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MSAE REGRESSION: A MORE ROBUST ALTERNATIVE TO THE LEAST SQUARES REGRESSION

by

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Abstract

In this paper, our objective is to introduce the minimum sum of absolute errors regression which is a more robust alternative to the popular least squares regression whenever there are outliers in the values of the response variable or the errors follow a long tailed error distribution or the loss function is proportional to the absolute errors rather than their squared values. We do so with a real application from the medical field.

Key words : interstitial lung disease; least squares; minimum sum of absolute errors regression; outliers; variables selection.

1. INTRODUCTION

In medical studies, quantitative models have been used to diagnose and assess the response to therapy. The least squares regression is one of the most often used model; however, it is very sensitive to outliers. There are several ways to deal with this problem, for example, one may identify the outliers, reject them and fit the model to the remaining observations, or one may use a more robust procedure than least squares procedure to estimate the parameters. Sometimes the first alternative is not acceptable or desirable because the observations are legitimate and therefore should not be rejected. The second alternative of using a more robust technique presents another difficulty of choosing a technique from among several available techniques.

Our objective, in this paper, is to introduce the minimum sum of absolute errors MSAE regression, an alternative to the least squares regression which is more robust to outliers. It is also more appropriate than least squares when the errors follow a long tailed error distribution or the loss function is proportional to absolute value of the errors than their squared value. We introduce the technique and the process of model selection with an actual case study from medicine. The rest of the paper is organized as follows: In Section 2, we describe the medical study which started us on this problem. In Section 3, we give

the least squares and the minimum sum of absolute errors analysis for the model and discuss the results. In Section 4, we give a brief overview of the MSAE regression and conclude the paper with a few comments in Section 5.

2. BACKGROUND

Interstitial Lung Disease(ILD) refers to a diffuse inflammatory process that occurs predominantly within the interstitial spaces and supporting structures of a lung. Clinical chart and x-rays (radiological pictures) of a patient with ILD usually suggest an open-chest lung biopsy to establish the diagnosis and to provide additional information on activity and stage of disease.

Pathological assessment is important to determine the prognosis and response of ILD to therapy, Carrrington, Gaensler, Coutu, Fitzgerald, and Grupta (1978), Katzeinstein, and Askin (1990) and Crystal, Bitterman, Rennard, Hance, and Keogh (1984). However, in routine practice, the proper quantitation of the extension and severity of pulmonary involvement is sometimes difficult and subject to frequent disagreement among different pathologists. Therefore, semi-quantitative scoring systems have been proposed, Cherniak, Colby, Flint, Thurlbeck, Waldron, Ackerson, and King (1991), Watters, King, Schwarz, Waldron, Styanford, and Cherniak (1986) and Fulmer, Robert, von Gal, and Crystal (1979), to provide the practicing pathologists a more rational basis to establish the severity of ILD.

The idea embodied in using pathological scoring systems is that the amount of alterations detected when analyzing the biopsy specimen express the severity of patient's functional and clinical impairment. However, because ILD usually affects a large part of pulmonary parenchyma, one has to be cautious when trying to establish structural-clinical correlations based on a small tissue sample. Thus, studies trying to correlate morphological alterations of lung biopsies with data more representative of entire lung function (such as pulmonary function tests) are necessary.

In an elegant study, Watters, et. al. (1986) demonstrated that histopathological alterations of open-chest lung biopsies of patients with ILD, as determined by semi-quantitative scoring, significantly correlate with clinical, radiological and functional parameters. This finding encourages further studies focusing the role of applying quantitative histological criteria to lung biopsies to assess the severity of ILD. In this context, it is possible that the combination of conventional histopathological assessment of ILD may improve the accuracy of histopathological evaluation of lung biopsy, adding important information about the severity of disease.

This study was designed to verify the association between objective indicators of lung damage and severity of functional impairment in ILD patients. For this purpose, stereological and semi-quantitative techniques were employed on 24 open-chest lung biopsies of patients with diffuse interstitial involvement.

Patients:

Twenty four biopsies of patients with ILD were selected from the file cases of open chest lung biopsies of Surgical Pathology Service of the teaching hospital of Faculdade de Medicina da Universidade de Sao Paulo. Biopsies were selected for this study on the basis of availability of patient's complete clinical and radiological data. In addition, this set of patients had the pulmonary function measurements gathered within 30 days before the biopsy.

