A kind of multi-treatment adaptive designs with assignment probabilities depending on the estimated parameters*

ZHANG Li-XIN †

Department of Mathematics, Zhejiang University

Abstract

The Play-the-Winner (PW) rule is an important method in clinical trials for patient allocation with two treatments, in which the probability a treatment is assigned to the coming patient depends upon the response of the previous patient. In this paper, we consider a general kind of PW rule for multi-treatment adaptive designs, in which the probability a treatment is assigned to the coming patient depends upon both the response of the previous patient and an estimated parameter, say, the estimated success rate. Using this kind of adaptive designs, more information of previous stages are used to update the model at each stage, and more patients may be assigned to better treatments. The strong consistency, the asymptotic normality and the strong approximation are established for the proportion of patients assigned to each treatment.

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†Department of Mathematics, Zhejiang University, Hangzhou 310028, P. R. China, E-mail: lxzhang@mail.hz.zj.cn
1 Introduction.

In comparing two treatments 1 and 2 with dichotomous response (success and failure), suppose subjects arrive to the experiment sequentially and must be assigned immediately to treatment 1 or 2. Zelen (1969) proposed the well-known Play-the-Winner (PW) rule: *A success on a particular treatment generates a future trial on the same treatment with a new patient. A failure on a treatment generates a future trial on the alternate treatment.* The PW rule are used for the ethical consideration in which more patients are assigned to a better treatment. As an extension of PW rule, Wei and Durham (1978) proposed the Randomized Play-the-Winner (RPW) rule based on the urn model. Wei (1979) extended the RPW rule to multi-treatment clinical trials and defined a generalized Polya’s urn design. The asymptotic properties of the RPW rule and its various generalizations to multi-treatment cases based on the generalized Polya urn (GPU) have been studied by many authors (cf., Wei 1979, Smythe and Rosenberger 1995, Smythe 1996, Bai and Hu 1999, 2000, etc.). Recently, Bai, Hu and Shen (2002) proposed a new multi-arm design whose rule to update the urn depends on the sample success rates. Such design can assign more patients to better treatments than Wei’s design does. However, the asymptotic distribution of the allocation proportion is unknown.

When the cure rate of each treatment is large (close to 1), the asymptotic distribution of the allocation proportion is unknown in using the RPW rule or its generalizations to multi-treatment cases based on the GPU. The variability of the RPW rule and the GPU model is very high unless all treatments have low cure rates. The variability of allocation can have a strong effect on power. This has been demonstrated by the simulation studies of Melfi and Page (1998) as well as Rosenberger, Stallard, Ivanova, Harper and Ricks (2001) and theoretically by Hu and Rosenberger (2003). Due to the unknown distribution and high variability, the designs in using urn models become less practicable when the treatments have high cure rates, since it is difficult for us to use the statistical method to test whether or not a design truly assign more patients to better treatments or the design fit the desirable goals.

In this paper, we consider another kind of generalizations of the PW rule and define a new adaptive design. In this new adaptive design, instead of using the urn model, we assign each patient directly with a certain probability. But the assigning probabilities are random and depend upon an estimated parameter, say, the sample success rate. A special case (see Example 2.1) of this new adaptive design seems similar to the one proposed by Bai, Hu and Shen (2002), while, the asymptotic normality holds for this new design in almost all cases. Another special case (see Example 2.3) is the sequential maximum likelihood procedure proposed by Melfi and Page (1998, 2000) and Melfi, et al. (2001). The new design is defined and some examples are given in Section 2. The asymptotic
properties, including the strong consistency and its convergence rate, the strong approximation and the asymptotic normality, are given in Section 3. The technical proofs of the strong consistency and its convergence rate are given in Section 4, and the proofs of the strong approximation and the asymptotic normality are given in Section 5.

2 The design and examples.

Consider a \( d \)-treatment clinical trial. Patients are recruited into the clinical trial sequentially and respond immediately to treatments. Suppose at stage \( m \), the \( m \)th patient is assigned to treatment \( i \). We wait for the response \( \xi_{m,i} \) of the \( m \)th patient on treatment \( i \), which is a random variable coming from a distribution family \( \{ P_{\theta_i}; \theta_i \in \Theta_i \} \). Then the \( (m+1) \)th patient will be assigned to treatment \( j \) according to a certain probability, which depends on the response \( \xi_{m,i} \) of the \( m \)th patient. Denote this probability by \( d_{ij}(\xi_{m,i}) \). After \( n \) assignments, for \( i = 1, \ldots, d \), we let \( N_{ni} \) be the number of patients assigned to treatment \( i \), and let \( X_{ni} = 1 \) if the \( n \)th patient is assigned to treatment \( i \) and 0 otherwise. Write \( N_n = (N_{n1}, \ldots, N_{nd}), X_n = (X_{n1}, \ldots, X_{nd}) \) and \( \theta = (\theta_1, \ldots, \theta_d) \). It is obvious that \( N_n 1' = N_{n1} + \cdots + N_{nd} = n \), where \( 1 = (1, \ldots, 1) \). Also,

\[
P(X_{m+1,j} = 1|X_{m,i} = 1, \xi_{m,i}) = d_{ij}(\xi_{m,i}) \quad i, j = 1, \ldots, d.
\]

Such a design is a generalization of the two-treatment Markov-Chain adaptive design proposed by Bai, et al. (2001). We write \( \xi_m = (\xi_{m,1}, \ldots, \xi_{m,d}) \), and assume that the responses \( \{ \xi_{m}, m = 1, 2, \ldots \} \) is a sequence of i.i.d. random vectors. In the clinical trial, \( \xi_{i,k} \) appears only when the \( i \)th patient is assigned to treatment \( k \), i.e., when \( X_{i,k} = 1 \). But we assume that all the responses \( \{\xi_{i,k}\} \) are there, and only those \( X_{i,k}\xi_{i,k}'s \) of non-zero are selected in the trial.

In many cases, the parameters \( \theta_k \)'s can be regarded as rules to judge whether a treatment is good or not. If \( \theta_1, \ldots, \theta_d \) are known, it is reasonable to use them to optimize the design. In such case, the assignment probability \( d_{ij} \) depends on \( \theta \), i.e.,

\[
P(X_{m+1,j} = 1|X_{m,i} = 1, \xi_{m,i}) = d_{ij}(\theta, \xi_{m,i}) \quad i, j = 1, \ldots, d.
\]

And then

\[
P(X_{m+1,j} = 1|X_{m,i} = 1) = h_{ij}(\theta) = \mathbb{E}[d_{ij}(\theta, \xi_{m,i})] \quad i, j = 1, \ldots, d.
\]

It follows that \( \{X_n; n \geq 1\} \) is a homogeneous Markov chain with transition matrix:

\[
H = H(\theta) = (h_{ij}(\theta))_{i,j=1}^d.
\]

However, the parameter \( \theta \) is usually unknown. We shall replace it by its estimator. This leads us
to consider the following adaptive design. Throughout this paper, we assume that \( \theta = \mathbb{E}\xi_m \). So, we can use the sample mean to estimate \( \theta \).

**Adaptive Design 1:** Suppose the previous \( m - 1 \) patients are assigned and the responses observed. Let \( \hat{\theta}_{m-1} = (\hat{\theta}_{m-1,1}, \ldots, \hat{\theta}_{m-1,d}) \) be an estimate of \( \theta \), where \( \hat{\theta}_{m-1,k} = \frac{\sum_{i=1}^{m-1} X_{i,k} \xi_{i,k} + \theta_{0,k}}{N_{m-1,k} + 1} \), \( k = 1, \ldots, d \). Here, \( \theta_0 = (\theta_{0,1}, \ldots, \theta_{0,d}) \) is a guessed value of \( \theta \), or an estimator of \( \theta \) from other early trials.

