Bias Correction in Non-Differentiable Estimating Equations for Optimal Dynamic Regimes

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Abstract

A dynamic regime is a function that takes treatment and covariate history and baseline covariates as inputs and returns a decision to be made. Robins (2004) proposed g-estimation using structural nested mean models for making inference about the optimal regime in a multi-interval trial. The method provides clear advantages over traditional parametric approaches.

Robins' g-estimation method always yields consistent estimators, but these can be asymptotically biased under a given structural nested mean model for certain longitudinal distributions of the treatments and covariates, termed exceptional laws. In fact, under the null hypothesis of no treatment effect, every distribution constitutes an exceptional law under structural nested mean models which allow for interaction of current treatment with past treatments or covariates. This paper provides an explanation of exceptional laws and describes a new approach to g-estimation which we call Zeroing Instead of Plugging In (ZIPI). ZIPI shares all of the asymptotic properties of recursive g-estimates at non-exceptional laws while providing substantial reduction in the bias at exceptional laws when decision rule parameters are not shared across intervals.

KEYWORDS: Dynamic treatment regimes; Optimal structural nested mean models; Asymptotic bias; g-estimation; Pre-test estimators.

1. INTRODUCTION

In a study aimed at estimating the mean effect of a treatment on a time-dependent outcome, dynamic treatment regimes are an obvious choice to consider. A dynamic regime is a function that has treatment and covariate history as arguments; the value returned by the function is the treatment to be given at the current time. A recently proposed method of inference (Robins 2004) is g-estimation using structural nested mean models. This method is semi-parametric and is robust to certain types of mis-specification. In this regard it is superior to traditional parametric approaches. However, g-estimation is asymptotically biased under specific data distributions which Robins has termed the *exceptional laws*. At exceptional laws, g-estimates of parameters for optimal structural nested mean models are asymptotically biased and exhibit non-regular behaviour.

The aim of this paper is to provide a means of reducing the asymptotic bias of g-estimates in the presence of exceptional laws. Exceptional laws are discussed in the optimal dynamic regimes literature only by Robins (2004); there, a method of detecting these laws and improving coverage of confidence intervals, but not the bias of point estimates, is proposed.

Structural nested mean models and g-estimation are discussed in section 2.1, followed by a detailed explanation of exceptional laws in g-estimation in section 2.2. Section 3.2 describes a method of reducing the asymptotic bias due to exceptional laws which we call *Zeroing Instead of Plugging In* (ZIPI), with theoretical properties derived in section 3.3. Sections 3.4 and 3.5 compare ZIPI to g-estimation and to the Iterative Minimization for Optimal Regimes (IMOR) method proposed by Murphy (2003). Section 4 concludes.

2. INFERENCE VIA G-ESTIMATION AND EXCEPTIONAL LAWS

2.1 Inference for optimal dynamic regimes: structural nested mean models and g-estimation

We consider the estimation of treatment effect in a sequential study. All of the methods discussed in this paper are appropriate for a finite number of treatment intervals. We shall focus on the two-interval case where a single covariate is used to determine the optimal rule at each interval.

Notation Notation is adapted from Murphy (2003) and Robins (2004). Treatments are taken at K fixed times, $t_1, ..., t_K$. L_j are the covariates measured prior to treatment at the beginning of the j^{th} interval, while A_j is the treatment taken subsequent to having measured L_j. Y is the outcome observed at the end of the second interval; larger values of Y are favorable. Specific or observed values are denoted in lower-case. Denote a variable X_j at t_j and its history, $(X_1,X_2,...,X_j)$, by $\bar{X}_j$. Finally, denote a treatment decision at t_j that depends on history, $\bar{L}_j, \bar{A}_{j-1}$, by $D_j \equiv D_j(\bar{L}_j, \bar{A}_{j-1})$.

In the two-interval case treatments are taken at two fixed times, t_1 and t_2. L_1 and L_2 are the covariates measured prior to treatment at the beginning of the first and second intervals, respectively, i.e. at t_1 and t_2. In particular, L_1 represents baseline covariates and L_2 includes time-varying covariates which may depend on treatment received at t_1. A_j, $j = 1, 2$, is the treatment given subsequent to observing L_j. Thus, the data are, chronologically, (L_1, A_1, L_2, A_2, Y).

Throughout this paper, models shall be explained in terms of *potential outcomes*: the value of a covariate or the outcome that would result if a subject were assigned to different treatments. In the two-interval case we denote by $L_2(a_1)$ a subject's potential covariate at the beginning of the second interval if treatment a_1 is taken by that subject, and $Y(a_1, a_2)$ denotes the potential end-of-study outcome if regime (a_1, a_2) is followed.

Potential outcomes adhere to the *axiom of consistency*: $L_2(a_1) = L_2$ whenever treatment a_1 is actually received and $Y(a_1, a_2) = Y$ whenever (a_1, a_2) is received. That is, the actual and counterfactual covariates (or outcome) are equal when the regime in question is the regime actually received.

Assumptions To estimate the effect of a dynamic regime, we require the *stable unit treatment value assumption* (Rubin 1978), which states that a subject's outcome is not influenced by other subjects' treatment allocation, and *no unmeasured confounders* (Robins 1997), which says that for any regime $\bar{a}_K$, $A_j \perp\!\!\!\perp (\bar{L}_j(\bar{L}_{j-1}, \bar{a}_{j-2}), ..., Y(\bar{L}_K, \bar{a}_{K-1}))|\bar{L}_j, \bar{a}_{j-1}$. Under sequential randomization, the latter assumption always holds. In two intervals for any a_1, a_2 we have that $A_1 \perp (L_2(a_1), Y(a_1, a_2))|L_1$ and $A_2 \perp Y(a_1, a_2)|(L_1, a_1, L_2)$. That is, conditional on history, treatment received in any interval is independent of any future potential outcome.

Without further assumptions, the optimal regime may only be estimated from among the set of *feasible* regimes (Robins 1994); feasibility requires some subjects to have followed a particular regime in order to make non-parametric inference about that regime.

Structural nested mean models and g-estimation Robins (2004, p. 209-214) produced a number of estimating equations for finding optimal regimes using structural nested mean models (SNMM) (Robins 1986). We use a subclass of SNMMs called the *optimal blip-to-zero* functions, denoted by $\gamma_j(\cdot)$, defined as the expected difference in outcome when using the "zero" regime instead of treatment a_j at t_j, in subjects with treatment and covariate history $\bar{l}_j, \bar{a}_{j-1}$ who subsequently receive the optimal regime. The "zero" regime, which we denote 0_j should be thought of as placebo or standard care; the optimal regime is denoted $d_j^{opt}\left(\bar{l}_j, \bar{a}_{j-1}\right)$. The treatment prescribed by the optimal (or zero) regime may differ depending on past treatment, i.e. what is optimal subsequent to t_j may depend on the treatment received at t_j. In the two-interval case, this gives blip functions

$$
\begin{aligned}
\gamma_1(l_1, a_1) &= E\Big[Y\Big(a_1, d_2^{opt}\Big(l_1, a_1, L_2(a_1)\Big)\Big) - Y\Big(0_1, d_2^{opt}\Big(l_1, 0_1, L_2(0_1)\Big)\Big)\Big|L_1 = l_1\Big], \\
\gamma_2(\bar{l}_2, \bar{a}_2) &= E\Big[Y(a_1, a_2) - Y(a_1, 0_2)\Big|(\bar{L}_2, A_1) = (\bar{l}_2, a_1)\Big].
\end{aligned}
$$

At the last (here, the second) interval there are no subsequent treatments, so the blip $\gamma_2(\cdot)$ is simply the expected difference in outcomes for having taken treatment a_2 as compared to the zero regime, 0_2, among people with history $\bar{l}_2, a_1$. At the first interval, the blip $\gamma_1(\cdot)$ is the expected (conditional) difference between the counterfactual outcome that would be observed if treatment a_1 was given in the first interval and optimal treatment was given in the second, and the counterfactual outcome that would be observed if the zero regime was given in the first interval and optimal treatment was given in the second interval.

Optimal blip functions are typically parameterized with parameters ψ. For example, a linear blip $\gamma_j(\bar{l}_j, \bar{a}_j) = a_j(\psi_0 + \psi_1 l_j + \psi_2 l_j^2 + \psi_3 a_{j-1})$ implies that the expected effect of treatment a_j on outcome provided optimal treatment is subsequently given is quadratic in the covariate l_j and linear in the treatment received in the previous interval.

Robins (2004, p. 208) proposes finding the parameters ψ of the optimal blip-to-zero function via g-estimation. For two intervals, let

$$\begin{aligned} H_1(\psi) &= Y - \gamma_1(l_1;\psi) + \left[\gamma_2(\bar{l}_2, (a_1, d_2^{opt});\psi) - \gamma_2(\bar{l}_2, \bar{a}_2;\psi)\right], \\ H_2(\psi) &= Y - \gamma_2(\bar{l}_2, \bar{a}_2;\psi). \end{aligned}$$

$H_1(\psi)$ and $H_2(\psi)$ equal, in expectation, the potential outcomes $Y\Big(0_1, d_2^{opt}\big(l_1, 0_1, L_2(0_1)\big)\Big)$ and $Y(a_1, 0_2)$, respectively. For the purpose of constructing an estimating procedure, we must specify a function $S_j(a_j) = s_j(a_j, \bar{l}_j, \bar{a}_{j-1}) \in \mathbb{R}^{dim(\psi_j)}$ which depends on variables that are thought to interact with treatment to influence outcome. For example, if the optimal blip at the second interval is linear, e.g. $\gamma_2(\bar{l}_2, \bar{a}_2) = a_2(\psi_0 + \psi_1 l_2 + \psi_2 a_1 + \psi_3 l_2 a_1)$, a common choice for this function is $S_2(a_2) = \frac{\partial}{\partial\psi}\gamma_2(\bar{l}_2, \bar{a}_2) = a_2 \cdot (1, l_2, a_1, l_2 a_1)^T$ since the blip suggests that the effect of the treatment at t_2 on outcome is influenced by covariates at the start of the second interval and by treatment at t_1. Let

$$U_j(\psi) = (H_j(\psi) - E[H_j(\psi)|\bar{L}_j, \bar{A}_{j-1}])\{S_j(A_j) - E[S_j(A_j)|\bar{L}_j, \bar{A}_{j-1}]\}. \tag{1}$$

For distributions that are not "exceptional" (see definition in the next session), with $U(\psi) = \sum_{j=1}^{2} U_j(\psi)$, $E[U(\psi)] = 0$ is an unbiased estimating equation from which consistent estimates $\hat{\psi}$ of ψ may be found. Robins proves that estimates found by solving (1) are consistent provided *either* the expected counterfactual model, $E[H_j(\psi)|\bar{L}_j, \bar{A}_{j-1}]$ is correctly specified, *or* the treatment model, $p_j(a_j|\bar{L}_j, \bar{A}_{j-1})$, used to calculate $E[S_j(A_j)|\bar{L}_j, \bar{A}_{j-1}]$) is correctly specified. Since, for consistency, only one of the nuisance models need be correct, this procedure is said to be *doubly-robust*. The estimators are asymptotically normal under standard regularity conditions but are not in general efficient without a special choice of the function $S_j(A_j)$.

A less efficient, singly-robust version of equation (1) simply omits the expected counterfactual model:

$$U_j^*(\psi) = H_j(\psi)\{S_j(A_j) - E[S_j(A_j)|\bar{L}_j, \bar{A}_{j-1}]\}. \tag{2}$$

Estimates found via equation (2) are consistent provided the treatment model, $p_j(a_j|\bar{L}_j, \bar{A}_{j-1})$, is correctly specified.

Recursive, closed-form g-estimation Exact solutions to equations (1) and (2) can be found when optimal blips are linear in ψ and parameters are not shared between intervals. For details of the recursive procedure, see Robins (2004) or Moodie, Richardson and Stephens (2007). An algorithm for the doubly-robust (equation (1)) two-interval case is as follows, using $\mathbb{P}_n$ to denote the empirical average operator:

1. Estimate the nuisance parameters α_2 in the treatment model $p_2(a_2|\bar{L}_2, A_1; \alpha_2)$. Assume a linear model for the expected counterfactual, $E[H_2(\psi_2)|\bar{L}_2, A_1; \varsigma_2]$; then the nuisance parameter ς_2 can be written as a function of the data and the unknown parameter, ψ_2.

