppose the testing stage is not stopped either after 6 patients are treated or after 9 patients are treated and the observed $(W_{41}^\star, W_{42}^\star)$ is $(11, 8)$. In Figure 3.3.1.1, $(11, 8)$ is not in the optimal continuation region at $s^\star = 20$, therefore, the testing stage is then terminated after 12 patients are allocated. Since $(W_{41}^\star, W_{42}^\star) = (11, 8)$
is in the region $T_2$, the treatment Pentamidine with Steroid is selected for the remaining 285 patients.
CHAPTER IV

THE ASYMPTOTICALLY EXPECTED OVERJUMP

OF A 2-DIMENSIONAL RANDOM WALK

4.1 Introduction

This chapter presents the solution of the asymptotically expected excess over the boundary by a 2-dimensional random walk. This solution can be used to approximate the difference between the solution of the continuous version of the stopping problem discussed in Chapter II and that of discrete version.

The random walk considered in this chapter is defined as follows: Let $(X_n, Y_n)$ be a random walk in two dimensions, where

$$(X_n, Y_n) = (X_{n-1} \pm 1, Y_{n-1}) \text{ or } (X_{n-1}, Y_{n-1} \pm 1)$$

each with probability $1/4$. The boundary considered is two parallel lines of equations:

$$ax + by = \pm c,$$

for some integers $a$, $b$, and a positive integer $c$.

In Section 4.2 the distance between $(X_m, Y_m)$ and the boundary is studied for specified $a$ and $b$ and some $m$ such that $(X_m, Y_m)$ is the first time the random walk crosses the boundary. The distance is
called the "overjump". The solution of the asymptotically expected overjump for $0 < a \leq b$ is given by Theorem 4.2.1.

In Section 4.3, some numerical results of Theorem 4.2.1 are computed. The application of the numerical results is discussed.

4.2 The Asymptotically Expected Overjump

The region inside the boundary is called the continuation region and is denoted by $C$. The complement of $C$ is called the stopping region and is denoted by $S$. The random walk begins at a random point in continuation region $C$ and stops as soon as it reaches stopping region $S$. Therefore, it "walks" until it reaches the stopping region $S$. Let $\rho_{S}(x,y)$ be the probability that a random walk starting at $(x,y)$ eventually hits the stopping region $S$. Then,

$$\rho_{S}(x,y) = \sum_{(u,v) \in S} P[(x,y),(u,v)] + \sum_{(u,v) \in C} P[(x,y),(u,v)] \rho_{S}(u,v),$$

where $P[(x,y),(u,v)]$ is the conditional probability that $(X_{1},Y_{1})$ is equal to $(x,y)$ given that $(X_{0},Y_{0})$ is equal to $(u,v)$ (Hoel, Port and Stone (1972), p.25).

Partition the continuation region into several strips by the lines: $aX + bY = -c+1$, $aX + bY = -c+2$, ..., $aX + bY = c-2$, $aX + bY = c-1$, in case that the boundary is of equations $aX + bY = \pm c$ for some specified $a$, $b$ and $c$. The $i$-th closest strip to the line $aX + bY = c$ is called the $i$-th strip. Figure 4.2.1 shows this partition for the specific case $a = 1$, $b = 2$ and $c = 8$.

The next result is used in the proof of Theorem 4.2.1.
Lemma 4.2.1. Let the boundary of the walk and the overjump be as defined in Section 4.1.

(i) If the random walk begins at a random point \((x_0, y_0)\) in the \(i\)-th strip for \(1 \leq i \leq a\) such that \((X_1, Y_1) = (x_0+1, y_0)\), the overjump in X-direction is uniformly distributed on the interval

\[((a-i)/a, (a-i+1)/a).\]

(ii) If the random walk begins at a random point \((x_0, y_0)\) in the \(i\)-th strip for \(1 \leq i \leq b\) such that \((X_1, Y_1) = (x_0, y_0+1)\), the overjump in the X-direction is uniformly distributed on the interval

\[((b-i)/a, (b-i+1)/a).\]

Proof: (i) The continuation region is partitioned into \(2c\) strips by the lines:

\[aX + bY = c-j, \text{ where } j = 1, 2, \ldots, 2c-1.\]

The distance of the lines \(aX + bY = c-j\) and \(aX + bY = c-j-1\), where \(j = 0, 1, 2, \ldots, 2c-1\), in the X-direction is \(1/a\). Hence, if the random walk begins at a point in the \(k\)-th strip for \(k > a\), it will not reach the stopping region by just walking one unit in the X-direction. On the other hand, if the random walk begins at a point in \(k\)-th strip for \(1 \leq k \leq a\) and walks one unit in the X-direction, it reaches the stopping region and the overjump is between \((a-k)/a\) and \((a-k+1)/a\). The overjump depends on where the random walk begins in the strip.

The result then follows from the assumption that the walk begins at a random point in the strip.

(ii) The proof is similar to (i). \(\Box\)
Let $p_i$ be the probability that a 2-dimensional random walk starting at a random point in the $i$-th strip eventually reaches the stopping region $S$. Then, if $a \leq b < 2c-b$, (4.2.1) implies

\[
(4.2.2) \quad p_i = \begin{cases} 
\frac{1 + 1 + p_{i+b} + p_{i+a}}{4} & 1 \leq i \leq a, \\
\frac{1 + p_{i-a} + p_{i+b} + p_{i+a}}{4} & a < i \leq b, \\
\frac{p_{i-b} + p_{i-a} + p_{i+b} + p_{i+a}}{4} & b < i \leq 2c-b.
\end{cases}
\]

The following notations will be used for the Theorem 4.2.1 and Corollary 4.2.1 which follow. For some integers $a$, $b$, and a positive integer $c$, let

\[
\tau_c = \inf \{ n : \left| aX_n + bY_n \right| \geq c \},
\]

\[
D_c = \left( \frac{\left| aX_{\tau_c} + bY_{\tau_c} \right| - c}{(a^2 + b^2)^{1/2}} \right).
\]

\[
H_c = \begin{cases} 
\frac{|X_{\tau_c} - (c-bY_{\tau_c})|}{a}, & (aX_{\tau_c} + bY_{\tau_c}) > c, \\
\frac{|X_{\tau_c} - (-c-bY_{\tau_c})|}{a}, & (aX_{\tau_c} + bY_{\tau_c}) < -c.
\end{cases}
\]

\[
V_c = \begin{cases} 
\frac{|Y_{\tau_c} - (c-aX_{\tau_c})|}{b}, & (aX_{\tau_c} + bY_{\tau_c}) > c, \\
\frac{|Y_{\tau_c} - (-c-aX_{\tau_c})|}{b}, & (aX_{\tau_c} + bY_{\tau_c}) < -c.
\end{cases}
\]