Now, if the \( n \)th patient is assigned to treatment \( i \) and the response observed, then we assign the \((m + 1)\)th patient to treatment \( j \) with probability \( d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i}) \), \( j = 1, \ldots, d \). However, to insure that each treatment is tested by enough patients, i.e., \( N_{ni} \rightarrow \infty \) a.s., \( i = 1, \ldots, d \), \( d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i}) \) shall be modified by \((1 - 1/m)d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i}) + 1/(md) \) if necessary. That is

\[
P(X_{m+1,j} = 1|F_m, X_{m,i} = 1, \xi_{m,i}) = (1 - \frac{1}{m})d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i}) + \frac{1}{md} \quad i, j = 1, \ldots, d. \tag{2.1}
\]

Here \( F_n = \sigma(X_1, \ldots, X_n, \xi_1, \ldots, \xi_{n-1}) \) is the history sigma field. We also let \( h_{ij}(\hat{\theta}_{m-1}) = E[d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i})|F_{m-1}] \) and write \( H(\hat{\theta}_{m-1}) = (h_{ij}(\hat{\theta}_{m-1}))_{i,j=1}^d \).

**Remark 2.1** If

\[
\sum_{m=2}^{\infty} \min_{i} h_{ij}(\hat{\theta}_{m-1}) = \infty \text{ a.s.,} \quad j = 1, \ldots, d, \tag{2.2}
\]

then the modification of \( d_{ij}(\hat{\theta}_{m-1}, \xi_{m,i}) \) is not necessary. For example, if \( \Theta = \{x: h_{ij}(x) > 0, i, j = 1, \ldots, d\} \) is a rectangle in \( \mathbb{R}^d \) of the form \( (a, b), (a, b] \) etc, and also \( \Theta \subset \Theta \), \( \hat{\theta}_{m-1} \in \Theta \) for each \( m \), then (2.2) is satisfied (see the proof in Section 4).

**Remark 2.2** Usually, many cases, in which the parameter \( \theta \) is not a mean of the response \( \xi_n \), can be transferred to the case we study above. In fact, if for each \( k \), the estimator \( \tilde{\theta}_{n,k} = \tilde{\theta}_{n,k}(\xi_{j,k} : j = 1, 2, \cdots, n) \) of \( \theta \) can be written in the following form:

\[
\tilde{\theta}_{n,k} = \frac{1}{n} \sum_{j=1}^{n} f_k(\xi_{j,k}) + o(n^{-1/2-\delta}), \quad \text{for some } \delta > 0, \tag{2.3}
\]

then in the Adaptive Design 1, we can define

\[
\hat{\theta}_{m-1,k} = \tilde{\theta}_{n,k}(\xi_{j,k} : X_{j,k} = 1, j = 1, 2, \cdots, m - 1).
\]

Many maximum likelihood estimators and moment estimators satisfy (2.3).

As a function of \( \hat{\theta} \), \( H(\hat{\theta}) \) is assumed to be continuous at \( \theta \), i.e., \( H(x) \rightarrow H = H(\theta) \) as \( x \rightarrow \theta \). It is obvious that \( H1' = 1 \). So, \( \lambda_1 = 1 \) is an eigenvalue of \( H \). Let \( \lambda_2, \ldots, \lambda_d \) be other \( d - 1 \) eigenvalues, and let \( \lambda = \max\{|\lambda_2|, \ldots, |\lambda_d|\} \). Then \( \lambda \leq 1 \). Also, we let \( v = (v_1, \ldots, v_d) \) be the left eigenvector of
corresponding to its maximal eigenvalue \( \lambda_1 = 1 \) with \( \mathbf{v} \mathbf{1}' = 1 \). Then \( v_i \geq 0, \ i = 1, \ldots, d \). In the next section, we will claim that under some suitable conditions (stated in Section 3) on the function \( \mathbf{H}(\cdot) \) and moments of the responses,

\[
\frac{N_n}{n} \to \mathbf{v} \text{ a.s. and } n^{1/2} \left( \frac{N_n}{n} - \mathbf{v} \right) \xrightarrow{\mathcal{D}} N(0, \mathbf{A}),
\]

(2.4)

if \( \lambda < 1 \), where \( \mathbf{A} \) is defined as in (3.4).

Next, we give some examples on the special case that the treatments have dichotomous outcomes, the success and failure. Let \( p_k \) be the success probability of a patient on treatment \( k \), and \( q_k = 1 - p_k \), \( k = 1, \ldots, d \). We assume that \( 0 < p_k < 1 \), \( k = 1, \ldots, d \). As an extension of the PW rule to the multi-treatment case, Hoel and Sobel (1972) proposed the Cyclic Play-the-Winner (PWC) rule: If the response on treatment \( k \) is a success, we assign a coming patient to the same treatment. If the response is a failure, we assign a coming patient to the treatment \( k + 1 \), and \( d + 1 \) means 1. In using the PWC rule, one has

\[
\frac{N_{nk}}{n} \xrightarrow{\mathcal{D}} v_{i_{PWC}} := \frac{1}{q_i} \sum_{j=1}^{d} \frac{1}{q_j}, \quad i = 1, \ldots, d.
\]

(2.5)

The PWC rule tends to put more patients to better treatments. However, one may argue, when there is a failure on treatment \( k \), why we assign the next patient to treatment \( k + 1 \), not some one of the other treatments, or some of the \( d - 1 \) treatments with certain probabilities. When there is a failure on treatment \( k \), it should be more reasonable to assign the next patient with higher probability to a better treatment among the other \( d - 1 \) treatments. Motivated by this, the following adaptive is considered.

**Example 2.1** If the response on treatment \( k \) is a success, we assign a coming patient to the same treatment. If the response is a failure, we assign a coming patient to other \( d - 1 \) treatments with probabilities proportional to the estimated success rates, i.e, at stage \( m \), when the response of the \( m \)th patient on treatment \( k \) is a failure, we assign the \((m + 1)\)th patient to treatment \( j \) with probability

\[
\frac{\hat{p}_{m-1,j}}{(M_{m-1} - \hat{p}_{m-1,k})},
\]

for all \( j \neq k \), where \( M_{m-1} = \sum_{j=1}^{d} \hat{p}_{m-1,j}, \ 
\hat{p}_{m-1,j} = \frac{S_{m-1,j} + 1}{N_{m-1,j} + 1}, \) and \( S_{m-1,j} \) denotes the number of successes of treatment \( j \) in all the \( N_{m-1,j} \) trials of previous \( m - 1 \) stages, \( j = 1, \ldots, d \).

For this design, we have

\[
\mathbf{H} = \begin{pmatrix}
  p_1 & \frac{p_2}{M - p_1}q_1 & \cdots & \frac{p_d}{M - p_1}q_1 \\
  \frac{p_1}{M - p_2}q_2 & p_2 & \cdots & \frac{p_d}{M - p_2}q_2 \\
  \cdots & \cdots & \cdots & \cdots \\
  \frac{p_1}{M - p_d}q_d & \frac{p_2}{M - p_d}q_d & \cdots & p_d
\end{pmatrix},
\]

where \( M = \sum_{j=1}^{d} p_j \), and

\[
v_i = \frac{p_i(M - p_i)/q_i}{\sum_{j=1}^{d} p_j(M - p_j)/q_j}, \quad i = 1, \ldots, d.
\]
The next example is an extension of Example 2.1.