2. To find $\hat{\psi}_2$, solve

$$\mathbb{P}_n U_2(\psi_2) = \mathbb{P}_n(H_2(\psi_2) - E[H_2(\psi_2)|\bar{L}_2, A_1; \hat{\varsigma}_2(\psi_2)])\{S_2(A_2) - E[S_2(A_2)|\bar{L}_2, A_1; \hat{\alpha}_2]\} = 0.$$

3. Estimate the nuisance parameters α_1 in $p_1(a_1|L_1; \alpha_1)$. Plug $\hat{\psi}_2$ into $H_1(\psi_1, \psi_2)$ so that only ψ_1 is unknown. If $E[H_1(\psi_1, \hat{\psi}_2)|L_1; \varsigma_1]$ is assumed to be linear, $\hat{\varsigma}_1$ can be expressed in terms of ψ_1 and $\hat{\psi}_2$.

4. Solve $\mathbb{P}_n(H_1(\psi_1, \hat{\psi}_2) - E[H_1(\psi_1, \hat{\psi}_2)|L_1; \hat{\varsigma}_1(\psi_1, \hat{\psi}_2)])\{S_1(A_1) - E[S_1(A_1)|L_1; \hat{\alpha}_1]\} = 0$, that

is, solve $\mathbb{P}_n U_1(\psi_1, \hat{\psi}_2) = 0$ to find $\hat{\psi}_1$.

2.2 Asymptotic bias under exceptional laws

The cumulative distribution function of the observed longitudinal data is *exceptional* if, at some interval j, the optimal treatment decision depends on at least one component of covariate and treatment history *and* there is a positive probability that the optimal rule is not unique (Robins 2004, p. 225). Suppose, for example, that the blip function is linear, depending only on the current covariate and the previous treatment: $\gamma_j(\bar{L}_j, \bar{A}_j; \psi) = A_j(\psi_{j0} + \psi_{j1}L_j + \psi_{j2}A_{j-1})$. The distribution is exceptional if either $\psi_{j1} \neq 0$ or $\psi_{j2} \neq 0$ and, in addition, it puts positive probability on values of L_j and A_{j-1} such that $\psi_{j0}+\psi_{j1}L_j+\psi_{j2}A_{j-1} = 0$. The combination of three factors make a law exceptional: (i) the form of the blip model (whether it depends on past treatment or covariates), (ii) the true value of the blip model parameters, and (iii) the distribution of treatments and covariates. Thus a law is exceptional with respect to a family of blip models.

Robins (2004, p. 308) uses a simple scenario to explain the bias at exceptional laws. Suppose a random variable X_i is drawn from a normal distribution with mean η, and we wish to estimate $I[\eta > 0]\eta$. The MLE of $I[\eta > 0]\eta$ is a transformation of the sample mean, $\widetilde{X}_j = I[\bar{X}_j > 0]\bar{X}_j$. In the usual frequentist vein, suppose that under repeated sampling a collection of sample means, $\bar{X}_1, \bar{X}_2, ...\bar{X}_k$, are found. If $\eta = 0$, approximately half of the sample means will be negative and half positive so that the *average* of the collection would be nearly 0. By truncating the negative statistics to zero to calculate $\widetilde{X}_j$, we average over a collection of statistics that are all non-negative and so $E[\widetilde{X}_j] \geq E[\bar{X}_j] = \eta$.

Now suppose the usual two-interval set-up, with linear optimal blips $\gamma_1(l_1, a_1) = a_1(\psi_{10} + \psi_{11}l_1)$ and $\gamma_2(\bar{l}_2, a_1, a_2) = a_2(\psi_{20} + \psi_{21}l_2 + \psi_{22}a_1 + \psi_{23}l_2a_1)$. Let $\eta_2 = \psi_{20} + \psi_{21}l_2 + \psi_{22}a_1 + \psi_{23}l_2a_1$; likewise $\hat{\eta}_2 = \hat{\psi}_{20} + \hat{\psi}_{21}l_2 + \hat{\psi}_{22}a_1 + \hat{\psi}_{23}l_2a_1$. The g-estimating function for ψ_2 is unbiased, so $E[\hat{\eta}_2] = \eta_2$. The sign of η_2 is used to decide optimal treatment at the second interval: $d_2^{opt} = I[\eta_2 > 0] = I[(\psi_{20} + \psi_{21}l_2 + \psi_{22}a_1 + \psi_{23}l_2a_1) > 0]$ and $\hat{d}_2^{opt} = I[\hat{\eta}_2 > 0]$ so that now the g-estimating equation solved for ψ_1 at the first interval contains:

$$
\begin{aligned}
H_1(\psi_1) &= Y - \gamma_1(l_1, a_1; \psi_1) + [\gamma_2(\bar{l}_2, (a_1, \hat{d}_2^{opt}); \hat{\psi}_2) - \gamma_2(\bar{l}_2, (a_1, a_2); \hat{\psi}_2)] \\
&= Y - \gamma_1(l_1, a_1; \psi_1) + [(\hat{d}_2^{opt} - a_2)(\hat{\psi}_{20} + \hat{\psi}_{21} l_2 + \hat{\psi}_{22} a_1 + \hat{\psi}_{23} l_2 a_1)] \\
&= Y - \gamma_1(l_1, a_1; \psi_1) + I[\hat{\eta}_2 > 0]\hat{\eta}_2 - a_2 \hat{\eta}_2 \\
&\overset{E}{\geq} Y - \gamma_1(l_1, a_1; \psi_1) + I[\eta_2 > 0]\eta_2 - a_2 \eta_2 = 0,
\end{aligned}
$$

where $\overset{E}{\geq}$ denotes "greater than or equal to in expectation". The quantity $\left[\gamma_2(\bar{l}_2, (a_1, d_2^{opt}); \psi_2) - \gamma_2(\bar{l}_2, (a_1, a_2); \psi_2)\right]$ in $H_1(\psi)$ – or more generally, $\sum_{k>j} \left[\gamma_k(\bar{l}_k, (\bar{a}_{k-1}, d_k^{opt}); \psi_k) - \gamma_k(\bar{l}_k, \bar{a}_k; \psi_k)\right]$ in $H_j(\psi_j)$ – corresponds to $I[\eta > 0]\eta$ in the simple scenario with random variables X_i, which is upwardly biased as observed above. By using a biased estimate of $I[\eta_2 > 0]\eta_2$ in $H_1(\psi)$, some non-mean-zero value is added into the g-estimating equation for ψ_1. The estimating function no longer has expectation zero and hence is asymptotically biased.

Simulated example Consider a concrete example, with randomly assigned treatments A_1, A_2 that take on the value 0 or 1 with equal probability and data: $L_1 \sim \mathcal{N}(0, 3)$; $L_2 \sim \text{round}(\mathcal{N}(0.75, 0.5))$; and $Y \sim \mathcal{N}(1, 1) - |\gamma_1(l_1, a_1)| - |\gamma_2(\bar{l}_1, \bar{a}_2)|$ (see, for example, Murphy (2003)). Note that the second interval covariate, L_2, is discrete. Suppose that the blip function is linear. For example, taking $\psi_1 = (1.6, 0.0)$ and $\psi_2 =$ (-3.0,2.0,1.0,0.0), whenever $L_2 = A_1 = 1.0$, $\psi_{20} + \psi_{21} L_2 + \psi_{22} A_1 + \psi_{23} L_2 A_1 = -3 + 2 \cdot 1 + 1 \cdot 1 + 0 \cdot 1 = 0$ even though not all components of ψ_2 equal zero. Table 1 summarizes the results of the simulations, including the bias of the first-interval g-estimates (absolute and relative to standard error) and the coverage of Wald and score confidence intervals for $n = 250$ and 1000. The bias in the first interval estimate of ψ_{10} is not negligible. Coverage is incorrect in smaller samples in part because of slow convergence of the estimated covariance matrix but perhaps also because of the exceptional law. Score intervals generally provide coverage closer to the nominal level than Wald intervals.

Robins proves that under the scenario of an exceptional law such as the above, estimates

$\hat{\psi}_1$ are $n^{1/2}$-consistent but are neither asymptotically normal nor asymptotically unbiased (Robins 2004, p. 313-315). For a graphical interpretation of asymptotic bias and consistency coinciding, we examine bias maps; these plots depict the bias of a parameter as sample size and another parameter are varied. Bias maps throughout this article focus on the absolute bias in ψ_{10} as a function of sample size and one of the second interval parameters, ψ_{20}, ψ_{21}, ψ_{22}, or ψ_{23}. Note that there are several combinations of parameters that lead to exceptional laws: as well as (-3.0, 2.0, 1.0, 0.0) if $p(A_1 = L_2 = 1) > 0$, exceptional laws occur with (-2.0, 2.0, 1.0, 0.0) and (-3.0, 3.0, 1.0, 0.0) if $p(A_1 = 0, L_2 = 1) > 0$.

These results of Robins give that estimates of ψ_{10}, ψ_{11} are asymptotically unbiased and converge to the true values, for parameters that do not change with n and a law such that $\psi_{20} + \psi_{21}L_2 + \psi_{22}A_1 + \psi_{23}L_2A_1 \neq 0$. Consistency may be visualized by looking at a horizontal cross-section of any one of the bias maps in Figure 1: eventually, sample size will be great enough that bias of first-interval estimates is smaller than any fixed, positive number. However, if we consider a sequence of data generating processes in which the ψ_2's decrease with increasing n, so that $\eta_2 = \psi_{20} + \psi_{21}L_2 + \psi_{22}A_1 + \psi_{23}L_2A_1$ is $O(n^{-1/2})$, then asymptotic bias is observed so that $E[\sqrt{n}(\hat{\psi}_1 - \psi_1)] > 0$. Contours of constant bias can be found along the lines on the bias map traced by plotting $\eta_2 = kn^{-1/2}$ against n. Note that the asymptotic bias is bounded. In finite samples, the proximity to the exceptional law and the sample size both determine the bias of the estimator (Figure 1).

In Figure 2, L_2 is not rounded so that $P(\psi_{20} + \psi_{21}L_2 + \psi_{22}A_1 + \psi_{23}L_2A_1 = 0) = 0$ and the law is not exceptional. Virtually no small- or large-sample bias is observed. For a law to not be exceptional, it is sufficient for the blip function to contain a continuous covariate with a non-zero coefficient. However in finite samples, it is also necessary that the derivative of the blip function with respect to a continuous covariate L_j, $\frac{\partial}{\partial L_j}\gamma_j(\bar{L}_j, \bar{A}_j)$, is large (that is, greater than $kn^{-1/2}$ for some k) whenever $\gamma_j(\bar{L}_j, \bar{A}_j)$ is in a neighbourhood of zero so as to be able to distinguish a unique optimal regime from those that are not unique.

Asymptotic bias calculation for two intervals It is useful in the ensuing discussion to express the blip as $\gamma_j(\bar{L}_j, \bar{A}_j; \psi_j) = A_j g_j(\bar{L}_j, \bar{A}_{j-1}; \psi_j)$. Using this form, the optimal rule and the definition of exceptional laws can be written in terms of the function $g_j(\bar{L}_j, \bar{A}_{j-1}; \psi_j)$. For binary treatment, the optimal rule is defined by the indicator $I[g_j(\bar{L}_j, \bar{A}_{j-1}; \psi_j) > 0]$. Exceptional laws exist when $P(g_j(\bar{L}_j, \bar{A}_{j-1}; \psi_j) = 0) > 0$ and $g_j(\bar{L}_j, \bar{A}_{j-1}; \psi_j)$ depends on at least one component of $\bar{L}_j, \bar{A}_{j-1}$.

