

# Serial correlation of quality control data – on the use of proper control charts

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*Background:* Biochemical quality control (QC) data have been reported to be autocorrelated. Serial correlation may increase the rate of false alarms if the traditional exponentially weighted moving average (EWMA) control chart to monitoring the process mean is used. False alarms are the focus of this paper, where an alarm is defined as the occurrence of a QC value outside the three standard deviation control limits. *Methods:* Daily QC measurements of common biochemical (Vitros 500) and hematological (SF-3000 and Behring Coagulation Timer (BCT)) quantities were recorded during several months while methods and analyzers showed no signs of malfunctioning. The time series were examined for autocorrelation and the performance of the EWMAST chart was compared with that of the EWMA chart when autocorrelation was present. *Results:* Many of the time series showed significant signs of autocorrelation. Using the EWMA chart to monitor the process mean, false alarms were noted for positively autocorrelated time series, while this was seldom the case when the EWMAST chart was used. For some quantities, the EWMAST chart gave alarms. However, when the process autocorrelation and therefore the limits of the control chart were updated, the alarms given by the EWMAST chart were reduced or disappeared. In some cases the mean level changed over time, which is expected due to calibrations. This problem will be the topic of a subsequent paper. *Conclusions:* Positive autocorrelation may be present in QC data. In this case the EWMAST chart should be used in place of the EWMA chart.

*Key words:* autocorrelation; control charts; EWMA chart; EWMAST chart; quality control; statistics

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## INTRODUCTION

The use of most control charts is based on the assumption that all quality control (QC)

values follow the same distribution while the analyzer is in operational control. Furthermore, it is assumed that all values are statistically independent.

If serial autocorrelation is present this latter condition is no longer fulfilled. A serial autocorrelation of lag 1 is present if each value ( $x_t$ ) (starting with the second value) in a time series of values is correlated with  $x_{t-1}$ , the value preceding it. Usually, when the autocorrelation of lag 1 is positive, we say the process is positively autocorrelated. A serial correlation of lag  $k$  is present if  $x_t$  is correlated with  $x_{t-k}$ .

In 1988, Alwan & Bissell [1] showed that QC values measured twice daily for 4 months on a Kodak (Vitros) analyzer for the majority of quantities demonstrated significant positive autocorrelation and in some cases near non-stationarity with a wandering mean. They also showed that it was possible to fit various models (auto-regressive integrated moving average (ARMA) models (see Box & Jenkins [2]) to QC data. Apparently, this important paper received relatively little attention.

Usually an  $\bar{X}$  chart is used in clinical chemistry where the process standard deviation (SD) is calculated using the formula  $\sum_{i=1}^N (x_i - \bar{x})^2 / (N-1)$  based on data  $\{x_1, \dots, x_N\}$  rather than based on the moving range that is usually recommended in textbooks of industrial quality control [3]. This chart does not produce too many false alarms (condition when a value falls outside the 3 SD limits while the process is in statistical control) where a positive autocorrelation is present. But it is less sensitive to changes in the mean level than the exponentially weighted moving average (EWMA) chart.

Zhang [4], however, showed that when a process is positively autocorrelated, the autocorrelation has a considerable impact on the cumulative sum (CUSUM) chart and EWMA chart. In this case, these control charts will give frequent false alarms.

Alwan & Bissell [1] suggested two types of control charts be used: one depicting the predicted value of the process (using the ARMA model, see above) and one (the  $\bar{X}$  residual chart) depicting the residuals, i.e. the deviations between observed and predicted values. Then the Westgard *et al.* rules [5] may be applied using the  $\bar{X}$  residual chart. This chart, however, has been shown to have a poor performance in detecting a process mean shift in Harris & Ross [6], Zhang [7, 8], Longnecker & Ryan [9], and Wardell [10] when applied to a positively autocorrelated process (an AR [1] process with a positive parameter). Furthermore,

the use of the residual chart has a serious drawback in that it requires that the model is estimated. Recently, an alternative control chart, the EWMAST chart proposed in Zhang [7], has been developed. This chart is similar to the well-known EWMA chart but with the important exception that its control limits depend on the autocorrelation of the process. Furthermore, when using the EWMAST chart it is not necessary to find the time series model fitting the data.