**Example 2.2** Let $0 \leq \alpha < \infty$. At the $m$th stage, if the response is a failure, we assign the $(m+1)$th patient to treatment $j$ with probability 
\[
\frac{\hat{p}_{m-1,j}^\alpha}{\sum_{j=1}^d \hat{p}_{m-1,j}^\alpha} \quad \text{for all } j \neq k, \text{ instead, where } M_{m-1,\alpha} = \sum_{j=1}^d \hat{p}_{m-1,j}^\alpha.
\]
In this case, $H(x) = (h_{k,j}(x), k, j = 1, \ldots, d)$, where $h_{k,k}(x) = p_k$ and $h_{k,j}(x) = \frac{x_\alpha q_k}{\sum_{i \neq k} x_i}$ for $k \neq j$. Also,
\[
H = H^{(\alpha)} = \left( \begin{array}{cccc}
\frac{p_1}{M_{\alpha}-p_1}q_1 & \frac{p_2}{M_{\alpha}-p_2}q_2 & \cdots & \frac{p_d}{M_{\alpha}-p_d}q_d \\
\frac{p_2}{M_{\alpha}-p_2}q_2 & \frac{p_1}{M_{\alpha}-p_1}q_1 & \cdots & \frac{p_d}{M_{\alpha}-p_d}q_d \\
\vdots & \vdots & \ddots & \vdots \\
\frac{p_d}{M_{\alpha}-p_d}q_d & \frac{p_d}{M_{\alpha}-p_d}q_d & \cdots & \frac{p_d}{M_{\alpha}-p_d}q_d
\end{array} \right),
\]
where $M_\alpha = \sum_{j=1}^d p_j^\alpha$, and
\[
v_i = v_i^{(\alpha)} = \frac{p_i(M_\alpha - p_i)/q_i}{\sum_{j=1}^d p_j^\alpha(M_\alpha - p_j^\alpha)/q_j}, \quad i = 1, \ldots, d.
\]
For these two examples, (2.4) holds. Example 2.1 is a special case of Example 2.2 with $\alpha = 1$. When $\alpha = 0$, then $H^{(\alpha)}$ and $v_i^{(\alpha)}$ become
\[
H^{(0)} = \left( \begin{array}{cccc}
p_1 & \frac{1}{d-1}q_1 & \cdots & \frac{1}{d-1}q_1 \\
\frac{1}{d-1}q_2 & p_2 & \cdots & \frac{1}{d-1}q_2 \\
\vdots & \vdots & \ddots & \vdots \\
\frac{1}{d-1}q_d & \frac{1}{d-1}q_d & \cdots & p_d
\end{array} \right)
\]
and
\[
v_i^{(0)} = \frac{1}{q_i} \frac{1}{\sum_{j=1}^d 1/q_j}, \quad i = 1, \ldots, d.
\]
By comparing the values of $v^{(\alpha)}$'s, one can find that the larger $\alpha$ is, the more patients will be assigned to a better treatment. It is obvious that $v_i^{(0)} = v_i^{\text{PWC}}$, $i = 1, \ldots, d$. So, the design in Example 2.1 or Example 2.2 assigns more patients to better treatments than the PWC rule does. Also, when there is a failure, the assignment is random in the designs in these two examples. So, these designs are not so deterministic as the PWC rule.

**Remark 2.3** When $d = 2$, the designs in Examples 2.1 and 2.2 are all the PW rule.

**Remark 2.4** Using the generalized Polya urn model, Bai, Hu and Shen (2002) proposed a design similar to that in Examples 2.1. But for the GPU model, to study the asymptotic normality, we need a very stringent condition that $\max\{\text{Re}(\lambda_2), \ldots, \text{Re}(\lambda_d)\} \leq 1/2$. Even in the 3-treatment case, such a condition is not easy to check.
At last we give an example for the two-treatment case.

**Example 2.3** We consider the two-treatment adaptive design. At the $m$th stage, no matter what the response of the $m$th patient is, we assign the $(m+1)$th patient to treatment $j$ with probability

\[
\hat{q}_{m-1,j} \frac{1-x_{m+2}}{(1-x_1)+(1-x_2)} \frac{1-x_1}{(1-x_1)+(1-x_2)}
\]

This is the sequential maximum likelihood procedure proposed by Melfi and Page (1998, 2000) and Melfi, et al. (2001). If $0 < p_1, p_2 < 1$, then

\[
H(x) = \begin{pmatrix}
\frac{1-x_2}{(1-x_1)+(1-x_2)} & \frac{1-x_1}{(1-x_1)+(1-x_2)} \\
\frac{1-x_2}{(1-x_1)+(1-x_2)} & \frac{1-x_1}{(1-x_1)+(1-x_2)}
\end{pmatrix} \rightarrow H = \begin{pmatrix}
\frac{q_2}{q_1+q_2} & \frac{q_1}{q_1+q_2} \\
\frac{q_2}{q_1+q_2} & \frac{q_1}{q_1+q_2}
\end{pmatrix}.
\]

We have the following asymptotic properties:

\[
N_{n,1} - \frac{q_2}{q_1+q_2} = O\left(\sqrt{\frac{\log \log n}{n}}\right) \quad \text{and} \quad N_{n,2} - \frac{q_1}{q_1+q_2} = O\left(\sqrt{\frac{\log \log n}{n}}\right) \quad \text{a.s.}
\]

and

\[
n^{1/2} \left( N_{n,1} - \frac{q_2}{q_1+q_2} \right), \left( N_{n,2} - \frac{q_1}{q_1+q_2} \right) \overset{D}{\rightarrow} N(0,\sigma^2)(1,-1),
\]

where

\[
\sigma^2 = \frac{q_1 q_2 (2 + p_1 + p_2)}{(q_1 + q_2)^3}.
\]

This design gives the same limiting proportions as the PW rule does.

### 3 Asymptotic properties.

To study the precise asymptotic properties, we first need some assumptions.

**Assumption 3.1** For the matrix $H$ and the vector $v$, we assume that $\lambda < 1$ and $v_i > 0$, $i = 1, \ldots, d$.

This assumption is satisfied if $H$ is a regular transition matrix of a Markov chain, i.e., all of the elements of $H^q$ are strictly positive for some $q = 1, 2, \ldots$. So the assumption is satisfied for all the designs in Examples 2.1-2.3 since $h_{ij} > 0$ for all $i, j = 1, \ldots, d$.

**Assumption 3.2** For the responses $\xi_n$, we assume that

\[
E\|\xi_n\|^{2+\delta} \leq c_0 < \infty \quad \text{for some} \quad \delta > 1.
\]

And write $\sigma_k^2 = \text{Var}(\xi_{1,k})$, $k = 1, \ldots, d$.

**Assumption 3.3** For the matrix function $H(x)$, we assume that

\[
H(x) - H = H(x) - H(\theta) = O(\|x - \theta\|) \quad \text{as} \quad x \rightarrow \theta.
\]
Assumption 3.4 For the matrix function $H(x)$, we assume that for $\delta > 0$,

$$H(x) - H = \sum_{k=1}^{d} \frac{\partial H(x)}{\partial x_k} \bigg|_{x=\theta} (x_k - \theta_k) + O(\|x - \theta\|^{1+\delta}) \quad \text{as} \quad x \to \theta.$$ 

Using the notation and assumptions defined as above, we can now establish the following results.