Robins (2004, p. 315) calculates the asymptotic bias of $\hat{\psi}_1(\psi_2)$ found using equation (2) on two intervals for linear blips in the special case where exceptional laws occur when $L_j = A_{j-1} = 1$. We generalize the result here:

Suppose a linear blip where $g_2(\bar{L}_2, A_1; \psi_2)$ depends on at least one of L_1, L_2, A_1 so that $g_2(\bar{L}_2, A_1; \psi_2) = 0$ whenever $\sum_{j=0}^{|\psi_2|-1} \psi_{2j} \cdot X_2 = 0$, where $|\psi_2|$ is the dimension of the vector ψ_2 and X_2 denotes the matrix consisting of a vector of 1's and the covariates in $g_2(\bar{L}_2, A_1; \psi_2)$ (in our simulations, $X_2 = (1, L_2, A_1, L_2 A_1)$). Let $\psi_1^\dagger$, $\psi_2^\dagger$ denote the true values of ψ_1 and ψ_2 and let $\Delta_1^g(\hat{\psi}_2, \psi_2^\dagger) = U_1^*(\psi_1, \hat{\psi}_2) - U_1^*(\psi_1, \psi_2^\dagger)$. As indicated by the notation, $\Delta_1^g(\hat{\psi}_2, \psi_2^\dagger)$ does not depend on ψ_1 when blips are linear. For linear blip functions,

$$
\begin{aligned}
\Delta_1^g(\hat{\psi}_2, \psi_2^\dagger) &= U_1^*(\psi_1, \hat{\psi}_2) - U_1^*(\psi_1, \psi_2^\dagger) \\
&= I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) = 0]\, \{S_1(A_1) - E[S_1(A_1)|L_1]\} \left(I[g_2(\bar{L}_2, A_1; \hat{\psi}_2) > 0] - A_2\right) \times \\
&\qquad g_2(\bar{L}_2, A_1; \hat{\psi}_2) \;+\; I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) \neq 0]\, \{S_1(A_1) - E[S_1(A_1)|L_1]\} \cdot \\
&\qquad\quad \Big\{ \left(I[g_2(\bar{L}_2, A_1; \hat{\psi}_2) > 0] - A_2\right) g_2(\bar{L}_2, A_1; \hat{\psi}_2) - \\
&\qquad\qquad \left(I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) > 0] - A_2\right) g_2(\bar{L}_2, A_1; \psi_2^\dagger) \Big\} \qquad (3)
\end{aligned}
$$

To find the asymptotic bias of $\hat{\psi}_1$, we perform a Taylor expansion, which gives

$$
\begin{aligned}
(\hat{\psi}_1 - \psi_1^\dagger) &= -\left(E\left[\frac{\partial}{\partial \psi_1} U_1^*(\psi_1^\dagger, \psi_2^\dagger)\right]\right)^{-1} \mathbb{P}_n U_1^*(\psi_1^\dagger, \hat{\psi}_2) + o_p(n^{-1/2}) \\
&= -\left(E\left[\frac{\partial}{\partial \psi_1} U_1^*(\psi_1^\dagger, \psi_2^\dagger)\right]\right)^{-1} \mathbb{P}_n \left(U_1^*(\psi_1^\dagger, \psi_2^\dagger) + \Delta_1^g(\hat{\psi}_2, \psi_2^\dagger)\right) + o_p(n^{-1/2}).
\end{aligned}
$$

The asymptotic bias is equal to

$$
\begin{aligned}
\lim_{n\to\infty} E[\sqrt{n}(\hat{\psi}_1 - \psi_1^{\dagger})] &= -\lim_{n\to\infty} \sqrt{n}\left(E\left[\frac{\partial}{\partial\psi_1}U_1^*(\psi_1^{\dagger},\psi_2^{\dagger})\right]\right)^{-1} E\left[\mathbb{P}_n\left(U_1^*(\psi_1^{\dagger},\psi_2^{\dagger}) + \Delta_1^g(\hat{\psi}_2,\psi_2^{\dagger})\right)\right] \\
&= -\lim_{n\to\infty} \sqrt{n}\left(E\left[\frac{\partial}{\partial\psi_1}U_1^*(\psi_1^{\dagger},\psi_2^{\dagger})\right]\right)^{-1} E\left[\mathbb{P}_n\Delta_1^g(\hat{\psi}_2,\psi_2^{\dagger})\right]
\end{aligned}
$$

since the g-estimating function $U_1^*(\psi_1^{\dagger},\psi_2^{\dagger})$ *that contains the true values* $\psi_1^{\dagger},\psi_2^{\dagger}$ is zero in expectation. Therefore, we must examine $E\left[\Delta_1^g(\hat{\psi}_2,\psi_2^{\dagger})\right]$, which is equal to $E\left[\mathbb{P}_n\Delta_1^g(\hat{\psi}_2,\psi_2^{\dagger})\right]$.

To proceed, we require an additional piece of information. We know that $\hat{\psi}_2$ is regular since $U_2^*(\psi_2)$ is smooth as a function of ψ_2, and so a Taylor expansion gives

$$
\begin{aligned}
(\hat{\psi}_2 - \psi_2^{\dagger}) &= -\mathbb{P}_n\left(\left(E\left[\frac{\partial}{\partial\psi_2}U_2^*(\psi_2^{\dagger})\right]\right)^{-1} U_2^*(\psi_2^{\dagger})\right) + o_p(n^{-1/2}) \\
&= \mathbb{P}_n(IF_{20}, IF_{21}, ..., IF_{2,|\psi_2|-1})^T + o_p(n^{-1/2}) = \mathbb{P}_n IF_2 + o_p(n^{-1/2}), \qquad (4)
\end{aligned}
$$

where IF_{2j} denotes $-\left(E\left[\frac{\partial}{\partial\psi_{2j}}U_2^*(\psi_2^{\dagger})\right]\right)^{-1} U_2^*(\psi_2^{\dagger})$ and IF_2 is the vector of such functions.

To simplify the expressions we consider, we will examine $E\left[\Delta_1^g(\hat{\psi}_2,\psi_2^{\dagger})\right]$ under non-exceptional laws and exceptional laws separately.

Calculations under non-exceptional laws: Under non-exceptional laws, $g_2(\bar{L}_2, A_1; \psi_2^{\dagger}) \neq 0$ and

$$
\begin{aligned}
\Delta_1^g(\hat{\psi}_2,\psi_2^{\dagger}) &= \{S_1(A_1) - E[S_1(A_1)|L_1]\}\cdot\Big\{\Big(I[g_2(\bar{L}_2,A_1;\hat{\psi}_2)>0] - A_2\Big)g_2(\bar{L}_2,A_1;\hat{\psi}_2) \\
&\qquad - \Big(I[g_2(\bar{L}_2,A_1;\psi_2^{\dagger})>0] - A_2\Big)g_2(\bar{L}_2,A_1;\psi_2^{\dagger})\Big\} \qquad (5) \\
&= \{S_1(A_1) - E[S_1(A_1)|L_1]\}\cdot\Big\{\Big(I[g_2(\bar{L}_2,A_1;\psi_2^{\dagger})>0] - A_2\Big)g_2(\bar{L}_2,A_1;\hat{\psi}_2) \\
&\qquad - \Big(I[g_2(\bar{L}_2,A_1;\psi_2^{\dagger})>0] - A_2\Big)g_2(\bar{L}_2,A_1;\psi_2^{\dagger})\Big\} \qquad (6) \\
&= \{S_1(A_1) - E[S_1(A_1)|L_1]\}\cdot\Big(I[g_2(\bar{L}_2,A_1;\psi_2^{\dagger})>0] - A_2\Big)\cdot \\
&\qquad \Big(g_2(\bar{L}_2,A_1;\hat{\psi}_2) - g_2(\bar{L}_2,A_1;\psi_2^{\dagger})\Big) \qquad (7) \\
&= \{S_1(A_1) - E[S_1(A_1)|L_1]\}\cdot\Big(I[g_2(\bar{L}_2,A_1;\psi_2^{\dagger})>0] - A_2\Big)\Big((\hat{\psi}_2 - \psi_2^{\dagger})\cdot X_2\Big) \qquad (8)
\end{aligned}
$$

$$= \quad \{S_1(A_1) - E[S_1(A_1)|L_1]\} \cdot \left(I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) > 0] - A_2\right)(\mathbb{P}_n IF_2 \cdot X_2) + o_p(n^{-1/2})$$

Briefly, we explain the steps. Equality of (5) and (6) follow since $I[g_2(\bar{L}_2, A_1; \hat{\psi}_2) > 0]$ takes on the same sign as $I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) > 0]$ with probability approaching 1 (Robins, 2004, p. 314), so the latter is substituted for the former. The next equality is a collecting of terms. Equality of (7) and (8) follow since, for linear blips, $g_2(\bar{L}_2, A_1; \hat{\psi}_2) - g_2(\bar{L}_2, A_1; \psi_2^\dagger)$ can be expressed as $\hat{\psi}_2 \cdot X_2 - \psi_2^\dagger \cdot X_2$. The final line results from a substitution using equation (4).

We break may the expectation of $\Delta_1^g(\hat{\psi}_2, \psi_2^\dagger)$ into a product of expectations as follows:

$$E\left[\Delta_1^g(\hat{\psi}_2, \psi_2^\dagger)\right] = E\left[\{S_1(A_1) - E[S_1(A_1)|L_1]\}\left(I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) > 0] - A_2\right)\right] \times$$
$$E\Big[X_2 \cdot E\left[\mathbb{P}_n IF_2 | X_2\right]\Big] + o_p(n^{-1/2}).$$

From this, we conclude that $E\left[\Delta_1^g(\hat{\psi}_2, \psi_2^\dagger)\right] = o_p(n^{-1/2})$ since X_2, which consists of some or all of the covariates in $(\bar{L}_2, A_1)$, is ancillary for $\psi_2^\dagger$ and so IF_2 has mean zero given X_2. Therefore there is no asymptotic bias when laws are not exceptional.

<u>Calculations under exceptional laws:</u> Under exceptional laws, $g_2(\bar{L}_2, A_1; \psi_2^\dagger) = 0$ and

$$\begin{aligned}
\Delta_1^g(\hat{\psi}_2, \psi_2^\dagger) &= \{S_1(A_1) - E[S_1(A_1)|L_1]\}\left(I[g_2(\bar{L}_2, A_1; \hat{\psi}_2) > 0] - A_2\right) g_2(\bar{L}_2, A_1; \hat{\psi}_2) && (9)\\
&= \{S_1(A_1) - E[S_1(A_1)|L_1]\}\left(I[g_2(\bar{L}_2, A_1; \hat{\psi}_2) - g_2(\bar{L}_2, A_1; \psi_2^\dagger) > 0] - A_2\right) \cdot \\
&\qquad \left(g_2(\bar{L}_2, A_1; \hat{\psi}_2) - g_2(\bar{L}_2, A_1; \psi_2^\dagger)\right) && (10)\\
&= \{S_1(A_1) - E[S_1(A_1)|L_1]\}\left(I[\sqrt{n}(\hat{\psi}_2 - \psi_2^\dagger) \cdot X_2 > 0] - A_2\right) \cdot \\
&\qquad \left((\hat{\psi}_2 - \psi_2^\dagger) \cdot X_2)\right) && (11)\\
&= \{S_1(A_1) - E[S_1(A_1)|L_1]\}\left(I[\sqrt{n}\mathbb{P}_n IF_2 \cdot X_2 > 0] - A_2\right)(\mathbb{P}_n IF_2 \cdot X_2) + o_p(n^{-1/2})
\end{aligned}$$

Equality of (9) and (10) follow since the law is exceptional, so $g_2(\bar{L}_2, A_1; \hat{\psi}_2) = 0$ and hence this zero can be added into the equation. Equality of expressions (10) and (11) follow by noting that for linear blips, $g_2(\bar{L}_2, A_1; \hat{\psi}_2) - g_2(\bar{L}_2, A_1; \psi_2^\dagger) = \hat{\psi}_2 \cdot X_2 - \psi_2^\dagger \cdot X_2$; the final expression results from a substitution using equation (4) and the fact that given X_2, $\sqrt{n}(\hat{\psi}_2 - \psi_2^\dagger)$ converges in distribution to $\sqrt{n}\mathbb{P}_n IF_2$ and thus these quantities have the same sign with probability converging to 1.

The expectation of $\Delta_1^g(\hat{\psi}_2, \psi_2^\dagger)$ may again be broken into a product of expectations:

$$
\begin{aligned}
E\left[\Delta_1^g(\hat{\psi}_2, \psi_2^\dagger)\right] &= E\left[\{S_1(A_1) - E[S_1(A_1)|L_1]\}\left(I[\mathbb{P}_n IF_2 \cdot X_2 > 0] - A_2\right)\left(\mathbb{P}_n IF_2 \cdot X_2\right)\right] + o_p(n^{-1/2}) \\
&= E\left[\{S_1(A_1) - E[S_1(A_1)|L_1]\} I[\mathbb{P}_n IF_2 \cdot X_2 > 0]\mathbb{P}_n IF_2 \cdot X_2\right] \\
&\qquad - E\left[\{S_1(A_1) - E[S_1(A_1)|L_1]\} A_2 \left(\mathbb{P}_n IF_2 \cdot X_2\right)\right] + o_p(n^{-1/2}) \\
&= E\left[\{S_1(A_1) - E[S_1(A_1)|L_1]\}\right] E\left[I[\mathbb{P}_n IF_2 \cdot X_2 > 0]\mathbb{P}_n IF_2 \cdot X_2\right] + o_p(n^{-1/2})
\end{aligned}
$$

Note that the final equality results from the fact that IF_2 has mean zero given X_2.

