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# Model Related Instabilities in High Dimensional Linear Models Brimacombe $M^*$ and Bimali M

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### Abstract

The use of high dimensional linear models is common in large database settings. The linearity of such models is often assumed. In sparse settings with the number of subjects (*n*) less than the number of variables (*p*) standard algorithms include the *lars-LASSO* approach which often provides stable convergence. In some cases the underlying data may be more appropriately modeled with a nonlinear model. The use of a linear model in such cases creates model mis-specification and instability for *lars-LASSO* based approaches. This is studied by using simulations with various relative sample sizes, correlation structures and error distributions.

**Keywords:** High dimensional models; Linear models; Model misspecification; Nonlinear models

#### Introduction

The onset of large databases in many sciences and the need to organize data into information has lead to heightened interest in the analytic and algorithmic methods that guide the analysis of these databases. This has arisen organically in fields such as genomics, imaging, health outcomes, epidemiology and clinical science [1]. Developing stable and interpretable approaches to the organization, analysis and modeling of such databases is a challenge, especially as they often are not subject to formal design standards during data collection.

A very large number of variables and relatively few subjects (large p and small n problems) are typical of such data. Often there is limited theoretical modeling and much of the research is empirically driven, falling under the data science or analytics label [2]. Standard methods of statistical analysis often do not hold up well in such settings [3]. Multiple comparison issues arise requiring careful interpretation and measures of statistical accuracy and significance often lose their meaning.

Correlation and nonlinear relationships may cause difficulty even in the application of simple linear models. The presence of correlated data structures may increase model sensitivity to outliers and anomalies in the data, creating instabilities in the predictive model and affecting identifiability [2]. The mis-specified use of linear models when the data reflect nonlinear patterns will also create bias and other difficulties [4].

For model-data settings with p>n new techniques and modified models have been developed to deal with such restricted or sparse situations including least angle regression (LARS) and the application of least absolute shrinkage and selection operator (LASSO) [5]. These have been shown to be stable in basic settings where linear models are appropriate. Approaches which extend older statistical techniques include restricted least squares, ridge regression, forward stagewise variable selection and principal components [2]. While application of new "large data" settings are growing [6], Data Science or BigData approaches to identifying patterns in these large sets of collected data often reflect a mix of algorithmic methods drawn from engineering, computer science and mathematics [7].

Stability in the linear modeling of large databases is a necessity as modelling in p>n settings requires a restriction of some sort to provide an identifiable model. This is usually a sparsity restriction and we have as a typical model;

 $y = X\beta + \varepsilon$  $\sum_{i=1}^{n} |\beta_i| \le t$ 

for a chosen *t*. The sparsity restriction imposes onto the linear model context the assumption that only a few of the parameter values will differ from zero. While a variety of different weightings can be used in developing a sparsity restriction, the basic idea of formally limiting the number of variables to be considered remains the same. Typically a forward stage-wise approach is used to fit these models [5], working within the LASSO assumption that only a few key variables are actually relevant.

In terms of correlations and associations among the variables, if p>n and P is large, work in Hall et al. [8] and Ahn et al. [9] examined the p>n situation generally and showed that for large p the data vectors in such a restricted setting cluster at the vertices of an n dimensional simplex. Further these n directions lie approximately perpendicular to each other in forming the simplex structure. This implies that as  $p \rightarrow \infty$  any randomness in the dataset is generated by random rotations of the n vertices of the simplex. The eigenvalues for example from a principal components based analysis of the data converge to equality, limiting the usefulness of clustering methods.

Note that in general the principles of least squares based model fitting provide an approach to obtaining optimal estimators and a fitted model. In the case of using a sparsity restriction, this is not so direct in its application and interpretation. Often there is a phase threshold expressed in terms of p and n at or beyond which least squares based convergence will not occur [10].

Often more applicable but time consuming is the use of algorithmic search techniques [11]. These cycle through all possible value combinations for the elements of the unknown  $\beta$  vector until an

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optimal choice is found, minimizing the sum of squared errors subject to the sparsity restrictions. As computers become exponentially faster it is worth noting that such conceptually simpler approaches may become more common [11].