Theorem 3.1 For the Adaptive Design 1, suppose $E\|\xi_1\| < \infty$ and $\lambda_j \neq 1$, $j = 2, \ldots, d$. Then

$$\frac{N_n}{n} \to v \quad \text{a.s.}$$

Theorem 3.2 For the Adaptive Design 1, under the Assumptions 3.1-3.3,

$$\frac{N_n}{n} - v = O\left(\sqrt{\log \log n}\right) \quad \text{a.s.} \quad (3.1)$$

The next theorem gives us the strong approximation of $N_n$.

Theorem 3.3 For the Adaptive Design 1, suppose the Assumptions 3.1, 3.2 and 3.4 are satisfied. Define $\tilde{H} = H - 1'v$ and

$$\Sigma = (I - \tilde{H}')^{-1}(\text{diag}(v) - H'\text{diag}(v)H)(I - \tilde{H})^{-1},$$

$$f_k = v \frac{\partial H(x)}{\partial x_k} \bigg|_{x=\theta}, \quad F = (f_1', \ldots, f_d'),$$

$$F_\parallel = F(I - \tilde{H})^{-1}, \quad \Sigma_\parallel = F'(\text{diag}(\sigma_1^2/v_1, \ldots, \sigma_d^2/v_d))F_\parallel. \quad (3.2)$$

Then possibly in a richer underlying probability space in which there exist two independent $d$-dimensional standard Brownian motions $\{B_t\}$ and $\{W_t\}$, we can redefine the sequence $\{X_t\}$, without changing its distribution, such that

$$\hat{\theta}_n - \theta = \frac{1}{n} W_n \text{diag}(\sigma_1/\sqrt{v_1}, \ldots, \sigma_d/\sqrt{v_d}) + o(n^{1/2 - \kappa})$$

$$N_n - n v = B_n \Sigma^{1/2} + \int_0^n \frac{W_t}{t} dt \Sigma^{1/2} + o(n^{1/2 - \kappa}) \quad \text{a.s.,} \quad (3.3)$$

for some $\kappa > 0$. In particular,

$$n^{1/2}\left(\frac{N_n}{n} - v, \hat{\theta}_n - \theta\right) \xrightarrow{D} N\left(0, \begin{pmatrix} \Lambda & F_\parallel \Lambda_\parallel \\ \Lambda_\parallel F_\parallel & \Lambda_\parallel \end{pmatrix}\right),$$

where

$$\Lambda = \Sigma + 2\Sigma_\parallel \quad \text{and} \quad \Lambda_\parallel = \text{diag}(\sigma_1^2/v_1, \ldots, \sigma_d^2/v_d), \quad (3.4)$$

and also

$$n^{-1/2}(N_{[nt]} - nt v) \xrightarrow{D} B_t \Sigma^{1/2} + \int_0^t \frac{W_s}{s} ds \Sigma^{1/2}$$

in the space $D[0,1]$ with the Skorohod topology.
Remark 3.1 Notice that the all eigenvalues of $\tilde{H}$ are 0, $\lambda_2, \ldots, \lambda_d$, and the all eigenvalues of $I - \tilde{H}$ are $1, 1 - \lambda_2, \ldots, 1 - \lambda_d$. So, if $\lambda_i \neq 1$, $i = 2, \ldots, d$, then $(I - \tilde{H})^{-1}$ exists.

Remark 3.2 If the assignment probabilities do not depend on the estimated parameters, i.e., $H(x) \equiv \tilde{H}$, then $\Sigma_i = 0$. So, the second term in the right hand of (3.3) and (3.4) will not appear.

Remark 3.3 From the proof of Theorem 3.3, we may estimate $\Lambda$ (the asymptotic covariance matrix of $n^{-1/2}N_n$) based on the following procedure:

(i) Let $\hat{\nu}_k = N_{n,k}/n$, $k = 1, \ldots, d$, and $\hat{\nu} = (\hat{\nu}_1, \ldots, \hat{\nu}_d)$. Estimate $H$ by $\hat{H} = H(\hat{\theta})$, and $f_k$ by $\hat{f}_k = v\partial H(x)/\partial x_k|_{x = \hat{\theta}}$, $k = 1, \ldots, d$. Write $\tilde{F} = (\hat{f}_1', \ldots, \hat{f}_d')'. $

(ii) Estimate $\sigma_k^2$ by $\hat{\sigma}_k^2$ if $X_{i,k} = \xi_{i,k} - \hat{\theta}_k)^2/N_{n,k}$, $k = 1, \ldots, d$, and estimate $\Lambda_1$ by $\hat{\Lambda}_1 = \text{diag}(\hat{\sigma}_1^2/\hat{\nu}_1, \ldots, \hat{\sigma}_d^2/\hat{\nu}_d)$.

(iii) Let $\hat{H} = H - 1\hat{\nu}$ and estimate $\Lambda$ by

$$\hat{\Lambda} = [(I - \hat{H})^{-1}]' \left[\text{diag}(\hat{\nu}) - \hat{H}'\text{diag}(\hat{\nu})\hat{H} + 2\hat{F}'\hat{\Lambda}_1\hat{F}\right] (I - \hat{H})^{-1}.$$

Based on $\hat{\Lambda}$, we can assess the variation of designs.

Remark 3.4 If the responses $\xi_n$, $n \geq 1$, are not identically distributed, then under the conditions in Theorems 3.1-3.3, we have respectively,

$$N_n - n\nu = O \left(\sum_{m=1}^n \|E\xi_m - \theta\|\right) \quad \text{a.s.},$$

$$N_n - n\nu = O \left(\sqrt{n \log \log n} + O \left(\sum_{m=1}^n \|E\xi_m - \theta\|\right)\right) \quad \text{a.s.},$$

$$N_n - n\nu = B_n \Sigma^{1/2} + \int_0^n \frac{W_t}{\ell} dt \Sigma^{1/2} + o(n^{1/2-\kappa})$$

$$+ O \left(\sum_{m=1}^n \|E\xi_m - \theta\|\right) + O \left(\sum_{m=1}^d \sum_{i=1}^d \text{Var}(\xi_{m,i} - \sigma_i^2) \right)^{1/2+\delta} \quad \text{a.s.}$$

4 Proofs of Theorems 3.1 and 3.2

In this section we prove the strong consistency and its convergence rate. We need some lemmas first.

Lemma 4.1 If $E\|\xi_1\| < \infty$, then $\hat{\theta}_{n,k} \rightarrow \theta_k$ a.s. as $n \rightarrow \infty$ on the event $\{N_{n,k} \rightarrow \infty\}$, $k = 1, \ldots, d$.

Furthermore, if $E\|\xi_1\|^2 < \infty$, then $\hat{\theta}_{n,k} - \theta_k = O(\sqrt{\log \log N_{n,k}} / N_{n,k})$ a.s. as $n \rightarrow \infty$ on the event $\{N_{n,k} \rightarrow \infty\}$, $k = 1, \ldots, d$.