From this, we find that the asymptotic bias of $\hat{\psi}_1$, $\lim_{n\to\infty} E[\sqrt{n}(\hat{\psi}_1 - \psi_1^\dagger)]$, equals

$$
\begin{aligned}
-\left(E\left[\frac{\partial}{\partial \psi_1} U_1^*(\psi_1^\dagger, \psi_2^\dagger)\right]\right)^{-1} &\Big\{ E\left\{I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) \neq 0]\right\} 0 \\
&+ E\left\{I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) = 0]\{S_1(A_1) - E[S_1(A_1)|L_1]\}\right\} E\left\{I\left[Z_{2+} > 0\right] Z_{2+}\right\} \Big\},
\end{aligned}
$$

where Z_{2+} is normal with mean 0 and variance equal to that of $IF_2 \cdot X_2$, or simply

$$
-\left(E\left[\frac{\partial}{\partial \psi_1} U_1^*(\psi_1^\dagger, \psi_2^\dagger)\right]\right)^{-1} E\left\{I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) = 0]\{S_1(A_1) - E[S_1(A_1)|L_1]\}\right\} E\left\{I\left[Z_{2+} > 0\right] Z_{2+}\right\}.
$$

Thus, when optimal regimes are not unique, $I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) = 0] = 1$ with non-zero probability and the g-estimates have bounded asymptotic bias equal to

$$
-\left(E\left[\frac{\partial}{\partial \psi_1} U_1^*(\psi_1^\dagger, \psi_2^\dagger)\right]\right)^{-1} E\left\{S_1(A_1) - E[S_1(A_1)|L_1]\right\} \cdot E[Z_{2+}|Z_{2+} > 0]P[Z_{2+} > 0].
$$

For more than two intervals, the asymptotic bias calculation is more complex. Consider a three-interval problem where non-unique optimal rules exist at the last interval. The asymptotic bias at the second (middle) interval proceed as above, so that, with Z_{3+} normal with mean 0 and variance $\mathrm{Var}\Big[\left(E\left[\frac{\partial}{\partial\psi_3}U_3^*(\psi_3^\dagger)\right]\right)^{-1}U_3^*(\psi_3^\dagger)\cdot X_3\Big]$, the asymptotic bias in $\hat{\psi}_2$ is

$$-\left(E\left[\frac{\partial}{\partial\psi_2}U_2^*(\psi_1,\psi_2^\dagger,\psi_3^\dagger)\right]\right)^{-1}E\left\{S_2(A_2)-E[S_2(A_2)|L_1,A_1,L_2]\right\}\cdot E[Z_{3+}|Z_{3+}>0]P[Z_{3+}>0].$$

Note that in the recursive estimation setting, $U_2^*(\psi_1,\psi_2,\psi_3) = U_2^*(\psi_2,\psi_3)$. The asymptotic bias calculation at the first interval can be found by examining $\Delta_1^g(\hat{\psi}_2,\psi_2^\dagger,\hat{\psi}_3,\psi_3^\dagger) = U_1^*(\psi_1,\hat{\psi}_2,\hat{\psi}_3) - U_1^*(\psi_1,\psi_2^\dagger,\psi_3^\dagger)$. This function is more complex than that derived above because it requires plug-in estimates of both the regular estimator $\hat{\psi}_3$ and the asymptotically biased, non-regular estimator $\hat{\psi}_2$.

The asymptotic bias for the doubly-robust equation (1) assuming a simple linear form for the expected counterfactual model is provided in Appendix A. Doubly-robust g-estimation is more efficient than singly-robust estimation and has the advantage that blip functions which do not allow for covariate and treatment interactions do not lead to exceptional laws.

2.3 Detecting exceptional laws

It is not necessary for all parameters to equal zero for a law to be exceptional, thus a simple F-test is not a sufficient check. Robins (2004, p. 317) suggests the following steps for when parameters are not shared across intervals:

1. Compute g-estimates of ψ_j for $j = 1, ..., K$ and Wald confidence intervals about each parameter.

2. At each interval j, compute $\left|d_j^{opt}\in \mathrm{CI}\right|_i$ as the number of optimal rules possible at time j for each subject i under all values ψ_j in the confidence set. E.g., if all values of ψ_j in the confidence set give the same optimal rule then $\left|d_j^{opt}\in \mathrm{CI}\right|_i = 1$.

3. If the fraction of $\left\{\left|d_j^{opt} \in \mathrm{CI}\right|_1, \left|d_j^{opt} \in \mathrm{CI}\right|_2, \ldots, \left|d_j^{opt} \in \mathrm{CI}\right|_n\right\}$ that is greater than 1, denoted by $p_{op,j}$, is small (e.g. $p_{op,j} < 0.05$) then the law at interval j is likely not exceptional and inference based on Wald confidence sets is reliable for earlier intervals $m < j$.

The idea behind this approach is that if there are few instances for which $\left|d_j^{opt} \in \mathrm{CI}\right|_i > 1$, then the confidence set is far away from values of ψ_j that, in combination with the distribution of covariate and treatment history, would produce an exceptional law. In our simulations, Robins' method detects exceptional laws in all samples in which they are present (Table 1) so that in all cases, score confidence intervals are recommended. In general, the score confidence intervals improve coverage at both time intervals, particularly in smaller samples.

This method may save the analyst having to find a more computationally-intensive confidence set if score intervals are not recommended, but could itself be quite time-consuming. We suggest here some additional guidelines:

- When parameters are not shared, exceptional laws at the k^{th} interval do not affect the regularity of estimates for ψ_j, $j > k$; hence it is sufficient to consider $\left|d_j^{opt} \in \mathrm{CI}\right|_i$ only for the intervals $k, \ldots, K$.

- If, at every interval, the Wald confidence interval for the parameter of at least one continuous variable (with no "spikes" or point-masses) excludes zero, the law is likely not exceptional.

- If at any interval, there is no effect of treatment (i.e., the Wald confidence set for ψ_j includes the vector 0), the law is likely exceptional.

If a law is exceptional, Wald confidence intervals will not have the correct coverage; score confidence intervals will still be uniformly of the correct level (Robins 2004, p. 222). However the asymptotic bias remains.

3. BIAS-CORRECTION AT EXCEPTIONAL LAWS: ZEROING INSTEAD OF PLUGGING IN (ZIPI)

3.1 Exceptional laws: an issue of subpopulations

In this section, we propose a modification to g-estimation (when no there is no parameter sharing) that not only detects exceptional laws but reduces bias when exceptional laws exist. The method relies on the supposition that – at any interval j – the sample of study participants is drawn from two populations, $\mathcal{M}_j^0$ and $\mathcal{M}_j^1$, where those who are members of $\mathcal{M}_j^0$ do not have a unique optimal treatment decision interval j, while there is only a single optimal treatment for all those belonging to $\mathcal{M}_j^1$. Let m_j^0 denote the members of the sample drawn from $\mathcal{M}_j^0$, and define m_j^1 similarly. The method that we propose attempts to determine an individual's membership in $\mathcal{M}_j^0$ or $\mathcal{M}_j^1$ and then treats the data collected on individuals from the two groups differently. In practice, m_j^0 and m_j^1 are unknown and must be estimated.

3.2 Zeroing Instead of Plugging In

As seen in section 2.2, bias enters the g-estimating equation of ψ_1 through the addition of the upwardly-biased estimate of $I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) > 0]g_2(\bar{L}_2, A_1; \psi_2^\dagger)$ into $H_1(\psi)$ when $g_2(\bar{L}_2, A_1; \psi_2^\dagger)$ is at or close to zero. Our algorithm searches for individuals for whom it is likely that $g_2(\bar{L}_2, A_1; \psi_2^\dagger) = 0$ and then uses the "better guess" of zero for $I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) > 0]g_2(\bar{L}_2, A_1; \psi_2^\dagger)$ instead of the estimate obtained by plugging in $\hat{\psi}_2$ for $\psi_2^\dagger$. We call this *Zeroing Instead of Plugging In* (ZIPI). Specifically, ZIPI is performed by starting at the last interval:

1. Compute $\hat{\psi}_K$ using the usual g-estimation (singly- or doubly-robust). Set $j = K$.

2. Estimate m_j^0, m_j^1 by calculating the 95% (or 80%, or 90%, etc.) Wald confidence interval, W_{ji}, about $g_j(\bar{l}_{j,i}, \bar{a}_{j-1,i}; \psi_j^\dagger)$ for each individual i in the sample. Let $\hat{m}_j^0 = \{i | 0 \in W_{ji}\}$, and $\hat{m}_j^1 = \{i | 0 \notin W_{ji}\}$.

3. For individual i, set

$$H^0_{j-1,i} = Y_i - \gamma_{j-1}(\bar{l}_{j-1,i}, \bar{a}_{j-2,i}; \psi_{j-1}) + \sum_{k>j} I[i \in \hat{m}^1_k][\gamma_k(\bar{l}_{k,i}, (\bar{a}_{k-1,i}, d^{opt}_{k,i}); \hat{\psi}_k) - \gamma_k(\bar{l}_{k,i}, \bar{a}_{k-1,i}; \hat{\psi}_k)].$$

I.e., if at any interval k, $k > j$, the confidence interval about $g_k(\bar{l}_{k,i}, \bar{a}_{k-1,i}; \psi^\dagger_k)$ includes zero, $\gamma_k(\bar{l}_{k,i}, (\bar{a}_{k-1,i}, d^{opt}_{k,i}); \psi_k) - \gamma_k(\bar{l}_{k,i}, \bar{a}_{k-1,i}; \psi_k)$ is set to 0 in $H^0_{j-1,i}$, otherwise it is estimated by plugging in $\hat{\psi}_k$.

4. Using $H^0_{j-1,i}$ as defined above, find the ZIPI estimate for ψ_{j-1} by replacing $H^0_{j-1,i}$ with $H_{j-1,i}$ in equation (1) or (2).

5. Repeat steps 2-4 with j replaced by $j-1$ until all parameters have been estimated.

The last interval ZIPI estimate, $\hat{\psi}_K$, is equal to the usual recursive g-estimate and thus is always consistent and asymptotically normal. Table 2 compares g-estimation with ZIPI using different confidence levels to select individuals who are likely to have non-unique optimal rules, keeping to the simulation scenario used in all previous examples. The bias reduction observed by using 0 instead of the estimate $I[g_j(\bar{L}_{2,i}, A_{1,i}; \hat{\psi}_2) > 0]g_j(\bar{L}_{2,i}, A_{1,i}; \hat{\psi}_2)$ is good at and far from exceptional laws, with performance dependent on the level of the confidence interval used to estimate m^0_2 and m^1_2. Coverage is very the nominal level.

In finite samples, some misclassification of individuals into m^0_j and m^1_j will always occur if type I error is held fixed and both sets are non-empty. In this context, a type I error consists of falsely classifying subject i as having a unique rule when in fact he does not: $P(i \in \hat{m}^1_j | i \in m^0_j)$. Correspondingly, type II error is the incorrect classification of subject i as having a non-unique optimal regime when in truth his optimal rule is unique: $P(i \in \hat{m}^0_j | i \in m^1_j)$. An unfortunate consequence is that ZIPI introduces bias where none exists using ordinary recursive g-estimation in regions of the parameter space that are moderately close to the exceptional laws (Figure 3). As sample size increases, the magnitude of the bias and the region of "moderate proximity" to the exceptional law where bias is observed both decrease. The maximum bias observed using ZIPI is smaller than that observed using usual g-estimation: 0.033 with 80% CI selection and 0.040 with 95% CI selection as compared to 0.060 with g-estimation (Figures 1, 3-4).

ZIPI falls into the class of pre-test estimators that are frequently used in a variety of statistical settings. (Variable or model selection constitutes a common example.) Even in better-understood scenarios, the optimal choice of threshold is a complicated problem; see, for example, Giles, Lieberman and Giles (1992) or Kabaila and Leeb (2006).

3.3 Consistency and asymptotic bias of ZIPI estimates

ZIPI estimates that have all of the desirable asymptotic properties exhibited by ordinary g-estimates at non-exceptional laws, with the added benefit of reduced asymptotic bias at exceptional laws.

Theorem 3.1. *Under non-exceptional laws, ZIPI estimates converge to the usual recursive g-estimates and therefore are asymptotically consistent, unbiased, and normally distributed.*

The proof is trivial. Of greater interest is the performance of ZIPI estimates under exceptional laws. We begin assuming that m_j^0 and m_j^1 are known for all j.

Theorem 3.2. *When the distribution is exceptional and m_j^0, m_j^1 are known at every interval, ZIPI estimates are asymptotically consistent, unbiased, and normally distributed.*

Proof: The statement is proved in the singly-robust (equation (2)) two-interval context. The generalization to K intervals or to the use of equation (1) follows readily.

