# Multiblock modelling to assess the overall risk factors for a composite outcome

#### S. BOUGEARD<sup>1\*</sup>, C. LUPO<sup>1</sup>, S. LE BOUQUIN<sup>1</sup>, C. CHAUVIN<sup>1</sup> AND E. M. QANNARI<sup>2</sup>

(Accepted 9 March 2011; first published online 14 April 2011)

#### SUMMARY

Research in epidemiology may be concerned with assessing risk factors for complex health issues described by several variables. Moreover, epidemiological data are usually organized in several blocks of variables, consisting of a block of variables to be explained and a large number of explanatory variables organized in meaningful blocks. Usual statistical procedures such as generalized linear models do not allow the explanation of a multivariate outcome, such as a complex disease described by several variables, with a single model. Moreover, it is not easy to take account of the organization of explanatory variables into blocks. Here we propose an innovative method in the multiblock modelling framework, called multiblock redundancy analysis, which is designed to handle most specificities of complex epidemiological data. Overall indices and graphical displays associated with different interpretation levels are proposed. The interest and relevance of multiblock redundancy analysis is illustrated using a dataset pertaining to veterinary epidemiology.

**Key words**: Epidemiology, generalized linear model, multiblock modelling, multiblock redundancy analysis, risk factor.

#### INTRODUCTION

Research in epidemiology may be concerned with assessing risk factors for complex health issues described by several variables. As an example in veterinary epidemiology, a disease can be jointly described by clinical signs observed in animals, post-mortem lesions on organs under study or diagnostic test results about viruses or bacterial pathogenicity. The key

idea that several variables may describe a latent con-

(Email: Stephanie.bougeard@anses.fr)

<sup>&</sup>lt;sup>1</sup> Department of Epidemiology, French Agency for Food, Environmental, and Occupational Health Safety (ANSES), Zoopole, Ploufragan, France

<sup>&</sup>lt;sup>2</sup> Department of Chemometrics and Sensometrics, Nantes-Atlantic National College of Veterinary Medicine, Food Science and Engineering (ONIRIS), Nantes, France

cept can be extended to the structure of explanatory variables. Veterinary epidemiological surveys usually consist of data gathered from animal characteristics, farm, transport conditions, slaughterhouse features, and laboratory results. As a consequence, explanatory variables may be organized into meaningful blocks related to the production stages. In a more formal way, epidemiological data are organized in (K+1) blocks of variables, consisting of a block of variables to be explained (Y) and a large number of explanatory variables organized in K meaningful blocks  $(X_1, ..., X_K)$ . All these variables are measured in the same epidemiological units, e.g. animals or farms.

<sup>\*</sup> Author for correspondence: Dr S. Bougeard, Department of Epidemiology, French Agency for Food, Environmental, and Occupational Health Safety (ANSES), Zoopole, BP 53, 22440 Ploufragan, France.

The statistical procedures usually performed pertain to generalized linear models (GLMs), especially complex models of logistic regression [1]. These models have appealing features that justify their wide use. However, in the case of a multivariate outcome such as a complex disease described by several variables (i.e. dependent variables), the epidemiologist needs to utilize successive GLMs using each dependent variable in turn, or, alternatively, a pooled variable which sums up the various dependent variables [2]. Moreover, all the potential explanatory variables can not be included in a single model because very often they are plagued by quasi-collinearity. It is well-known that under these circumstances, the relevance and the stability of the results obtained from GLMs are impaired [3]. For this reason, several authors have advocated that explanatory variables should be subjected to a selection procedure or alternatively summarized onto latent variables (or components) (see e.g. [4, 5]). Finally, the organization of the explanatory variables into meaningful blocks (e.g. environment, infectious agents, alimentary factors, management habits) is usually omitted in GLMs. This is a drawback because assessment of the importance of each block in the explanation of the dependent variables (Y) is of paramount interest to the epidemiologist.

Considering the aim and the specificity of such complex data, the research work focuses on methods related to the multiblock modelling framework. Within this framework, the well-known method is structural equation modelling (SEM), also known as LISREL [6]. It can be viewed as a joint point between path and factor analysis [7]. On the one hand, path models give direct relationships between explanatory variables and variables to be explained [8]. On the other hand, factor analysis summarizes the variable blocks, as expression of different concepts, with latent variables [9]. SEM is a confirmatory model to assess the relationships among several datasets through latent variables. It is based on a conceptual model which should be set up by the user beforehand. It is used extensively in economics, business and social science. As an alternative to SEM, partial least squares path modelling (PLS-PM) [10] is a distribution-free data analysis approach and appears to be more adapted to biological data. It requires neither distributional nor sample size assumptions [11]. However, PLS-PM lacks a well-identified global optimization criterion and the iterative algorithm convergence is only proven in few particular cases [12]. For our purpose of exploring and modelling the relationships between

a dataset Y and several datasets  $(X_1, ..., X_K)$ , these problems can be circumvented by using multiblock (K+1) methods. Multiblock partial least squares (PLS) [13, 14] is a widely used multiblock modelling technique. It is designed as an extension of PLS regression [15], a popular method for linking two datasets X and Y. Multiblock PLS is mainly used in the field of process monitoring [16], chemometrics [17] and sensometrics [18].