To examine the stability of sparsity related linear models numerical simulation is a useful approach. True parameter values can be defined, data generated from the true model and the convergence of the resulting estimated model to these true values examined. Nonlinearity and mis-specification issues that arise in the analysis of large databases using linear models can be studied. In many settings the true underlying relationship may be a simple nonlinear relationship that can easily be missed when using linear methods or associated correlation based methods. The use of residuals in developing related diagnostic measures of convergence may be difficult as the residuals themselves may be biased and correlated [12], not at all *i.i.d* in nature.

Note that in some cases simulated databases should reflect the context of the science within which the statistical models are defined. In the context of population oriented genomics a more genetically relevant process should be used to generate datasets. These should reflect in some way the population genetic structures that exist through generations and underlie the analysis of current generations [13]. Here we define the simulation setting more broadly and do not use such restrictions.

In this paper we study the stability of linear models with sparsity, examining the cases n > p, n=p and p > n. The lars-LASSO approach is the most directly applicable and stable approach to fitting these types of restricted linear models, converging quickly, and is used throughout the simulations. The stability of the method is well understood and has a geometric basis [5]. Here we generate datasets to model a variety of specific distribution and correlation structures in the data, different relative levels of p versus n and mis-specification of the model in question, examining the frequency with which the lars-LASSO based linear model correctly chooses the true set of explanatory variables used to generate the response. The usefulness of these approaches in p > n high dimensional settings is then discussed.

### Model Stability

Model stability in a linear model can be affected by various properties of the model-data combination. There are some standard challenges and modifications. Sensitivity to rescaling and transformations of the response [14], the presence of heterogeneity [15], and use of ridge regression to limit effects of collinearity [16]. These are aimed at improving the application and stability of the model-data combination and resulting fitted model. In the fitting of linear models these issues also extend to diagnostic measures for detecting the effects of outliers and anomalies in the data [16]. From a broader algorithmic perspective, the ordinary least squares estimator can be seen as a very simple yet accurate one-step algorithm, guided and justified by calculus and geometric concepts.

In fitting higher dimensional linear models, the use of residuals in developing diagnostic measures of convergence, a common approach in standard linear models, may be inappropriate when p > n as the residuals may themselves be biased and correlated, not at all *i.i.d.* in nature. A standard diagnostic measure and fitting criterion is the  $C_{p,m}$  diagnostic which is an estimator based on a total mean square error (*MSE*) criterion;

$$C_{p,m} = \frac{SSE_p}{MSE(X_1, \dots, X_m)} - (n - 2p)$$

where *p* is the overall number of variables [16]. A property of  $C_{p,m}$  is  $E[C_{p,m}]=p$ , so we can use the value of  $C_{p,m}$  to estimate the number of variables to include in the model. Typically we determine  $C_{p,m}$  for each value of *m* choosing the value for *p* at which the  $C_{p,m}$  value stabilizes [16]. This is often viewed graphically. Note that the  $C_{p,m}$  criterion is based on the assumption that the *MSE* from the full model is an unbiased estimate of  $\sigma^2$ .

If the full model happens to contain a large number of parameters that are not significantly different from zero, the *MSE* will be larger than the estimate of  $\sigma^2$  obtained from a model in which more variables are significant. This is because the variables that are not contributing to decreasing the  $SSE_p$  are still included in the degrees of freedom when computing *MSE*. If this is the case, the  $C_{p,m}$  may not be a suitable criterion for determining a useful model [16]. Further if we have a nonlinear component to the data affecting model convergence, then this caveat regarding the application of  $C_{p,m}$  as a model fitting criterion may apply and caution should be exercised.

The LASSO related sparsity restriction that is placed on the set of linear models being considered is given by;

$$\sum_{i=1}^{m} |\beta_i| < t.$$

This places a restriction on the fitting of the linear models(s) being considered and will alter the set of  $C_{p,m}$  values to be considered. This is easily incorporated into the *lars* algorithm [17].