Proof. For $k = 1, \ldots, d$, define $\tau_i^k = \min\{j : N_{j,k} = i\}$, where $\min\emptyset = +\infty$. Let $\{\eta_{k}\}$ be an independent copy of $\{\xi_{i,k}\}$, which is also independent of $\{X_i\}$. Define $\Xi_{i,k} = \xi_{\tau_i^k,k} I\{\tau_i^k < +\infty\} +$
η_{i,k}I\{\tau^k_i = +\infty\}, i \geq 1. Then \{\Xi_{m,k}, m = 1, 2, \ldots\} is a sequence of i.i.d. random variables, with the same distribution as that of \xi_{1,k} (cf. Bai, Hu and Shen, 2002). Also, \hat{\theta}_{n,k} = \frac{1}{N_{n,k+1}}(\sum_{i=1}^{N_{n,k}} \Xi_{m,k} + 1) on the event \{N_{n,k} \to \infty\}. The results follow by the law of large numbers and the law of the iterated logarithm for sums of i.i.d. random variables.

**Lemma 4.2** For the Adaptive Design 1, we have

\[ N_{n,k} \to \infty \quad \text{a.s.,} \quad k = 1, \ldots, d. \]

**Proof.** For each fixed \(k\), it is obvious that

\[ \sum_{m=2}^{\infty} P(X_{m+1,k} = 1|\mathcal{F}_m) \geq \sum_{m=2}^{\infty} \frac{1}{md} = +\infty \quad \text{a.s.}, \]

which implies that \(P(X_{m,k} = 1, \text{i.o.}) = 1\) by the generalized Borel-Cantelli lemma. It follows that \(N_{n,k} \to \infty\) a.s. If (2.2) is satisfied, then the proof is similar.

**Proof of Theorem 3.1.** Write

\[ h_{ij}(m) = (1 - \frac{1}{m})h_{ij}(\hat{\theta}_{m-1}) + \frac{1}{md} \quad \text{and} \quad H_m = (h_{ij}(m))_{i,j=1}^d. \]

From (2.1), it follows that

\[ P(X_{m+1,j} = 1|\mathcal{F}_m, X_{m,i} = 1) = h_{ij}(m) \quad i, j = 1, \ldots, d, \]

i.e.,

\[ P(X_{m+1} = e_j|X_m = e_i, \mathcal{F}_m) = h_{ij}(m), \]

where \(e_i\) is a vector whose \(i\)th component is 1 and other components are 0, \(i = 1, \ldots, d\). It follows that

\[ E[X_{m+1}|\mathcal{F}_m] = X_m H_m. \quad (4.1) \]

So, \(\{X_m\}\) looks like a non-homogeneous Markov chain with transition matrix \(H_n\).

Let \(Z_n = X_n - E[X_n|\mathcal{F}_{n-1}]\), and \(M_n = \sum_{k=1}^{n} Z_n\). By (4.1), it is easily seen that

\[ X_n = Z_n + X_{n-1}H_{n-1} = Z_n + (X_{n-1} - v)H + v + X_{n-1}(H_{n-1} - H) = Z_n + (X_{n-1} - v)\tilde{H} + v + X_{n-1}(H_{n-1} - H) \]

since \(vH = v\) and \((X_{n-1} - v)1' = 1 - 1 = 0\). So,

\[ \sum_{k=1}^{n}(X_k - v) = M_n + \sum_{k=1}^{n}(X_k - v)\tilde{H} + \sum_{k=1}^{n} X_k(H_k - H) + E[X_1|\mathcal{F}_0] - E[X_{n+1}|\mathcal{F}_n]. \]

It follows that

\[ (N_n - nv)(I - \tilde{H}) = M_n + \sum_{k=1}^{n} X_k(H_k - H) + E[X_1] - E[X_{n+1}|\mathcal{F}_n]. \quad (4.2) \]
On the other hand, it is obvious that $\|Z_n\| \leq 2$. By the law of the iterated logarithm for martingales (c.f., Theorem 5.4.1 of Stout (1974)), one has

\[ M_n = O(\sqrt{n \log \log n}) \quad \text{a.s.} \quad (4.3) \]

Now, by Lemmas 4.1 and 4.2, we have $\hat{\theta}_n \rightarrow \theta$ a.s. as $n \rightarrow \infty$. So, $H(\hat{\theta}_n) \rightarrow H(\theta)$ a.s. $n \rightarrow \infty$. It follows that $H_n \rightarrow H$. Hence

\[ \sum_{k=1}^{n} \|H_k - H\| = o(n) \quad \text{a.s.,} \]

which together with (4.2) and (4.3) implies $(N_n - n \nu)(I - \tilde{H}) = o(n)$ a.s. Notice that $(I - \tilde{H})^{-1}$ exists under the condition that $\lambda_j \neq \lambda_1 = 1$ for $j \neq 1$. The proof is now completed.

**Proof of Theorem 3.2.** From Theorem 3.1, it follows that

\[ \frac{1}{N_{n,k}} \sim \frac{1}{nv_k} \quad \text{a.s.} \quad (n \rightarrow \infty), \quad k = 1, \ldots, d. \]

So, by Lemmas 4.1 and 4.2,

\[ \hat{\theta}_{n,k} - \theta_k = O\left(\sqrt{\log \log \frac{N_{n,k}}{n}}\right) = O\left(\sqrt{\log \log \frac{n}{n}}\right) \quad \text{a.s.} \quad k = 1, \ldots, d. \]

Thus

\[ \hat{\theta}_n - \theta = O\left(\sqrt{\log \log \frac{n}{n}}\right) \quad \text{a.s.,} \quad (4.4) \]

which, together with Assumption 3.4, implies that

\[ H_n - H = H(\hat{\theta}_{n-1}) - H(\theta) + O\left(\frac{1}{n}\right) = O\left(\sqrt{\log \log \frac{n}{n}}\right) \quad \text{a.s.} \quad (4.5) \]

Hence

\[ \sum_{k=1}^{n} \|H_k - H\| = \sum_{k=1}^{n} O\left(\sqrt{\log \log \frac{k}{k}}\right) = O\left(\sqrt{n \log \log n}\right) \quad \text{a.s.} \]

By combining (4.2), (4.3) and the above equation, we conclude that $(N_n - n \nu)(I - \tilde{H}) = O(\sqrt{n \log \log n})$ a.s. The proof is now completed.

**The proof of (2.2) in Remark 2.1:** By Lemma 4.1, $\hat{\theta}_{m,j} \rightarrow \theta_j$ a.s. on the event $\{N_{m,j} \rightarrow \infty\}$. Also, on the event $\{\sup_m N_{m,j} < \infty\}$, there exists an $m_0$ such that $\hat{\theta}_{m,j} = \hat{\theta}_{m_0,j}$ for all $m \geq m_0$. It follows that

the closure of $\{\hat{\theta}_m; m = 1, 2, \ldots\} \subset \{x : h_{ij}(x) > 0, i, j = 1, \ldots, d\}$ a.s.

So, by the continuity of $H(x)$, with probability one there is an $c_0 > 0$ such that

\[ h_{ij}(\hat{\theta}_m) \geq c_0 \quad \text{for all} \quad i, j = 1, \ldots, d \quad \text{and} \quad m \geq 1. \]

(2.2) is proved.
5 Proof of Theorem 3.3.

Recall (4.2), in which the martingale $M_n$ can be approximated by a Wiener process. If the term $\sum_{k=1}^{n} X_k(H_k - H)$ is asymptotically negligible, then the strong approximation of $N_n$ follows easily. However, by (4.5), the fast convergence rate of the mentioned term is $O(\sqrt{n \log \log n})$. So, we need to do some more things on this term. We need some lemmas. The first one tells us that this term can be approximated by $\sum_{k=1}^{n} v(H_k - H)$.