We propose yet another (K+1) multiblock method called multiblock redundancy analysis. This method of analysis is more focused towards the explanation of the Y variables than multiblock PLS [19, 20]. It can be viewed as an extension of redundancy analysis [21] which is designed to explore the relationships between two datasets. The underlying principle is that each dataset is summed up by latent variables which are linear combinations of the variables in the dataset under consideration. These latent variables are sought by maximizing a criterion which reflects the extent to which each latent variable from the explanatory blocks are linked to the latent variables from the Y block. The solution to this maximization problem is directly derived from a matrix eigenanalysis. Moreover, multiblock redundancy analysis gives valuable tools for the explanation and the investigation of the relationships among variables and datasets. The associated models explain each variable in Y with explanatory variables, through orthogonalized regression. As the method aims at describing datasets with a large numbers of variables, the epidemiologist needs to sum up the complex links between them and between the datasets. Overall indices and graphical displays associated with different interpretation levels are proposed.

The interest of multiblock redundancy analysis is illustrated using a dataset from an observational study devoted to the assessment of the overall risk factors for losses in broiler chicken flocks (Y) described by four variables, i.e. the first-week mortality rate, the mortality rate during the rest of the rearing, the mortality rate during the transport to the slaughterhouse and the condemnation rate at slaughterhouse. As a matter of fact, most studies reported in the literature focus on particular reasons for losses. For the epidemiologist interested in determining the most appropriate focus to contain losses in broiler chickens, integrating results from separate analysis into an overall approach is difficult and probably not relevant. Moreover, the investigation of risk factors in epidemiological surveys is consistently resulting from

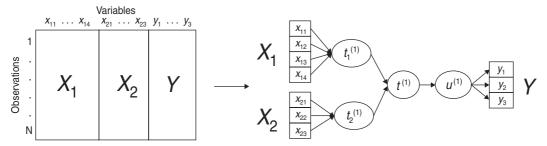


Fig. 1. Example of multiblock data structure and associated conceptual scheme of multiblock redundancy analysis, highlighting the relationships between the variable blocks  $(X_1, X_2, Y)$  and their associated components  $(t_1^{(1)}, t_2^{(1)}, u^{(1)})$  for the first dimension.

complex interactions between variables. Our objectives are to model the relationships between the losses as a composite block to be explained, with explanatory variables organized in thematic blocks related to the various production stages. In particular, we aim at assessing the impact of the different production stages on the whole losses and the specific risk factors for each element of losses. This pinpoints which production stages need to be improved and meets the specific expectations of the various factors in the poultry production chain confronted with health event complexity.

#### MATERIAL AND METHOD

#### Multiblock redundancy analysis

An original method, called multiblock redundancy analysis, is proposed in the multiblock modelling framework, adapted to the setting in which a block Y of several variables is to be explained by K explanatory variable blocks  $(X_1, ..., X_K)$ . The main idea is that each dataset is summed up by a latent variable (or component) which is a linear combination of the variables derived from this dataset. Multiblock redundancy analysis can be considered as a componentbased estimation technique where the latent variable estimation plays a central role. More precisely, the method derives a global component  $t^{(1)}$ , related to all the explanatory variables merged in the dataset  $X = [X_1|...|X_K]$ , closely related to a component  $u^{(1)}$ , linear combination of the variables in Y. Moreover, the component  $t^{(1)}$  sums up the partial components  $(t_1^{(1)}, ..., t_K^{(1)})$ , respectively, associated with the blocks  $(X_1, ..., X_K)$ . A simplified example of a conceptual scheme, highlighting the relationships between the variable blocks and their associated components is proposed in Figure 1.

The global component  $t^{(1)}$  sums up the partial components and is sought such as its squared covariance with  $u^{(1)}$  is as large as possible. The solutions are derived from the eigenanalysis of a matrix which involves the datasets Y and  $(X_1, ..., X_K)$ . Thereafter, the partial components  $t_1^{(1)}, ..., t_K^{(1)}$  are given by the normalized projection of  $u^{(1)}$  on each subspace spanned by variables in blocks  $X_1, X_2, ..., X_K$ . It follows that the global component  $t^{(1)}$  is a synthesis of the partial components  $(t_1^{(1)}, ..., t_K^{(1)})$  and therefore, the relationships of a given block  $X_k$  with Y is investigated through the relationships of  $t_k^{(1)}$  with  $t^{(1)}$ . (For a detailed account of multiblock redundancy analysis see [19, 20].)