Then, $D_c$ is the overjump perpendicular to the boundary, $H_c$ is the overjump in the $X$-direction and $V_c$ is the overjump in the $Y$-direction.
The limits \( \lim_{c \to \infty} ED_c \), \( \lim_{c \to \infty} EH_c \) and \( \lim_{c \to \infty} EV_c \) exist from renewal theory (Hogan (1986)). Let

\[(4.2.3) \quad ED = \lim_{c \to \infty} ED_c,\]

\[(4.2.4) \quad EH = \lim_{c \to \infty} EH_c,\]

and

\[(4.2.5) \quad EV = \lim_{c \to \infty} EV_c.\]

**Theorem 4.2.1.** ED and EH are defined as above. For integers \(a, b\) where \(0 < a \leq b\), if \((r_1, r_2, \ldots, r_b)\) is a solution of the following set of equations:

\[q_i = r_1 + r_2 w_1^i + r_3 w_2^i + \ldots + r_b w_{b-1}^i,\]

where \(i = -(b-1), -(b-2), \ldots, -1, 0,\)

\[q_i = \frac{1 - 2i}{2a},\]

and \(w_1, w_2, \ldots, w_{b-1}\) are the roots with magnitude less than 1 of the equation:

\[1 + z^{b-a} - 4z^b + z^{b+a} + z^{2b} = 0,\]

then

\[EH = r_1,\]

\[EV = ar_1/b,\]

and

\[ED = ar_1/(a^2 + b^2)^{1/2}.\]
Proof: Let $e_i$ be the expected overjump in the X-direction by the random walk beginning at a random point in the $i$-th strip if the boundary is $aX + bY = c$ for some specific positive integers $a$, $b$ and $c$ such that $a \leq b$.

Then, by Lemma 4.2.1 and (4.2.2), we have

$$e_i = \begin{cases} \frac{[(2(b-i)+1)/2a+(2(a-i)+1)/2a+e_{i+b}+e_{i+a}]}{4} & 1 \leq i \leq a, \\ \frac{[(2(b-i)+1)/2a+e_{i-a}+e_{i+b}+e_{i+a}]}{4} & a < i \leq b, \\ \frac{[e_{i-b}+e_{i-a}+e_{i+b}+e_{i+a}]}{4} & b < i \leq 2c-b. \end{cases}$$

(4.2.6)

Actually, (4.2.6) can be rewritten as the following:

$$e_{i-b} + e_{i-a} - 4e_i + e_{i+a} + e_{i+b} = 0,$$

(4.2.7)

where $i = 1, 2, \ldots, 2c-b$, such that

$$e_i = (1-2i)/2a, \quad i = -b+1, -b+2, \ldots, 1, 0.$$

It is clear that (4.2.7) is a homogeneous linear difference equation. A solution of this linear difference equation is

$$e_i = r_1 + r_2 w_1^i + r_3 w_2^i + \ldots + r_b w_{b-1}^i,$$

where $w_1, w_2, \ldots, w_{b-1}$ are the roots with magnitude less than 1 of the equation:

$$1 + z^{b-a} - 4z^b + z^{b+a} + z^{2b} = 0.$$

By the boundary conditions of the linear difference equation, we can get a solution of $(r_1, r_2, \ldots, r_b)$. Since

$$|w_i| < 1, \quad i = 1, 2, 3, \ldots, b-1.$$
we get

\[ e_n \rightarrow r_1 \text{ as } n \rightarrow \infty. \]

In other words, the expected overjump in the X-direction tends to \( r_1 \) as \( c \) goes to infinity. Therefore, the expected overjump in the Y-direction and the expected overjump perpendicular to the boundary tend to

\[ ar_1/b \]

and

\[ ar_1/(a^2+b^2)^{1/2}. \]

respectively, as \( c \) goes to infinity.

The following is analytic solutions for some special cases of Theorem 4.2.1:

1. If \( a = 1 \) and \( b = 1 \),
   \[ \text{ED} = 1/(2\sqrt{2}); \]

2. If \( a = 1 \) and \( b = 2 \),
   \[ \text{ED} = \sqrt{5}/5 - 1/10; \]

3. If \( a = 1 \) and \( b = 3 \),
   \[ \text{ED} = \sqrt{5}/(2\sqrt{2}) - \]
   
   \[ (1/10)(6\sqrt{10} - 2(10\sqrt{5} - 20)^{1/2})/(5+\sqrt{5} - (\sqrt{5} - 2)^{1/2} - (\sqrt{5}+2)^{1/2}). \]

The asymptotically expected overjump in the X-direction when the boundary has slope \(-a/b\) is the same as the asymptotically expected overjump in the Y-direction when the boundary has slope \(-b/a\). Thus, Corollary 4.2.1 follows.
**Corollary 4.2.1.** For integers $a$ and $b$ where $0 < b \leq a$, if $(r_1, r_2, \ldots, r_a)$ is a solution of the following set of equations:

$$q_i = r_1 + r_2 w_1^i + r_3 w_2^i + \ldots + r_a w_{a-1}^i,$$

where $i = -(a-1), -(a-2), \ldots, 1, 0$,

$$q_i = \frac{1 - 2i}{2b},$$

and $w_1, w_2, \ldots, w_{a-1}$ are the roots with magnitude less than 1 of the equation:

$$1 + z^{a-b} - 4z^a + z^{a+b} + z^{2a} = 0.$$

then

$$EV = r_1,$$

$$EH = br_1/a,$$

and

$$ED = \frac{br_1}{(a^2 + b^2)^{1/2}}.$$

A program in Turbo Pascal is coded to simulate the asymptotically expected overjump. The numerical evidence generated by the program strongly supports the Theorem.
Figure 4.2.1: Boundary: $X + 2Y = 8$ or $-8$
4.3 Numerical Results

Because of symmetry, if the boundary has slope \(-p/q\), where \(p < 0 < q\), the asymptotically expected overjumps can be obtained from the Theorem 4.2.1.