Decompose the usual first-interval g-estimation function into two components:

$$\mathbb{P}_n(U_1^*(\psi_1, \hat{\psi}_2)) = \frac{1}{n}\sum_{i=1}^{n} U_{1i}^*(\psi_1, \hat{\psi}_2) = \frac{1}{n}\sum_{i\in m_2^0} U_{1i}^*(\psi_1, \hat{\psi}_2) + \frac{1}{n}\sum_{i\in m_2^1} U_{1i}^*(\psi_1, \hat{\psi}_2).$$

For $i \in m_2^1$, $g_2(\bar{l}_{2,i}, a_{1,i}; \psi_2) \neq 0$ and so $E\left[\frac{1}{n}\sum_{i\in m_2^1} U_{1i}^*(\psi_1, \hat{\psi}_2)\right] = 0$. For $i \in m_2^0$, on the other hand, $E[U^{*}_{1i}(\psi_1, \hat{\psi}_2)] \neq 0$ since

$$H_{1,i}(\psi_1, \hat{\psi}_2) = Y_i - \gamma_1(l_{1,i}; \psi_1) + \left[(\hat{d}^{opt}_{2,i} - a_{2,i})(\hat{\psi}_{20} + \hat{\psi}_{21} l_{2,i} + \hat{\psi}_{22} a_{1,i} + \hat{\psi}_{23} l_{2,i} a_{1,i})\right]$$

is upwardly biased for $H_{1,i}(\psi_1, \psi_2^{\dagger})$, as described in section 2.2 and by Robins (2004).

Now let $H^0_{1,i}(\psi_1) = Y_i - \gamma_1(l_{1,i}; \psi_1)$ if subject i belongs to m^0_2 and $H^0_{1,i}(\psi_1) = H_{1,i}(\psi_1)$ otherwise. If $i \in m^0_2$, $H^0_{1,i}(\psi_1) = H_{1,i}(\psi_1, \psi_2^{\dagger})$, otherwise $E[H^0_{1,i}(\psi_1)] = H_{1,i}(\psi_1, \psi_2^{\dagger})$. The ZIPI estimating equation (corresponding to inefficient g-estimating equation (2)) is

$$E[U^{0*}_{1i}(\psi_1, \hat{\psi}_2)] = \frac{1}{n}\Big\{\sum_{i \in m^0_2} H^0_{1,i}(\psi_1)\{S_j(A_j) - E[S_j(A_j)|\bar{L}_j, \bar{A}_{j-1}]\} + \sum_{i \in m^1_2} H^0_{1,i}(\psi_1)\{S_j(A_j) - E[S_j(A_j)|\bar{L}_j, \bar{A}_{j-1}]\}\Big\}.$$

$E[U^{0*}_{1i}(\psi_1, \hat{\psi}_2)] = 0$, and therefore ZIPI estimates calculated under known m^0_2, m^1_2 are consistent and asymptotically unbiased for any ψ in the parameter space and at any law, exceptional or otherwise. □

Of course, m^0_j and m^1_j are not known and must always be estimated. Typically, some misclassification will occur. Recall type I error is that of using the estimate $\hat{\psi}_2$ rather than 0 in $H_{1,i}(\psi_1)$ and type II error that of using 0 when a plug-in estimate would have been desired. We now calculate the asymptotic bias and compare this to the result of section 2.2 to demonstrate that even when m^0_j and m^1_j are estimated, ZIPI exhibits less asymptotic bias than recursive g-estimation. As with ordinary g-estimation, generalization of the expression for the asymptotic bias for $K > 2$ intervals is not trivial because of the need to use both regular and asymptotically biased plug-in estimates.

Theorem 3.3. *When the distribution law is exceptional and m^0_2, m^1_2 are estimated, two-interval ZIPI estimates have smaller asymptotic bias than the usual recursive g-estimates provided estimates are not shared across intervals, and* $\inf_{\bar{L}_2, A_1} \{|g_2(\bar{L}_2, A_1; \psi_2^{\dagger})|\} \setminus \{0\} = \mu > 0$.

Proof: Misclassification arising from estimating m^0_2 and m^1_2 results in asymptotic bias in

ZIPI estimates at exceptional laws; however the magnitude of the bias is less than that of g-estimates. Since $|g_2(\bar{L}_2, A_1; \psi_2)| \geq \mu$ for some $\mu > 0$ for all subjects with a unique optimal rule at the second interval, it follows that there exists a sample size such that the power to detect whether $g_2(\bar{L}_{2,i}, A_{1,i}; \psi_2) \neq 0$ is effectively equal to 1 if classification of individuals into m_2^0, m_2^1 is performed using $1 - \epsilon$ confidence intervals with fixed type I error ϵ. However, $100\epsilon\%$ of the people with non-unique treatment rules will be falsely classified as belonging to $\mathcal{M}_2^1$.

Assume linear blips, so $\sum_{j=0}^{|\psi_2|-1} \psi_{2j}^{\dagger} \cdot X_2 = 0$ when laws are exceptional, where the true values of ψ_1, ψ_2 are denoted by $\psi_1^{\dagger}$, $\psi_2^{\dagger}$. Define $\Delta_1^z(\hat{\psi}_2, \psi_2^{\dagger}) = U_1^{0*}(\psi_1, \hat{\psi}_2) - U_1^*(\psi_1, \psi_2^{\dagger})$, a quantity in ZIPI estimation similar to $\Delta_1^g(\hat{\psi}_2, \psi_2^{\dagger})$ in the usual g-estimation procedure. Since, asymptotically, the only form of misclassification error in ZIPI is type I, $\Delta_1^z(\hat{\psi}_2, \psi_2^{\dagger})$ consists of three components:

i. If $i \in m_j^0$ and $i \in \hat{m}_j^0$, $\Delta_1^z(\hat{\psi}_2, \psi_2^{\dagger}) = 0$;

ii. If $i \in m_j^0$ and $i \in \hat{m}_j^1$,
$\Delta_1^z(\hat{\psi}_2, \psi_2^{\dagger}) = \{S_1(A_1) - E[S_1(A_1)|L_1]\} \cdot \Big(I[(\hat{\psi}_2 - \psi_2^{\dagger}) \cdot X_2 > 0] - A_2\Big)(\hat{\psi}_2 - \psi_2^{\dagger}) \cdot X_2$;

iii. If $i \in m_j^1$, $\Delta_1^z(\hat{\psi}_2, \psi_2^{\dagger}) = \{S_1(A_1) - E[S_1(A_1)|L_1]\} \cdot$
$\Big\{\Big(I[g_2(\bar{L}_2, A_1; \hat{\psi}_2) > 0] - A_2\Big) g_2(\bar{L}_2, A_1; \hat{\psi}_2) - \Big(I[g_2(\bar{L}_2, A_1; \psi_2^{\dagger}) > 0] - A_2\Big) g_2(\bar{L}_2, A_1; \psi_2^{\dagger})\Big\}$.

Similar to the calculation of section 2.2, asymptotic bias is proportional to $E[\Delta_1^z(\hat{\psi}_2, \psi_2^{\dagger})]$. The classification procedure in ZIPI incorrectly fails to use zeros for $100\epsilon\%$ of the sample with $\mathcal{M}_1^0$. Therefore we rewrite $\Delta_1^z(\hat{\psi}_2, \psi_2^{\dagger})$ in terms of $\Delta_1^g(\hat{\psi}_2, \psi_2^{\dagger})$ of recursive g-estimation: $\Delta_1^z(\hat{\psi}_2, \psi_2^{\dagger}) = \epsilon I[g_2(\bar{L}_2, A_1; \psi_2^{\dagger}) = 0]\Delta_1^g(\hat{\psi}_2, \psi_2^{\dagger}) + I[g_2(\bar{L}_2, A_1; \psi_2^{\dagger}) \neq 0]\Delta_1^g(\hat{\psi}_2, \psi_2^{\dagger})$. It follows directly that the asymptotic bias of first-interval ZIPI estimates at exceptional laws is

$$-\epsilon E\left[\frac{\partial}{\partial \psi_1} U_1^*(\psi_1^{\dagger})\right]^{-1} E\left\{S_1(A_1) - E[S_1(A_1)|L_1]\right\} \cdot E[Z_{2+}|Z_{2+} > 0]P[Z_{2+} > 0]. \qquad \square$$

In finite samples both type I *and* type II error will be observed, which leads to additional bias in the ZIPI estimates. When sample size is not sufficient for power to equal 1, $\Delta_1^z(\hat{\psi}_2, \psi_2^\dagger)$ is decomposed into *four* components (two of which are zero in expectation). If type II error is denoted by β, then, approximately, for two-intervals the bias will be proportional to $\epsilon\mathrm{P}(g_2(\bar{L}_2, A_1; \psi_2^\dagger) = 0)E[\Delta_1^g(\hat{\psi}_2, \psi_2^\dagger)] + \beta\mathrm{P}(g_2(\bar{L}_2, A_1; \psi_2^\dagger) \neq 0)\cdot$ $E\left[\{S_1(A_1) - E[S_1(A_1)|L_1]\}\left(I[g_2(\bar{L}_2, A_1; \psi_2^\dagger) > 0] - A_2\right) g_2(\bar{L}_2, A_1; \psi_2^\dagger)\right]$.

When covariates are integer-valued as in our simulations, there is good separation of $g_2(\bar{L}_2, A_1; \hat{\psi}_2)$ between those people with unique rules and those without; in this instance, simulations suggest that choosing a relatively large (e.g., 0.20) type I error provides a good balance between bias reduction *at* and *near* exceptional laws (Figures 3-4).

3.4 ZIPI versus simultaneous (non-recursive) g-estimation

With ZIPI g-estimation proving both theoretically and in simulation to be asymptotically less biased than recursive g-estimation when parameters are not shared between intervals, it is the obvious choice. The question then arises as to whether it is better than simultaneous (non-recursive) g-estimation when parameters are shared. Recall that Theorem 3.3 pertains to recursive, not simultaneous, estimation.

If parameters are believed to be shared, that is, $\psi_j = \psi_{j'}$ for some $j \neq j'$, recursive methods may still be used by pretending otherwise, using a recursive form of g-estimation (the usual or ZIPI) then averaging the interval-specific estimates of ψ. Inverse covariance weighted recursive g-estimates have the advantage of being easier to compute than simultaneous estimates and are doubly-robust under non-exceptional laws (Robins 2004, p. 221). On the other hand, simultaneous g-estimation can incorporate the stationarity information into the estimating equations and search for estimates of the shared parameters directly without needing to average estimates from different intervals.

Robins (2004, p. 221-222) recommends simultaneous g-estimation for non-exceptional laws when there are few subjects who change treatment from one interval to the next: with few changes of treatment at interval j, estimates $\hat{\psi}_j$ are extremely variable and so the inverse variance weighting can introduce bias in the estimating equation for ψ_m, $m < j$, in a manner not unlike the bias caused by exceptional laws.

If there are a moderate number of treatment changes from one interval to the next (recursive) ZIPI estimation may be useful for the purposes of bias reduction in large samples. Figure 5 compares ZIPI with 80% confidence intervals used to estimate membership in m_j^0 or m_j^1, recursive g-estimation, and simultaneous g-estimation for data as before: $L_1 \sim \mathcal{N}(0,3)$; $L_2 \sim$ round($\mathcal{N}(0.75, 0.5)$); $Y \sim \mathcal{N}(1,1) - |\gamma_1(L_1, A_1)| - |\gamma_2(\bar{L}_2, \bar{A}_2)|$ but we now impose stationarity so that $\gamma_1(L_1, A_1) = A_1(\psi_0 + \psi_1 L_1)$ and $\gamma_2(\bar{L}_2, \bar{A}_2) = A_2(\psi_0 + \psi_1 L_2 + \psi_{22} A_1 + \psi_{23} L_2 A_1)$. Note the sharing of ψ_0 and ψ_1 in blips of both intervals.

In our simulations, simultaneous and recursive g-estimation are similar in terms of both bias and variability. Relative to simultaneous g-estimation, the recursive methods are easier to implement and do not suffer from the possibility of multiple roots under linear blip functions. At non-exceptional laws, ZIPI is asymptotically equivalent to the doubly-robust recursive g-estimation which, as noted above, is locally efficient. In our simulations, ZIPI's performance at exceptional laws was inconsistent, performing much better when $\psi_1 = 2$ as compared to when $\psi_1 = 3$ (Figure 5). These results demonstrate that inverse-covariance weighted ZIPI estimates are not always less biased than simultaneous g-estimates even in quite large samples.

3.5 ZIPI versus Iterative Minimization for Optimal Regimes

It is worth noting that the asymptotic bias due to exceptional laws is present in the Iterative Minimization for Optimal Regimes (IMOR) (Murphy 2003) method as well (Table 3). This is not surprising since IMOR and g-estimation are very closely related (Moodie et al. 2007). Nevertheless, when parameters are shared and the sample is not very large, IMOR may prove to be less biased at exceptional laws than ZIPI for the reasons noted in the previous subsection.

4. DISCUSSION

In this paper, we have discussed the asymptotic bias of optimal decision rule parameter estimates in the presence of exceptional laws. We also presented suggestions to reduce the computational burden of trying to detect exceptional laws using Robins' method.