In order to improve the prediction ability of the model, higher-order solutions are obtained by considering the residuals of the orthogonal projections of the datasets  $(X_1, ..., X_K)$  onto the subspace spanned by the first global component  $t^{(1)}$ . Thereafter, the second-order solution is performed by replacing the original datasets  $(X_1, ..., X_K)$  by their residuals in the criterion to maximize. This leads to determination of a second component  $u^{(2)}$  in the Y space, a second component  $t^{(2)}$  in the space spanned by the X variables and the associated latent variables in the various blocks of variables. The rationale behind this step is to investigate other directions in the space spanned by the X variables in order to shed light on the Y variables from various perspectives thus improving their prediction. Subsequent components  $(t^{(2)}, ..., t^{(H)})$  can be found by reiterating this process. As a consequence, these components can be expressed as linear combinations of X,  $t^{(h)} = Xw^{*(h)}$ , where  $w^{*(h)}$  is the vector of loadings associated with  $t^{(h)}$ . They are mutually orthogonal with each other and ranked by order of importance in explaining the total variation of Y. This allows orthogonalized regression which takes into account all the explanatory variables, and

Y is split up into  $Y = \sum_{l=1}^{h} t^{(l)} c^{(l)'} + Y^{(h)}$  for  $h=(1,...,H), Y^{(h)}$  being the matrix of residuals of the model based on h components. This leads to the model:  $Y = X[w^{*(1)}c^{(1)'} + \cdots + w^{*(h)}c^{(h)'}] + Y^{(h)}$  for h = (1, ..., H). From a practical point of view, the final model may be obtained by selecting the optimal number of components to be retained with a validation technique such as twofold cross-validation [22]. This consists of splitting the whole dataset into two sets, namely a calibration set and a validation set. The calibration set is used to select the parameters of the model and the fitting ability of the model, and the validation set is used to compute the prediction ability. Among all the models corresponding to the various values of h, a model with a satisfactory fitting ability and good prediction ability is retained. Orthogonalized regression handles the multicollinearity problem by selecting a subset of orthogonal components and avoiding the latest components which can be deemed to reflect noise only.

#### **Interpretation tools**

For the optimal dimension h, the exponential of the regression coefficients associated with each explanatory variable  $x_p$  and each variable to be explained  $y_q$ ,  $\beta_{pq}^{(h)} = \sum_{l=1}^{(h)} w^{*(h)} c^{(h)l}$ , are interpreted as the incidence rate ratio (IRR) [1]. Bootstrapping simulations are performed to provide standard deviations and tolerance intervals (TIs), associated with the regression coefficient matrix [23, 24]. An explanatory variable is considered to be significantly associated with a variable in Y if the 95% TI associated with the IRR does not contain 1. IRRs are interesting indices to link explanatory variables with each of the variables in Y.

However, if the number of variables in Y is large, the epidemiologist needs to sort the explanatory variables in a global order of priority. The variable importance for the projection (VIP) proposed in the PLS regression framework is a relevant tool [25, 26]. The VIP values sum up the overall contribution of each explanatory variable to the explanation of the Y block for a model involving  $(t^{(1)}, ..., t^{(h)})$  components. As the VIP indices verify, for a given dimension, the property  $\sum_{n=1}^{P} (VIP_n^2)/P = 1$ , where P is the total number of variables in X, they can be expressed as percentages. Associated standard deviations and tolerance intervals, computed using bootstrapped results, may additionally be computed. For the optimal dimension h, each explanatory variable is considered as significantly associated with the Y block if the 95 % TI associated with the VIP does not contain the threshold value 0.8 [27].

Finally, it interesting for the epidemiologist to assess the contributions of the explanatory blocks to the modelling task. Several indices are proposed in the literature and the block importance in the prediction (BIP) appears to be the most relevant [28]. For an optimal dimension h, the BIP values are based on the weighted average values of the coefficients  $(a_1^{(h)2}, ..., a_K^{(h)2})$  which reflect the importance of each block  $X_k$  in the Y block explanation. Moreover, the BIP can also be computed to assess the importance of each block  $X_k$  in explaining each variable in Y. As the BIP indices verify, for a given dimension the property  $\sum_{k=1}^{K} (BIP_k^2)/K = 1$ , where K is the number of explanatory blocks, can be expressed as percentages. Associated standard deviations and tolerance intervals, computed using bootstrapped results, may be given. It follows that for the optimal dimension h, each block  $X_k$  is considered to be significantly associated with the overall block Y or with each variable in Y, if the 95% TI associated with the BIP does not contain the threshold value 0.8 [28].

#### **Software**

Statistical procedures and associated interpretation tools were performed using code programs developed in Matlab<sup>®</sup> (The MathWorks Inc., USA) and also made available in R (http://www.r-project.org/). The code source is available upon request from the corresponding author.

#### Illustration dataset

Both in human and veterinary epidemiological surveys, it frequently occurs that the data at hand can be organized into blocks. The complex health issue (Y block), described by several variables, needs to be explained with a large number of explanatory variables organized into meaningful blocks ( $X_1, ..., X_K$ ), related to feeding, environment, genetic heritage, among others.