The purpose of the present study was 1) to gain an impression of the generality of the problem, i.e. to find whether it is only the Vitros control values that are autocorrelated and 2) to examine the performance of the EWMA and the EWMAST control charts in the presence of autocorrelation under conditions where the analyzer is in operational control. Therefore, we have examined QC data covering a selection of commonly measured biochemical and hematological quantities and three different analyzers, the Vitros 500, the Sysmex SF-3000 and the Behring Coagulation Timer (BCT) during periods where there were no assignable causes of variation due to malfunctioning of the analyzers. [Commercial equipment is identified in this paper to describe the experimental procedure. Identification does not imply recommendation or endorsement by the National Institute of Standards and Technology, nor does it mean that the equipment is necessarily the best available for the purpose.]

## MATERIALS AND METHODS

### *QC data material*

Measurements of control material were made daily between 08.00 h and 10.00 h using the Vitros 500, the SF-3000 hematology analyzer and the BCT.

Commercial QC material was used on the Vitros 500 and the Sysmex SF-3000, namely the Vitros products Performance verifier Johnson & Johnson Clinical Diagnostics covering low values and the Vitros products Performance verifier II, Johnson & Johnson Clinical Diagnostics covering high values on the Vitros 500 and the SF-check-L covering low values, the SF-check-M covering normal values and the SF-check-H covering high values on the SF-3000 analyzer.

Since commercial QC material was not used daily on the BCT, a plasma pool (P-Pool) comprising blood donor material was prepared and distributed into vials which were kept at  $-80^{\circ}\text{C}$  until used, with one vial being used per day during the study period.

#### *The Vitros analyzer*

QC-Glucose;  $\text{c}/\text{mmol}/\text{L}$  (GLU), QC-Urea;  $\text{c}/\text{mmol}/\text{L}$  (UREA), QC-Creatinin;  $\text{c}/\mu\text{mol}/\text{L}$  (CREA), QC-Potassium-ion;  $\text{c}/\text{mmol}/\text{L}(\text{K})$  and QC-Sodium-ion;  $\text{c}/\text{mmol}/\text{L}$  (Na) values measured in the two Vitros QC materials during the period 4 April 1998 to 12 December 1998 using the Vitros 500 were examined. Since recurrent problems with the lamp of the Vitros 500 were recorded from 9 September until 27 October 1998, at which time the lamp was removed and replaced by a new one, data from this period were excluded from the study. The QC prefixed to the component name symbolizes the system, i.e. a quality control material. The names in parentheses symbolize the quantities divided by their respective units. For each of the 10 above-mentioned quantities (5 components in 2 QC materials) all time series satisfying the following conditions were extracted from the remaining data:

- 1) no technical or other problems with Vitros 500 as evidenced from the log book;
- 2) all measurements were made on QC material from the same lot;
- 3) no missing values in any of the series;
- 4) each series included at least 50 consecutive data points.

#### *The SF-3000 analyzer*

QC-MCV;  $\text{volume}/\text{fl}$  (MCV), QC-RBC;  $\text{numberfr.}/10^{12}/\text{L}$  (RBC), QC-PLT;  $\text{numberfr.}/10^9/\text{L}(\text{PLT})$  and QC-WBC;  $\text{numberfr.}/10^9/\text{L}$  (WBC) measured daily on the SF-check-H, M and L QC materials using the Sysmex SF-3000 located at the Esbjerg Community Hospital during the period 17 November 1998 to 4 January 1999 were recorded and included in the study. The QC prefixed to the component name symbolizes the system, i.e. a quality control material. The names in the parentheses symbolize the quantities divided by their

respective units. During the period, the following conditions were all satisfied:

- 1) according to the log books there were no technical or other problems with the Sysmex SF-3000 analyzer;
- 2) for each quantity, QC material from the same lot was used.

There were no missing values except on days 12 and 13. The missing data points were substituted by data constructed from linear interpolation between the results obtained on day 11 and day 14.