Hence, the asymptotically expected overjump perpendicular to the boundary is the same for a boundary with slope \(-a/b\), \(-b/a\), \(a/b\) or \(b/a\), for some positive integers \(a\) and \(b\). Therefore, we only compute the asymptotically expected overjumps for boundaries with rational slope \(-a/b\), where \(a\) and \(b\) are relatively prime, positive integers and \(a < b\). A program coded in Gauss provides the numerical results.

Figures 4.3.1-3 illustrate the numerical results. Table 4.3.1 provides the asymptotically expected overjumps for the boundaries with some selected slopes. The largest value of \(b\) considered is 150.

Finally, Theorem 4.2.1 can be applied as follows. Let's consider the discrete version of the stopping problem defined in Section 2.6 in which the spacing of the time variable is \(\Delta\). Assume that part of the boundary of the optimal continuation region for this problem can be described by the equation:

\[ aX + bY = c \]

for some positive integers \(a\), \(b\) and \(c\). By Theorem 4.2.1, the suggested approximation for the solution of the continuous time problem is

\[ aX + bY = c \pm \lfloor 1-(a^2+b^2)^{1/2}ED \rfloor \sqrt{2\Delta} \]

where \(ED\) is defined in (4.2.3) and the sign is determined so as to make the continuation region for the continuous time problem larger.
Figure 4.3.1: Perpendicular Expected Overjumps vs Slopes
Figure 4.3.2: Horizontal Expected Overjumps vs Slopes
Figure 4.3.3: Vertical Expected Overjumps vs Slopes
Table 4.3.1
Asymptotically Expected Overjumps

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APPENDIX A  PROGRAM LISTING

/* PURPOSE: THIS CODE IS FOR SOLVING THE LAST CONTINUATION POINTS INVOLVING A 2-DIMENSIONAL RANDOM WALK. */

#include <math.h>
#include <stdio.h>
#include <stdlib.h>
#define out "t.int"  /*
#define right "rg.int"  /* define the name of output files */
#define left "lf.int"  /*
#define w1dim 445  /* the number of grid levels in V1 */
#define w2dim 445  /* the number of grid levels in V2 */
#define negdim 100  /* the number of negative grid levels in V2 */
#define leftdim no_steps+negdim+10
        /* the size of the vector storing the locations of the "left-last continuation points for negative grid levels in V2 */
#endif

#define starting_s 1
#define starting_dels 0.125
        /* the spacing of the time variable in the first phase */

#define spacing 1
#define no_stages 2  /* the number of phases */
#define no_steps 111  /* the number of steps in each phase */

double b();

main()
{
/* VARIABLE DECLARATIONS */
        /*
        */
        /*
        */

double w2[w2dim];  /* stores the grid levels in V2 */
double w1[w1dim];  /* stores the grid levels in V1 */
double neww2[w2dim];  /* stores the grid levels in V2 for next phase */
double neww1[w1dim];  /* stores the grid levels in V1 for next phase */
double \*w[w2dim], \*wr[w2dim]; \/* stores the risk for the current step */
\*rr[w2dim]; \/* stores the risk for the previous step */
int iid[2], \/* indicators for applying Proposition 3.2.4 */
rindp[w2dim], \/* stores the locations of the "right-last" 
continuation points at the previous step */
rind[w2dim], \/* stores the locations of the "right-last" 
continuation point at the current step */
lindp[leftdim], \/* stores the locations of the "left-last" 
continuation points at the previous step */
lind[leftdim], \/* stores the locations of the "left-last" 
continuation points at the current step */

int flend, \/* the location of the "left-last" continuation 
point corresponding to the V2 grid level which 
is smallest in V2 grid levels having "left-last" 
continuation points at the current step */
flid, \/* indicating if the value of flend is updated */
pflend, \/* the location of the "left-last" continuation 
point corresponding to the V2 grid level which 
is smallest in V2 grid levels having "left-last" 
continuation points at previous step */
ilend, \/* indicator for applying Proposition 3.2.4 */
irend, \/* indicator for applying Proposition 3.2.4 */
out0, \/* indicator to see if (o,v2) is written in the 
output file graphleft */
mlow, \/* the number of negative grid levels in V2 in the 
output file */
larger, \/* indicating if the matrices r and rr are large 
enough */
rend, \/* the rightmost grid level in V1 necessary to be 
checked for the current V2 grid level */
lend, \/* the leftmost grid level in V1 necessary to be 
checked for the current V2 grid level */
nleft, \/* the size of the vectors lind and lindp */
c, \/* the factor to decrease the s spacing from each 
phase to the next */
ng, \/* indicator for the output: 1 means the result of 
the current step will be output */
nstage, \/* the number of phases */
ns, \/* the number of steps */
nw1, \/* the number of grid levels in V1 */
nw2, \/* the number of grid level in V2 */
w2ind, \/* indicating whether the interpolation is 
appropriate */
w2id, is, beg, bed, twlk, \/* index variables */
i, j, ii, jj, id, wlk, wlik, \/* for */
wikk, w2k, w2kk, w2kkk; \/* computations */
double s, \/* the time variable */
s0; \/* the initial value of the time variable */
```c
double  dels,  /* the time variable spacing */
       delw,  /* the spacing of V1 and V2 */
       td, d,  /* stores the stopping risk */
       ted, ed,  /* stores the bayes risk */
       aed, a;  /* for updating the risk in the continuation
            region only */
double  sqrt3;  /* stores sqrt(3) */
FILE  *graph, *graphleft, *outfile;

/******
/ ALLOCATING TWO 2-DIMENSIONAL MATRICES */
/******

for (i=0; i<w2dim; i++)
{
    r[i]=(double *)malloc((wldim)*sizeof(double));
    if (r[i]==NULL)
    {
        fprintf(stderr,"Memory allocation fails: r[%d]\n",i);
        exit(-1);
    }
    rr[i]=(double *)malloc((wldim)*sizeof(double));
    if (rr[i]==NULL)
    {
        fprintf(stderr,"Memory allocation fails: rr[%d]\n",i);
        exit(-1);
    }
}

/******
/ OPEN THREE OUTPUT FILES */
/******

if ((outfile=fopen(out, "wt"))==NULL)
{
    printf("cannot open file outfile. \n");
    exit(1);
}
if ((graph=fopen(right, "wt"))==NULL)
{
    printf("Cannot open file right. \n");
    exit(1);
}
if ((graphleft=fopen(left, "wt"))==NULL)
{
    printf("Cannot open file left. \n");
    exit(1);
}

/******
/ SET THE INITIAL VALUES FOR SOME VARIABLES */

s0=starting_s;
c=spacing;
dels=starting_dels/(double)c;
larger=0;
sqrt3=sqrt((double)3.0);
ng=0;
```
/* DECIDE THE NUMBERS OF GRID LEVELS IN V1 AND V2 
   AND THE NUMBERS OF STEPS AND PHASES. */