In the p > n > m setting there is a de facto limitation on the values for  $C_{p,m}$  reflecting the relationship of p to n to m or the set of variables to be considered at one time. In the case of underlying nonlinearity, the dependence of the measure on the squared length of the orthogonal projection (I - P)y where  $P = X(X'X)^{-1}X'$  and  $X = [x_1,...,x_p]$ , gives rise to difficulties as the mis-specified linear model will be biased and as such the mean value of  $C_{p,m}$  may not be useful as a measure of p [16]. Thus the criteria can be easily misapplied when linearity cannot be assumed. If this criteria is an essential aspect of the model fitting approach under assumed linearity, the chosen models may be misleading if the true underlying model is nonlinear. Here we apply the  $C_{p,m}$  criteria throughout for consistency.

### **Results of Numerical Study**

The *lars-LASSO* algorithm was used to fit all models. This is a very stable algorithm with convergence occuring quickly, so simulations were repeated only 30 times in each setting reported here. All models were examined using centered data. Several distributions along with various standard correlation structures (auto-regressive (AR), compound symmetry (CS) and diagonal heterogeneity (DH) with correlations given by  $0.8^{|i-j|}$  and  $0.2^{|i-j|}$ ) were examined for various levels of p versus n. Again, the fitting criteria used throughout for comparability is the  $C_{p,m}$  criteria. The overall set of distributions, correlation structures, levels of (n,p) and models considered are summarized in Table 1.

Using a response *y* generated from the linear model

 $y = 1 + 5.0x_1 + 4.7x_3 + 7.8x_6 + 0.6x_7 + 0.5x_9 + 0.4x_{10}$ 

in combination with various correlation structures and assumed normal error for all variables  $x_1$  to  $x_{10}$ , the simulation results given in Table 2 were observed.

The pattern in this table reveals a large amount of stability in the predictive accuracy of the lars-LASSO approach across various correlation structures. There was some observed instability in models with p >> n and n small and this occured across all correlation structures considered.

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Distributions	Correlation Structures	Р	n	Model
Normal	AR, CS, DH	30, 300	50, 30, 10	Linear, Non-linear
Multivariate-t	AR, CS, DH	30, 300	50, 30, 10	Linear, Non-linear
Skew-Normal	AR, CS, DH	30, 300	50, 30, 10	Linear, Non-linear

Table 1: Summary of simulation studies.

Correlation Type, n, p	<b>X</b> <sub>1</sub>	X <sub>3</sub>	X <sub>6</sub>	<b>X</b> <sub>7</sub>	X,	X <sub>10</sub>	Other
AR, 50, 30	30	30	30	30	30	30	0
AR, 30, 30	30	30	30	30	30	30	0
AR, 10, 30	8	8	24	16	5	4	21
AR, 50,300	26	26	29	29	29	22	7
AR,30, 300	27	29	30	30	28	27	2
AR,10, 300	1	2	3	8	6	3	21
CS, 50, 30	30	30	30	30	30	30	0
CS, 30, 30	30	30	30	30	30	30	0
CS, 10, 30	11	16	20	25	15	8	23
CS, 50,300	28	26	30	28	28	26	7
CS,30, 300	30	30	30	30	29	28	1
CS,10, 300	3	1	8	1	3	2	30
DH1,50,30	30	30	30	30	30	30	0
DH1,30,30	30	30	30	30	30	30	0
DH1,10,30	12	6	17	22	10	6	22
DH1,50,300	27	27	29	29	29	28	2
DH1,30,300	20	19	27	22	15	14	9
DH1,10,300	1	0	7	2	1	0	23
DH2,50, 30	30	30	30	30	30	30	0
DH2,30, 30	30	30	30	30	30	30	0
DH2,10, 30	13	7	19	18	10	6	22
DH2,50,300	27	27	28	29	27	24	6
DH2,30,300	19	18	27	26	16	13	9
DH2.10.300	0	0	10	2	2	0	24

 Table 2: Results of Simulations for Various (n,p) Combinations Using A Multivariate Normal with Several Correlation Structures, 30 Replications and Linear Model.

 Generated response and true model:  $y=1+5.0x_1+4.7x_3+7.8x_6+0.6x_9+0.4x_{10}$ .