We introduced Zeroing Instead of Plugging In, a recursive form of g-estimation in which zeros are used rather than estimates in those individuals who are likely to have non-unique optimal treatments at some intervals. When parameters are non-stationary, ZIPI is consistent and asymptotically unbiased at all laws when individuals with non-unique optimal rules can be identified without error. In practice, ZIPI estimates are asymptotically biased at exceptional laws due the estimation of m_j^0 and m_j^1, however the bias is smaller than that of recursive g-estimates when parameters are non-stationary and the quantity that determines optimal treatment is bounded away from zero. Therefore whenever parameters are not shared between intervals ZIPI is to be preferred over recursive g-estimation if there is a possibility of laws being exceptional. Future work will include determination of the best choice of threshold in ZIPI.

Asymptotic bias due to exceptional laws cannot be avoided by using methods that do not require plug-in estimates such as simultaneous g-estimation or IMOR, even when parameters are stationary. When the sample is very large and there are moderate to large numbers of people receiving treatment in each interval, inverse covariance weighted ZIPI estimates may provide a good alternative to either simultaneous g-estimation or IMOR, though this is not guaranteed.

We conclude by observing that one of g-estimation's primary points of appeal is that, unlike traditional approaches such as dynamic programming, estimates are asymptotically unbiased under the null hypothesis of no treatment effect even if the distribution law is mis-specified provided the true law is not exceptional. However for a blip function that includes at least one component of treatment and covariate history, *under the hypothesis of no treatment effect, every distribution is an exceptional law* and therefore g-estimation is asymptotically biased under the null for all such blip functions and laws. Thus when primary concern is in performing a valid test of the null hypothesis of no treatment effect, we may consider fitting a "null" blip model which does not include any covariates (using the doubly robust estimator), proceeding to richer blip models only if the "null" blip model cannot be rejected.

APPENDIX A. ASYMPTOTIC BIAS OF DOUBLY-ROBUST G-ESTIMATES

The doubly-robust g-estimating equation (1) can be expressed in terms of the singly-robust equation (2): $U_j(\psi) = U_j^*(\psi) - E[H_j(\psi)|\bar{L}_j, \bar{A}_{j-1}; \varsigma_2]\{S_j(A_j) - E[S_j(A_j)|\bar{L}_j, \bar{A}_{j-1}]\}$. Knowing the asymptotic bias of (2), it is therefore sufficient to consider $E[H_j(\psi)|\bar{L}_j, \bar{A}_{j-1}]\{S_j(A_j) - E[S_j(A_j)|\bar{L}_j, \bar{A}_{j-1}; \varsigma_2]\}$ to find the asymptotic bias of (1). The doubly-robust procedure has the advantage that blip functions which do not allow for covariate and treatment interactions never lead to exceptional laws. We proceed in a two-interval setting.

Let $\delta_1^g(\psi_1, \hat{\psi}_2, \psi_2^\dagger) = E[(H_2(\hat{\psi}_2) - H_2(\psi_2^\dagger))|\bar{L}_2, A_1; \varsigma_2]\{S_2(A_2) - E[S_2(A_2)|\bar{L}_2, A_1]\}$. To be concrete, assume that the expected counterfactual is modelled by a simple linear form $E[H_2(\psi_2)|\bar{L}_2, A_1] = W \cdot \varsigma_2(\psi_2)$, where W is some subset of the covariate and treatment history, L_1, A_1, L_2, and a vector of 1's. The ordinary least squares estimator is $\hat{\varsigma}_2(\psi_2) = (W'W)^{-1}W'H_2(\psi_2)$. If laws are not exceptional, $H_2(\hat{\psi}_2)$ converges to $H_2(\psi_2^\dagger)$ and a continuous mapping theorem provides that $\hat{\varsigma}_2(\hat{\psi}_2)$ converges to $\varsigma_2(\psi_2^\dagger)$. Then, asymptotically, $E[(H_2(\hat{\psi}_2) - H_2(\psi_2^\dagger))|\bar{L}_2, A_1; \varsigma_2] = 0$ so that $\delta_1^g(\psi_1, \hat{\psi}_2, \psi_2^\dagger) = 0$.

On the other hand, when laws are exceptional $g_2(\bar{L}_2, A_1; \psi_2^\dagger) = 0$ and

$$\begin{aligned}
\delta_1^g(\psi_1, \hat{\psi}_2, \psi_2^\dagger) &= W(W'W)^{-1}W' \left(I[g_2(\bar{L}_2, A_1; \hat{\psi}_2) > 0] - A_2\right) g_2(\bar{L}_2, A_1; \hat{\psi}_2) \times \\
&\qquad\qquad \{S_1(A_1) - E[S_1(A_1)|L_1]\} \\
&= W(W'W)^{-1}W' \left(I[g_2(\bar{L}_2, A_1; \hat{\psi}_2) - g_2(\bar{L}_2, A_1; \psi_2^\dagger) > 0] - A_2\right) \times \\
&\qquad \left(g_2(\bar{L}_2, A_1; \hat{\psi}_2) - g_2(\bar{L}_2, A_1; \psi_2^\dagger)\right) \{S_1(A_1) - E[S_1(A_1)|L_1]\} \\
&= W(W'W)^{-1}W' \left(I[(\hat{\psi}_2 - \psi_2^\dagger) \cdot X_2 > 0] - A_2\right) (\hat{\psi}_2 - \psi_2^\dagger) \cdot X_2 \times \\
&\qquad\qquad \{S_1(A_1) - E[S_1(A_1)|L_1]\}
\end{aligned}$$

where $(\hat{\psi}_2 - \psi_2^\dagger) \cdot X_2 = g_2(\bar{L}_2, A_1; \hat{\psi}_2) - g_2(\bar{L}_2, A_1; \psi_2^\dagger)$ when blips are linear. Letting Z_{2+} denote a normal random variable with mean zero and variance $\mathrm{Var}\Big[\Big(E\left[\frac{\partial}{\partial \psi_2} U_2(\psi_2^\dagger)\right]\Big)^{-1} U_2(\psi_2^\dagger) \cdot X_2\Big]$, we have $E[\delta_1^g(\psi_1, \hat{\psi}_2, \psi_2^\dagger)] = E\Big[\{S_1(A_1) - E[S_1(A_1)|L_1]\} W(W'W)^{-1}W'\Big] E[Z_{2+}|Z_{2+} > 0] P[Z_{2+} > 0] + o_p(n^{-1/2})$. Further,

$$\begin{aligned}
(\hat{\psi}_1 - \psi_1^\dagger) &= -\left(E\left[\frac{\partial}{\partial \psi_1} U_1(\psi_1^\dagger, \psi_2^\dagger)\right]\right)^{-1} \mathbb{P}_n U_1(\psi_1^\dagger, \hat{\psi}_2) + o_p(n^{-1/2}) \\
&= -\left(E\left[\frac{\partial}{\partial \psi_1} U_1(\psi_1^\dagger, \psi_2^\dagger)\right]\right)^{-1} \mathbb{P}_n \left(U_1(\psi_1^\dagger, \psi_2^\dagger) + \Delta_1^g(\hat{\psi}_2, \psi_2^\dagger) - \delta_1^g(\psi_1, \hat{\psi}_2, \psi_2^\dagger)\right) + o_p(n^{-1/2}).
\end{aligned}$$

Thus, the asymptotic bias of $\hat{\psi}_1$ found via doubly-robust g-estimation equals

$$\begin{aligned}
-\left(E\left[\frac{\partial}{\partial \psi_1} U_1(\psi_1^\dagger, \psi_2^\dagger)\right]\right)^{-1} E\left\{S_1(A_1) - E[S_1(A_1)|L_1](1 - W(W'W)^{-1}W')\right\} \times \\
E[Z_{2+}|Z_{2+} > 0] P[Z_{2+} > 0].
\end{aligned}$$

Under a more complex form for $E[H_2(\psi_2)|\bar{L}_2, A_1]$, and indeed under its correct specification (Moodie et al. 2007), it maybe the case that $\delta_1^g(\psi_1, \hat{\psi}_2, \psi_2^\dagger)$ depends on ψ_1. This is not so when a simple linear model is assumed, as is typically done for closed-form, recursive g-estimation.

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Tables

Table 1: Summary statistics of g-estimates and Robins' (2004) proposed method of detecting exceptional laws from 1000 data-sets of sample sizes 250 and 1000.

n	ψ	$\hat{\psi}$	|Bias|	$\|t\|^a$	rMSE	Cov.[b]	Cov.[c]
250							
	ψ_{10} = 1.6	1.657	0.057	0.306	0.245	95.1	94.2
	ψ_{11} = 0.0	-0.001	0.001	0.027	0.057	94.2	94.7
	ψ_{20} = -3.0	-3.001	0.001	0.001	0.424	92.5	94.5
	ψ_{21} = 2.0	2.006	0.006	0.017	0.460	92.0	93.5
	ψ_{22} = 1.0	1.004	0.004	0.003	0.615	93.5	93.6
	ψ_{23} = 0.0	-0.001	0.001	0.008	0.693	94.2	94.7
		$p_{op,2}$: Mean (Range): 63.8 (30.4, 92.0)					
1000							
	ψ_{10} = 1.6	1.629	0.029	0.321	0.121	95.5	95.4
	ψ_{11} = 0.0	-0.001	0.001	0.026	0.028	96.1	95.2
	ψ_{20} = -3.0	-3.001	0.001	0.017	0.203	95.3	95.3
	ψ_{21} = 2.0	2.002	0.002	0.007	0.225	94.2	94.7
	ψ_{22} = 1.0	1.000	0.000	0.002	0.298	95.4	94.9
	ψ_{23} = 0.0	-0.006	0.006	0.032	0.348	94.5	95.2
		$p_{op,2}$: Mean (Range): 35.7 (28.2, 70.2)					

[a] $|t| = |Bias(\hat{\psi})/\mathrm{SE}(\hat{\psi})|$

[b] Coverage of 95% Wald confidence intervals

[c] Coverage of 95% score confidence intervals

[d] Estimated proportion of sample with non-unique optimal rules (see section 2.3)

Table 2: Parameter estimates under exceptional laws: summary statistics of g-estimation using Zeroing Instead of Plugging In (ZIPI) and the usual g-estimates from 1000 data-sets of sample sizes 250, 500 and 1000 using 80%, 90%, and 95% CIs for ZIPI. Second interval parameter estimates are omitted for all but 80% CI exclusions since the exclusions affect only first-interval parameters when using ZIPI (see section 3.2).

CI		ZIPI					Usual g-estimation				
exclusion	ψ	$\hat{\psi}$	SE	$\lvert t\rvert^a$	rMSE	Cov.^{b}	$\hat{\psi}$	SE	$\lvert t\rvert^a$	rMSE	Cov.^{b}
$n = 250$											
80%	$\psi_{10} = 1.6$	1.631	0.167	0.174	0.229	94.3	1.659	0.179	0.322	0.243	95.7
	$\psi_{11} = 0.0$	-0.001	0.042	0.031	0.057	94.3	-0.001	0.042	0.029	0.057	94.6
	$\psi_{20} = -3.0$	-2.991	0.299	0.016	0.413	92.8	-2.991	0.299	0.016	0.413	93.3
	$\psi_{21} = 2.0$	1.977	0.325	0.095	0.461	92.3	1.977	0.325	0.095	0.461	92.4
	$\psi_{22} = 1.0$	0.992	0.444	0.020	0.606	94.2	0.992	0.444	0.020	0.606	94.3
	$\psi_{23} = 0.0$	0.014	0.505	0.015	0.696	93.1	0.014	0.505	0.015	0.696	93.4
90%	$\psi_{10} = 1.6$	1.622	0.165	0.126	0.227	94.3					
	$\psi_{11} = 0.0$	-0.001	0.042	0.031	0.057	94.1					
95%	$\psi_{10} = 1.6$	1.617	0.164	0.098	0.225	94.4					
	$\psi_{11} = 0.0$	-0.001	0.042	0.030	0.057	94.2					
$n = 500$											
80%	$\psi_{10} = 1.6$	1.615	0.118	0.108	0.164	92.6	1.636	0.126	0.281	0.172	94.2
	$\psi_{11} = 0.0$	0.000	0.030	0.003	0.041	94.8	0.000	0.030	0.002	0.041	94.7
	$\psi_{20} = -3.0$	-2.998	0.212	0.006	0.288	93.5	-2.998	0.212	0.006	0.288	94.1
	$\psi_{21} = 2.0$	1.993	0.233	0.047	0.317	93.7	1.993	0.233	0.047	0.317	93.9
	$\psi_{22} = 1.0$	0.996	0.314	0.013	0.432	93.9	0.996	0.314	0.013	0.432	94.3
	$\psi_{23} = 0.0$	-0.002	0.360	0.018	0.495	93.3	-0.002	0.360	0.018	0.495	93.7
90%	$\psi_{10} = 1.6$	1.609	0.117	0.062	0.161	93.2					
	$\psi_{11} = 0.0$	0.000	0.030	0.003	0.041	94.9					
95%	$\psi_{10} = 1.6$	1.605	0.116	0.032	0.160	93.3					
	$\psi_{11} = 0.0$	0.000	0.030	0.002	0.041	94.9					
$n = 1000$											
80%	$\psi_{10} = 1.6$	1.616	0.083	0.180	0.114	94.9	1.632	0.090	0.348	0.121	95.3
	$\psi_{11} = 0.0$	-0.001	0.021	0.041	0.028	94.8	-0.001	0.021	0.042	0.028	95.1
	$\psi_{20} = -3.0$	-2.995	0.150	0.025	0.207	93.4	-2.995	0.150	0.025	0.207	93.7
	$\psi_{21} = 2.0$	1.997	0.165	0.030	0.225	93.8	1.997	0.165	0.030	0.225	94.0
	$\psi_{22} = 1.0$	0.992	0.222	0.036	0.305	94.2	0.992	0.222	0.036	0.305	94.5
	$\psi_{23} = 0.0$	0.003	0.255	0.003	0.348	94.8	0.003	0.255	0.003	0.348	95.0
90%	$\psi_{10} = 1.6$	1.611	0.083	0.127	0.113	95.1					
	$\psi_{11} = 0.0$	-0.001	0.021	0.042	0.028	94.8					
95%	$\psi_{10} = 1.6$	1.608	0.082	0.089	0.112	95.1					
	$\psi_{11} = 0.0$	-0.001	0.021	0.042	0.028	94.7					