nw2=w2dim-1;
wl1=w1dim-1;
olon=negdim;
lef=leftdim;
stage=no_stages;
ns=no_steps;
if (sO<=0)
{
    fprintf(outfile, "ERROR-------INITIAL S <= 0!! sO = %f\n", sO);
go to finish;
}
else
{
id=1;

/* LOOP FOR DIFFERENT GRID SPACINGS */

for do
{
delw=sqrt((double)2.0*dels);
    if ( id>1 )
{
        for (j=0; j<=nw2; j++)
            neww2[j]=w2[ns]+j*delw;
        for (j=0; j<=nw1; j++)
            neww1[j]=(-1+j)*delw;
        for (j=0; j<=nw2; j+=2)
{
            w2ind=ns+j/2;
            if (w2ind>(nw2-ns))
                fprintf (outfile,"ERROR----interpolating too many");
            if (neww2[j]!=w2[w2ind])
                fprintf (outfile,"error in rescaling");
            if (neww2[j]<0)
                for (i=0; i<=nw1; i++)
                {
                    if ( (neww1[i]<w1[1indp[w2ind]])     
                      (neww1[i]>w1[rindp[w2ind]]) )
                      r[j][i]=b(neww1[i],neww2[j],s,s0)*s0*s0/(s-s0);
                    else
                    {
                        if (((x2)==0))
                            r[j][i]=(rr[w2ind][i/2]+rr[w2ind][(i+2)/2])/2;
                        else
                            r[j][i]=rr[w2ind][(i+1)/2];
                    }
                }
            else
                {
                }
        }
    }
}
for (i=0; i<=nw1; i++)
{
    if ( (neww1[i]>w1[rindp[w2ind]]) )
        r[j][i]=b(neww1[i].neww2[j].s,s0)*s0/s0/(s-s0);
    else
    
        if ((i%2)==0)
            r[j][i]=rr[w2ind][(i+2)/2]/2;
        else
            r[j][i]=rr[w2ind][(i+1)/2];
}
}
}

for (j=1; j<=nw2; j+=2)
{
    for (i=0; i<=nw1; i++)
        r[j][i]=(r[j-1][i]+r[j+1][i])/2;
}

fprintf (outfile, "\n\n");

fprintf (outfile, "STAGE : %3d\n", id);
if (id=1) s=s0;

fprintf (outfile, "INITIAL VALUE OF S : %8.6f\n", s);

fprintf (outfile, "SPACING OF S : %8.6f\n", dels);

fprintf (outfile, "SPACING OF V1 & V2 : %8.6f\n", delw);

fprintf (outfile, "\n");

fprintf (outfile, "%12s %9s %9s %9s \n", "s", "V1", "V2", "ed\n");

/* SET THE INITIAL VALUE OF THE VECTORS STORING THE LOCATIONS 
   OF THE LAST CONTINUATION POINTS */

flend=0;
for (i=0; i<=nw2; i++)
{
    rindp[i]=0;
    rind[i]=0;
}
for (i=0; i<=nleft; i++)
{
    lindp[i]=0;
    lind[i]=0;
}

if (id==1)
{
    s=s0+dels;

    /* SET THE GRID LEVELS OF V1 AND V2 */

    for (i=0; i<=nw2; i++) w2[i]=(-1*nlow-1*ns+1)*delw;
        for (i=0; i<=nw1; i++) w1[i]=(-1+i)*delw;

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/* EVALUATE THE STOPPING RISK WHEN S=S0+DELS */

for (j=0; j<nw2; j++)
    for (i=0; i<nw1; i++)
        rr[j][i]=b(w1[i],w2[j],s,s0)*s0*s/(s-s0);

else

/* SET THE GRID LEVELS OF V1 AND V2 FOR INTERPOLATION */

for (i=0; i<nw2; i++) w2[i]=neww2[i];
for (i=0; i<nw1; i++) w1[i]=neww1[i];

/* EVALUATE THE STOPPING RISK WHEN S=STARTING-S AT THIS PHASE */

for (j=0; j<nw2; j++)
    for (i=0; i<nw1; i++)
        rr[j][i]=r[j][i];

/* AT EACH STEP, FOR EACH GRID LEVEL IN V2, V20 SAY, FIND
THE CORRESPONDING V1, V10 SAY, TO MAKE (V10,V20) A LAST
CONTINUATION POINT */

/* LOOP FOR EACH STEP, S=S0+IS*DELS, IS=2,3,... */

for (is=1; is<ns; is++)
{
    out0=0;
    flid=0;
    flend=0;
    ng=0;
    if ( (is==5) :: (is==10) :: (is==20) :: (is==40) )

    if (id==nstage) ng=1;
    s=s+dels;
    w2k=is-1;
    a=s0*s/(s-s0);  /* a=1/(1/s0-1/s) */
    aed=(s-dels-s0)*s/((s-dels)*s0);  /* aed=(1/(s-dels)-1/s0)/(1/s0) */

    /* AT TIME S2, DETERMINE THE LAST CONTINUATION POINT */

    if ( is==1 )