Lemma 5.1 If $\lambda = \max\{\|\lambda_2|, \cdots, |\lambda_d|\} < 1$, then

$$\|\sum_{k=1}^{n} X_k(H_k - H) - \sum_{k=1}^{n} v(H_k - H)\| \leq C + C\|\sum_{k=2}^{n} Z_k(I - \tilde{H}^{-1})(H_{k-1} - H)\|$$

$$+ C\sum_{k=2}^{n} \|H_k - H_{k-1}\| + C\sum_{k=1}^{n} \|H_k - H\|^2. \quad (5.1)$$

Proof. Without loss of generality, we assume that $\|x\|$ is the Euclidian norm of $x \in \mathbb{R}^d$, and $\|M\| = \sup_{x \neq 0} \|xM\|/\|x\|$ is the norm of a $d \times d$ matrix $M$. Write $H_0 = e'_1EX_1$. For $k \leq 0$, let $X_k = aX_1, H_k = H_0, \mathcal{F}_k = \mathcal{F}_0$ and $Z_k = 0$. Then for $p \geq n \geq 1$,

$$\sum_{k=1}^{n} X_k(H_k - H) = \sum_{k=1}^{n} Z_k(H_k - H) + \sum_{k=1}^{n} X_{k-1}H_{k-1}(H_k - H) + \sum_{k=1}^{n} X_kH_{k-1}(H_k - H) - H_kH_k$$

$$= \sum_{k=1}^{n} Z_k(H_k - H) + \sum_{k=1}^{n} X_{k-1}H(H_k - H) + \sum_{k=1}^{n} X_k(H_k - H)(H_k - H)$$

$$= \sum_{k=1}^{n} Z_k(H_k - H) + \sum_{k=1}^{n} Z_{k-1}H(H_k - H) + \sum_{k=1}^{n} X_kH(H_k - H)$$

$$= \cdots = \sum_{k=1}^{n} \sum_{j=0}^{p} Z_{k-j}H^j(H_k - H) + \sum_{k=1}^{n} X_{k-p}H^p(H_k - H)$$

$$+ \sum_{k=1}^{n} \sum_{j=1}^{p} X_{k-j}(H_k - H)H^{j-1}(H_k - H).$$

Observe that $X_j1' = 1, Z_j1' = 0, H_j - 1'v = (H - 1'v)^j = H^j$ and $(H_j - H)1' = 1' - 1' = 0$. We have

$$X_{k-p}H^p(H_k - H) = X_{k-p}(H^p - 1'v)(H_k - H) + X_{k-p}1'v(H_k - H)$$

$$= X_{k-p}H^p(H_k - H) + v(H_k - H),$$

$$Z_{k-j}H^j(H_k - H) = Z_{k-j}H^j(H_k - H).$$

and

$$X_{k-j}(H_k - H)H^{j-1}(H_k - H) = X_{k-j}(H_k - H)\tilde{H}^{j-1}(H_k - H).$$
We conclude that

\[ \sum_{k=1}^{n} X_k(H_k - H) \]

\[ = \sum_{k=1}^{n} v(H_k - H) + \sum_{k=1}^{n} \sum_{j=0}^{p} Z_{k-j} \tilde{H}^j(H_k - H) \]

\[ + \sum_{k=1}^{n} \sum_{j=1}^{p} X_{k-j} (H_{k-j} - H) \tilde{H}^{j-1}(H_k - H) + \sum_{k=1}^{n} X_{k-p} \tilde{H}^p(H_k - H) \]

\[ = \sum_{k=1}^{n} v(H_k - H) + \sum_{k=1}^{n} \sum_{j=0}^{p} Z_{k-j} \tilde{H}^j(H_{k-j-1} - H) + \sum_{k=1}^{n} \sum_{j=0}^{p} Z_{k-j} \tilde{H}^j(H_k - H_{k-j-1}) \]

\[ + \sum_{k=1}^{n} \sum_{j=1}^{p} X_{k-j} (H_{k-j} - H) \tilde{H}^{j-1}(H_k - H) + \sum_{k=1}^{n} X_{k-p} \tilde{H}^p(H_k - H) \]

\[ =: \sum_{k=1}^{n} v(H_k - H) + I_1 + I_2 + I_3 + I_4. \quad (5.3) \]

Notice that \( \lim_{j \to \infty} \| \tilde{H}^j \|^{1/j} = |\lambda| < 1 \). So, for \( |\lambda| < \rho < 1 \), there exists a constant \( C > 0 \) such that

\[ \| \tilde{H}^j \| \leq C \rho^j, \quad j \geq 0. \]

It follows that

\[ \| I_1 \| = \| \sum_{k=1}^{n} \sum_{j=0}^{n} Z_{k-j} \tilde{H}^j(H_{k-j-1} - H) \| = \| \sum_{j=0}^{n} \sum_{k=j}^{n} Z_{k-j} \tilde{H}^j(H_{k-j-1} - H) \| \]

\[ = \| \sum_{j=0}^{n} \sum_{l=0}^{j} Z_l \tilde{H}^j(H_{l-1} - H) \| = \| \sum_{l=0}^{n} \sum_{j=0}^{l} Z_l \tilde{H}^j(H_{l-1} - H) \| \]

\[ = \| \sum_{l=0}^{n} \sum_{j=n-l}^{\infty} Z_l \tilde{H}^j(H_{l-1} - H) \| = \| \sum_{l=0}^{n} \sum_{j=n-l}^{\infty} Z_l \tilde{H}^j(H_{l-1} - H) \| \]

\[ \leq \| \sum_{l=0}^{n} Z_l (I - \tilde{H})^{-1}(H_{l-1} - H) \| + C \sum_{l=0}^{n} \sum_{j=n-l}^{\infty} \rho^j \| H_{l-1} - H \| \]

\[ \leq \| \sum_{l=1}^{n} Z_l (I - \tilde{H})^{-1}(H_{l-1} - H) \| + C/(1 - \rho)^2, \quad (5.4) \]

\[ \| I_2 \| \leq C \sum_{k=1}^{n} \sum_{j=0}^{p} \rho^j \| H_k - H_{k-j-1} \| \leq C \sum_{k=1}^{n} \sum_{j=0}^{p} \rho^j \sum_{i=0}^{j} \| H_{k-i} - H_{k-i-1} \| \]

\[ \leq C \sum_{k=1}^{n} \sum_{i=0}^{j} \rho^j \sum_{i=0}^{n} \| H_{k-i} - H_{k-i-1} \| \leq C \sum_{k=1}^{n} \rho^j \sum_{i=0}^{n} \| H_{k} - H_{k-1} \| \]

\[ \leq C \sum_{k=1}^{n} \| H_k - H_{k-1} \|, \quad (5.5) \]
Lemma 5.2
Let
\[
\|I_3\| \leq C \sum_{k=1}^{n} \sum_{j=1}^{p} \|H_{k-j} - H\| \cdot \rho^{j-1} \cdot \|H_k - H\| = C \sum_{j=1}^{p} \rho^{j-1} \sum_{k=1}^{n} \|H_{k-j} - H\| \cdot \|H_k - H\|
\]
\[
\leq C \sum_{j=1}^{p} \rho^{j-1} \left( \sum_{k=1}^{n} \|H_{k-j} - H\|^2 \right)^{1/2} \left( \sum_{k=1}^{n} \|H_k - H\|^2 \right)^{1/2} \leq C \sum_{j=1}^{p} \rho^{j-1} \sum_{k=1}^{n} \|H_k - H\|^2
\]
\[
= C \sum_{j=1}^{p} j \rho^{j-1} \|H_0 - H\|^2 + C \sum_{j=1}^{p} \rho^{j-1} \sum_{k=1}^{n} \|H_k - H\|^2
\]
\[
\leq C \|H_0 - H\|^2 + C \sum_{k=1}^{n} \|H_k - H\|^2
\]
(5.6)

and

\[
\|I_4\| \leq C \rho^p \sum_{k=1}^{n} \|H_k - H\|.
\]
(5.7)

Substituting (5.4)-(5.7) into (5.2) and letting \( p \to \infty \) yields (5.1).