^{a} $|t| = |Bias(\hat{\psi})/\mathrm{SE}(\hat{\psi})|$
^{b} Coverage of 95% Wald confidence intervals

Table 3: Parameter estimates under exceptional laws: summary statistics of g-estimation using Zeroing Instead of Plugging In (ZIPI) and the IMOR from 1000 data-sets of sample sizes 250, 500 and 1000 using 80% CIs for ZIPI.

		ZIPI				IMOR			
n	ψ	$\hat{\psi}$	SE	rMSE	Cov.[a]	$\hat{\psi}$	SE	rMSE	Cov.[a]
250									
	$\psi_{10} = 1.6$	1.628	0.167	0.233	93.3	1.643	0.193	0.259	95.9
	$\psi_{11} = 0.0$	0.002	0.042	0.058	93.6	-0.002	0.043	0.059	92.7
	$\psi_{20} = -3.0$	-3.017	0.296	0.409	92.4	-3.042	0.391	0.524	95.7
	$\psi_{21} = 2.0$	2.011	0.325	0.451	92.1	2.040	0.381	0.516	94.1
	$\psi_{22} = 1.0$	1.022	0.442	0.606	94.6	1.046	0.496	0.675	94.4
	$\psi_{23} = 0.0$	-0.020	0.507	0.693	94.9	-0.047	0.516	0.699	95.1
500									
	$\psi_{10} = 1.6$	1.625	0.118	0.160	95.0	1.640	0.137	0.180	96.7
	$\psi_{11} = 0.0$	0.000	0.030	0.041	94.4	0.000	0.030	0.041	94.6
	$\psi_{20} = -3.0$	-2.993	0.212	0.288	93.4	-2.997	0.276	0.369	95.5
	$\psi_{21} = 2.0$	1.995	0.234	0.319	93.6	2.000	0.269	0.362	94.5
	$\psi_{22} = 1.0$	0.994	0.313	0.419	95.7	1.000	0.349	0.470	96.0
	$\psi_{23} = 0.0$	0.009	0.361	0.482	95.8	0.002	0.363	0.488	96.3
1000									
	$\psi_{10} = 1.6$	1.608	0.083	0.116	92.7	1.619	0.097	0.129	95.3
	$\psi_{11} = 0.0$	0.000	0.021	0.028	96.2	0.000	0.021	0.028	96.2
	$\psi_{20} = -3.0$	-3.010	0.151	0.206	93.8	-3.020	0.197	0.265	95.9
	$\psi_{21} = 2.0$	2.009	0.166	0.227	94.0	2.017	0.191	0.258	95.2
	$\psi_{22} = 1.0$	1.015	0.222	0.305	94.0	1.023	0.249	0.342	94.0
	$\psi_{23} = 0.0$	-0.013	0.256	0.347	94.0	-0.018	0.258	0.353	94.3

[a] Coverage of 95% Wald confidence intervals

Figures: Titles and Artwork

Figure 1. Absolute bias of $\hat{\psi}_{10}$ as sample size varies at and near exceptional laws. In each figure, one of $\psi_{20}, \psi_{21}, \psi_{22}, \psi_{23}$ is varied while the remaining are fixed at one of -3.0, 2.0, 1.0, or 0.0, respectively. Note that there are several combinations of parameters that lead to exceptional laws: as well as (-3.0, 2.0, 1.0, 0.0) with $p(A_1 = L_2 = 1) > 0$, exceptional laws occur with (-2.0, 2.0, 1.0, 0.0) and (-3.0, 3.0, 1.0, 0.0) if $p(A_1 = 0, L_2 = 1) > 0$.

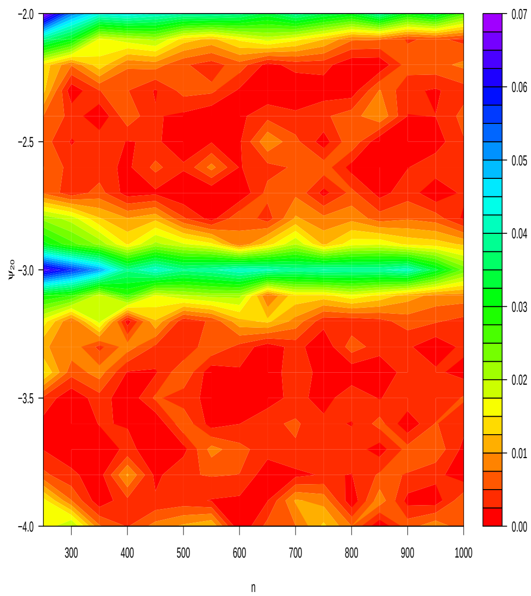
Figure 2. Lack of bias of $\hat{\psi}_{10}$ as sample size varies for non-exceptional laws. In each figure, one of $\psi_{20}, \psi_{21}, \psi_{22}, \psi_{23}$ is varied while the other three parameters are fixed at one of -3.0, 2.0, 1.0, or 0.0, respectively. L_2 is continuous Normal so that $p(A_1 = L_2 = 1) = p(A_1 = 0, L_2 = 1) = 0$ and its co-efficient in the blip function is sufficiently larger than zero so that no optimal rules appear to be non-unique in samples of size 200 or greater.

Figure 3. Absolute bias of $\hat{\psi}_{10}$ as sample size varies at and near exceptional laws using Zeroing Instead of Plugging In (ZIPI) when 95% confidence intervals suggest exceptional laws. In each figure, one of $\psi_{20}, \psi_{21}, \psi_{22}, \psi_{23}$ is varied while the other three parameters are fixed at one of -3.0, 2.0, 1.0, or 0.0, respectively.

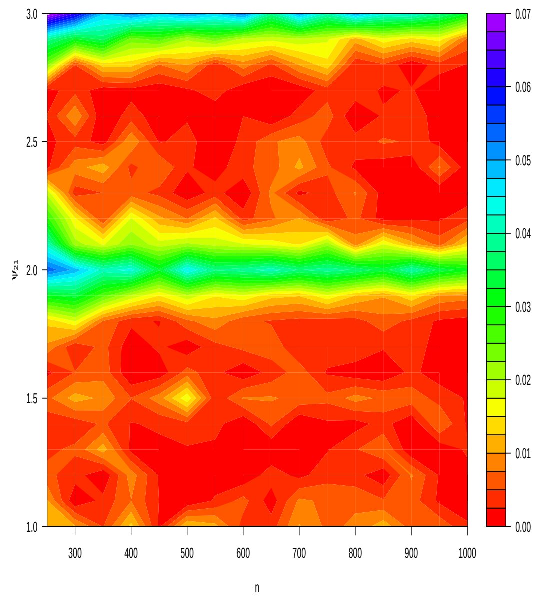
Figure 4. Absolute bias of $\hat{\psi}_{10}$ as sample size varies at and near exceptional laws using Zeroing Instead of Plugging In (ZIPI) when 80% confidence intervals suggest exceptional laws. In each figure, one of $\psi_{20}, \psi_{21}, \psi_{22}, \psi_{23}$ is varied while the other three parameters are fixed at one of -3.0, 2.0, 1.0, or 0.0, respectively.

Figure 5. Absolute bias in $\hat{\psi}_0$ as n varies about exceptional laws assuming stationarity: inverse-covariance weighted ZIPI estimates with 80% CIs, inverse-covariance weighted recursive g-estimates, and simultaneous g-estimates [left, center, and right columns]. Rows: the true value of one of $\psi_0, \psi_1, \psi_{22}, \psi_{23}$ is varied; the rest are fixed at -3.0, 2.0, 1.0, or 0.0, respectively.

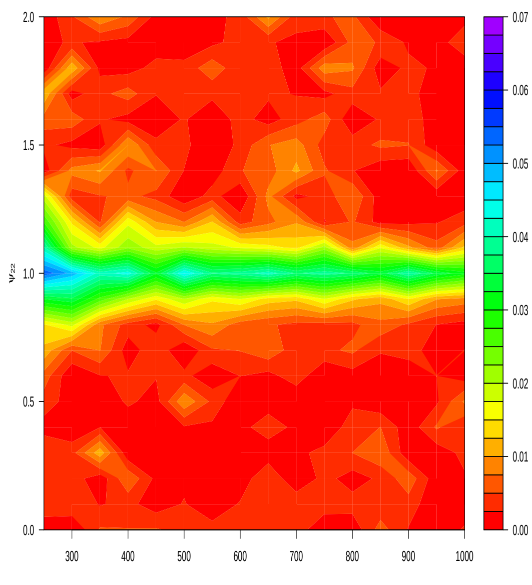
Figure 1:



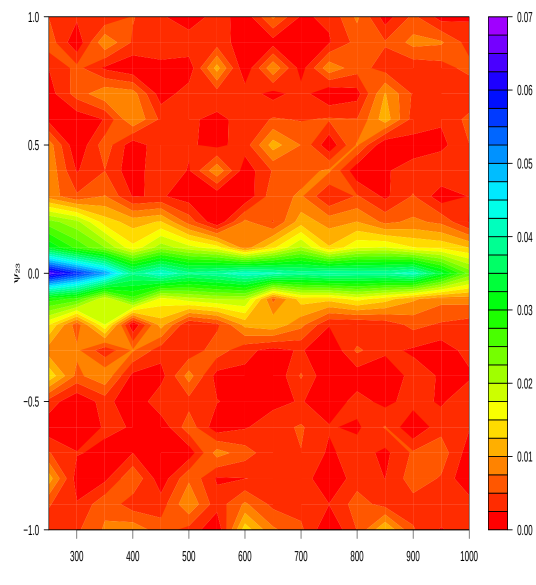
(a) Bias in $\hat{\psi}_{10}$, varying ψ_{20}