    /* FOR EACH GRID LEVEL IN V2, V20 SAY, FIND THE CORRESPONDING
V1, V10 SAY, TO MAKE (V10,V20) A LAST CONTINUATION POINT */

    while ( w2k<=(nw2-2) )
    {
beg=0;
bend=0;
w1k=0;
w2kk=w2k+1;
w2kkk=w2kk+1;
tw1kk=0;
td=0;
ted=0;
if ( w2[w2kk]>0 )
{
    while ( w1k<=(nw1-2) )
    {
        w1kk=w1k+1;
        w1kccc=w1kkk+1;
        d=a*b(w1[w1kk],w2[w2kk],s,s0);
        ed=aed*d;
        rr=w2kk[w1k]+rr[w2kk][w1kk]+rr[w2kk][w1kk]+rr[w2kkk][w1kk])/4;
        if ( ed<d )
        {
            if ( w1kk==(nw1-1) )
            {
                larger=1;
                goto finish;
            }
            r[w2kk][w1kk]=ed;
            if ( w1kk==2 )
                r[w2kk][0]=r[w2kk][2];
            bed=1;
            td=d;
            ted=ed;
        }
        else if ( bed==1 )
        {
            rind[w2kk]=w1k;
            if ( (w2kk>ns) && (w2kk<=(nw2-ns)) && (ng==1) )
            {
                td=td/a;
                ted=ted/a;
                fprintf(outfile, "%8.5f %8.2f %8.2f %14.6f\n", s, w2[w2kk], w1[w1k], ted);
                fprintf(graph,"%8.6f %14.6f %14.6f\n", s, w1[w1k], w2[w2kk]);
            }
            w1k=nw1;
        }
        else
        {
            w2k=nw2;
            w1k=nw1;
        }
    }
}

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wlk=wlk+1;
}
}
else
{
    while ( wlk<=(nw1-2) )
    {
        wlk=wlk+1;
        wkk=wlkk+1;
        d=a*b(w1[wlkk],w2[w2kk],s,s0);
        ed=a*d;
        rr[w2kk][wlk]+rr[w2kk][wlkk]+rr[w2kk][wlkk]+rr[w2kk][wlkk])/4;
        if ( ed<d )
        {
            if (flid==0)
            {
                flend=wlkk;
                flid=1;
            }
            if (wlkk==nw1-1)
            {
                larger=1;
                goto finish;
            }
        }
        r[w2kk][wlkk]=ed;
        if ( wlk==2 )
            r[w2kk][0]=r[w2kk][2];
        if ( beg==0 )
        {
            beg=1;
            lind[w2kk]=wlkk;
            if (((out0==0) && (wlkk==1))
            {
                out0=1;
                if ( (w2kk==ns) && (w2kk<=(nw2-ns))
                    && (ng==1) )
                {
                    d=d/a;
                    ed=ed/a;
                    fprintf(outfile,
"%8.5f %8.2f %8.2f %14.6f\n",
                    s, w2[w2kk], w1[wlkk], ed);
                    fprintf(graphleft,"%8.6f %14.6f %14.6f\n",
                    s, w1[wlkk], w2[w2kk]);
                }
            }
        }
    }
}
else if ( (wlkk>1) && (w2kk==ns)
    && (w2kk<=(nw2-ns)) && (ng==1) )
    {
        d=d/a;
        ed=ed/a;
    }
}
fprintf(outfile, " %8.5f %8.2f %8.2f %14.6f\n", 
    s, w2[w2kk], w1[w1kk], ed);
    fprintf(graphleft, " %8.6f %14.6f %14.6f\n", 
    s, w1[w1kk], w2[w2kk]);
}
}
else
{
    bed=1;
    tw1kk=w1kk;
    td=d;
    ted=ed;
}
}
else if ( (beg==1) && (bed==1) )
{
    w1k=nw1;
}
    w1k=w1k+1;
}

/* DECIDE THE VALUES OF VECTORS STORING THE LOCATIONS
   OF THE LAST CONTINUATION POINTS */

/*
if (beg==0)
{
    lind[w2kk]=0;
    rind[w2kk]=0;
}
else if (bed==0)
{
    rind[w2kk]=lind[w2kk];
}
else
{
    rind[w2kk]=tw1kk;

    if ( (ng==1) && (w2kk>=ns) && (w2kk<=(nw2-ns)) )
    {
        td=td/a;
        ted=ted/a;
        fprintf(outfile, " %8.5f %8.2f %8.2f %14.6f\n", 
            s, w2[w2kk], w1[tw1kk], ted);
        fprintf(graph, " %8.6f %14.6f %14.6f\n", 
            s, w1[tw1kk], w2[w2kk]);
    }
}
}
    w2k=w2k+1;
}
}
else
/* APPLY THE PROPERTIES OF THE LAST CONTINUATION POINTS */
/* AT TIME S3, S4, S5, .... FOR EACH GRID LEVEL OF V2, V20 SAY, FIND THE CORRESPONDING
V1. V10 SAY, TO MAKE (V10,V20) A LAST CONTINUATION POINT */

while ( w2k<(nw2-is-1) )
{
    beg=0;
    bed=0;
    w2kk=w2k+1;
    w2kdkk=w2kk+1;
    tw1kk=0;
    td=0;
    ted=0;
    if ( w2[w2kk]>=0 )
{
    /* DECIDE THE NUMBER OF GRID LEVELS IN V1 WHICH HAVE TO
BE CHECKED FOR THE CURRENT GRID LEVEL OF V2 */