Pulmonary Function Measurements:

Forced Vital Capacity (FVC) was measured with a computerized modular lung analyzer as recognized by the American Thoracic Society (1991) and expressed in terms of the predicted value for each patient, according to patient's age and physical characteristics, Morris, Koski, and Johnson (1971).

Morphological Analysis:

Fragments were fixed in 10% buffered formalin and embedded in paraffin for processing by routine histological procedures. Semi-thin sections (2 micrometers) were obtained from the paraffin blocks using the technique described by Junqueira, Silva, and Torloni(1989). Slides were stained with ematoxylineosin.

Pathological studies were carried out without knowledge of patient's clinical or physiological status. In the first step, morphometric studies were done at the level of alveolar interstitium to determine the areal fractions of cellular infiltration (CELL) and septal vascularization (VES) at alveoplar level. For this purpose, twelve randomly selected non-coincident 1000x power fields of lung parenchyma were studied, excluding axial components such as large bronchi and vessels. The areal fraction of each component of alveolar tissue was determined by standard-point-counting procedure, i.e., by counting 1,420 points per biopsy. In addition, differential counting of cells within the interstitial space was performed at the same moment. Cells in the pulmonary interstitium were classified into four-categories based on their appearance at light microscopy, Saldiva, Brentani, Carvalho, Auler, Calheiros, and Pacheco (1985): epithelial cells(EPIT), elongated cells(FUSI), olymorphonuclear cells(POLY) and mononucleated cells(MONO). At a lower magnification(40x), more general aspects of parenchyma remodeling were quantified by a semi-quantitative scoring system. The presence of vascular sclerosis(SCLEVASC), obliterate bronchiolitis(BOBLIT), smooth muscle hyperplasia(MUSCLE), honeycombing(HONEY), and desquamative pneumonia(DESQ) were individually graded from zero to four. For each of the preceding alterations, a degree zero corresponds to the absence of alteration; the degree one indicates that less than 25% of the structures of interest are altered ; the degree two indicates that 25 to 50% of the structures under analysis are affected; the degree three indicates that more than 50% but less than 75% of structures are altered; and, finally, degree four signifies that more than 75% of the structures are abnormal. Pathological scoring was carried out simultaneously by two pathologists, in double observation microscope.

In addition to the pulmonary function measurements and morphological variables, variables such as the age in years(AGE), sex(SEX) and if the patient smoked or not (SMOK) were also observed. The list of variables and the data are given in the Appendix.

3. PROBLEM STATEMENT AND ANALYSIS

The objective of the study was to build a model to assess prognosis and response to treatment for ILD patients. It is desirable to develop a parsimonious model that is effective and easy to understand, explain and maintain.

Because there are 14 variables, we began the analysis of the data using a stepwise least squares regression. The resulting model is:

$$CVF = 46.7 + 0.614\ AGE - .0615\ EPIT + 108\ CELL - 10.6\ HONEY,$$

with $R^2 = 0.708$. That is, this model explains 70.8 % of the variation in the response variable. An analysis of the residuals for this model identified two outliers. On further investigation of the data, it was confirmed that these observations were correct. Therefore, it was decided not to eliminate them and to use a more robust procedure than least squares to estimate the parameters of the model. The minimum sum of absolute errors MSAE regression is one such alternative.

After consultations, it was decided that a model with fewer than three variables may be too small whereas a model with more than six variables may not be more useful than one with fewer variables. A way to select the best model with p predictors variables (p = 3,...,6) using the MSAE criterion is to determine the set of p variables from among $\binom{k}{p}$-$\binom{14}{p}$ possible subsets of size p that results in the smallest MSAE value. Using the computer program given in Wellington and Narula (1981), we found the following models with three to six variables having the minimum sum of absolute errors:

Model with three variables is:

$$CVF = 67.76 - 0.062\ EPIT - 9.53\ HONEY + 141.76\ CELL, \qquad (1)$$

with R_2, the coefficient of determination for MSAE regression (McKean and Sievers (1987)), equal to 0.600 .

Model with four variables is:

$$CVF = 56.55 - 0.069\ EPIT - 10.39\ HONEY + 116.67\ CELL + 0.423\ AGE, \qquad (2)$$

with $R_2 = 0.632$.