Simulations using the same correlation structures but with multivariate-t and skew-normal multivariate error distributions were then conducted and the results shown in Tables 3 and 4. Again there was weakness in variable selection with *n* small and p >> n across all correlation structures. The more robust error distributions did not alter the general pattern.

The same basic linear model fitting was then examined from the perspective of total variation explained, with results given in Table 4. For p=5000 and n=100, 250 and 500 using the same set of error distributions and correlation structures, the number of principal components [18] accounting for 75-80% of variation was determined for all models. Note that in the p>n case the number of principal components is limited by the sample size n and the percent reported here is the number of principal components divided by the number of available eigenvectors.

As shown in Table 5 the percent of non-zero principal components required to explain 75-80% of total variation was in the 45-68% range of non-zero principal components. For all distributions and correlation structures, as n decreased in relation to p, the percent of principal components required to explain the given level of total variation in the data increased. This reflects the geometric arguments mentioned in [8,9] as the principal components here converge towards equality and more of them are required to explain a given level of total variation.

The compound symmetry correlation structure leads to slightly

lower levels of variation explained. This pattern held for all error distributions with slightly lower levels in the multivariate-t distribution case where outlier generation is more common.

Overall, the results reported in Table 1 through Table 4 indicate the stability of the *lars-LASSO* stagewise approach in linear models, especially when  $p \le n$ . For levels of p >> n the predictive aspect of the model is weak across the various types of correlation structures and error distributions considered.

### Nonlinearity and model mis-specification

The use of a linear model when underlying nonlinearity exists in the data can lead to misleading results. The curvature of the underlying nonlinear model can be substantial and effect the accuracy of the model [19]. This was examined here using a simulated partially nonlinear regression model of the form;

$$y = 1.4exp(-4.5x_1 - 6x_2) + 3.2x_3 + 2.3x_6 + 1.1x_7 + 0.8x_9 + 0.6x_{10}$$

Restricting our study to cases of  $p \ge n$ , nonlinearity had a strong effect on the model fitting, even when limited to only a few variables. We deliberately mis-specified the model using a linear model for fitting when the underlying relationship in the data was nonlinear with the  $C_{p,m}$  criteria used for comparative purposes, but may this not be stable for variable selection. Thirty replications were simulated using n=(10,30,50) and p=(30,300) and a similar set of error distributions and correlation structures as in Tables 1-4 with a linear model assumption.

Correlation Type, n, p	<b>X</b> <sub>1</sub>	X <sub>3</sub>	<b>X</b> <sub>6</sub>	<b>X</b> <sub>7</sub>	X,	<b>X</b> <sub>10</sub>	Other
AR, 50, 30	30	30	30	30	30	30	0
AR, 30, 30	30	30	30	30	30	30	0
AR, 10, 30	3	17	24	17	13	6	23
AR, 50,300	29	29	29	27	27	24	8
AR,30, 300	28	28	29	30	24	27	6
AR,10, 300	1	3	11	4	3	1	22
CS, 50, 30	30	30	30	30	30	30	0
CS, 30, 30	30	30	30	30	30	30	0
CS, 10, 30	4	12	12	12	13	4	28
CS, 50,300	30	29	30	29	29	26	3
CS,30, 300	27	25	30	30	22	27	6
CS,10, 300	0	3	6	3	1	0	30
DH1,50,30	30	30	30	30	30	30	0
DH1,30,30	30	30	30	30	30	30	0
DH1,10,30	12	7	14	18	9	4	21
DH1,50,300	27	25	30	28	28	26	7
DH1,30,300	22	16	25	21	11	10	11
DH1,10,300	2	0	7	3	0	0	26
DH2,50, 30	30	30	30	30	30	30	0
DH2,30, 30	30	30	30	30	30	30	0
DH2,10, 30	12	7	17	15	9	4	23
DH2,50,300	26	26	27	29	24	21	8
DH2,30,300	20	16	26	22	13	10	10
DH2,10,300	2	0	7	1	0	0	25

AR: Auto-Regressive, CS: Compound Symmetry, DH1: Diagonal Heterogeneity with correlation given by 0.8<sup>[i-j]</sup>, DH2: Diagonal Heterogeneity with correlation given by 0.2<sup>[i-j]</sup>.