The next two lemmas are on the strong approximation for a martingale.

Lemma 5.2 Let \( \{S_n = \sum_{k=1}^{n} \Delta S_k, \mathcal{F}_n; n \geq 1\} \) be a \( \mathbb{R}^K \)-valued martingale sequence, and let

\[
T_n = \sum_{k=1}^{n} \mathbb{E} \left[ \left( \Delta S_k \right) \left( \Delta S_k \right) \right] \mathcal{F}_{k-1}.
\]

Suppose there exist a constant \( 0 < \epsilon < 1 \) such that

\[
\sup_n \mathbb{E} \|X_n\|^{2+\epsilon} < \infty.
\]
(5.8)

Furthermore, suppose \( T \) is a covariance matrix measurable with respect to \( \mathcal{F}_k \) for some \( k \geq 0 \). Then for any \( \delta > 0 \), possibly in a richer underlying probability space in which there exists a \( K \)-dimensional standard Brownian \( \{B_t\} \), we can redefine the sequence \( \{S_n\} \) and \( T \), without changing their distributions, such that \( \{B_t\} \) is independent of \( T \), and

\[
S_n - B_nT^{1/2} = O(n^{1/2-\kappa}) + O(\alpha_n^{1/2+\delta}) \text{ a.s.}
\]
for some \( \kappa > 0 \). Here \( \alpha_n = \max_{m \leq n} \|T_m - mT\| \).

Proof. This lemma is proved by Zhang (2004), we omit the details here.

Lemma 5.3 Denote \( \Sigma_1 = \text{diag}(v) - H \text{diag}(v)H \). Let \( Q_n = (Q_{n,1}, \ldots, Q_{n,d}) = \sum_{k=1}^{n} q_k \), where \( q_k = X_k \text{diag}(\xi_k - \theta) \). Suppose Assumption 3.2 is satisfied. Then for any \( \delta > 0 \), there are two independent \( d \)-dimensional standard Brownian motions \( B_t \) and \( W_t \) and a positive number \( \kappa > 0 \), such that

\[
M_n - B_n \Sigma_1^{1/2} = O(n^{1/2-\kappa}) + O((\sum_{k=1}^{n} \|H_n - H\|)^{1/2+\delta}) \text{ a.s.},
\]
\[
Q_n - W_n \text{diag} (\sigma_1 \sqrt{v_1}, \ldots, \sigma_d \sqrt{v_d}) = O(n^{1/2-\kappa}) + O((\sum_{k=1}^{n} \|H_n - H\|)^{1/2+\delta}) \text{ a.s.}
\]
Proof. It is obvious that

$$E[Z'_n q_n | F_{n-1}] = E[Z'_n X_n | F_{n-1}] diag(E[\xi_n - \theta]) = 0. \quad (5.9)$$

and

$$\sum_{k=2}^{n} E[q'_k q_k | F_{n-1}] = \sum_{k=2}^{n} diag(\sigma^2_1, \cdots, \sigma^2_d) diag(X_{k-1}H_{k-1})$$

$$= diag(\sigma^2_1, \cdots, \sigma^2_d) diag(\sum_{k=1}^{n-1} X_kH) + diag(\sigma^2_1, \cdots, \sigma^2_d) diag(\sum_{k=1}^{n-1} X_k(H_k - H))$$

$$= (n-1) diag(\sigma^2_1, \cdots, \sigma^2_d) diag(vH) + diag(\sigma^2_1, \cdots, \sigma^2_d) diag((N_{n-1} - (n-1)v)H)$$

$$+ diag(\sigma^2_1, \cdots, \sigma^2_d) diag(\sum_{k=1}^{n-1} X_k(H_k - H)).$$

It follows that

$$\left\| \sum_{k=1}^{n} E[q'_k q_k | F_{n-1}] - n diag(\sigma^2_1 v_1, \cdots, \sigma^2_d v_d) \right\|$$

$$\leq C + C \|N_n - nv\| + C \sum_{k=1}^{n} \|H_k - H\| \leq C \sqrt{n \log \log n} + C \sum_{k=1}^{n} \|H_k - H\| \ a.s., \quad (5.10)$$

by (4.2) and (4.3).

On the other hand, we can verify that

$$E[Z'_n Z_n | F_{n-1}] = E[Z'_n X_n | F_{n-1}] - (E[X_n | F_{n-1}])' E[X_n | F_{n-1}]$$

$$= diag(X_{n-1}H_{n-1}) - H'_n diag(X_{n-1})H_{n-1}$$

$$= diag(vH) - H' diag(v)H - H' diag(X_{n-1} - v)H + diag((X_{n-1} - v)H)$$

$$+ diag(X_{n-1}(H_{n-1} - H)) - H'_n diag(X_{n-1}) (H_{n-1} - H) - (H_{n-1} - H)' diag(X_{n-1})H.$$ 

It follows that

$$\left\| \sum_{k=1}^{n} E[Z'_k Z_k | F_{k-1}] - n \Sigma_1 \right\|$$

$$\leq \left\| H' diag(N_{n-1} - nv)H \right\| + \left\| diag((N_{n-1} - nv)H) \right\| + C \sum_{k=1}^{n} \|H_k - H\| + C$$

$$\leq C \|N_n - nv\| + C \sum_{k=1}^{n} \|H_k - H\| + C \leq C \left( \sqrt{n \log \log n} \right) + C \sum_{k=1}^{n} \|H_k - H\| \quad (5.11)$$

by (4.2) and (4.3) again. By (5.11), (5.9) and (5.10), applying Lemma 5.2 to the martingale sequence 
$$\{\sum_{k=1}^{n} (Z_k, q_k); n \geq 1\}$$ completes the proof of Lemma 5.3.