Model with five variables is:

$$CVF = 76.77 - 0.063\ EPIT - 11.11\ HONEY + 109.74\ CELL + 0.249\ AGE - 8.29\ SEX, \qquad (3)$$

with $R_2 = 0.698$.

Model with six variables is:

$$CVF = 81.59\text{-}0.061\ EPIT\ \text{-}9.87\ HONEY + 95.35\ CELL + 0.223\ AGE\ \text{-}8.76\ SEX\ \text{-}\ 1.40\ BOBLIT, \quad (4)$$

with $R_2 = 0.72$.

The minimum sum of absolute errors model found by the stepwise procedure proposed by Andre, Elian, Narula, and Aubin (1996) is:

$$CVF = 81.59 - 0.061\ EPIT - 9.87\ HONEY + 95.34\ CELL + 0.223\ AGE - 8.76\ SEX - 1.40\ BOBLIT, \quad (6)$$

with $R_2 = 0.72$. It may be observed that the six variable model (6) selected by the stepwise procedure is the same as the one (4) computed by the implicit enumeration procedure; however, this is not always true.

Model Selection

Here, as in most practical problems, as a rule there does not exist a single "best" model but rather many "equally good" models. One possible and objective method is to compute the sum of predictive absolute errors SPAE for each model as follows:

Leave out an observation, i say, and fit the model to the remaining n-1 observations. Predict the value of the response variable for the i^{th} observation using this model. Compute the difference between the observed and predicted values of the response variable for the i^{th} observation. Repeat this operation for i = 1, ..., n and compute the sum of the predictive absolute errors.

Choose the model which minimizes the sum of predictive absolute errors.

In our problem we got the SPAE equal to 231.37, 195.98, 222.37 and 237.71 respectively for the models with three, four, five and six variables presented above. So the choosen model by this criterion is the four variable model. Observe that the variables in this model are the same as that selected by the usual stepwise procedure in least -squares regression.

In selecting the final model, however, one should always use experience, professional judgment in the subject area, and other practical and economic consideration.

4. THE MSAE REGRESSION

The minimum sum of absolute errors MSAE regression offers a robust alternative to the least squares regression whenever the data contains outliers or the errors follow a long tailed error distribution such as the Laplace or the Cauchy distribution, or the loss function is proportional to the absolute value of the errors rather than their squared values, Narula and Wellington (1977, 1985). Although proposed fifty years before the least squares procedure, the MSAE criterion has not been popular because of the computational problems and the lack of statistical properties and inference procedures for the estimators.

Now a number of very efficient and effective algorithms and computer programs are available to solve the simple and multiple linear MSAE regression models, Narula (1987). The computer programs have been included in popular statistical packages like SAS and IMSL. Algorithms and computer programs for selecting variables are also available, Narula and Wellington (1979) and Wellington and Narula (1981). Andre, Elian, Narula, and Aubin (1996) have proposed stepwise procedures for selection of variables. Their procedure can be easily implemented with the popular statistical package SAS. Therefore, at present, the computational difficulties associated with the use of the MSAE regression do not exist.

It has been shown that the estimators of the MSAE regression model are completely determined by the number of observations equal to the number of parameters in the model. These observations have zero residuals. Just as the sample mean is not effected by making the observations above the median larger or the observations below the median smaller, similarly, the fitted MSAE regression hyperplane remains unchanged if the observations above the regression hyperplane remain above it and those below it remain below, Narula and Wellington (1985). This is very unlike the least squares regression where any change in the values of an observation results in a change in the values of the least squares estimates of the parameters. Furthermore, the fitted MSAE regression remains unchanged if the values of the predictor variables for the observations with nonzero residuals remain within certain intervals. The procedures to compute such intervals have been proposed, Narula, Sposito and Wellington (1993). These intervals give the analyst useful information about the imprecision of the observations which leave the fitted MSAE regression unchanged.

It has been shown that the MSAE estimators of the parameters of the regression model are asymptotically unbiased and have a multinormal distribution, Basset and Koenker (1978). Furthermore, the confidence ellipsoid for these estimators is smaller than that for the least squares estimators whenever the sample median is a more efficient estimator than the sample mean for the location parameter of the error distribution. Based on the asymptotic distribution results and the results of the Monte Carlo studies, statistical inference procedures have also been proposed, Narula (1987).