    /* ----------------------------------------------- */
    /* */
    /* */
    /* */
    if ( rindp[w2kk]==0 )
    {
        if ( (rindp[w2k]>0) || (rindp[w2kdkk]>0) )
        {
            if (rindp[w2k]==rindp[w2kk])
                rend=rindp[w2k];
            else
                rend=rindp[w2kdkk];
        }
        else
            rend=1;
    }
    else if ( (rindp[w2k]>rindp[w2kk]) ||
               (rindp[w2kdkk]>rindp[w2kk]))
    {
        if (rindp[w2k]==rindp[w2kk])
            rend=rindp[w2k];
        else
            rend=rindp[w2kdkk];
    }
    else
    {
        rend=rindp[w2kk]+1;
    }
    /* ----------------------------------------------- */

    w1k=rindp[w2kk];
    while ( w1k<rend )
    {
        w1k+w1k+1;
        w1kdkk=w1kk+1;
        d=awb(w1[w1k],w2[w2kk],s,s0);
    }
ed=aed
    (rr[w2kk][w1kk]+rr[w2kk][w1kkk]+
     rr[w2kk][w1kk]+rr[w2kkk][w1kk])/4;
    if ( ed<d )
    {
        if ( w1kkk==nw1-1 )
            {larger=1;
             goto finish;
            }
        bed=1;
        tw1kkk=w1kk;
        td=d;
        ted=ed;
    }
    else
    {
        wlk=nw1;
    }
    wlk=w1k+1;
}
if ( bed==1 )
{
    rind[w2kkk]=tw1kkk;
    if ( (w2kk>k==ns) && (w2kkk<(nw2-ns)) && (ng==1) )
    {
        td=td/a;
        ted=ted/a;
        fprintf(outfile,
            " %8.5f %8.2f %8.2f %14.6f\n",
            s, w2[w2kk], w1[tw1kk], ted);
        fprintf(graph," %8.6f %14.6f %14.6f\n",
            s, w1[tw1kkk], w2[w2kkk]);
    }
}
else
{
    rind[w2kk]=rindp[w2kk];
    if ( rind[w2kk]>0 )
    {
        d=b(w1[rind[w2kk]],w2[w2kk],s,s0);
        ed=aed#
            (rr[w2kk][rind[w2kkk]-1]+rr[w2kk][rind[w2kk]+1]+
             rr[w2k][rind[w2kk]]+rr[w2kkk][rind[w2kkk]])/(4*a);
        if ( (w2kk>k==ns) && (w2kkk<(nw2-ns)) && (ng==1) )
        {
            fprintf(outfile,
                " %8.5f %8.2f %8.2f %14.6f\n",
                s, w2[w2kk], w1[rind[w2kk]], ed);
            fprintf(graph," %8.6f %14.6f %14.6f\n",
                s, w1[rind[w2kk]], w2[w2kk]);
        }
    }
}

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if ( rind[w2kk]==0 )
    w2k=nw2;
}
else
{
if ( (lindp[w2kk]==0) && (rindp[w2kk]==0) &&
    (lindp[w2k]==0) && (rindp[w2k]==0) &&
    (lindp[w2kkk]==0) && (rindp[w2kkk]==0) )
{
lend=pflend;
    ilend=0;
    while ( (ilend<1) && (lend>0) )
    {
        for (i=0; i<1; i++) iid[i]=0;
if ( ((w1[lend+1]+sqt3*w2[w2kk]) <= 0) &&
    ((w1[lend+1]-sqt3*w2[w2kk]) >= 0) ) iid[1]=1;
if ( ((w1[lend]+sqt3*w2[w2kk+1]) <= 0) &&
    ((w1[lend]-sqt3*w2[w2kk+1]) >= 0) ) iid[0]=1;
    ilend=iid[0]*iid[1];
if ( (ilend==0) && lend==lend-1; )
}
w1k=lend;
    while ( w1k<=(nw1-2) )
    {
        w1kk=w1k+1;
        w1kkk=w1kk+1;
        d=nb(w1[w1kk],w2[w2kk],s,s0);
ed=ed*#
    (rr[w2kk][w1k]+rr[w2kk][w1kk]+rr[w2k][w1kk]+rr[w2kkk][w1kk])/4;
    if ( ed<d )
    {
if ( flid==0)
    {
flend=w1kk;
    flid=1;
}
if ( w1kk==(nw1-1) )
    {
larger=1;
goto finish;
}
if ( beg==0 )
    {
    beg=1;
lind[w2kk]=w1kk;
    if ( ((out0==0) && (w1kk==1))
    {
    out0=1;
    if ( (w2kk>=ns) && (w2kk<=(nw2-ns)) &&
        (ng==1) )
    {
    d=d/a;
ed=ed/a;

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fprintf(outfile,
   " %8.5f %8.2f %8.2f %14.6f\n",
   s, w2[w2kk], w1[w1kk], ed);
    fprintf(graphleft, "%8.6f %14.6f %14.6f\n",
   s, w1[w1kk], w2[w2kk]);
}
}
else if ( (w2kk>=ns) && (w2kk<=(nw2-ns)) &&
   (w1kk>=1) && (ng==1) )
{
   d=d/a;
   ed=ed/a;
   fprintf(outfile,
      " %8.5f %8.2f %8.2f %14.6f\n",
   s, w2[w2kk], w1[w1kk], ed);
    fprintf(graphleft, "%8.6f %14.6f %14.6f\n",
   s, w1[w1kk], w2[w2kk]);
}
}
else
{
    bed=1;
    tw1kk=w1kk;
    td=ed;
    ted=ed;
}
}
else if ( (beg==1) || (bed==1) )
{
    w1k=nw1;
}
else
{
    irend=0;
    for (i=0; i<1; i++) iid[i]=0;
    if ( (((w1[w1k]+sqt3*w2[w2kk]) >= 0) &&
      (((w1[w1k]) >= 0))) )
    iid[0]=1;
    if ( (((w1[w1kk]+sqt3*w2[w2kk-1]) >= 0) &&
      (((w1[w1kk]) >= 0))) )
    iid[1]=1;
    irend=iid[0]*iid[1];
    if ( (irend==1) w1k=nw1;
}
    w1k=w1k+1;
}
if ( (beg==0) )
{
    lind[w2kk]=0;
    rind[w2kk]=0;
}
else if ( (bed==0) )
{

rind[w2kk]=lind[w2kk];
}
else
{
    rind[w2kk]=tw1kk;
    if ( (ng==1) && (w2kk>=ns) && (w2kk<=(nw2-ns)) )
    {
        td=td/a;
        ted=ted/a;
        fprintf(outfile,
" %8.5f %8.2f %8.2f %14.6f\n",
        s, w2[w2kk], w1[tw1kk], ted);
        fprintf(graph," %8.6f %14.6f %14.6f\n",
        s, w1[tw1kk], w2[w2kk]);
    }
}
else
{