**Table 3:** Results of Simulations for Various (n,p) Combinations Using A Multivariate-t Distribution with Several Correlation Structures, 30 Replications, and Linear Model: Generated response and true model:  $y=1+5.0x_1+4.7x_3+7.8x_6+0.6x_7+0.5x_6+0.4x_{10}$ .

The results for the nonlinear models are given in Tables 6-8.

While some discussion of error distribution and correlation structure may be useful, we can see that the mis-specification of a linear model when the true model is nonlinear gives poor results. Variable selection is uniformly poor and the rate at which the model picks up variables that have little or no support in the actual simulation is relatively high. The cause of this is the nature of the lars algorithm which uses orthogonal projections of the remaining residual vectors at each stage to find the next predictive variable to which it is highly correlated.

In the linear model setting this algorithm creates a fast stepwise convergence to an optimal answer. However the use of both orthogonal projection and correlation is challenging when nonlinearity is present. Nonlinear patterns are less likely to be detected when correlation is present and orthogonal projections onto linear subspaces are not appropriate by definition when model fitting with nonlinear models [20]. In addition, as noted above the  $C_{p,m}$  criteria is poorly defined and can be misleading.

## Mis-specification and sparsity restriction

The issue of mis-specification arises as there is no guarantee that the use of a linear model will necessarily agree with the underlying data structure, as seen above. Problems will arise if the data are actually nonlinear in pattern. This is common in many natural phenomena, especially in relation to growth patterns. When this is the case models that focus on linearity may miss non-linear patterns in the data. The effects of nonlinearity can be difficult to deal with as the least squares or maximum likelihood estimates in fitting models may be correlated and correlation can be very misleading in the presence of noninear patterns. Thus the effects of mis-specification in regard to a small number of variables will impact the fitting of the entire model.

To more formally address the mis-specification issue with sparsity we express the linear model as function of two sets of variables;

$$y = X\beta + \varepsilon = X_1\beta_1 + X_2\beta_2 + \varepsilon$$

where initially n > p. Let us assume that the key significant variables are grouped in the  $X_1$  ( $n \times p_1$ ) matrix with  $p_1$  variables, the  $X_2$  ( $n \times p_2$ ) matrix has  $p_2$  additional variables, where  $p_1 << p_2$  and  $p_1 + p_2 = p$ . The error term  $\varepsilon$  ( $n \times 1$ ) is assumed to have the distribution  $\varepsilon \sim N(0, \sigma^2 I)$ . The goal here is to identify the variables in the  $X_1$  matrix. Now assume the aspect of interest is a nonlinear model underlying the  $X_1$  set of variables. In this setting we wish to assess to what extent the LASSO [5] or related technique may not detect the set of variables embedded in the nonlinear model. We re-express our initial model as;

$$y = F(X_1\beta_1) + X_2\beta_2 + \varepsilon$$
$$\sum_{i=1}^{m} |\beta_i| \le t$$

where  $F(X_1 \beta_1)$  is a nonlinear model for the  $X_1$  subset of variables and we focus the sparsity restriction on the  $X_1$  set of variables, selecting  $k < p_1$  non-zero coefficients in the sparsity restriction. Replacing  $F(X_1 \beta_1)$  with its Taylor expansion about  $\beta_{10}$  to the second order we obtain;

$$\nu = [X_1\beta_{10} + F'(X_1\beta_1)(\beta_1 - \beta_{10})] + X_2\beta_2 + \varepsilon$$
(1)