An example is given in the field of veterinary epidemiology. The population consists of a cohort of slaughtered broiler chicken flocks from all the European Union licensed slaughterhouses in France [29]. A large number (351) of broiler chicken flocks are randomly selected by two-stage sampling, stratified per slaughterhouse and based on random selection of the day of slaughter and of the flock sequence

number in the slaughtering schedule of that day. On the one hand, the information collected on each flock is prospective at slaughterhouse, and consists of recording the transport conditions to the slaughterhouse, the number of dead animals on arrival, the slaughtering conditions, the condemnation rate and the official sanitary reasons for condemnation. On the other hand, retrospective information is collected and involves the conditions during the rearing period, health history, daily mortality, catching and loading conditions. The aim is to assess the overall risk factors for a composite outcome: losses in broiler chickens (Y), described by four variables, i.e. the first-week mortality rate, the mortality rate during the rest of the rearing, the mortality rate during the transport to the slaughterhouse, and the condemnation rate at the slaughterhouse.

The explanatory variables are first selected on the basis of the main factors reported in the literature and of an earlier univariate screening applied to each dependent variable. These 68 selected variables are organized in four thematic blocks related to farm structure and systematic husbandry management practices  $(X_1, 16 \text{ variables})$ , flock characteristics and on-farm history of the chicks at placement  $(X_2, 14 \text{ variables})$ , flock characteristics during the rearing period  $(X_3, 17 \text{ variables})$  and catching, transport and lairage conditions, slaughterhouse and inspection features  $(X_4, 21 \text{ variables})$ . Indicator (dummy) variables are considered for the categorical variables. All the 68 putative explanatory variables are included in the multiblock analysis, fitted with a backwards-selection procedure.

As all the variables are expressed in different units, they are column centred and scaled to unit variance. As the explanatory variables have been standardized, the total variance in each block is equal to the number of variables in this block. This motivates the block scaling in order to put the blocks on the same footing [30]. For this purpose, each of the (K=4) explanatory block is accommodated with a scaling factor to set them at the same total variance 1/K.

#### RESULTS

#### **Preliminary results**

Among the 68 explanatory variables, 20 were significant risk factors for at least one variable relating to the losses and are retained for the final analysis. Among these 20 variables, five pertain to the farm structure and the systematic husbandry management

practices  $(X_1)$ , four are selected from the flock characteristics and the on-farm history of the chicks at placement  $(X_2)$ , six relate to the flock characteristics during the rearing period  $(X_3)$ , and five relate to the catching, transport and lairage conditions, slaughterhouse and inspection features  $(X_4)$ . The twofold cross-validation results led us to a model with (h=4) components  $(m_{cv} = 500 \text{ cross-validated samples})$ . This model explains 93% of the variation in Y, 15% in  $X_1$ , 30% in  $X_2$ , 30% in  $X_3$  and 27% in  $X_4$ .

#### Risk factors for each element of the dependent block

A predictive model is set up by regressing the variables to be explained upon the first four global components. The regression coefficients, transformed into IRRs, the associated standard deviations and the tolerance intervals ( $m_{\rm bt}$ =500 bootstrapped samples) of the 20 explanatory variables are computed for each dependent variable. Table 1 gives the explanatory variables which are significantly associated with the four variables related to the losses.

Each variable in Y is significantly related to a specific set of explanatory variables. First, the first-week mortality rate is related to four variables, two of which pertain to the farm structure. The mortality rate during the rest of the rearing is significantly linked with seven variables, four of which pertain to the flock characteristics during the rearing period. The mortality rate during the transport to the slaughterhouse is associated with eight variables, among which four pertain to the catching, transport and lairage conditions, slaughterhouse and inspection features. Finally, the condemnation rate at slaughterhouse is related to 15 variables, six of these variables refer to flock characteristics during the rearing period. Some explanatory variables are specifically related to one variable in Y, e.g. the chick homogeneity (from  $X_2$ ), whereas others are linked with up to three (out of four) variables in Y, e.g. the genetic strain (from  $X_3$ ).

#### Risk factors for the dependent block (Y)

In order to sort these explanatory variables by a global order of priority thus highlighting their overall contribution to the explanation of the Y block, the VIP are computed. Figure 2 depicts the VIP<sup>2</sup> expressed as percentages, of the main explanatory variables.

It turns out that four explanatory variables have a significant impact on the overall losses: the stress occurrence during rearing ( $VIP_{Stress}^2 = 13.3\%$ , 95% TI

342

Table 1. Contribution of the explanatory variables to the explanation of the four variables of losses  $Y = [y_1, y_2, y_3, y_4]$ , by means of significant incidence rate ratio (IRR) associated with their 95% tolerance interval