/* DECIDE THE NUMBER OF GRID POINTS HAVE TO BE CHECKED
FOR THE CURRENT GRID LEVEL OF V2 */

//--------------------------------------------------------------------------
//
// if ( (rindp[w2k]>rindp[w2kk]) \\
// (rindp[w2kkk]>rindp[w2kk]) )
//
// {  
//    if (rindp[w2kk]>rindp[w2kkk])
//        rend=rindp[w2k];
//    else
//        rend=rindp[w2kkk];
// }  
// else
//    rend=rindp[w2kk]+1;
//
// /* LOOP FOR APPLYING PROPOSITION 3.2.4 */

irend=0;
while (irend < 1)
{
    for (i=0; i<=1; i++) iid[i]=0;
    if ( (w1[rend-1]+sqt3*w2[w2kk]) >= 0) &&
        (w1[rend-1] >= 0) )
        iid[0]=1;
    if ( (w1[rend]+sqt3*w2[w2kk-1]) >= 0) &&
        (w1[rend] >= 0) )
        iid[1]=1;
    irend=iid[0]*iid[1];
    if (irend==0) rend=rend+1;
}
if (lindp[w2kk]>2)
{

if ((lindp[w2k]<lindp[w2kk]) && (lindp[w2k]>1))
{
    if ( (lindp[w2kk]<lindp[w2k]) &&
         (lindp[w2kk]>1) )
        lend=lindp[w2kk]-1;
    else if (lindp[w2k]>1)
        lend=lindp[w2k]-1;
    else
        lend=lindp[w2k]-2;

else
    lend=lindp[w2kk]-2;
}
else
    lend=0;

/* LOOP TO APPLY PROPOSITION 3.2.4 */

ilend=0;
while ((ilend < 1) && (lend>0))
{
    for (i=0; i<=1; i++) iid[i]=0;
    if ( ((w1[lend+1]+sqrt3*w2[w2kk]) <= 0) &&
         ((w1[lend+1]-sqrt3*w2[w2kk]) > 0) ) iid[1]=1;
    if ( ((w1[lend]+sqrt3*w2[w2kk+1]) <= 0) &&
         ((w1[lend]-sqrt3*w2[w2kk+1]) > 0) ) iid[0]=1;
    ilend=iid[0]*iid[1];
    if (ilend==0) lend=lend-1;
}
wlk=lend;

/*------------------------------------------*/

if ((lindp[w2kk]==0) && (rindp[w2kk]==0))
{
    while (wlk<=rend)
    {
        w1kk=wlk+1;
        w1kkk=wlkk+1;
        d=abs(w1[w1kk],w2[w2kk],s,s0);
        ed=ed^2
        (rr[w2kk][wlk]+rr[w2kk][wlkk]+rr[w2k][wlkk]+rr[w2kkk][wlkk])/4;
        if (ed<d)
        {
            if (flid==0)
            {
                flend=wlkk;
                flid=1;
            }
            if (wlkk=(nw1-1))
            {
                larger=1;
            }
        }
    }
goto finish;
}
if ( beg==0 )
{
    beg=1;
lind[w2kk]=w1kk;
    if (((out0==0) && (w1kk==1))
    {
        out0=1;
        if ( (w2kk==ns) && (w2kk<(nw2-ns)) &&  
        (ng==1) )
        {
            d=d/a;
ed=ed/a;
            fprintf(outfile,
" %8.5f %8.2f %8.2f %14.6f\n",  
    s, w2[w2kk], w1[w1kk], ed);
            fprintf(graphleft,
" %8.6f %14.6f %14.6f\n",  
    s, w1[w1kk], w2[w2kk]);
    }
    }
    else if ( (w1kk>1) && (w2kk==ns)  
        && (w2kk<(nw2-ns)) && (ng==1) )
    {
        d=d/a;
ed=ed/a;
            fprintf(outfile,
" %8.5f %8.2f %8.2f %14.6f\n",  
    s, w2[w2kk], w1[w1kk], ed);
            fprintf(graphleft," %8.6f %14.6f %14.6f\n",  
    s, w1[w1kk], w2[w2kk]);
    }
    }
else
{
    bed=1;
tw1kk=w1kk;
td=d;
ted=ed;
}
}
else if ( (beg==1) || (bed==1) )
{
    w1k=nw1;
}
w1k=w1k+1;
}
if ( (beg==0) )
{
    lind[w2kk]=0;
    rind[w2kk]=0;
}
else if ( (bed==0) )
{
    rind[w2kk]=lind[w2kk];
}
else
{
    rind[w2kk]=tw1kk;
    if ( (ng==1) && (w2kk>ns) && (w2kk<=(nw2-ns)) )
    {
        td=td/a;
        ted=ted/a;
        fprintf(outfile,
                " %8.5f %8.2f %8.2f %14.6f\n",
                s, w2[w2kk], w1[tw1kk], ted);
        fprintf(graph," %8.6f %14.6f %14.6f\n",
                s, w1[tw1kk], w2[w2kk]);
    }
}
else
{
    while (w1k < rend)
    {
        if ( (w1k>=1end) && (w1k<=lindp[w2kk]-2) )
        {
            w1kk=w1k+1;
            w2kk=w1kk+1;
            d=a*b(w1[w1kk],w2[w2kk],s,s0);
            ed=a*ed*
                (rr[w2kk][w1k]+rr[w2kk][w1kkk]+rr[w2k][w1kk]+rr[w2kk][w1kkk])/4;
            if ( ed<d )
            {
                if (f1id==0)
                {
                    f1end=w1kk;
                    f1id=1;
                }
                if (beg==0)
                {
                    beg=1;
                    lind[w2kk]=w1kk;
                    if ( (out0==0) && (w1kk==1) )
                    {
                        out0=1;
                        if ( (w2kk>ns) && (w2kk<=(nw2-ns)) &&
                                (ng==1) )
                        {
                            d=d/a;
                            ed=ed/a;
                            fprintf(outfile,
                                    " %8.5f %8.2f %8.2f %14.6f\n",
                                    s, w2[w2kk], w1[w1kk], ed);
                        }
                    }
                }
            }
        }
    }
}
fprintf(graphleft,
" %8.6f %14.6f %14.6f
",
  s, w1[w1kk], w2[w2kk]);
}
}
else if ( (w2kk>=ns) && (w2kk<=(nw2-ns)) &&
  (w1kk>1) && (ng==1) )
{
d=d/a;
ed=ed/a;
fprintf(outfile,
" %9.5f %8.2f %8.2f %14.6f\n",
  s, w2[w2kk], w1[w1kk], ed);
fprintf(graphleft,
" %8.6f %14.6f %14.6f\n",
  s, w1[w1kk], w2[w2kk]);
}
w1k=rindp[w2kk]-1;
}
}
else if ( (w1k=rindp[w2kk]) && (w1k<rend) )
{
  w1kk=w1k+1;
  w1kkk=w1kk+1;
  d=a*b(w1[w1kk],w2[w2kk],s,s0);
ed=aed
  (rr[w2kk][w1k]+rr[w2kk][w1kkk]+
   rr[w2k][w1kk]+rr[w2kkk][w1kk])/4;
if ( ed<d )
{
  bed=1;
  tw1kk=w1kk;
  td=d;
  ted=ed;
}
else
  w1k=nw1;
}
w1k=w1k+1;
}
if ( (beg==0 )
{
  lind[w2kk]=lindp[w2kk];
  if ( lind[w2kk]==0 )
{
    d=b(w1[lind[w2kk]],w2[w2kk],s,s0);
ed=aed
    (rr[w2kk][lind[w2kk]-1]+rr[w2kk][lind[w2kk]+1]
     +rr[w2kk-1][lind[w2kk]]+rr[w2kkk][lind[w2kk]])
    /(4*a);
    if ( (out0==0) && lind[w2kk]==1)
    {
      out0=1;
      -131-
if ((w2kk>=ns) && (w2kk<=(nw2-ns)) &&
(ng==1))
{
    fprintf(outfile,
        " %8.5f %8.2f %8.2f %14.6f\n",
        s, w2[w2kk], w1[lind[w2kk]], ed);
    fprintf(graphleft," %8.6f %14.6f %14.6f\n",
        s, w1[lind[w2kk]], w2[w2kk]);
}
else if ((lind[w2kk]>1) && (w2kk>=ns) &&
        (w2kk<=(nw2-ns)) && (ng==1))
{
    fprintf(outfile,
        " %8.5f %8.2f %8.2f %14.6f\n",
        s, w2[w2kk], w1[lind[w2kk]], ed);
    fprintf(graphleft," %8.6f %14.6f %14.6f\n",
        s, w1[lind[w2kk]], w2[w2kk]);
}