$$\sum_{i=1}^{m} |\beta_i| < t \tag{2}$$

Type, n, p	<b>X</b> <sub>1</sub>	X <sub>3</sub>	X <sub>6</sub>	<b>X</b> <sub>7</sub>	X,	<b>X</b> <sub>10</sub>	Other
AR, 50, 30	30	30	30	30	30	30	0
AR, 30, 30	30	30	30	30	30	30	0
AR, 10, 30	7	14	23	25	9	6	12
AR, 50,300	29	24	29	28	25	25	10
AR,30, 300	27	27	30	28	28	25	4
AR,10, 300	2	3	18	10	6	0	21
CS, 50, 30	30	30	30	30	30	30	0
CS, 30, 30	30	30	30	30	30	30	0
CS, 10, 30	11	20	26	18	14	5	19
CS, 50,300	28	28	26	29	29	26	7
CS,30, 300	19	20	29	25	23	20	9
CS,10, 300	4	5	8	4	1	0	30
DH1,50,30	30	30	30	30	30	30	0
DH1,30,30	30	30	30	30	30	30	0
DH1,10,30	11	12	17	18	10	11	12
DH1,50,300	29	29	30	29	29	30	2
DH1,30,300	21	19	30	24	18	16	6
DH1,10,300	2	1	6	5	4	3	23
DH2,50, 30	30	30	30	30	30	30	0
DH2,30, 30	30	30	30	30	30	30	0
DH2,10, 30	11	12	15	18	11	11	12
DH2,50,300	29	29	30	29	29	30	3
DH2,30,300	21	19	30	24	16	14	6
DH2,10,300	3	1	8	3	4	3	22

AR: Auto-Regressive, CS: Compound Symmetry, DH1: Diagonal Heterogeneity with correlation given by 0.8<sup>[i-j]</sup>, DH2: Diagonal Heterogeneity with correlation given by 0.2<sup>[i-j]</sup>.

**Table 4:** Results of Simulations for Various (n,p) Combinations Using A MultivariateSkew Normal Distribution with Several Correlation Structures, 30 Replications, andLinear Model: Generated response and true model:  $y=1+5.0x_1+4.7x_3+7.8x_6+0.6x_7$  $+0.5x_9+0.4x_{10}$ .

Distribution	Covariance Structure	Number of Principal Components (% Non-zero components)
		68 (68%)
	Autoregressive	159 (64%)
		293 (59%)
		44 (44%)
Normal	Compound Symmetry	102 (41%)
		187 (37%)
		70 (70%)
	Diagonal Heterogeneity	166 (66%)
		312 (62%)
		50 (50%)
	Autoregressive	114 (46%)
		216 (43%)
		29 (29%)
Multivariate-t	Compound Symmetry	57 (23%)
		113 (23%)
		51 (51%)
	Diagonal Heterogeneity	117 (47%)
		227 (45%)
		65 (65%)
	Autoregressive	149 (60%)
		264 (53%)
		60 (60%)
Skew-Normal	Compound Symmetry	136 (54%)
		242 (48%)
		67 (67%)
	Diagonal Heterogeneity	158 (63%)
		289 (58%)

Table 5: Number of Principal Components Accounting for 75-80% of Total Variation
for p=5000 and (n=100, 250 and 500).

Distribution	Covariance Structure	n	р	X1	<i>X</i> <sub>2</sub>	Xs	X <sub>6</sub>	<b>X</b> 7	X <sub>9</sub>	<i>X</i> 10
		10	30	1	0	1	2	2	6	4
		10	300	0	0	0	0	0	0	0
	Autorograpoixo	30	30	11	9	22	16	10	13	13
	Autoregressive	30	300	0	0	2	0	2	2	1
		50	30	5	8	22	18	11	12	13
		50	300	0	0	0	2	3	3	3
	Compound Symmetry	10	30	2	2	5	7	2	2	2
		10	300	0	0	0	0	0	0	0
Normal		30	30	16	5	20	10	10	18	10
Normai		30	300	1	0	1	7	0	1	1
		50	30	8	5	23	13	6	15	12
		50	300	0	0	6	1	10	1	4
		10	30	0	0	5	6	1	5	8
		10	300	0	0	0	3	0	0	0
	Diagonal	30	30	11	5	15	16	14	11	14
	Heterogeneity	30	300	0	0	1	0	3	7	1
		50	30	0	7	15	11	14	20	12
		50	300	0	0	2	0	0	2	2

 Table 6: Variable Selection Rates for 30 Replications, Normal Error and Various Correlation Structures.