#### *The BCT analyzer*

P-Pool-F (II, VII, X);  $\text{time}/\text{s}$  (F(II, VII, X)), P-Pool-APTT;  $\text{time}/\text{s}$  (APTT), P-Pool-ATIII;  $\text{arb. units}/\text{l}$  (ATIII) and P-Pool-Fib (functional method);  $\text{c}/\mu\text{mol}/\text{L}$  (Fib) measured daily on the P-Pool using the BCT during the period 24 December 1998 to 28 February 1999 were recorded and included in the study. The P-Pool in front of the component name symbolizes the system, i.e. the quality control material. The names in parentheses symbolize the quantities divided by their respective units. During the period when the measurements were made the following conditions were all satisfied:

- 1) according to the log books there were no technical or other problems with the BCT;
- 2) all results obtained measuring commercial QC material once daily on Monday through Friday were within the control limits specified by the company (The Dade Behring Company)
- 3) There were no missing P-Pool values during the study period covering 67 days

A quantity includes a system, a component and kind of quantity. The system in this context is a QC material referred to in this paper as L, M or H symbolizing materials covering low, normal and high values, respectively. Thus L-GLU symbolizes the quantity L-Glucose; c divided by its unit  $\text{mmol}/\text{L}$ .

#### *Time series analysis*

Measurements of QC materials were subjected to various statistical analyses. First, we introduce some basic concepts for time series analyses.

One such concept is the stationarity of a time series. A time series  $\{X_t; t=1, 2, \dots\}$  is said to be (weakly) stationary if (a)  $E[X_t] = \mu$ , i.e. a constant mean not depending on the time  $t$ ; (b) the covariance between  $X_t$  and  $X_{t+k}$  depends only on  $k$ .

In particular, it follows from (b) that the process variance is a constant. For a stationary process, the correlation between  $X_t$  and  $X_{t+k}$  is called the autocorrelation of lag  $k$  denoted by  $\rho(k)$ . The function  $\rho(k)$  ( $k=1, 2, \dots$ ) is called the autocorrelation function (ACF) of the process. The simplest stationary process is white noise which has  $\mu=0$  and  $\rho(k)=0$  when  $k \neq 0$ . If a process has zero mean and a Gaussian distribution, an independently identically distributed (IID) sequence is the same as white noise. A simple process is the first order autoregressive (AR(1)) process  $\{X_t; t=1, 2, \dots\}$  which is defined as

$$X_t - \mu = \phi(X_{t-1} - \mu) + a_t$$

where the parameter  $\phi$  is a constant,  $\mu$  is the process mean, and  $a_t$  is white noise with a finite variance  $\sigma_a^2$ . Loosely speaking, the parameter  $\phi$  defines the “memory” effect.  $\phi=0$  corresponding to white noise or an IID when the process is normally distributed while  $\phi>0$  for positive autocorrelation. When  $|\phi|<1$ , the process  $\{X_t\}$  is stationary. In this case,  $\sigma_x^2 = \sigma_a^2 / (1 - \phi^2)$  and  $\rho(k) = \phi^k$  for  $k \geq 0$ .

For each observed series, we first inspected whether it was autocorrelated or just white noise. We used the plot of the autocorrelation function of the series and the Ljung–Box Test (Ljung & Box [11]) to determine this.

For illustrative purposes, we will review the analysis of the quantity L-NA-1. The time series plot is shown in Figure 1. The sample autocorrelation function of the series with a 95% confidence band is displayed in Figure 2. The autocorrelations at the first and second lags are significantly different from zero. That means the process is not white noise or an IID process.

### *The EWMAST chart*

The EWMAST chart is an extension of the traditional EWMA chart designed to monitor a stationary process. For a time series  $\{X_t\}$ , the chart is constructed by plotting the EWMA ( $Z_t$ ), which is defined as:

$$Z_t = (1 - \lambda)Z_{t-1} + \lambda X_t$$

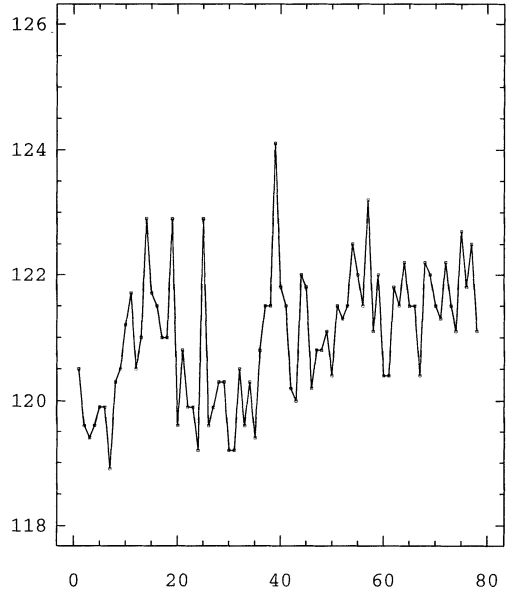


FIG. 1. The time series plot of the quantity L-Na-1.