if (bed==0)
{
    rind[w2kk]=rindp[w2kk];
    if (rind[w2kk]>0)
    {
        d=b(w1[rind[w2kk]], w2[w2kk], s, s0);
        ed=aedx;
        (rr[w2kk][rind[w2kk]-1]+rr[w2kk][rind[w2kk]+1]
        +rr[w2kk-1][rind[w2kk]]+rr[w2kk][rind[w2kk]])
        /((4*a));
        if ((w2kk>=ns) && (w2kk<=(nw2-ns)) && (ng==1))
        {
            fprintf(outfile,
                " %8.5f %8.2f %8.2f %14.6f\n",
                s, w2[w2kk], w1[rind[w2kk]], ed);
            fprintf(graph," %8.6f %14.6f %14.6f\n",
                s, w1[rind[w2kk]], w2[w2kk]);
        }
    }
}
else
{
    rind[w2kk]=tw1kk;
    if ((w2kk>=ns) && (w2kk<=(nw2-ns)) && (ng==1))
    {
        td=td/a;
        ted=ted/a;
        fprintf(outfile,
            " %8.5f %8.2f %8.2f %14.6f\n",
            s, w2[w2kk], w1[tw1kk], ted);
    }
}
```c
fprintf(graph,"%8.6f %14.6f %14.6f\n", s, w1[w1kk], w2[w2kk]);
}

if (w2[w2kk]>=0)
  jj=1;
else if (lind[w2kk]<=1)
  jj=1;
else
  jj=lind[w2kk];
for (j=jj; j<=rind[w2kk]; j++)
{
  r[w2kk][j]=aedw
    (rr[w2kk][j-1]+rr[w2kk][j+1]
    +rr[w2kk-1][j]+rr[w2kk][j])/4;
  if (j==2) r[w2kk][0]=r[w2kk][2];
}
if (flid==1) pflend=frend;
w2k=w2k+1;
}

/* UPDATE MATRICES AND VECTORS rr, rindp, lindp, FOR
 COMPUTATIONS OF THE NEXT TIME STEP */

for (j=is; j<=(nw2-is); j++)
{
    if (w2[j]>=0 ) ii=1;
    else if ( lind[j]==0 ) ii=1;
    else ii=lind[j];
for (i=ii; i<=rind[j]; i++)
{
  rr[j][i]=r[j][i];
  if (i==2 ) rr[j][0]=rr[j][2];
}
for (i=0; i<=nw2; i++) rindp[i]=rind[i];
for (i=0; i<=nleft; i++) lindp[i]=lind[i];
for (i=0; i<=nleft; i++)
{
    if ( (is==ns) && (i==is ) )
      printf("%f %f %d %d\n", s, w2[i], lind[i], rind[i]);
}
    id=id+1;
dels=dels/4;
)
while (id<nstage);
}
```

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fprintf(offile, "need more VI grid to find the last continuation points\n");
fprintf(offile, "the last value of S considered is: is=ld and s=lf.\n", is, s);
}
close(offile);
close(graph);
close(graphleft);

double b(w1, w2, s, s0)
double w1, w2, s, s0;
{
    double sqrt2, sqrt3, sqrt6;
    sqrt2=sqrt((double)2.0);
    sqrt3=sqrt((double)3.0);
    sqrt6=sqrt((double)6.0);
    if (((w1+sqrt3*w2) <= 0) && ((w1-sqrt3*w2) >= 0))
        return ((1/s-1/s0)*(-1*sqrt6*w2));
    else if (((w1 <=0) && ((w1-sqrt3*w2) < 0))
        return (((1/s)-(1/s0))*((sqrt6/2)*w2-(3*sqrt2/2)*w1));
    else if ((w1 >0) && ((w1+sqrt3*w2) > 0))
        return (((1/s)-(1/s0))*((sqrt6/2)*w2+(3*sqrt2/2)*w1));
}

THE END OF THE PROGRAM
BIBLIOGRAPHY


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