If we were to apply a linear model to this setting we would in essence be using a local linear approximation rather than the true model, giving;

$$y = X_1 \beta_{10} + X_2 \beta_2 + \varepsilon$$
$$\sum_{i=1}^{m} |\beta_i| < t$$

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where  $\varepsilon^* = \varepsilon + F'(X_1\beta_1)(\beta_1 - \beta_{10})$  and in fitting this, we will both potentially miss the nonlinear aspect of the data and apply an approach which employs a biased error distribution  $\varepsilon^* \sim N(F'(X_1\beta_1)(\beta_1 - \beta_{10}), \sigma^2 I)$ .

In the p>n setting sparseness will not help alleviate the misspecification issue. Indeed the mis-specification effect may be augmented over the restrictions implicit in the use of the sparsity restriction. The  $C_{p,m}$  criteria defined here in this context will not be unbiased [16] and use of residuals in diagnostic measures may be inappropriate as noted above.

Note that if the underlying model is mis-specified, the sparseness restriction may not actually make sense, as it applies a linear scale to the relative importance of the estimated parameter coefficients. Note further that the centering of the data, a key component in the *LASSO-lars* algorithm [5], may actually increase the bias in the model if there is underlying nonlinearity [21]. Indeed the effect of centering in such

Distribution	Covariance Structure	n	р	<b>X</b> <sub>1</sub>	<b>X</b> <sub>2</sub>	<b>X</b> 3	<i>x</i> <sub>6</sub>	<b>X</b> <sub>7</sub>	<i>x</i> <sub>9</sub>	<b>X</b> <sub>10</sub>
		10	30	0	0	0	3	3	7	10
		10	300	0	0	0	0	0	1	1
	Autorogrossivo	30	30	10	9	16	15	17	21	20
	Autoregressive	30	300	0	0	0	2	0	0	2
		50	30	0	0	3	2	3	6	0
		50	300	0	0	0	5	6	12	1
	Compound	10	30	0	0	4	5	0	8	6
		10	300	0	0	0	0	0	0	0
Multivoriato t		30	30	7	8	11	18	17	18	15
wullivanale-l	Symmetry	30	300	0	0	0	0	1	0	0
		50	30	8	4	9	10	21	16	12
		50	300	1	0	1	0	6	8	1
		10	30	0	0	5	10	7	10	11
		10	300	0	0	0	0	0	1	3
	Diagonal	30	30	10	14	14	20	19	21	17
	Heterogeneity	30	300	0	0	2	4	0	3	1
		50	30	12	11	21	19	17	10	17
		50	300	0	0	0	3	0	1	2

 Table 7: Variable Selection Rates for 30 Replications, Multivariate-t Error and Several Correlation Structures.

Distribution	Covariance Structure	n	р	<b>x</b> <sub>1</sub>	x <sub>2</sub>	<b>x</b> <sub>3</sub>	<b>X</b> <sub>6</sub>	<b>x</b> <sub>7</sub>	<b>x</b> <sub>9</sub>	<b>x</b> <sub>10</sub>
		10	30	0	0	1	3	7	3	6
		10	300	0	0	0	0	0	0	0
	Autorograpojuo	30	30	10	12	15	9	13	13	19
	Autoregressive	30	300	0	0	0	0	0	1	5
		50	30	2	6	2	29	15	22	4
		50	300	0	0	0	6	7	1	1
	Compound	10	30	0	0	5	5	2	10	2
		10	300	0	0	2	0	1	0	0
Skow Normal		30	30	12	11	13	12	17	9	16
Skew-Norman	Symmetry	30	300	0	0	0	0	0	3	1
		50	30	0	6	5	29	13	9	0
		50	300	0	0	0	2	3	3	3
		10	30	0	0	3	1	3	11	2
		10	300	0	0	0	0	1	0	0
	Diagonal	30	30	11	11	14	12	12	14	18
	Heterogeneity	30	300	0	0	0	1	0	3	1
		50	30	1	2	2	28	13	7	0
		50	300	0	0	0	6	2	1	0

 $\label{eq:table_state} \begin{array}{l} \textbf{Table 8:} Variable Selection Rates for 30 Replications, Skew-Normal Error and Various Correlation Structures. \end{array}$ 

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a mis-specified settings may alter depending on each set of variables considered in the stagewise fitting process.