	First-week mortality rate (y <sub>1</sub> )	Mortality rate during the rest of the rearing (y <sub>2</sub> )	Mortality rate during the transport to slaughterhouse ( <i>y</i> <sub>3</sub> )	Condemnation rate at slaughterhouse (y <sub>4</sub> )
% of the Y variation explained by the model ( $h=4$ dimensions)	82.6%	93.6%	97.0%	95·2%
X <sub>1</sub> block: Farm structure and systematic husbandry management practices Total area for chicken on the farm [Area]* Cleaning step in decontamination of chicken house: yes (vs. no) [Soak] Heating system in the chicken house: gas heater (vs. radiant) [Heat] Sorting practice: yes (vs. no) [Sort] Age of the facilities: > 12 years (vs. recent or renovated) [Renov]	n.s. n.s. 0·77 (0·65–0·91) 1·24 (1·05–1·46) n.s.	n.s. 0·85 (0·75–0·96) 0·83 (0·71–0·96) n.s. n.s.	1·25 (1·05–1·49) 0·77 (0·65–0·90) n.s. n.s.	1·31 (1·07–1·60) 0·80 (0·66–0·96) n.s. n.s. 1·20 (1·01–1·43)
X <sub>2</sub> block: Flock characteristics and on-farm history of the chicks at placement Vitamins and minerals during the starting period: yes (vs. no) [Vitamin] Frequency of farmer visits during the starting period [Freqchick] Homogeneity of chicks at placement: yes (vs. no) [Homochick] Number of chicks at placement [Nbchick]	n.s. n.s. 0·60 (0·49–0·72) n.s.	0·90 (0·82–0·99) n.s. n.s. n.s.	n.s. n.s. n.s. 1·20 (1·03–1·40)	0.88 (0.79–0.97) 0.81 (0.72–0.92) n.s. 1.21 (1.01–1.44)
X <sub>3</sub> block: Flock characteristics during the rearing period  Production type: standard (vs. others†) [Typrod]  Homogeneity of chickens at the end of rearing: yes (vs. no) [Homochicken]  Genetic strain: X (vs. other) [Strain]  Locomotor disorder observed: yes (vs. no) [Locpb]  Stress occurrence‡ during rearing: yes (vs. no) [Stress]  Frequency of farmer visits during rearing [Freqchicken]	n.s. n.s. n.s. n.s. n.s.	1·41 (1·16–1·72) n.s. 0·59 (0·45–0·79) 1·52 (1·08–2·14) 2·16 (1·58–2·96) n.s.	n.s. n.s. 0·83 (0·70–0·98) n.s. n.s.	0·79 (0·65–0·97) 0·75 (0·59–0·96) 0·73 (0·61–0·87) 1·37 (1·06–1·78) 1·40 (1·11–1·75) 0·80 (0·70–0·93)
X <sub>4</sub> block: Catching, transport and lairage conditions, slaughterhouse and inspection features  Type of loading system: mechanical (vs. manual) [LoadType]  Meteorological conditions during lairage: rain and/or wind (vs. neither rain nor wind) [RainWind]  Stocking density in transport crates [StockingD]  Average duration of waiting time on lairage [Dlairage]  Withdrawal of carcasses at the evisceration line: yes (vs. no) [Evisc]	n.s. n.s. n.s. 0·84 (0·73–0·98) n.s.	n.s. n.s. n.s. n.s.	2·03 (1·56–2·64) 1·37 (1·12–1·69) 1·53 (1·23–1·89) 1·34 (1·04–1·74) n.s.	n.s. n.s. 0·82 (0·67–0·99) 0·81 (0·70–0·94) 1·64 (1·38–1·95)

n.s., Non-significant.

<sup>\*</sup> Abbreviation of the variable name given within square brackets.
† 'Others' includes light or heavy production types.
‡ Stress occurrence gathers feeding system defection, electrical defect, etc.

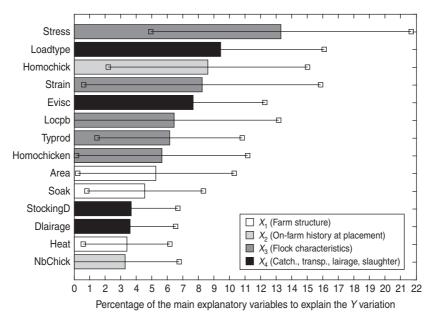


Fig. 2. Contribution of the main explanatory variables [variable importance for the projection  $(VIP)^2 \ge 3\%$ ] to the explanation of the overall losses (Y), through  $VIP^2$  (expressed as percentages) associated with their 95% tolerance interval.

4·9–21·7), the type of loading system (VIP $^2_{\text{LoadType}}$  = 9·4%, 95% TI 2·8–16·1), chick homogeneity (VIP $^2_{\text{HomoChick}}$  = 8·6%, 95% TI 2·2–15·0) and carcass withdrawal at the evisceration line (VIP $^2_{\text{Evisc}}$  = 7·6%, 95% TI 3·0–12·3). Because of its high variability, the genetic strain has a relatively important although non-significant impact (VIP $^2_{\text{Strain}}$  = 8·2%, 95% TI 0·6–15·9).

## Explanatory block importance for the dependent block (Y) explanation

Figure 3 depicts the relative importance of the four production stages, i.e. the four explanatory blocks, in the overall losses explanation, highlighting the significant importance of two blocks.

More precisely,  $42 \cdot 2\%$  (95% TI  $32 \cdot 2-52 \cdot 2$ ) of the overall losses variation are explained by the flock characteristics during the rearing period ( $X_3$ ) and  $26 \cdot 8\%$  (95% TI  $19 \cdot 1-34 \cdot 6$ ) by the catching, transport and lairage conditions, slaughterhouse and inspection features ( $X_4$ ). In addition, the relative importance of the four production stages in the explanation of each element of the losses is given in Table 2.

Neither the farm structure  $(X_1)$  nor the on-farm history at placement  $(X_2)$  have a significant impact on any variable of the losses. The most important findings are that the mortality rate during the rest of the rearing and the condemnation rate at slaughterhouse are mainly explained by the flock characteristics

during rearing  $(X_3)$ , and that the mortality rate during the transport to slaughterhouse is mainly related to the catching, transport and lairage conditions, slaughterhouse and inspection features  $(X_4)$ .

#### DISCUSSION

### Multiblock modelling for complex epidemiological data

On the whole, multiblock modelling results match up with those obtained from particular cases of GLMs, as both approaches lead to identification of specific risk factors related to each specific element of losses. (See e.g. [31] for risk factors associated with the firstweek mortality rate; see [32] for risk factors for the mortality rate during the remainder of the rearing; see [33] for risk factors for the mortality rate during transport and see [29] for risk factors for condemnation at slaughterhouse.) Although this classical risk factor analysis gives complete, accurate and sensible results, the epidemiologist needs to obtain overall results to pass them on to professionals. Multiblock redundancy analysis gives all the specific risk factors for each element of a composite outcome from a single analysis and gives additional information. It is welladapted to complex health issues and integrates an overall epidemiological approach. The method gives operational conclusions to the multifactorial origin of complex outcome. The model under study explains 93% of the variation that occurred in overall losses.

Table 2. Contribution of the explanatory blocks  $(X_1, ..., X_4)$  to the explanation of each variable of the losses  $Y = [y_1, y_2, y_3, y_4]$ , by means of block importance in the prediction (BIP<sup>2</sup> expressed as percentages) associated with their 95% tolerance interval

	First-week mortality rate $(y_1)$	Mortality rate during the rest of the rearing $(y_2)$	Mortality rate during the transport to slaughterhouse $(y_3)$	Condemnation rate at slaughterhouse $(y_4)$
% of the <i>Y</i> variation explained by the model ( <i>h</i> = 4 dimensions)	82.6%	93.6%	97.0 %	95·2 %
Farm structure and systematic husbandry management practices $(X_1)$	12·8 % (5·6–20·0) n.s.	14·1% (6·7–21·4) n.s.	11·6% (4·2–18·9) n.s.	18·5 % (9·5–27·5) n.s.
Flock characteristics and on-farm history at placement $(X_2)$	22·4 % (10·4–34·5) n.s.	12·4 % (3·8–20·9) n.s.	20·3 % (10·4–30·1) n.s.	13·8 % (4·5–23·0) n.s.
Flock characteristics during rearing $(X_3)$	31.0% (13.3–48.8)*	<b>50·4%</b> (37·9–62·8)*	26·9 % (10·2–43·6) n.s.	<b>53·0</b> % (38·6–67·4)*
Catching, transport, lairage, slaughterhouse $(X_4)$	33.7% (18.6–48.8)*	23·2% (11·1–35·3) n.s.	<b>41·3</b> % (24·0–58·5)*	14·7 % (2·3–27·1) n.s.

n.s., Non-significant.

<sup>\*</sup> Significant association.

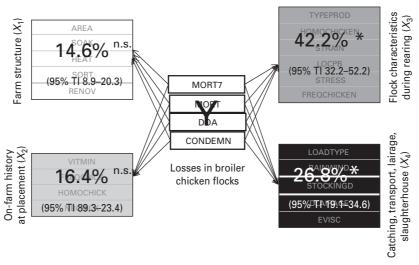


Fig. 3. Contribution of the four explanatory blocks  $(X_1, ..., X_4)$  to the explanation of the overall losses (Y), through block importance in the prediction (BIP<sup>2</sup>; expressed as percentages) associated with their 95% tolerance interval (TI). \* Significant association; n.s., non-significant.

The main part of this variation, i.e. 13·3%, can be explained by the stress occurrence during rearing and 9·4% by the mechanical catching method, among others. If particular care is taken with respect to the four most important variables, i.e. stress during rearing, type of loading system, chick homogeneity at

placement and genetic strain, the explained losses could be reduced by 39.6%. As a final remark, the variation in overall losses is explained by the flock characteristics during rearing (42.2% of explained variation) and the catching, transport and lairage conditions, slaughterhouse and inspection features

(26.8% of explained variation). One of the main advantages of multiblock redundancy analysis is to assess measurable and relevant impacts of variable blocks in a single analysis. Moreover, these weights can be compared to each other and this provides valuable information for epidemiologists. These findings may be useful for global management decisions. The relevant process stages on which to focus can be determined, as a decision-support aid in health management. This meets the specific expectations of the various factors in the production chain confronted with health complexity.

#### Alternative multiblock methods

The structure of epidemiological data together with the specific aim of epidemiologists led us to develop a new multiblock method, called multiblock redundancy analysis. This method is adapted to the setting where a block of several variables is to be explained by several explanatory blocks. Some other methods that could also meet the epidemiologists' expectations, are proposed within the framework of canonical analysis [34] or PLS regression [13]. Multiblock redundancy analysis was chosen considering its balanced behaviour with respect to robustness to multicollinearity and good fitting ability.

#### Multiblock modelling vs. successive GLMs

The overall approach of multiblock modelling can be compared to the standard approach which consists in setting up successive GLMs. GLMs boast some major advantages that justify their wide use in the epidemiological framework. First, the link between explanatory and dependent variables can be fitted (e.g. Poisson link function for the condemnation rate) whereas, in multiblock modelling, this link is the linear link function. Second, the explanatory variable status, i.e. quantitative or categorical, is taken into account in GLMs. By comparison, in the multiblock framework, dummy variables are considered for categorical variables and with this coding they are considered along with the quantitative variables. Third, in GLMs, explanatory variables can be selected in relation to the dependent variable under study. As an example, variables from the block relating to the catching, transport and lairage, and slaughterhouse are not selected to explain the first-week mortality. A limitation of multiblock modelling is the selection

of all explanatory variables available in order to explain all the variables to be explained at the same time, even if some are not relevant. This may lead to the selection of irrelevant variables as risk factor (e.g. the average duration of waiting time on lairage as a significant risk factor for the first-week mortality). Finally, GLMs are well-known methods that are fully available on software.

Multiblock redundancy analysis is based on a single criterion that reflects the objectives to be addressed. The criterion is based on the determination of latent variables which highlight the relationships among the datasets. This method fits within the general framework of multivariate techniques and factor analysis. The appealing feature of these methods is that they provide visualization tools which can be helpful for researchers to unveil hidden patterns and relationships among variables. As this method is mainly exploratory, its results are expressed in relation to the explanatory variables. Using latent variables as a summary of manifest variables makes it possible to include a large number of variables in a single model. In comparison with GLMs, the multiblock approach does not necessitate recourse to the univariate step, whose aim is to select a subset of explanatory variables; as these variables are organized in blocks the method is less sensitive to multicollinearity. Moreover, multiblock redundancy analysis is likely to recover more variations in the Y dataset than GLMs because new dimensions can be added if necessary in order to explain additional variability in the data.

Multiblock modelling uses additional information available for grouping the variables into meaningful blocks and allows several variables to be explained at the same time. This avoids the necessity of setting up separate models or combining several dependent variables into one single variable. Multiblock redundancy analysis provides both standard epidemiological results, such as IRRs, and specific estimations, such as VIPs and BIPs. The structure of explanatory variables within thematic blocks can be used to estimate their respective weights (i.e. the BIP indices) in the dependent variable explanation. Multiblock redundancy analysis makes it possible to shed light on the significant explanatory variables affecting a composite dependent variable and to pinpoint the problems in the various explanatory blocks. Furthermore, multiblock redundancy analysis allows many possibilities for graphical displays and combines tools from factor analysis with tools pertaining to regression.

#### Research perspectives for multiblock modelling

Notwithstanding their high benefits, multiblock methods still present some limitations in comparison with GLMs and further investigations will be undertaken to handle more epidemiological data specificities. For instance, multiblock modelling does not efficiently handle the information from relevant external variables, such in hierarchical GLMs. At present, this information could be highlighted in graphical displays, but it is of paramount interest to include it in the criterion to be optimized. Furthermore, multiblock redundancy analysis could be adapted to more complex data, e.g. explanation of several blocks of health events, each being described by several variables, or the evolution of a complex health event at different periods of time. As in LIS-REL or PLS-PM framework, these kinds of methods can also be extended to situations where the explanatory blocks of variables are linked with each other, while integrating this information in the criterion. Further developments in multiblock analysis should lead to new breakthroughs in the statistical processing of epidemiological data. These developments together with the increase of the volume and complexity of data in biology will certainly contribute to making the use of multiblock modelling increasingly popular.

#### **ACKNOWLEDGEMENTS**

The authors thank the French Ministry of Agriculture and Fisheries and the Office de l'Elevage for funding this research project, the Official Veterinary Services and Jean Peraste for extensive data collection, and the farmers and slaughterhouses for their participation in the survey.

#### **DECLARATION OF INTEREST**

None.

#### REFERENCES

- Dohoo IR, Martin W, Stryhn H. Veterinary Epidemiologic Research. Prince Edward Island, Canada: Atlantic Veterinary College Inc., University of Prince Edward Island, 2003, pp. 706.
- Rose N, et al. Risk factors for Salmonella persistence after cleansing and disinfection in French broilerchicken houses. Preventive Veterinary Medicine 2000; 44: 9–20.
- 3. **Dohoo IR**, *et al.* An overview of techniques for dealing with large numbers of independent variables in

- epidemiologic studies. *Preventive Veterinary Medicine* 1997; **29**: 221–239.
- 4. **Berghaus RD**, *et al.* Factor analysis of a Johne's disease risk assessment questionnaire with evaluation of factor scores and a subset of original questions as predictors of observed clinical paratuberculosis. *Preventive Veterinary Medicine* 2005; 72: 291–309.
- Boklund A, et al. Biosecurity in 116 Danish fattening swineherds: descriptive results and factor analysis. Preventive Veterinary Medicine 2004; 66: 49–62.
- 6. **Joreskog KG.** A general method for analysis of covariance structure. *Biometrika* 1970; **57**: 239–251.
- Musil CM, Jones SL, Warner CD. Structural equation modeling and its relationship to multiple regression and factor analysis. *Research in Nursing and Health* 1998; 21: 271–281.
- 8. Woods PSA, et al. Path analysis of subsistence farmers' use of veterinary services in Zimbabwe. Preventive Veterinary Medicine 2003; 61: 339–358.
- Manske T, Hultgren J, Bergsten C. Prevalence and interrelationships of hoof lesions and lameness in Swedish dairy cows. *Preventive Veterinary Medicine* 2002; 54: 247–63.
- Wold H. Soft modelling: the basic design and some extensions. In: Jöreskog KG, Wold H, eds. System Under Indirect Observation, Part 2. Amsterdam: North-Holland, 1982, pp. 1–54.
- Rougoor CW, et al. Relationships between dairy cow mastitis and fertility management and farm performance. Preventive Veterinary Medicine 1999; 39: 247–264.
- 12. **Hanafi M.** PLS path modelling: computation of latent variables with the estimation mode B. *Computational Statistics and Data Analysis* 2007; **22**: 275–292.
- 13. **Wold S.** Three PLS algorithms according to SW. In: Wold S, ed. *Symposium MULDAST (Multivariate Analysis In Science And Technology)*. Umea University, Sweden, 1984, pp. 26–30.
- 14. Wangen LE, Kowalski BR. A multiblock partial least squares algorithm for investigating complex chemical systems. *Journal of Chemometrics* 1988; 3: 3–20
- 15. **Wold H.** Estimation of principal components and related models by iterative least squares. In: Krishnaiah, ed. *Multivariate analysis*. New York: Academic Press, 1966, pp. 391–420.
- 16. **Kourti T.** Multivariate dynamic data modeling for analysis and statistical process control of batch processes, start-ups and grade transitions. *Journal of Chemometrics* 2003; **17**: 98–109.
- Kohonen J, et al. Multi-block methods in multivariate process control. *Journal of chemometrics* 2008; 22: 281–287.
- Tenenhaus M, et al. PLS methodology to study relationships between hedonic judgments and product characteristics. Food Quality and Preference 2005; 16: 315–325.
- Bougeard S, Qannari EM. Multiblock redundancy analysis. Application to epidemiological surveys. In: XIII International Conference of Applied Stochastic

- Models and Data Analysis. Vilnius (Lithuania), 2009, pp. 279–283.
- Bougeard S, et al. From multiblock partial least squares to multiblock redundancy analysis. A continuum approach. *Informatica* 2011; 22: 1–16.
- Rao CR. The use and interpretation of principal component analysis in applied research. *Sankhya*, A 1964;
   26: 329–358.
- Stone M. Cross-validatory choice and assessment of statistical predictions. *Journal of the Royal Statistical Society* 1974; 36: 111–147.
- 23. **Efron B, Tibshirani R**. *An Introduction to the Bootstrap*. New York: Chapman & Hall, 1993.
- Rebafka T, Clémençon S, Feinberg M. Bootstrap-based tolerance intervals for application to method validation. *Chemometrics and Intelligent Laboratory Systems* 2007; 89: 69–81.
- Chong IG, Jun CH. Performance of some variable selection methods when multicollinearity is present.
   Chemometrics and Intelligent Laboratory Systems 2005;
   78: 103–12
- 26. Wold S. PLS for multivariate linear modelling. In: Waterbeemd Hvd, ed. QSAR: Chemometric Methods in Molecular Design: Methods and Principles in Medicinal Chemistry. Weinheim, Germany: Verlag-Chemie, 1994.
- Gosselin R, Rodrigue D, Duchesne C. A Bootstrap-VIP approach for selecting wavelength intervals in spectral

- imaging applications. *Chemometrics and Intelligent Laboratory Systems* 2010; **100**: 12–21.
- 28. Vivien M, Verron T, Sabatier R. Comparing and predicting sensory profiles by NIRS: Use of the GOMCIA and GOMCIA-PLS multi-block methods. *Journal of Chemometrics* 2005; 19: 162–170.
- Lupo C, et al. Feasibility of screening broiler chicken flocks for risk markers as an aid for meat inspection. Epidemiology and Infection 2009; 137: 1086–1098.
- Westerhuis JA, Coenegracht PMJ. Multivariate modelling of the pharmaceutical two-step process of wet granulation and tableting with multiblock partial least squares. *Journal of Chemometrics* 1997; 11: 379– 392
- 31. Yassin H, et al. Field study on broilers' first-week mortality. Poultry Science 2009; 88: 798-804.
- Heier BT, Hogasen HR, Jarp J. Factors associated with mortality on Norwegian broiler flocks. *Preventive Veterinary Medicine* 2002; 53: 147–158.
- Chauvin C, et al. Factors associated with mortality of chicken broilers during transport to slaughterhouse. Animal (in press).
- 34. **Kissita G.** Generalized canonical analysis with generalized reference tables: theoretical and applied elements [in French] (Ph.D. thesis). Paris: University of Paris Dauphine IX, 2003, 184 pp.