Proof of Theorem 3.3. Recall (4.2). We first apply Lemma 5.1 to show that

$$\sum_{k=1}^{n} X_k(H_k - H) = \sum_{k=1}^{n} \frac{1}{k} Q_k diag(1/v_1, \cdots, 1/v_d)F + o(n^{1/2-\delta/3}) \ a.s. \quad (5.12)$$
By Assumption 3.4 and (4.4),
\[
H_{n+1} - H = H(\hat{\theta}_n) - H(\theta) + O\left(\frac{1}{n}\right)
\]
\[
= \sum_{k=1}^{d} \left. \frac{\partial H(x)}{\partial x_k} \right|_{x=\theta} (\hat{\theta}_{n,k} - \theta_k) + O(\|\hat{\theta}_n - \theta\|^{1+\delta}) + O\left(\frac{1}{n}\right)
\]
\[
= \sum_{k=1}^{d} \left. \frac{\partial H(x)}{\partial x_k} \right|_{x=\theta} (\hat{\theta}_{n,k} - \theta_k) + o(n^{-1/2-\delta/3}) \quad a.s.
\]  
(5.13)

Also, by noting that \(Q_n = O(\sqrt{n \log \log n})\) a.s., \(\hat{\theta}_{n,k} = \frac{\sum_{m=1}^{n} X_{m,k} \xi_{m,k+1}}{N_{n,k+1}}\), \(k = 1, \ldots, d\), and (3.1), we have
\[
\hat{\theta}_{n,k} - \theta_k = \frac{n}{N_{n,k} + 1} \left( Q_{n,k} + 1 - \theta_k \right)
\]
\[
= \frac{1}{v_k} \frac{1}{n} Q_{n,k} + \left( \frac{n}{N_{n,k} + 1} - \frac{1}{v_k} \right) \frac{1}{n} Q_{n,k} + \frac{1 - \theta_k}{N_{n,k} + 1}
\]
\[
= \frac{1}{v_k} Q_{n,k} + O\left( \sqrt{\log \log n} \right) \cdot O\left( \frac{\log \log n}{n} \right) + O\left( \frac{1}{n} \right)
\]
\[
= \frac{1}{v_k} Q_{n,k} + + O\left( \frac{1}{n} \right) \quad a.s.
\]

It follows that
\[
H_{n+1} - H = \frac{1}{v_k} \sum_{k=1}^{d} \left. \frac{\partial H(x)}{\partial x_k} \right|_{x=\theta} Q_{n,k} + o(n^{-1/2-\delta/3})
\]
(5.14)

So,
\[
v(H_{n+1} - H) = (\hat{\theta}_n - \theta)F + o(n^{-1/2-\delta/3})
\]
\[
= \frac{1}{n} Q_n \text{diag}(1/v_1, \ldots, 1/v_d)F + o(n^{-1/2-\delta/3}) \quad a.s.
\]  
(5.15)

We conclude that
\[
\sum_{k=1}^{n} v(H_k - H) = \sum_{k=1}^{n} \frac{1}{h_k} Q_k \text{diag}(1/v_1, \ldots, 1/v_d)F + o(n^{1/2-\delta/3}) \quad a.s.
\]  
(5.16)

Next we treat the terms in the left hand of (5.1). By (5.14),
\[
H_{n+1} - H_n = \frac{1}{v_k} \sum_{k=1}^{d} \left. \frac{\partial H(x)}{\partial x_k} \right|_{x=\theta} \left( \frac{Q_{n,k}}{n} - \frac{Q_{n-1,k}}{n-1} \right) + o(n^{-1/2-\delta/3})
\]
\[
= \frac{1}{v_k} \sum_{k=1}^{d} \left. \frac{\partial H(x)}{\partial x_k} \right|_{x=\theta} \frac{X_{n,k} (\xi_{n,k} - \theta_k)}{n} + O\left( \frac{\sqrt{n \log \log n}}{n(n-1)} \right) + o(n^{-1/2-\delta/3})
\]
\[
= O\left( \frac{\|\xi_n - \theta\|}{n} \right) + o(n^{-1/2-\delta/3}) = o(n^{-1/2-\delta/3}) \quad a.s.
\]

It follows that
\[
\sum_{k=1}^{n-1} \|H_{k+1} - H_k\| = o(n^{1/2-\delta/3}) \quad a.s.
\]  
(5.17)

By (4.5),
\[
\sum_{k=1}^{n} \|H_k - H\|^2 = O\left( (\log n) \log \log n \right) \quad a.s.
\]  
(5.18)
On the other hand, \( \{ \sum_{k=2}^{n} Z_k (I - \bar{H})^{-1} (H_{k-1} - H) ; n \geq 2 \} \) is a martingale sequence with

\[
\left\| \sum_{k=2}^{n} E \left[ (I - \bar{H})^{-1} (H_{k-1} - H) \right] Z_k Z_k^\prime (I - \bar{H})^{-1} (H_{k-1} - H) \right\| \leq C \sum_{k=2}^{n} \| H_{k-1} - H \|^2 = O((\log n) \log \log n) \quad \text{a.s.}
\]

By the law of the iterated logarithm for martingales, we have

\[
\sum_{k=2}^{n} Z_k (I - \bar{H})^{-1} (H_{k-1} - H) = O(\sqrt{\log n} \log \log n) \quad \text{a.s.} \quad (5.19)
\]

Combining (5.16)-(5.19) and (5.1) yields (5.12) immediately.

Now, by (4.2), (5.12) and Lemma 4.1, we obtain

\[
(N_n - n\nu)(I - \bar{H}) = B_n \Sigma_1^{1/2} + \sum_{k=1}^{n} W_k \text{diag}(\sigma_1/\sqrt{v_1}, \cdots, \sigma_d/\sqrt{v_d}) F + o(n^{1/2-\kappa})
\]

\[
= B_n \Sigma_1^{1/2} + \int_{0}^{n} W d\nu \text{diag}(\sigma_1/\sqrt{v_1}, \cdots, \sigma_d/\sqrt{v_d}) F + o(n^{1/2-\kappa}) \quad \text{a.s.}
\]

Also,

\[
\hat{\theta}_n - \theta = \frac{1}{n} Q_n \text{diag}(1/v_1, \cdots, 1/v_d) + o(n^{-1/2-\delta/3})
\]

\[
= \frac{1}{n} W_n \text{diag}(\sigma_1/\sqrt{v_1}, \cdots, \sigma_d/\sqrt{v_d}) + o(n^{-1/2-\kappa}) \quad \text{a.s.}
\]

The proof is now completed.

**A note on the proof of Example 2.3:** Write \( E = (1, -1)'(1, -1) \). Note that \( v_1 = \frac{q_2}{q_1 + q_2}, \)

\( v_2 = \frac{q_2}{q_1 + q_2}, \), \( \sigma_1^2 = p_1 q_1, \sigma_2^2 = p_2 q_2, \)

\[
H = \frac{1}{q_1 + q_2} \begin{pmatrix} q_2 & q_1 \\ q_2 & q_1 \end{pmatrix} = 1' \nu.
\]

So, \( \bar{H} = H - 1' \nu = 0 \) and \( \Sigma = \Sigma_1 = \frac{q_1 q_2}{(q_1 + q_2)^2} E. \) Also,

\[
\frac{\partial H(x)}{\partial x_1} \bigg|_{x=(p_1, p_2)} = \frac{q_2}{(q_1 + q_2)^2} \begin{pmatrix} 1 & -1 \\ 1 & -1 \end{pmatrix} \quad \text{and} \quad \frac{\partial H(x)}{\partial x_2} \bigg|_{x=(p_1, p_2)} = \frac{q_1}{(q_1 + q_2)^2} \begin{pmatrix} -1 & 1 \\ -1 & 1 \end{pmatrix}.
\]

It follows that

\[
F = \frac{1}{q_1 + q_2} (q_2, -q_1)'(1, -1) \quad \text{and} \quad \Sigma = F' \text{diag}(\sigma_1^2/v_1, \sigma_2^2/v_2) F = \frac{q_1 q_2 (p_1 + p_2)}{(q_1 + q_2)^3} E.
\]

Then

\[
\Lambda = \Sigma + 2\Sigma = \frac{q_1 q_2 (2 + p_1 + p_2)}{(q_1 + q_2)^3} E.
\]

The proof is completed.
References