## Discussion

The simulation and study of model fitting behavior in high dimensional settings is an interesting use of the computer as a tool of scientific inquiry. Simulation allows for the study of algorithm behavior across a wide set of assumptions. Here the accuracy and stability of the *lars-LASSO* algorithm in linear models with n > p and p > n to a lesser extent is demonstrated in this manner. The number of replications has been kept fairly small due to the known stability and accuray of the algorithm investigated.

Use of mis-specified nonlinear models can lead to a high level of observed instability and model sensitivity. The assumption of linearity in large databases is often a common approach to the initial modeling of the variables measured. If there is a scientific context for the variables in question this should be reviewed to ensure that a linear scaling is appropriate. Note that it may be necessary to rescale some variables before a linear predictive model is appropriate for application.

Standard diagnostic assessments of model robustness and fit must be carefully interpreted in these settings. Numerical studies conducted here show that nonlinearity and p > n are a potential basis of predictive error in high dimensional model settings. Further potential misspecification issues may be present, affecting the accuracy of predictive linear models. The *lars-LASSO* model can be extended by altering the definition of sparsity, but this does not necessarily imply robustness to nonlinear specification and correlation structure.

#### References

- 1. National Science Foundation (2007) Discovery in Complex or Massive Datasets: Common Statistical Themes.
- Brimacombe M (2014) High Dimensional Databases and Linear Models: A Review. Open Access Medical Statistics 4: 17-27.
- Lambert CG, Black LJ (2012) Learning from our GWAS mistakes: from experimental design to scientific method. Biostatistics 13: 195-203.

- White H (1981) Consequences and Detection of Misspecified Nonlinear Regression Models. J of the Amer Statist Assoc 76: 419-433.
- Tibshirani R (1996) Regression Shrinkage and Selection via the LASSO. J Royal Statist Soc 58: 267-288.
- Johnstone IM, Titterington DM (2009) Statistical challenges of high-dimensional data. Philos Trans A Math Phys Eng Sci 367: 4237-4253.
- Kambatla K, Kollias G, Kumar V, Grama A (2014) Trends in Big Data Analytics. J Parallel Distrib. Comput 74: 2561-2573.
- Hall P, Marron JS, Neeman A (2005) Geometric Representation of High Dimension, Low Sample Size, J.R. Statist. Soc. B 67: 427-444.
- Ahn J, Marron JS, Muller KM, Chi Y-Y (2007) The High-Dimension, Low Sample-Size Geometric Representation Holds Under Milder Conditions. Biometrika 94: 760-766.
- Donoho DL, Stodden V (2006) Breakdown Point of Model Selection when the Number of Variables Exceeds the Number of Observations.
- 11. Berger B, Peng J, Singh M (2013) Computational solutions for omics data. Nat Rev Genet 14: 333-346.
- 12. Cook RD, Tsai CH (1985) Residuals in Nonlinear Regression. Biometrika 72: 23-29.
- 13. Himmelstein DS, Greene CS, Moore JH (2011) Evolving hard problems: Generating human genetics datasets with a complex etiology. BioData Min 4: 21.
- Box GEP, Cox DR (1964) An analysis of transformations, Journal of the Royal Statistical Society, Series B 26: 211-252.
- 15. Box GEP (1953) Non-Normality and tests on variances. Bio-metrika 40: 318-335.
- Draper NR, Smith H (1981) Applied Regression Analysis, John wiley & sons Inc, USA.
- 17. Efron B, Hastie T, Johnstone I, Tibshirani R (2004) Least Angle Regression. Annals of Statistics 32: 407-451.
- Johnson RA, Wichern DW (1992) Applied Multivariate Statistical Analysis. Prentice Hall Inc., New Jersey.
- 19. Seber GAF, Wild CJ (1989) Nonlinear Regression. John Wiley, New York, USA.
- Brimacombe M (2016) A Note on Linear and Second Order Significance Testing in Nonlinear Models. International Journal of Statistics and Probability 5: 19-27.
- Brimacombe M (2016) Local Curvature and Centering Effects in Nonlinear Regression Models. Open Journal of Statistics 6: 76-84.