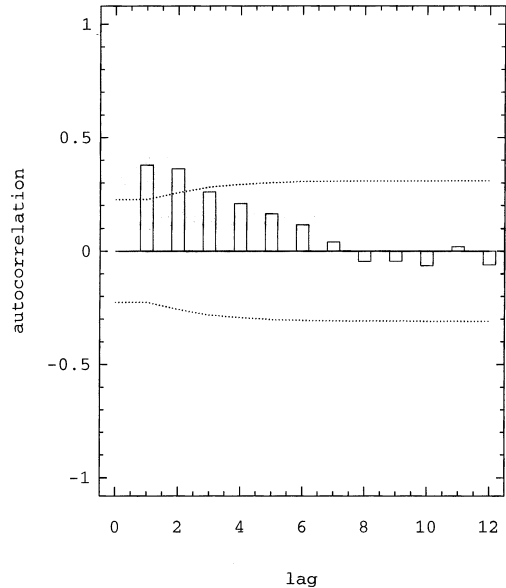


FIG. 2. The sample autocorrelation function of the L-Na-1 time series with a 95% confidence band.

for  $t=1, 2, \dots$ , where  $Z_0 = \mu$ . The parameter  $\lambda$  ( $0 < \lambda \leq 1$ ) is a constant.  $Z_t$  can be expressed as a weighted average of all previous  $X_t$ . Namely,

$$Z_t = \lambda X_t + \lambda(1 - \lambda)X_{t-1} + \lambda(1 - \lambda)^2 X_{t-2} + \dots + \lambda(1 - \lambda)^{t-1} X_1 + (1 - \lambda)^t Z_0$$

TABLE I. Comparisons of ARLs for the X-chart, X residual chart, the EWMA chart and the EWMAST chart applied to a positively autocorrelated process (AR(1) process with  $\phi > 0$ ).

$\Phi$	Shift	X chart	Residual chart	EWMA ( $\lambda=0.2$ )	EWMAST ( $\lambda=0.2$ )
0.0	0	370.4	370.4	547.7	547.7
	0.5	155.2	155.2	44.6	44.6
	1	43.9	43.9	10.8	10.8
	2	6.30	6.3	3.7	3.7
	3	2.00	2.0	2.4	2.4
0.25	0	381.6	370.4	139.6	664.6
	0.5	166.5	206.0	32.8	74.2
	1	46.6	75.4	10.7	17.5
	2	7.25	12.2	3.9	5.02
	3	2.21	2.85	2.4	2.93
0.50	0	400.7	370.4	56.0	829.5
	0.5	181.2	258.4	27.0	147.3
	1	56.4	123.8	10.8	31.9
	2	9.16	24.2	4.00	7.49
	3	2.60	4.14	2.50	3.93
0.75	0	496.0	370.4	30.4	1135.2
	0.5	236.0	311.2	21.6	333.8
	1	74.3	197.7	11.6	82.0
	2	14.4	40.2	4.39	14.9
	3	3.59	3.01	2.63	6.32
0.95	0	1382.2	370.4	30.8	2653.1
	0.5	753.2	331.0	25.4	1376.4
	1	286.1	138.8	16.8	446.3
	2	46.8	1.08	5.72	74.1
	3	9.13	1.00	2.83	18.8

ARL=average run length; EWMA=exponentially weighted moving average.

Notice that  $\lambda=1$  corresponds to the ordinary X chart. According to Zhang (7), the variance of  $Z_t$  ( $\sigma_z^2$ ) is given by the equation

$$\sigma_z^2 = \left[ \frac{\lambda}{2-\lambda} \right] \sigma_x^2 \left\{ 1 - (1-\lambda)^{2t} + 2 \sum_{k=1}^{t-1} \rho(k)(1-\lambda)^k [1 - (1-\lambda)^{2(t-k)}] \right\},$$

where  $\rho(k)$  is the process autocorrelation at lag  $k$  and  $\sigma_x^2$  is the variance of the process. For a large integer  $M$ , an approximate variance is

$$\sigma_z^2 \approx \left[ \frac{\lambda}{2-\lambda} \right] \sigma_x^2 \left\{ 1 + 2 \sum_{k=1}^M \rho(k)(1-\lambda)^k [1 - (1-\lambda)^{2(M-k)}] \right\}$$

when  $t > M$ .  $\lambda=0.2$  is selected for the EWMA and EWMAST charts in this paper. The control limits of the EWMAST chart are  $\mu \pm L\sigma_z$  where  $\mu$  is the process mean and  $L$  is a constant, usually 3. Notice that when the process is an IID sequence or white noise,  $\rho(k)=0$  when  $k \neq 0$ . In this case, the EWMAST chart and the traditional EWMA are same.

In this paper  $M=12$  is used, since for a time series of size  $N$ , a reliable estimate of autocorrelation  $\rho(k)$  may only be obtained when  $k \leq N/4$ . The mean, process variance and

autocorrelations are estimated from the data during a period in which the process was under control. It is noted that calculating the process variance does not require prior knowledge of the structure of the underlying process model. It is also noted that  $\sigma_x^2$  is estimated using the usual formula

$$\hat{\sigma}_x^2 = \frac{\sum_{t=1}^N (x_t - \bar{x})^2}{N-1}$$

For the estimation of the process variance of a stationary process, we refer to Zhang [12].

In Zhang [4, 7] comparisons of the EWMAST chart, the traditional EWMA chart, the X chart and the X residual chart were done based on the average run length (ARL). ARL is the mean of the run length, defined as the number of observations that must be plotted before a point indicates an out-of-control condition. A desired control chart should have large in-control ARLs and small out-of-control ARLs. The ARLs of the EWMAST chart, the EWMA chart, the X chart and the X residual chart for various

AR(1) processes with positive parameters are listed in Table I.

The ARLs were calculated for various step shifts of the process means according to a shift parameter (0, 0.5, 1, 2 and 3) to be multiplied with the process SD  $\sigma_X$ .

In Table I, the ARLs for the X chart are based on simulations with the exception of the value for  $\phi=0$ , which can be easily calculated. The ARLs for the residual chart were calculated with a formula devised by Zhang [8]. From Table I, it is clear that when the process is positively autocorrelated, the autocorrelation has a big impact on the EWMA chart. When  $\phi=0.25$ , the in-control ARL is reduced to 139.6 from 547.71 when  $\phi=0$ . Thus, even when the process is weakly autocorrelated, the EWMA chart will give frequent false alarms even when the process is stable and under control. When  $\phi=0.5$ , the in-control ARL for the EWMAST chart is 829.5, which is much larger than 56 for the EWMA chart and 400.7 for the X chart. For the relationship between the X chart and EWMAST chart, for small shifts (0.5, 1 and 2) and weak to moderate autocorrelation ( $\phi=0.25$  and 0.5) the EWMAST chart has a better performance (lower ARL). Table I shows that, overall, the EWMAST chart performs better than the residual chart, the X chart and the EWMA chart when the process is stationary ( $\phi<0.95$ ). The detailed discussion on the

comparisons among the three control charts can be found in Zhang [4, 7].

## RESULTS

For each biochemical time series examined, its size ( $N$ ), the mean, SD and the estimates of the autocorrelation coefficients of lags 1, 2 and 3 are shown in Table II. In Table III the corresponding results are shown for the hematological quantities. Only in 13 out of the 34 time series could the data be adequately modeled as IID or white noise. In the remaining cases the data were autocorrelated. The results obtained when the EWMA and the EWMAST charts were applied to each of the 11 time series that included more than 55 data points are presented in Table IV. For each chart, the chart parameters including the process mean, process variance and autocorrelations were calculated using the first 50 data points and the chart was then applied to the whole series. In 6 of the 9 series where significant process autocorrelations were demonstrated, all values fell within the control limits of the EWMAST chart. In one case (ATIII) a single value fell outside the limits and in two cases more than one value fell outside the limits (11 values in the case of APTT and 5 in the case of L-CREA series 1). However, the two last -mentioned time series

TABLE II. Mean, number of observations per time series and SD of biochemical QC values and the autocorrelations at the first three lags.

Quantity variate	Series #	N	Mean	SD	$\rho_1$	$\rho_2$	$\rho_3$
L-GLU	1	78	4.54	0.0604	0.315	0.328	0.324
	2	51	4.68	0.0517	0.362	0.137	-0.132
H-GLU	1	72	14.9	0.1477	0.595	0.377	0.203
	2	53	15.1	0.1926	0.560	0.341	0.303
L-UREA	1	78	5.73	0.1646	0.284	0.124	0.102
	2	51	5.76	0.1131	0.284	0.290	0.255
H-UREA	1	56	16.5	0.5168	IID		
	2	53	16.9	0.4518	0.335	-0.050	-0.076
L-CREA	1	78	80.6	1.684	0.590	0.475	0.513
	2	51	80.9	0.9697	IID		
H-CREA	1	79	552	5.379	0.274	-0.002	0.190
	2	53	550	7.877	0.479	0.440	0.371
L-NA	1	78	121	1.075	0.378	0.363	0.260
	2	51	120	1.160	0.507	0.534	0.435
H-NA	1	53	140	1.110	0.313	0.282	0.196
L-K	1	51	3.11	0.0412	0.371	0.206	0.147
H-K	1	73	5.08	0.0638	IID		
	2	52	5.10	0.1292	0.650	0.631	0.457

QC=quality control.

TABLE III. Mean, number of observations and SD of hematological QC values and the autocorrelations at the first three lags.

Quantity Variate	N	Mean	SD	$\rho_1$	$\rho_2$	$\rho_3$
L-MCV	49	71.38	0.509	0.251	-0.060	0.062
M-MCV	49	78.47	0.462	IID		
H-MCV	49	86.51	0.417	IID		
L-PLT	49	66.99	4.078	IID		
M-PLT	49	233.01	11.034	0.463	0.275	0.196
H-PLT	49	529.95	13.949	IID		
L-RBC	49	2.57	0.032	IID		
M-RBC	49	4.75	0.040	IID		
H-RBC	49	5.49	0.052	0.475	0.380	0.398
L-WBC	49	2.45	0.050	IID		
M-WBC	49	7.87	0.121	IID		
H-WBC	49	20.37	0.308	IID		
P-Pool-F(II,VII,X)	67	20.83	0.475		0.145	0.177
P-Pool-APTT	67	33.09	0.993	0.415	0.382	0.346
P-Pool-AT III	67	0.891	0.016	0.109	-0.155	0.037
P-Pool-FIB	67	10.55	0.379	IID		

QC=quality control.

were both strongly autocorrelated and the charts demonstrated that the mean probably did change during the period examined. By contrast, when the EWMA chart was used instead (see column 3 of Table IV), more than one point fell outside the limits in 6 of the 9 cases and one value fell outside the limits in 3 cases. These results show that the traditional EWMA chart is more likely to give false alarms in the presence of autocorrelation than the EWMAST is. The latter, therefore, is the chart of choice in the presence of autocorrelation, especially when the autocorrelation is positive.

Table V presents the results obtained when the appropriate control chart was constructed using the first 50 values of the first time series and then applied to the second time series of the

same quantity collected some time after the first one. If the model of the first time series was IID, the EWMA chart was used, and if not the EWMAST was used. In 6 out of the 8 cases several values fell outside the control limits (see column 3 of Table V). Column 4, Table V shows the results obtained when the autocorrelation of the second time series was used instead of that of series 1 when constructing the control chart (the mean value was still calculated using the first 50 values of series 1). In three cases (H-CREA, L-NA and H-K) all values now fell within the control limits indicating that the out-of-control condition had probably been caused by a change in the process autocorrelation and not a change in the mean level. In two of the cases (L-GLU and H-UREA) it is fair to

TABLE IV. Control chart constructed from the first 50 data points and applied to whole-time series.

Quantity variate	N	Number of EWMA's outside control limits	
		EWMA chart	EWMAST chart
H-K series1	73	1	-
L-NA series1	78	3	0
L-GLU series1	78	15	0
H-GLU series1	72	6	0
L-CREA series1	78	21	5
H-CREA series1	79	4	0
L-UREA series-1	78	1	0
P-Pool-ATPP	67	12	11
P-Pool-ATIII	67	1	1
FIB	67	0	-
F(II,VII,X)	67	1	0

TABLE V. Control chart applied to series 2 but constructed using the mean and autocorrelation of the first 50 data points of series 1 (A) or using the mean of the first 50 data points but autocorrelation of series 2 (B).

Quantity variate	N (of series 2)	Number of points outside limits	
		(A)	(B)
L-GLU	51	49	49
H-GLU	53	20	8
L-UREA	51	0	2
H-UREA	53	8	9
L-CREA	51	0	19
H-CREA	53	5	0
L-NA	51	3	0
H-K	52	33	0

conclude that the mean had changed significantly since the number of values outside the control limits did not change when the autocorrelation was updated. The interpretation of the remaining cases is less clear-cut.

These results demonstrate that (at least in the case of the analyzer examined) the process autocorrelation may not be stable. The same is true for the mean level. This has to be taken into account when the EWMAST chart is being applied.

## DISCUSSION

As mentioned in the introduction, the EWMAST chart was chosen because it has been shown to be superior to the X chart, the residual charts (Zhang [4, 8]) and the EWMA chart, and it is simple to use. Recently a new chart, the ARMAST chart, has been proposed for stationary processes by Jiang *et al.* [13] and the EWMAST chart can be treated as a special case of the ARMAST. Using the ARMAST chart in place of the EWMAST chart for the data of the present study, however, would only result in a marginal improvement of the ARLs. Since the use of the ARMAST chart is more complicated than that of the EWMAST chart, the ARMAST chart was not used in the present study.

Other approaches have been suggested when dealing with autocorrelation. For example, Montgomery & Mastrangelo [14] proposed to plot one-step-ahead EWMA prediction errors on a control chart. According to the simulation results of Zhang [7] and Jiang *et al.* [13],

however, this chart appears to be less effective than the EWMAST chart.

Essentially, the focus of this paper has been the problem of false alarms. We found that, in the presence of autocorrelation, a considerable number of values fell outside the control limits when the traditional EWMA chart was used while none of the values fell outside the control limits when the EWMAST chart was used (see Table IV). The reason is that the EWMAST chart accommodates the process autocorrelation and the limits of the chart are based on the process autocorrelation. Notice that the variances for EWMA chart and EWMAST chart differ by a factor of  $2 \sum_{k=1}^M \rho(k)(1-\lambda)^k [1 - (1-\lambda)^{2(M-k)}]$  shown previously. When this factor is positive, which is true when all or most  $\rho(k)$  s are positive, the control limits of the EWMAST chart are larger than those of the corresponding EWMA chart. In this case, the false alarms are reduced. We conclude that as long as the process autocorrelation remains stable, the EWMAST chart reduces the false alarms caused by the process autocorrelation.

It was noticed that on some occasions the process autocorrelation changed over time although the mean level remained stable, and as a consequence some values fell outside the control limits. Since the purpose of the chart is to control the mean level, we do not want the chart to be sensitive to a change in the process autocorrelation. To minimize this effect, the process autocorrelation could be updated continuously by using, say, the most recent 50 values to estimate the autocorrelation and adjusting the control limits accordingly.

Another approach is to find the cause of the autocorrelation and modify the system accordingly so that the autocorrelation disappears, or, alternatively, to model the underlying mechanism and to modify the calibration equation. An example of the latter approach would be the modeling of the carry-over in the old AMA II analyzers.

In their study [1] of the Vitros analyzer Alwan & Bissell observed that sometimes the time series were strongly and positively autocorrelated. In our study, the time series are not as strongly autocorrelated as those of Alwan & Bissell but they were also shorter than theirs. When we applied the EWMAST chart based on



one time series to a second time series of the same quantity but recorded several weeks later, we found that in some cases the mean level had changed significantly.

Recalibrations and/or changes of the reagents batches may account for this phenomenon. In a subsequent paper we examine this hypothesis.

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