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APPENDIX

THE LIST OF VARIABLES

Response variable:

FVC (forced vital capacity):

Predictor variables:

SEX: 0 = Male, 1 = Female
AGE (in years)
SMOK (smoking): 0 = Smoker, 1 = Nonsmoker
EPIT (epithelial cells): Area fraction of epitelial cells/10 000 μm^2 of alveolar tissue;
FUSI (elongated cells): Area fraction of fusiform cells/10 000 μm^2 of alveolar tissue;
MONO (mononucleated cells): Area fraction of mononucleated cells/10 000 μm^2 of alveolar tissue;
POLY (polymorphonuclear cells): Area fraction of polymorphonuclear cells /10 000 μm^2 of alveolar tissue;
CELL (cellular infiltration): Total cellularity/10 000 μm^2 of alveolar tissue;
VES (septal vascularization): Area fraction of capillaries/10 000 μm^2 of alveolar tissue;
BOBLIT (obliterate bronchiolitis): Score of bronchiolitis obliterans (zero to four);
MUSCLE (smooth muscle hyperplasia): Score of smooth muscle (zero to four);
SCLEVASC (sclerosis): Score of vascular sclerosis (zero to four);
HONEY (honeycombing): Score of honeycombing (zero to four);
DESQ (desquamative pneumonia): Score of intra alveolar cell disquarnation (zero to four);

APPENDIX

DATA FOR THE EXAMPLE

OBS	FVC	SEX	AGE	SOK	EPIT	FUSI	MONO	POLY	CELL	VES	BOBLIT	MUSCLE	SCLEVASC	HONEY	DESQ
1.	56	1	64	0	192.405	359.71	669.24	0.000	0.231	0.289	3	4	1	4	2
2.	75	2	39	0	398.588	441.53	163.06	20.706	0.251	0.578	0	0	3	0	0
3.	32	2	39	0	671.674	622.29	1728.57	49.308	0.043	0.203	3	0	0	0	0
4.	88	1	69	1	227.424	539.19	145.42	13.424	0.153	0.615	0	0	0	0	0
5.	83	1	41	0	310.136	419.39	88.11	3.525	0.143	0.551	0	0	0	0	0
6.	59	1	42	1	187.597	378.95	82.54	1.251	0.150	0.785	0	4	3	3	2
7.	51	1	32	1	405.836	411.85	261.54	30.062	0.225	0.240	0	0	0	0	0
8.	67	1	45	1	100.237	346.53	223.38	2.864	0.183	0.725	0	0	3	1	2
9.	60	2	53	0	144.290	397.77	129.99	0.000	0.176	0.696	3	1	4	2	0
10.	98	1	46	1	149.187	275.22	204.49	14.147	0.251	0.577	0	0	2	0	4
11.	48	2	44	0	211.614	398.81	278.35	4.883	0.174	0.703	0	1	3	0	2
12.	82	1	44	0	254.398	376.39	297.54	7.439	0.242	0.593	3	2	0	0	2
13.	86	2	57	0	167.728	384.79	4624.07	3.289	0.203	0.702	0	1	2	0	0
14.	103	2	49	0	337.145	597.76	614.08	12.410	0.313	0.554	0	0	2	0	0
15.	115	2	65	0	276.864	365.31	401.66	8.206	0.206	0.572	0	0	2	0	3
16.	64	2	26	0	309.206	512.22	99.65	27.510	0.224	0.579	0	0	3	0	1
17.	57	1	46	1	173.373	367.14	308.02	24.222	0.204	0.722	0	2	3	3	2
18.	82	1	28	1	238.277	375.29	223.85	64.037	0.178	0.685	0	0	2	0	1
19.	50	2	52	1	130.308	374.79	423.90	34.747	0.175	0.697	3	2	3	3	2
20.	48	1	49	1	165.546	318.45	284.34	37.911	0.203	0.674	4	2	2	4	2
21.	57	2	32	0	168.547	394.52	282.60	1.349	0.165	0.647	0	2	4	2	2
22.	45	1	57	0	621.861	1477.29	416.57	151.746	0.238	0.685	2	3	2	2	2
23.	77	1	72	0	607.268	171.91	2529.51	89.094	0.468	0.435	0	0	2	2	2
24.	92	1	57	1	404.735	1443.59	2022.71	93.677	0.293	0.618	0	0	3	0	0

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