A new strategy to monitor instrumental blank samples based on multivariate control charts

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Abstract. This paper proposes a methodology to monitor and assess the stability of instrumental blank samples of four elements (lead, cadmium, nickel and chromium), analysed through inductively coupled plasma mass spectrometry (ICP-MS). The proposed methodology, which is based on multivariate control charts, comprises an intra-day control, used as an internal quality control tool, to monitor and detect possible contaminations that may occur in the measurement process. The strategy used to evaluate the multivariate control chart performance was a direct comparison with a set of four univariate control charts build for each element. The findings (of this exploratory study) suggest that multivariate control charts have potential to be effectively used as an internal quality control tool in a daily base in IPC-MS. Taking into account the statistics used in this chart, Q-Statistics, their sensitivity should be improved, as well as the mathematical complexity involved.

1. Introduction
According to the World Health Organization, chronic diseases associated with poor eating habits affect more than a third of the European population. Globally, it is estimated that 60% of premature deaths are caused by these diseases. In this context, Lead, Cadmium, Nickel and Chromium are chemical elements considered dangerous to health, being the food intake the primary source of human exposure to these elements [1].

An accurate quantification of these elements, usually existing in food in trace concentrations, is crucial. The ICP-MS is one of the most suitable analytical techniques to quantify inorganic components at trace concentrations, offering to Internal Quality Control (ICQ)’ laboratory a huge challenge due to the wide number of analysis and matrices associated with sample preparation methods [2].

The use of blank samples is one of the main tools of IQC, and allows a quantitative evaluation of two fundamental method-performance characteristics: limit of detection (LOD) and limit of quantification (LOQ). In addition, it enables the analyst to ensure that the analytical signal is not affected by any source of contamination [3-4]. Control charts have been used to monitor blank samples and identify

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possible systematic deviations from regular performance in time, that may conduct to possible contamination situations, as advocated by [5-6]. The goal of this work is to present a multivariate control charts-based approach, grounded on Quesenberry Q-statistics [7], to monitor instrumental blank samples of four inorganic components (Pb, Cr, Cd and Ni) analysed by ICP-MS. Following the same strategy defined in [8], for the univariate case, the Quesenberry multivariate control chart will allow to establish a daily routine control scheme, allowing to monitoring possible contaminations in ICP-MS, as well as assessing the statistical consistency of instrumental blank samples of several elements at the same time.

2. Materials and methods

2.1. Instrumentation

Measurements were performed using a quadrupole inductively coupled plasma mass spectrometry (ICP-MS; Thermo Elemental, X-series 2, UK). ICP-MS tuning was performed on a daily basis with a diluted 10 mg L⁻¹ multi-element solution (Analytika, UNICAM, Portugal). Operating conditions for ICP-MS were for experience, optimized as follows:

| Parameter          | Setting       |
|--------------------|---------------|
| Extraction         | -113.7, 190   |
| Focus              | 10.0          |
| Pole Bias          | -0.1          |
| Hexapole Bias      | -3.0          |
| Nebulizer flow rate| 0.87 L min⁻¹  |
| Forward Power      | 191 1404 W    |
| Cool gas flow rate | 13.0 L min⁻¹  |
| Auxiliary gas flow rate | 0.90 L min⁻¹ |
| Sampling Depth     | 120, 192      |
| Standard Resolution| 135           |
| High Resolution    | 150           |
| Analogue Detector  | 1902          |
| PC Detector        | 3353          |

The parameters were monitored daily for elementary stability and sensitivity, mass calibration and for the presence of oxides and doubly charged ions, and the above conditions optimized accordingly.

2.2. Reagents

All reagents were of high analytical grade. All solutions were prepared using ultrapure water (18.2 MΩ cm) (Q-POD Millipore, Interface, Portugal) and Nitric acid pro analysis (65% v/v) (Merk, VWR, Portugal) was previously purified by sub-boiling distillation using a SubPur apparatus (Milestone, Unicam, Portugal). Hydrogen peroxide solutions acquired were of ultrapure grade. For the calibration curve, working multi-element standard solutions were prepared from mono-element high purity ICP stock standards containing 1000 mg/L of each element. IQC standard solutions were prepared using the multi-element standard solution, high purity ICP 100 mg/L, from Merck (21 elements diluted in nitric acid) containing all the elements under study. Taking into account the matrix under analysis internal standards were chosen between Yttrium, Indium and/or Rhodium (1000 mg L⁻¹; Merck).

2.3. Samples preparation and sample collection

All samples and standard preparation steps were carried out in clean room facilities. Blank samples were prepared on a daily basis by preparing a solution of 2% HNO₃ (V/V) with MILLI-Q water (18 MΩ) (Q-POD Millipore, Interface, Portugal). A nitric acid solution with 2% concentration was used for working standards and as rinsing solutions between samples for the ICP-MS. Internal standards were added to all samples and working standards, in order to correct instrumental drift.

To apply the univariate and multivariate control charts, a set of non-consecutive 16 working days collected during 2015 were considered, wherein only a single matrix was analysed in each day and the four elements in study (Pb, Cd, Ni and Cr) were simultaneously analysed (daily sample size range from 9 to 21 instrumental blanks obtained by ICP-MS).
3. Results and discussion

3.1. Statistical process control - univariate control charts

The ICP-MS equipment performed an auto-test at the beginning of each working day, ensuring the independence of the instrumental blanks collected in each day. This type of situations is characterised as a Short-Run process, where no in-control parameter estimation is possible given the small amount of data collected in each day. Based on Quesenberry Q-statistics [2], and following the methodology presented in Matos [1] for the intra-day control, a set of Q Short-Run control charts was built to monitor the four elements under study, as shown in figure 1.

Figure 1. Intra-day Q(X) chart for a) Pb, b) Cd, c) Ni and d) Cr.
3.2. Multivariate control charts

To avoid the complexity of interpreting one chart per each element analysed by ICP-MS, a multivariate control chart was built to simultaneously monitor the four instrumental blank samples shown in figure 1. Similarly, to the univariate control charts, the Quesenberry Q-Statistics was used considering a multivariate process. Considering the same 16 working days, a multivariate control chart was built (figure 2).

![Figure 2. Multivariate intra-day Q(X) chart considering the elements Pb, Cd, Ni and Cr.](image)

As shown in figure 2, the multivariate chart enabled to detect 8 possible especial causes of variation. When compared with the control charts presented in figure 1, two of the 8 out-of-controls situations were not justified by individual behaviours. On days 1 and 8 the out-of-control situations occur in Cr, on day 7 Ni was the responsible, whereas on day 14 was Pb. On days 2 and 9 the multivariate chart evidences an out-of-control, possibly with joint contribution of high values of Pb and Cr, as can be seen in figure 1 a) and d). However, the multivariate control chart identifies 2 out-of-controls (in days 9 and 16), which cannot be explained by none of the individual elements. These situations can be justified by a joint behaviour of two or more elements. In day 13 Ni and Cr showed out-of-control in the individual control charts, however, in the multivariate control chart no evidence was shown.

4. Conclusion

The findings suggest that, as an IQC tool, to implement an instrumental blank control in ICP-MS, considering a multielemental analysis, multivariate charts constitute an interesting alternative to univariate control charts. In this case, the multivariate chart allows identifying almost all problematic situations that occur in each univariate charts, though some disadvantages, such as the difficulty in its interpretation and the complex mathematical formulation associated with it, can be identified. Looking at the instrumental blank values involved in each out-of-control situation, only five of them present values near or upper the instrumental LOD. Further studies should be developed in order to improve the sensitivity of multivariate charts in the control of possible contaminations in IPC-MS.

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