(b) Bias in $\hat{\psi}_{10}$, varying ψ_{21}

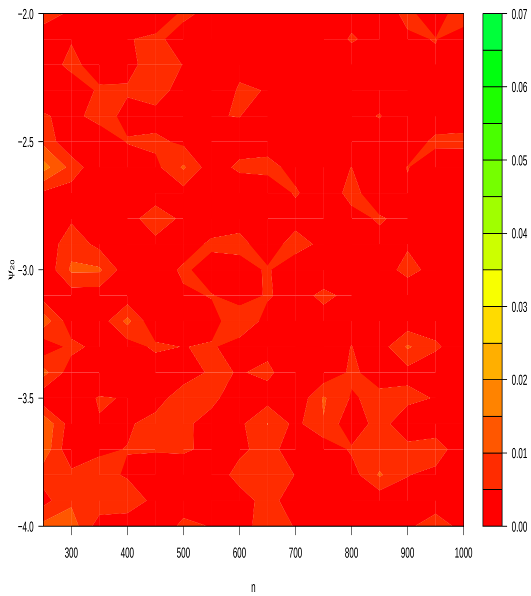


(c) Bias in $\hat{\psi}_{10}$, varying ψ_{22}

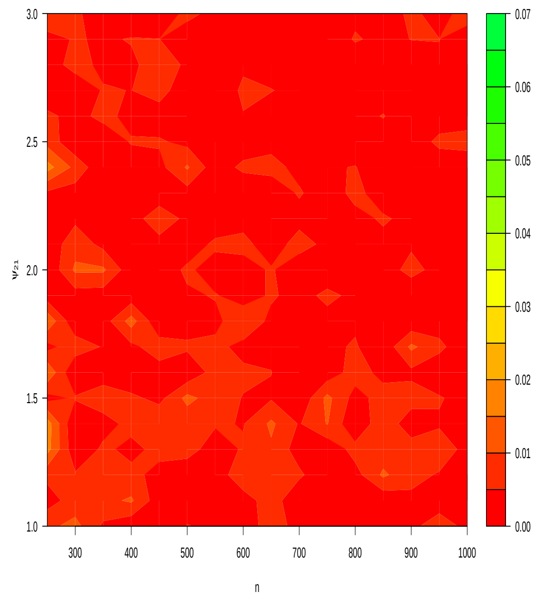


(d) Bias in $\hat{\psi}_{10}$, varying ψ_{23}

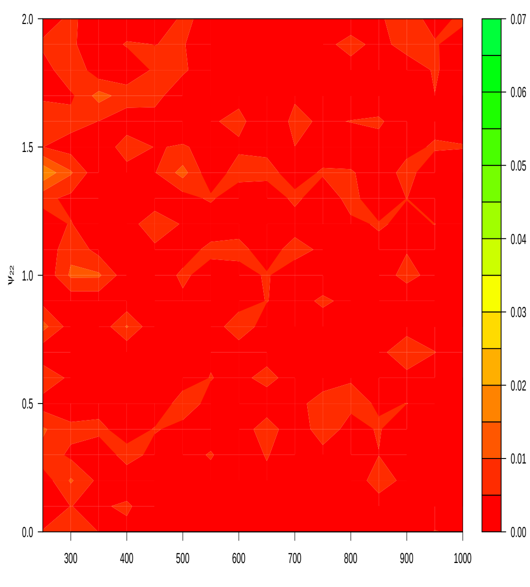
Figure 2:



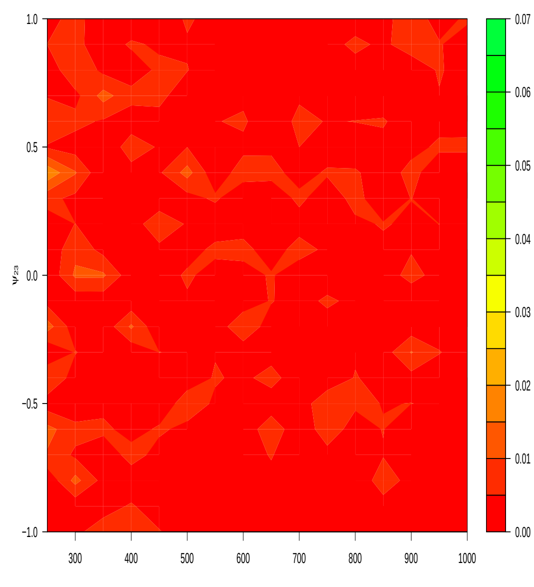
(a) Bias in $\hat{\psi}_{10}$, varying ψ_{20}



(b) Bias in $\hat{\psi}_{10}$, varying ψ_{21}

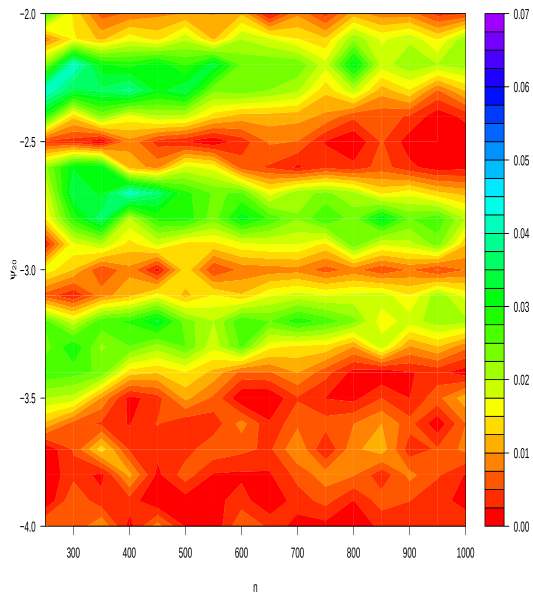


(c) Bias in $\hat{\psi}_{10}$, varying ψ_{22}

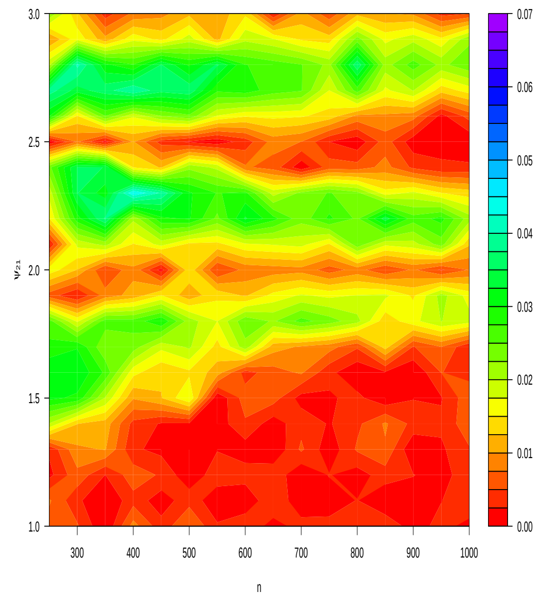


(d) Bias in $\hat{\psi}_{10}$, varying ψ_{23}

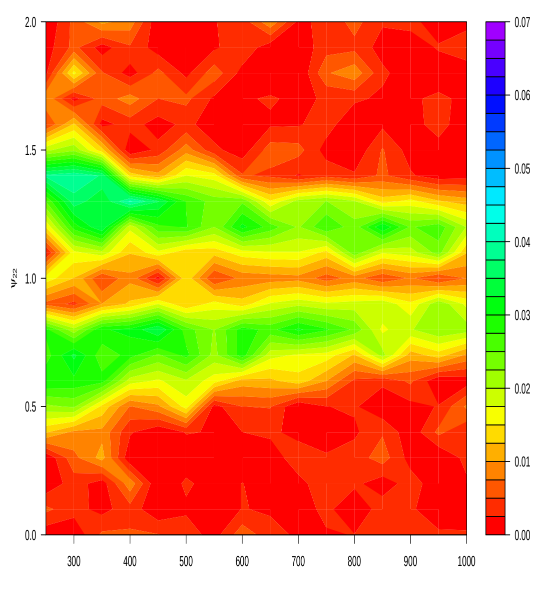
Figure 3:



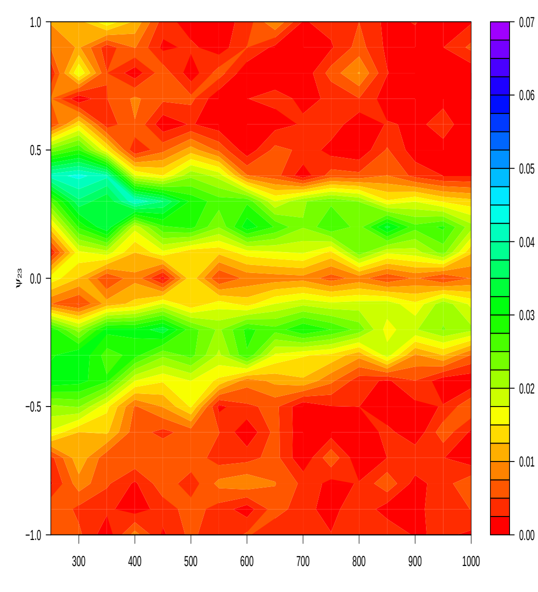
(a) Bias in $\hat{\psi}_{10}$, varying ψ_{20}



(b) Bias in $\hat{\psi}_{10}$, varying ψ_{21}

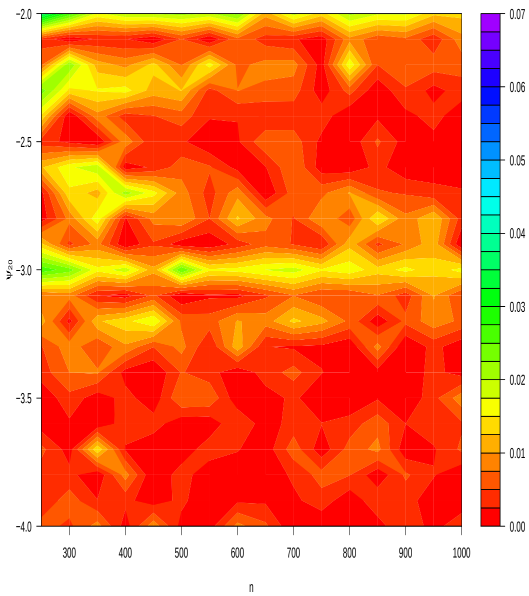


(c) Bias in $\hat{\psi}_{10}$, varying ψ_{22}

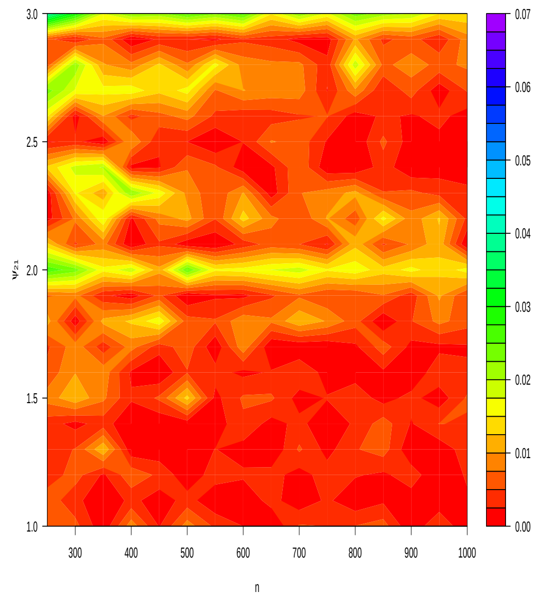


(d) Bias in $\hat{\psi}_{10}$, varying ψ_{23}

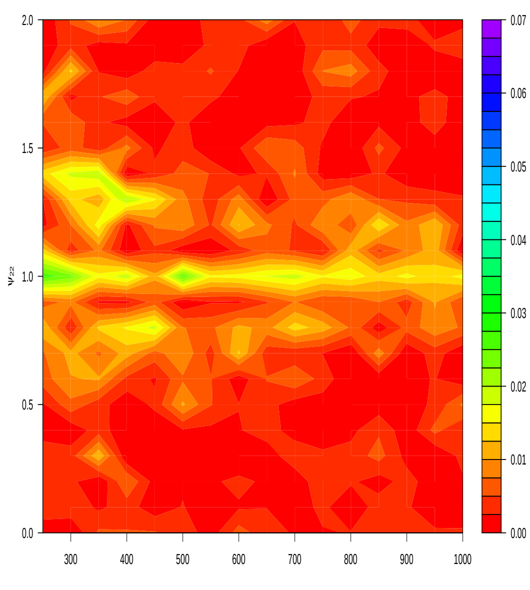
Figure 4:



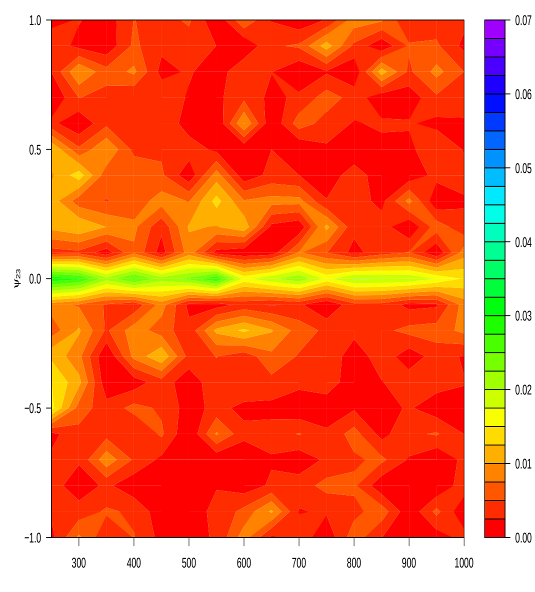
(a) Bias in $\hat{\psi}_{10}$, varying ψ_{20}



(b) Bias in $\hat{\psi}_{10}$, varying ψ_{21}



(c) Bias in $\hat{\psi}_{10}$, varying ψ_{22}



(d) Bias in $\hat{\psi}_{10}$, varying ψ_{23}

Figure 5: