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Concepts and a case study for a flexible class of graphical Markov models

Nanny Wermuth¹ and D. R. Cox²

Abstract With graphical Markov models, one can investigate complex dependences, summarize some results of statistical analyses with graphs and use these graphs to understand implications of well-fitting models. The models have a rich history and form an area that has been intensively studied and developed in recent years. We give a brief review of the main concepts and describe in more detail a flexible subclass of models, called traceable regressions. These are sequences of joint response regressions for which regression graphs permit one to trace and thereby understand pathways of dependence. We use these methods to re-analyze and interpret data from a prospective study of child development, now known as the ‘Mannheim Study of Children at Risk’. The two related primary features concern cognitive and motor development, at the age of 4.5 and 8 years of a child. Deficits in these features form a sequence of joint responses. Several possible risks are assessed at birth of the child and when the child reached age 3 months and 2 years.

1 Introduction

To observe and understand relations among several features of individuals or objects is one of the central tasks in many substantive fields of research, including the medical, social, environmental and technological sciences. Statistical models can help considerably with such tasks provided they are both flexible enough to apply to a wide variety of different types of situation and precise enough to guide us in thinking about possible alternative relationships. This requires in particular joint responses, which contain continuous random variables, discrete random variables or both types, in addition to only single responses.

Causal inquiries, the search for causes and their likely consequences, motivate much empirical research. They rely on appropriate representations of relevant pathways of dependence as they develop over time, often called data generating processes. Causes which start pathways with adverse consequences may be called risk factors or risks. Knowing relevant pathways offers in principle the opportunity to intervene, aiming to stop the accumulation of some of the risks, and thereby to prevent or at least alleviate their negative consequences.

Properties of persons or objects and features, such as attitudes or behavior of individuals, which can vary for the units or individuals under study, form the variables that are represented in statistical models. A relationship is called a strong positive dependence if knowing one feature makes it much more likely that the other feature is present as well. If, however,

¹Department of Mathematical Sciences, Chalmers University of Technology, Gothenburg, Sweden and International Agency of Research on Cancer, Lyon, France; wermuth@chalmers.se

²Nuffield College, Oxford, UK; david.cox@nuffield.ox.ac.uk

prediction of a feature cannot be improved by knowing the other, then the relation of the two is called an independence. Whenever such relations only hold under certain conditions, then they are qualified to be conditional dependences or independences.

Graphs, with nodes representing variables and edges indicating dependences, serve several purposes. These include to incorporate available knowledge at the planning stage of an empirical study, to summarize aspects important for interpretation after detailed statistical analyses and to predict, when possible, effects of interventions, of alternative analyses of a given set of data or of changes compared to results from other studies with an identical core set of variables.

Corresponding statistical models are called graphical Markov models. Their graphs are simple when they have at most one edge for any variable pair even though there may be different types of edge. The graphs can represent different aspects of pathways, such as the conditional independence structure, the set of all independence statements implied by a graph, or they indicate which variables are needed to generate joint distributions. In the latter case, the graph represents a research hypothesis on variables that make an important contribution. Theoretical and computational work has progressed strongly during the last few years.

In the following, we give first some preliminary considerations. Then we describe some of the history of graphical Markov models and the main features of their most flexible subclass, called traceable regressions. We illustrate some of the insights to be gained with sequences of joint regressions, that turn out to be traceable in a prospective study of child development, now known as the Mannheim Study of Children at Risk.

2 Several preliminary considerations

Graphical Markov models are of interest in different contexts. In the present paper, we stress data analysis and interpretation. From this perspective, a number of considerations arise. In a given study, we have objects or individuals, here children, and their appropriate selection into the study is important. Each individual has properties or features, represented as variables in statistical models.

A first important consideration is that for any two variables, either one is a possible outcome to the other, regarded as possibly explanatory, or the two variables are to be treated as of equal standing. Usually, an outcome or response refers to a later time period than a possibly explanatory feature. In contrast, an equal standing of two or more features is appropriate when they refer to the same time period or all of them are likely to be simultaneously affected by an intervention.

On the basis of this, we typically organize the variables for planned statistical analyses into a series of blocks, often corresponding to a time ordering. All relations between variables within a same block are undirected, whereas those between variables in different blocks are directed in the way described.

An edge between two nodes in the graph, representing a statistical dependence between two variables, may thus be of at least two types. To represent a statistical dependence of an outcome on an explanatory feature, we use a directed edge with an arrow pointing to the outcome from the explanatory feature. For relations between features of equal standing, we use undirected edges.

In fact, it turns out to be useful to have two types of undirected edge. A dashed line is used to represent the dependence between two outcomes or responses given variables in their past.

By contrast, a full line in the block of variables describing the background or context of the study and early features of the individuals under study, represents a conditional dependence given all remaining background variables.

From one viewpoint, the role of the graphical representation is to specify statistical independences that can be used to simplify understanding. From a complementary perspective, often the more immediately valuable, the purpose is to show those strong dependences that will be the base for interpreting pathways of dependence.

3 Some history of graphical Markov models

The development of graphical Markov models started with undirected, full line graphs; see Wermuth (1976), Darroch, Lauritzen and Speed (1980). The results built, for discrete random variables, on the log-linear models studied by Birch (1963), Goodman (1970), Bishop, Fienberg and Holland (1975), and for Gaussian variables, on the covariance selection models by Dempster (1972). Shortly later, the models were extended to acyclic directed graph models for Gaussian and for discrete random variables; see Wermuth (1980), Wermuth and Lauritzen (1983). With the new model classes, results from the beginning of the 20th century by geneticist Sewall Wright and by probabilist Andrej Markov were combined and extended.

These generalizations differ from those achieved with structural equations that were studied intensively in the 1950's within econometrics; see for instance Bollen (1989). Structural equation models extend sequences of linear, multiple regression equations by permitting explicitly endogenous responses. These have residuals that are correlated with some or all of the regressors. For such endogenous responses, equation parameters need not measure conditional dependences, missing edges in graphs of structural equations need not correspond to any independence statement and no simple local modelling may be feasible. This contrasts with traceable regressions; see Section 4.1.

Wright had used directed acyclic graphs, that is graphs with only directed edges and no variables of equal standing, to represent linear generating processes. He developed 'path analysis' to judge whether such processes were well compatible with his data. Path analyses were recognized by Tukey (1954) to be fully ordered, also called 'recursive', sequences of linear multiple regressions in standardized variables.

With his approach, Wright was far ahead of his time, since, for example, formal statistical tests of goodness of fit were developed much later; see Wilks (1938). Conditions under which directed acyclic graphs represent independence structures for almost arbitrary types of random variables were studied later still; see Pearl (1988), Studený (2005).

One main objective of traceable regressions is to uncover graphical representations that lead to an understanding of data generating processes. These are not restricted to linear relations although they may include linear processes as special cases. A probabilistic data generating process is a recursive sequence of conditional distributions in which response variables can be vector variables that may contain discrete or continuous components or both types. Each of the conditional distributions specifies both the dependences of a joint response, Y_a say, on components in an explanatory variable vector, Y_b , and the undirected dependences among individual response component pairs of Y_a .

Graphical Markov models generalize sequences of single responses and single explanatory variables that have been extensively studied as Markov chains. Markov had recognized at the

beginning of the 20th century that seemingly complex joint probability distributions may be radically simplified by using the notion of conditional independence.

In a Markov chain of random variables Y_1, \dots, Y_d , the joint distribution is built up by starting with the marginal density f_d of Y_d and generating then the conditional density $f_{d-1|d}$. At the next step, conditional independence of Y_{d-2} from Y_d given Y_{d-1} is taken into account, with $f_{d-2|d-1,d} = f_{d-2|d-1}$. One continues such that with $f_{i|i+1,\dots,d} = f_{i|i+1}$, response Y_i is conditionally independent of Y_{i+2}, \dots, Y_d given Y_{i+1} , written compactly in terms of nodes as $i \perp\!\!\!\perp \{i+2, \dots, d\} | \{i+1\}$, and ends, finally, with $f_{1|2,\dots,d} = f_{1|2}$, where Y_1 has just Y_2 as an important, directly explanatory variable.

The fully directed graph, that captures such a Markov chain, is a single directed path of arrows. For five nodes, $d = 5$, and node set $N = \{1, 2, 3, 4, 5\}$, the graph is

$$1 \longleftarrow 2 \longleftarrow 3 \longleftarrow 4 \longleftarrow 5.$$

This graph corresponds to a factorization of the joint density f_N given by

$$f_N = f_{1|2} f_{2|3} f_{3|4} f_{4|5} f_5.$$

The three defining local independence statements given directly by the above factorization or by the graph are: $1 \perp\!\!\!\perp \{3, 4, 5\} | 2$, $2 \perp\!\!\!\perp \{4, 5\} | 3$ and $3 \perp\!\!\!\perp 5 | 4$. One also says that in such a generating process, each response Y_i ‘remembers of its past just the nearest neighbour’, the nearest past variable Y_{i+1} .

Directed acyclic graphs are the most direct generalization of Markov chains. They have a fully ordered sequence of single nodes, representing individual response variables for which conditional densities given their past generate f_N . No pairs of variables are on an equal standing. In contrast to a simple Markov chain, in this more general setting, each response may ‘remember any subset or all of the variables in its past’.

Directed acyclic graphs are also used for Bayesian networks where the node set may not only consist of random variables, that correspond to features of observable units, but can represent decisions or parameters. As a framework for understanding possible causes and risk factors, directed acyclic are too limited since they exclude the possibility of an intervention affecting several responses simultaneously.

One early objective of graphical Markov models was to capture independence structures by appropriate graphs. As mentioned before, an independence structure is the set of all independence statements implied by the given graph. Such a structure is to be satisfied by any family of densities, f_N , said to be generated over a given graph.

In principle, all independence statements that arise from a given set of defining statements of a graph, may be derived from basic laws of probability by using the standard properties satisfied by any probability distribution and possibly some additional ones, as described for regression graphs in Section 4.1; see also Frydenberg (1990) for a discussion of properties needed to combine independence statements captured by directed acyclic graphs.

The above Markov chain implies for instance also

$$1 \perp\!\!\!\perp 4 | 3, \quad \{1, 2\} \perp\!\!\!\perp \{4, 5\} | 3, \quad \text{and} \quad 2 \perp\!\!\!\perp 4 | \{1, 3, 5\}.$$

For many variables, methods defined for graphs simplify considerably the task of deciding for a given independence statement whether it is implied by a graphs. Such methods have been called separation criteria; see Geiger, Verma and Pearl (1990), Lauritzen et al. (1990)

and Marchetti and Wermuth (2009) for different but equivalent separation criteria for directed acyclic graphs.

For ordered sequences of vector variables, permitting joint instead of only single responses, the graphs are directed acyclic in blocks of vector variables. These blocks are sometimes called the ‘chain elements’ of the corresponding ‘chain graphs’. Four different types of such graphs for discrete variables have been classified and studied by Drton (2009). He proves that two types of chain graph have the desirable property of defining always curved exponential families for discrete distributions; see for instance Cox (2006) for the latter concept.

This property holds for the ‘LWF-chain graphs’ of Lauritzen and Wermuth (1989) and Frydenberg (1990), and for the graphs of Cox and Wermuth (1993, 1996) that have more recently been slightly extended and studied as ‘regression graphs’; see Wermuth and Sadeghi (2012), Sadeghi and Marchetti (2012). With the added feature that each edge in the graph corresponds to dependence that is substantial in a given context, they become ‘traceable regressions’; see Wermuth (2012).

Most books by statisticians on graphical Markov models focus on undirected graphs and on LWF-chain graphs; see Højsgaard, Edwards and Lauritzen (2012), Edwards (2000), Lauritzen (1996), Whittaker (1990). In this class of graphical Markov models, each dependence between a response and a variable in its past is considered to be conditional also on all other components within the same joint response.

Main distinguishing features between different types of chain graph are the conditioning sets for the independences, associated with the missing edges, and for the edges present in the graph. For regression graphs, conditioning sets are always excluding other components of a given response vector, and criteria, to read off the graph all implied independences, do not change when the last chain element contains an undirected, full-line graph. It is in this general form, in which we introduce this class of models here. The separation criteria for these models are generalized versions of the criteria that apply to directed acyclic graphs.

Figure 1 shows two sets of joint responses and a set of background variables, ordered by time. The two related joint responses concern aspects of cognitive and motor development at age 8 years (abbreviated by Y_8, X_8 , respectively) and at age 4.5 years (Y_4, X_4). There are two risks, measured up to 2 years, Y_r, X_r , where Y_r is regarded as a main risk for cognitive development and X_r as a main risk for motor development. Two more potential risks are available already at age 3 months of the child. Detailed definitions of the variables, a description of the study design and of further statistical results are given in Laucht, Esser and Schmidt (1997) and summarized in Wermuth and Laucht (2012).

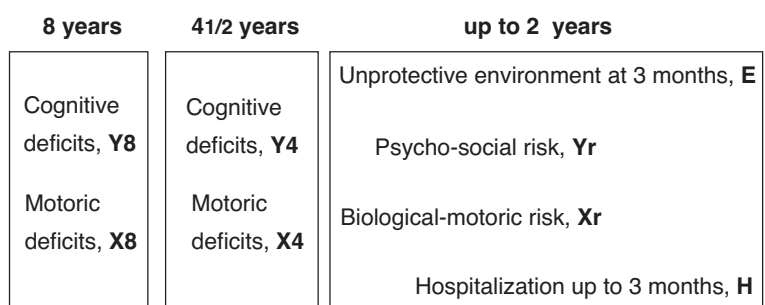


Figure 1: Ordering of the variables given by time; joint responses of primary interest are Y_8, X_8 , those of secondary interest are Y_4, X_4 , the context variables are risks known up to age 2.

4 Sequences of regressions and their regression graphs

The well-fitting regression graph in Figure 2 is for the variables of Figure 1 and for data of 347 families participating in the Mannheim study from birth of their first child until the child reached the age of 8 years. The graph results from the statistical analyses reported in Section 4.2. These are further discussed in Section 4.3.

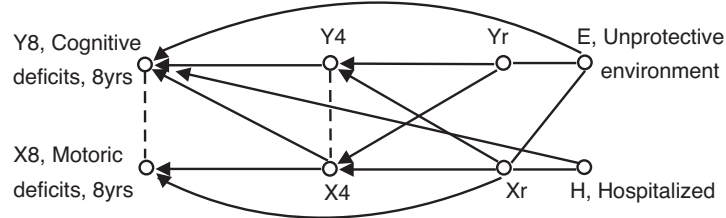


Figure 2: A well-fitting regression graph for data of the child development study; arrows pointing from regressors in the past to a response in the future; dashed lines for dependent responses given their past; full lines for dependent early risk factors given the remaining background variables.

The goodness-of-fit of the graph to the given data is assessed by local modeling which include here linear and nonlinear dependences. The following Table 1 gives a summary in terms of Wilkinson’s model notation that is in common use for generalized linear models and two coefficients of determination, R^2 . There is a good fit for quantitative responses when the changes from R^2_{full} to R^2_{sel} are small, that is from the regression of an individual response on all variables in its past to a regression on only a reduced set of selected regressors.

4.1 Explanations and definitions

In each regression graph, arrows point from the past to the future. An arrow is present, between a response and a variable in its past, when there is a substantively important dependence, that is also statistically significant, given all its remaining regressors. Regressors are recognized in the graph by arrows pointing to a given response node.

The undirected dependence between two individual components of a response vector is indicated here by a dashed line; some authors draw instead a bi-directed edge. Such an edge

Table 1: Fitted equations in Wilkinson’s notation

Response	Selected model	R^2_{full}	R^2_{sel}
Y_8 :	$Y_4 + X_4^2 + E + H$	0.67	0.67
X_8 :	$X_4^2 + X_r$	0.36	0.36
Y_4 :	$Y_r + X_r^2$	0.25	0.25
X_4 :	$Y_r + X_r^2$	0.37	0.36
Y_r :	E^2	0.57	0.56
X_r :	$E + H$	0.35	0.35

Note that any square term implies that also a main effect is included

is present if there is a substantial dependence between two response components given the past of the considered joint response. An undirected edge between two context variables is a full line. Such an edge is present when there is a substantial dependence given the remaining context variables. An edge is missing, when for this variable pair no dependence can be detected, of the type just described.

The important elements of this representation are node pairs i, k , possibly connected by an edge, and a full set ordering $g_1 < g_2 < \dots < g_J$ for the connected components g_j of a regression graph. The connected components of the graph are uniquely obtained by deleting all arrows from the graph and keeping all nodes and all undirected edges. In general, several orderings may be compatible with a given graph since different generating processes may lead to a same independence structure.

There is further an ordered partitioning of the node set into two parts, that is a split of N as $N = (u, v)$, such that response node sets g_1, \dots are in u and background node sets \dots, g_J are in v . In Figure 2, there are two sets in u : $g_1 = \{Y_8, X_8\}$ and $g_2 = \{Y_4, X_4\}$. The subgraph of the background variables is for $v = g_3 = \{Y_r, X_r, E, H\}$ and there is only one compatible ordering of the three sets g_j .

Within v , the undirected graph is commonly called a concentration graph, reminding us of the parameterization for a Gaussian distribution, where a concentration, an element in the inverse covariance matrix, is a multiple of the partial correlation given all remaining variables; see Cox and Wermuth (1996), Section 3.4, or Wermuth (1976).

Within u , the undirected graph induced by the set g_j is instead a conditional covariance graph given the past of g_j , the nodes in $g_{>j} = \{g_{j+1}, \dots, g_J\}$; see Wermuth, Cox and Marchetti (2009), Wiedenbeck and Wermuth (2010) for related estimation tasks. Arrows may point from any node in g_j for $j > 1$ to its future in $g_{<j} = \{g_1, \dots, g_{j-1}\}$ but never to its past. Thus within each g_j , there are only undirected edges and all arrows point from nodes in g_j to nodes in $g_{<j}$, where $g_{<1} = \emptyset$.

With $g_{>J} = \emptyset$, the basic factorization of a family of densities f_N , generated over a regression graph, G_{reg}^N , is

$$f_N = f_{u|v} f_v \text{ with } f_{u|v} = \prod_{g_j \subseteq u} f_{g_j|g_{>j}} \text{ and } f_v = \prod_{g_j \subseteq v} f_{g_j}, \quad (1)$$

and the family satisfies all independence constraints implied by the graph.

For i, k a node pair, and $c \subset N \setminus \{i, k\}$, we write $i \perp\!\!\!\perp k|c$ for Y_i, Y_k conditionally independent given Y_c . In terms of a joint conditional density $f_{ik|c}$, this is equivalent to the following constraints on conditional densities:

$$i \perp\!\!\!\perp k|c \iff (f_{i|kc} = f_{i|c}) \iff f_{ik|c} = (f_{i|c} f_{k|c}).$$

For every variable pair Y_i, Y_k making an important contribution to the generating process of f_N , we say it is conditionally dependent given Y_c for some $c \subset N \setminus \{i, k\}$ specified in Definition 1 below and write $i \pitchfork k|c$. A regression graph is said to be edge-minimal if every missing edge in the graph corresponds to a conditional independence statement and every edge present is taken to represent a dependence; see the following definition.

Definition 1 *Defining pairwise dependences of G_{reg}^N . An edge-minimal regression graph specifies with $g_1 < \dots < g_J$ a generating process for f_N where the following dependences*

$$\begin{aligned} i \text{---} k &: i \pitchfork k|g_{>j} && \text{for } i, k \text{ response nodes in } g_j \text{ of } u, \\ i \longleftarrow k &: i \pitchfork k|g_{>j} \setminus \{k\} && \text{for response node } i \text{ in } g_j \text{ of } u \text{ and node } k \text{ in } g_{>j}, \\ i \text{---} k &: i \pitchfork k|v \setminus \{i, k\} && \text{for } i, k \text{ context nodes in } v, \end{aligned} \quad (2)$$

define the edges present in G_{reg}^N . The meaning of each corresponding edge missing in G_{reg}^N results with the dependence sign \pitchfork replaced by the independence sign $\perp\!\!\!\perp$.

By equation (2), a unique independence statement is assigned to the missing edge of each uncoupled node pair i, k . To combine independence statements implied by a regression graph, two properties are needed, called composition and intersection; see Sadeghi and Lauritzen (2012). The properties are stated below in Definition 3(1) as a same joint independence implied by the two independence statements under bullet points 2 and 3 on the right-hand side. In their simplest form, the two properties can be illustrated with two simple 3-node graphs.

For all trivariate probability distributions, one knows $i \perp\!\!\!\perp hk \implies (i \perp\!\!\!\perp h \text{ and } i \perp\!\!\!\perp k)$ as well as $i \perp\!\!\!\perp hk \implies (i \perp\!\!\!\perp h|k \text{ and } i \perp\!\!\!\perp k|h)$. The reverse implications are the composition and the intersection property, respectively. Thus, whenever node i is isolated from the coupled nodes h, k in a 3-node regression graph, it is to be interpreted as $i \perp\!\!\!\perp hk$ and this type of subgraph in three nodes i, h, k results, under composition, by removing the ih -arrow and the ik -arrow in the following graph on the left and under intersection in the following graph on the right. These small examples show already that the two properties are used implicitly in the selection of regressors; the composition property for multivariate regressions and the intersection property for directed acyclic graph models.



For the tracing of dependences, we need both of these properties but also the following, called singleton transitivity. It is best explained in terms of the Vs of a regression graph, the subgraphs in 3 nodes having 2 edges. In a regression graph, there can be at most 8 different V-configurations. Such a V in three nodes, (i, o, k) say, has uncoupled endpoints i, k and inner node o .

The V configurations in G_{reg}^N are of two different types. In G_{reg}^N , the collision Vs are:

$$i \text{---} o \longleftarrow k, \quad i \longrightarrow o \longleftarrow k, \quad i \text{---} o \text{---} k,$$

and the transmitting Vs are:

$$i \longleftarrow o \longleftarrow k, \quad i \longleftarrow o \longrightarrow k, \quad i \longrightarrow o \longrightarrow k, \quad i \longleftarrow o \text{---} k, \quad i \longleftarrow o \longrightarrow k.$$

These generalize the 3 different possible Vs in a directed-acyclic graph. For such an edge-minimal graph, the two uncoupled nodes i, k of a transmitting V have either an important common-source node (as above on the right) or an important intermediate node (as above on the left), while the two uncoupled nodes i, k of a collision V with two arrows pointing to its inner node, have an important, common response.a

Singleton transitivity means that a unique independence statements is assigned to the end-points i, k of each V of an edge-minimal graph, either the inner node o is included or excluded in every independence statement implied by the graph for i, k . For the strange parametrisation under which singleton transitivity is violated in a trivariate discrete family of distributions; see Wermuth (2012).

Expressed equivalently, let node pair i, k be uncoupled in an edge-minimal G_{reg}^N and consider a further node o and a set $c \subseteq N \setminus \{i, o, k\}$. Under singleton transitivity, for both the independences $i \perp\!\!\!\perp k|c$ and $i \perp\!\!\!\perp k|oc$ to hold, one of the constraints $o \perp\!\!\!\perp i|c$ or $o \perp\!\!\!\perp k|c$ has to be

satisfied as well. Without singleton transitivity, the path of a V in nodes (i, o, k) can never induce a dependence for the endpoints i, k .

Definition 2 *Dependence-base regression graph.* An edge-minimal G_{reg}^N is said to form a dependence base when its defining independences and dependences are combined by using standard properties of all probability distributions and the three additional properties: intersection, composition and singleton transitivity.

A dependence base regression graph, G_{reg}^N , is edge-inducing by marginalizing over the inner node of a transmitting V and by conditioning on the inner node of a collision V . This can be expressed more precisely.

Theorem 1 Implications of V s in a dependence-base regression graph (Wermuth, 2012). For each V in three nodes, (i, o, k) of a dependence-base G_{reg}^N , there exists some $c \subseteq N \setminus \{i, o, k\}$, such that the graph implies $(i \perp\!\!\!\perp k | oc)$ and $i \pitchfork k | c$ when it is a transmitting V , while it implies $(i \perp\!\!\!\perp k | c)$ and $i \pitchfork k | oc$ when it is a collision V .

The requirement appears to be elementary, but some densities or families of densities f_N , even when generated over a dependence base G_{reg}^N , may have such peculiar parameterizations that both statements $i \perp\!\!\!\perp k | oc$ and $i \perp\!\!\!\perp k | c$ can hold even though both node pairs i, o and o, k are coupled by an edge. Thus, singleton-transitivity needs to be explicitly carried over to a generated density.

We sum up as follows. For a successful tracing of pathways of dependence in an edge-minimal regression graph, all three properties are needed: composition, intersection and singleton transitivity. Intersection holds in all positive distributions and the composition property holds whenever nonlinear and interactive effects also have non-vanishing linear dependences or main effects.

Singleton transitivity is satisfied in binary distributions; see Simpson (1951). More generally, it holds when families of densities are generated over G_{reg}^N that have a rich enough parametrization, such as the conditional Gaussian distributions of Lauritzen and Wermuth (1989) that contain discrete and continuous responses.

Definition 3 *Characterizing properties of traceable regressions.* Traceable regression are densities f_N generated over a dependence base G_{reg}^N , that have for disjoint subsets a, b, c, d of N

(1) three equivalent decompositions of the same joint independence

- $b \perp\!\!\!\perp ac | d \iff (b \perp\!\!\!\perp a | cd \text{ and } b \perp\!\!\!\perp c | d)$
- $b \perp\!\!\!\perp ac | d \iff (b \perp\!\!\!\perp a | d \text{ and } b \perp\!\!\!\perp c | d)$,
- $b \perp\!\!\!\perp ac | d \iff (b \perp\!\!\!\perp a | cd \text{ and } b \perp\!\!\!\perp c | ad)$, and

(2) edge-inducing V 's of G_{reg}^N are dependence-inducing for f_N .

One outstanding feature of traceable regressions is that many of their consequences can be derived by just using the graph, for instance when one is marginalizing over some variables in set M , and conditioning on other variables in set C . In particular, graphs can be obtained for node sets $N' = N \setminus \{C, M\}$ which capture precisely the independence structure implied by

G_{reg}^N , the generating graph in the larger node set N , for $f_{N|C}$, the family of densities of Y'_N given Y_C .

Such graphs are named independence-preserving, when they can be used to derive the independence structure that would have resulted from the generating graph by conditioning on a larger node set $\{C, c\}$ and marginalizing over the set $\{M, m\}$. Otherwise, such graphs are said to be only independence-predicting. Both types of graph transformations can be based on operators for binary matrices that represent graphs; see Wermuth, Wiedenbeck and Cox (2006), Wermuth and Cox (2004).

From a given generating graph, three corresponding types of independence-preserving graph result by using the same sets C, M . These are in a subclass of the much larger class of MC-graphs of Koster (2002), studied as the ribbon-less graphs by Sadeghi (2012a), or they are the maximal ancestral graphs of Richardson and Spirtes (2002) or the summary graphs of Wermuth (2011); see Sadeghi (2012a) for proofs of their Markov equivalence.

A summary graph shows when a generating conditional dependence, of Y_i on Y_k say, in f_N remains undistorted in $f_{N|C}$, parametrized in terms of conditional dependences, and when it be may become severely distorted; see Wermuth and Cox (2008). Some of such distortions can occur in randomized intervention studies, but they may often be avoided by changing the set M or the set C .

Therefore, these induced graphs are relevant for the planning stage of follow-up studies, designed to replicate some of the results of a given large study by using a subset of the variables, that is after marginalizing over some variables, and/or by studying a subpopulation, that is after conditioning on another set of variables.

For marginalizing alone, that is in the case of $C = \emptyset$, one may apply the following rules for inserting edges repeatedly, keep only one of several induced edges of the same type, and gets often again a regression graph induced by $N' = N \setminus M$. In general, a summary graph results; see Wermuth (2011). The five transmitting Vs induce edges by marginalizing over the inner node

$$i \leftarrow \emptyset \leftarrow k, \quad i \leftarrow \emptyset \text{---} k, \quad i \text{---} \emptyset \text{---} k, \quad i \leftarrow \emptyset \text{---} \text{---} k, \quad i \leftarrow \emptyset \text{---} \text{---} k$$

to give, respectively,

$$i \leftarrow k, \quad i \leftarrow k, \quad i \text{---} k, \quad i \text{---} \text{---} k, \quad i \text{---} \text{---} k.$$

The induced edges ‘remember the type of edge at the endpoints of the V’ when one takes into account that each edge $\circ \text{---} \text{---} \circ$ in G_{reg}^N can be generated by a larger graph, that contains $\circ \leftarrow \emptyset \text{---} \text{---} \circ$. Thereby, the independence structure implied by this graph, for the node set excluding the hidden nodes, $\{\emptyset\}$, is unchanged.

For any choice of C, M and a given generating graph G_{reg}^N , routines in the package ‘ggm’, contained within the computing environment R, help to derive the implications for $f_{N|C}$ by computing either one of the different types of independence-preserving graph; see Sadeghi and Marchetti (2012). Other routines in ‘ggm’ decide whether a given independence-preserving graph is Markov equivalent to another one or to a graph in one of the subfamilies, such as a concentration or a directed acyclic graph; see Sadeghi (2012b) for justifications of these procedures. This helps to contemplate and judge possible alternative interpretations of a given G_{reg}^N .

For two regression graphs, the Markov equivalence criterion is especially simple: the two graphs have to have identical sets of node pairs with a collision V; see Theorem 1 of Wermuth

and Sadeghi (2012). The result implies that the two sets may contain different ones of the 3 possible collision Vs. Also, the two sets of pairs with a transmitting V are then identical, though a given transmitting V in one graph may correspond in the other graph to another one of the 5 transmitting Vs that can occur in G_{reg}^N .

4.2 Constructing the regression graph via statistical analyses

As mentioned before, we use here data from the Mannheim Study of Children at risk. The study started in 1986 with a random sample of more than 100 newborns from the general population of children born in the Rhine-Neckar region in Germany. This sample was completed to give equal subsamples, in each of the nine level combinations of two types of adversity, taken to be at levels ‘no, moderate or high’. In other words, there was heavy oversampling of children at risk.

The recruiting of families stopped with about 40 children of each risk level combination and 362 children in the study. All measurements were reported in standardized form using the mean and standard deviation of the starting random sample, called here the norm group. Of the 362 German-speaking families who entered the study when their first, single child was born without malformations or any other severe handicap, 347 families participated still when their child reached the age of 8 years.

Two types of risks were considered, one relevant for cognitive the other for motor development. One main difference to previous analyses is that we averaged three assessments of each type of risk: taken at birth, at 3 months and at two years. This is justified in both cases by the six observed pairwise correlations being all nearly equal. The averaged scores, called ‘Psycho-social risk up to 2 years’, Y_r , and ‘Biological-motoric risk up to 2 years’, X_r , have smaller variability than the individual components. This points to a more reliable risk assessment and leads to clearly recognizable dependences, to the edges present in Figure 2.

The regression equations may be read off Tables 2 to 7 below. For instance for Y_8 , there are four regressors and one nonlinear dependence on X_4 with

$$E_{\text{lin}}(Y_8 | \text{past of } Y_8) = 0.03 + 0.78 Y_8 + (0.07 + 0.10 X_4) X_4 + 0.11 E + 0.12 H.$$

The test results of Table 2 imply that the previous measurement of cognitive deficits at age 4 years, Y_4 is the most important regressor and that the next important dependence is nonlinear and on motoric deficits at 4 years, X_4^2 .

For each individual response component of the continuous joint responses, the results of linear-least squares fittings are summarized in six tables. In each case, the response is regressed in the starting model on all the variables in its past. Quadratic or interaction terms are included whenever there is a priori knowledge or a systematic screening alerts to them; see Cox and Wermuth (1994).

The tables give the estimated constant term and for each variable in the regression, its estimated coefficient (coeff), the estimated standard deviation of the coefficient (s_{coeff}), as well as the ratio $z_{\text{obs}} = \text{coeff}/s_{\text{coeff}}$, often called a studentized value. Each ratio is compared to the 0.995 quantile of a standard Gaussian random variable Z , for which $\Pr(Z > |2.58|) = 0.01$. This relatively strict criterion for excluding variables assures that each edge in the constructed regression graph corresponds to a dependence that is considered to be substantively strong in the given context, in addition to being statistically significant for the given sample size.

At each backward selection step, the variable with the smallest observed value $|z_{\text{obs}}|$ is deleted from the regression equation, one at a time, until the threshold is reached so that no more variables can be excluded. The remaining variables are selected as the regressors of the response. An arrow is added for each of the regressors to the graph containing just the nodes, arranged in $g_1 < g_2 < \dots < g_J$.

The last column in each table shows the studentized value z'_{obs} , that would be obtained when the variable were included next into the selected regression equation. Wilkinson's model notation is added in the table to write the selected model in compact form. For continuous responses, the coefficient of determination is recorded for the starting model, denoted by R^2_{full} and for the reduced model containing the selected regressors, denoted by R^2_{sel} .

A dashed line is added, for a variable pair of a given joint response, when in the regression of one on the other, there is a significant dependence given their combined set of the previously selected regressors.

A full line is added for a variable pair among the background variables, when in the regression of one on all the remaining background variables, there is a significant dependence of this pair. This exploits that an undirected edge present in a concentration graph, must also be significant in such a regression; see Wermuth (1992).

Table 2: Regression results for Y_8

Response: Y_8 , cognitive deficits at 8 years							
explanatory variables	starting model			selected			excluded
	coeff	s_{coeff}	z_{obs}	coeff	s_{coeff}	z_{obs}	z'_{obs}
constant	0.00	—	—	0.03	—	—	—
Y_4 , cognitive deficits, 4.5yrs	0.78	0.05	15.36	0.78	0.05	15.70	—
X_4 , motoric deficits, 4.5yrs	0.05	0.04	—	0.07	0.04	—	—
Y_r , psycho-social risk, 2yrs	0.00	0.07	0.01	—	—	—	-0.13
X_r , biol.-motoric risk, 2yrs	0.07	0.07	1.07	—	—	—	1.08
E , Unprotect. environm., 3mths	0.10	0.06	1.81	0.12	0.04	2.62	—
H , Hospitalisation up to 3mths	0.09	0.05	1.91	0.12	0.04	3.00	—
X_4^2	0.09	0.01	6.53	0.10	0.01	7.15	—
$R^2_{\text{full}} = 0.67$ Selected model $Y_8 : Y_4 + X_4^2 + E + H$ $R^2_{\text{sel}} = 0.67$							

This strategy leads to a well-fitting model, unless one of the excluded variables has a too large contribution when it is added alone to a set of selected regressors. Such a variable would have to be included as an additional regressor. However, this did not happen for the given set of data.

Table 3: Regression results for X_8

Response: X_8 , motoric deficits at 8 years							
explanatory variables	starting model			selected			excluded
	coeff	s_{coeff}	z_{obs}	coeff	s_{coeff}	z_{obs}	z'_{obs}
constant	0.26	—	0,26	—	—	—	—
Y_4 , cognitive deficits, 4.5yrs	-0.01	0.06	-0.10	—	—	—	0.04
X_4 , motoric deficits, 4.5yrs	0.33	0.04	7.39	0.33	0.04	—	—
Y_r , psycho-social risk, 2yrs	0.01	0.08	0.19	—	—	—	0.43
X_r , biol.-motoric risk, 2yrs	0.17	0.08	2.27	0.19	0.06	2.97	—
E , Unprotect. environm., 3mths	0.01	0.07	0.17	—	—	—	0.44
H , Hospitalisation up to 3mths	0.01	0.08	0.26	—	—	—	0.26
X_4^2	0.18	0.23	3.41	0.05	0.02	2.89	—
$R_{\text{full}}^2 = 0.36$ Selected model $X_8 : X_4^2 + X_r$ $R_{\text{sel}}^2 = 0.36$							

The tests for the residual dependence of the two response components gives a weak dependence at age 8 with $z_{\text{obs}} = 2.4$ but a strong dependence at age 4.5 with $z_{\text{obs}} = 7.0$.

Table 4: Regression results for Y_4

Response: Y_4 , cognitive deficits at 4.5 years							
explanatory variables	starting model			selected			excluded
	coeff	s_{coeff}	z_{obs}	coeff	s_{coeff}	z_{obs}	z'_{obs}
constant	-0.29	—	—	-0.29	—	—	—
Y_r , psycho-social risk, 2yrs	0.36	0.08	4.81	0.36	0.05	6.77	—
X_r , biol.-motoric risk, 2yrs	0.17	0.09	—	0.18	0.07	—	—
E , Unprotect. environm., 3mths	-0.01	0.07	-0.14	—	—	—	0.39
H , Hospitalisation up to 3mths	0.14	0.04	3.36	—	—	—	-0.12
X_r^2	0.14	0.04	3.36	0.14	0.04	3.36	—
$R_{\text{full}}^2 = 0.25$, Selected model $Y_4 : Y_r + X_r^2$, $R_{\text{sel}}^2 = 0.25$							

Table 5: Regression results for X_4

Response: X_4 , motoric deficits at 4.5 years							
explanatory variables	starting model			selected			excluded
	coeff	s_{coeff}	z_{obs}	coeff	s_{coeff}	z_{obs}	z'_{obs}
constant	-0.47	—	—	-0.47	—	—	—
Y_r , psycho-social risk, 2yrs	0.33	0.10	3.44	0.28	0.07	4.21	—
X_r , biol.-motoric risk, 2yrs	0.62	0.11	5.50	0.50	0.09	—	—
E , Unprotect. environm., 3mths	-0.06	0.08	-0.66	—	—	—	-0.77
H , Hospitalisation up to 3mths	-0.13	0.07	-1.83	—	—	—	-1.88
$(X_r)^2$	0.21	0.05	3.97	0.23	0.05	4.43	—
$R^2_{\text{full}} = 0.37$ Selected model $X_4 : Y_r + X_r^2$ $R^2_{\text{sel}} = 0.36$							

Table 6: Regression results for Y_r

Response: Y_r , psycho-social risk up to 2 years							
explanatory variables	starting model			selected			excluded
	coeff	s_{coeff}	z_{obs}	coeff	s_{coeff}	z_{obs}	z'_{obs}
constant	-0.20	—	—	-0.21	—	—	—
X_r , biol.-motoric risk, 2yrs	-0.04	0.04	-0.81	—	—	—	-1.51
E , Unprotect. environm., 3mths	0.57	0.03	—	0.55	0.03	—	—
H , Hospitalisation up to 3mths	-0.03	0.04	-0.80	—	—	—	-1.50
E^2	0.16	0.03	6.12	0.16	0.03	6.20	—
$R^2_{\text{full}} = 0.57$ Selected model $Y_r : E^2$ $R^2_{\text{sel}} = 0.56$							

Table 7: Regression results for X_r

Response: X_r , biologic-motoric risk up to 2 years							
explanatory variables	starting model			selected			excluded
	coeff	s_{coeff}	z_{obs}	coeff	s_{coeff}	z_{obs}	z'_{obs}
constant	0.25	—	—	0.22	—	—	—
Y_r , psycho-social risk, 2yrs	-0.05	0.07	-0.81	—	—	—	-1.22
E , Unprotect. environm., 3mths	0.17	0.06	3.04	0.12	0.04	—	—
H , Hospitalisation up to 3mths	0.48	0.04	12.30	0.48	0.04	12.40	—
E^2	-0.04	0.03	-1.09	—	—	—	-1.42
$R^2_{\text{full}} = 0.35$ Selected model $X_r : E + H$ $R^2_{\text{sel}} = 0.35$							

A global goodness-of-fit test, with proper estimates under the full model, may depend on additional distributional assumptions and require iterative fitting procedures. For exclusively

linear relations of a joint Gaussian distribution, such a global test for the joint regressions would be equivalent to the fitting of a corresponding structural equation model, given the unconstrained background variables, and the global fitting of the concentration graph model to the context variables would correspond to estimation and testing for one of Dempster's covariance selection models.

4.3 Using a well-fitting graph

There are direct and indirect pathways from risks at three months to cognitive deficits at 8 years. The exclusively positive conditional dependences along different paths accumulate to positive marginal dependences, even for responses connected only indirectly to a risk, for instance for Y_8 to Y_r or X_8 to E .

Among the background variables, an unprotective environment for the 3 months-old child, E , is strongly related to the psycho-social risk up to 2 years, Y_r and hospitalization up to 3 months, H , to the biological-motoric risk up to 2 years, X_r . The weakest but still statistically significant dependence among these four risks occurs for an unprotective environment, E , and the biological-motoric risk, X_r .

Such a dependence taken alone can often best be explained by an underlying common explanatory variable, here for instance a genetic or a socio-economic risk. This would lead to replacing the full line for (E, X_r) in Figure 2 by the common-source V , shown in Figure 3. The inner node of this V is crossed out because it represents a hidden that is unobserved variable. Hidden nodes represent variables that are unmeasured in a given study but whose relevance and existence is known or assumed.

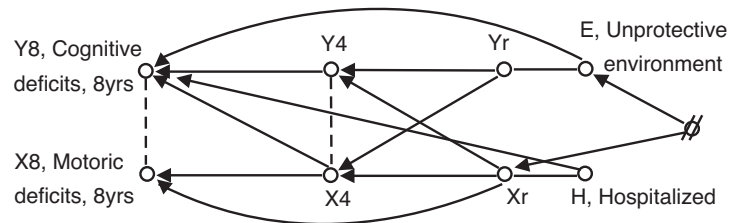


Figure 3: A graph equivalent to the one of Fig. 2 with one hidden, common explanatory variable

Though Figure 3 appears to contain only a small change compared to Figure 2, this change requires a Markov equivalence result for a larger class than regression graphs, as available for the ribbon-less graphs of Sadeghi (2012a), since a path of the type $i \text{---} o \leftarrow k$ does not occur in a regression graph. Given these results, it follows that graphs Figure 4(a) and (b) are Markov equivalent and that the structure of graph 4(b) can be generated by the larger graph 4(c) that includes a common, but hidden regressor node for the two inner nodes of the path.

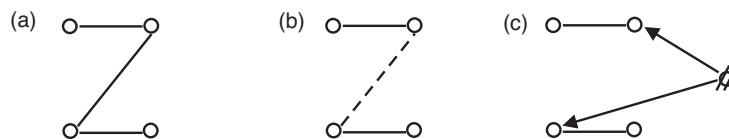


Figure 4: A hidden variable graph (c) generating two Markov equivalent graphs (a) and (b)

To better understand the distinguishing features of the pathways of dependence in Figure 2 leading to the joint responses of main interest at age 8, we generate the implied regressions graphs when the assessments at age 8 and at 4.5 years are available for only one of the two aspects. In that case one has ignored, that is marginalized over, the assessments of the other aspect at age 8 and 4.5.

The resulting graph, for Y_8 and Y_4 ignored, happens to coincide with the subgraph induced by the remaining, selected six nodes in Figure 1, as shown in Figure 5. Such an induced graph has the selected nodes and as edges all those present among them in the starting graph and no more.

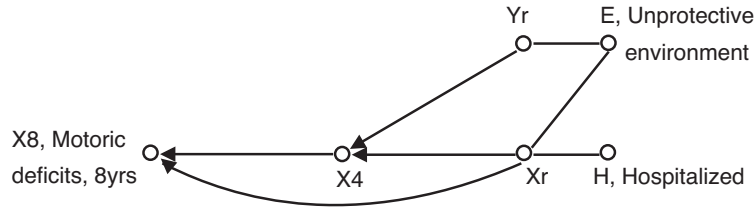


Figure 5: The regression graph induced by ignoring Y_8 and Y_4 in Figure 2; $M = \{Y_8, Y_4\}$, $C = \emptyset$

The graph of Figure 5 implies that possible psycho-social risks of a child up to age 2, Y_r , do not contribute directly to predicting motoric deficits at school-age, X_8 , also when the more recent information on cognitive deficits is not available.

By contrast, the regression graph in Figure 6 that results after ignoring X_8 and X_4 , shows two additional arrows compared to the subgraph induced in Figure 2 by Y_8, Y_4, Y_r, X_r, E, H .

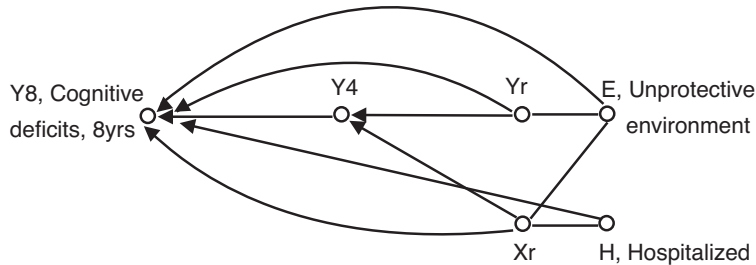


Figure 6: The regression graph induced by ignoring X_8 and X_4 in Figure 2; $M = \{X_8, X_4\}$, $C = \emptyset$

The induced arrows are for (Y_8, Y_r) and for (Y_8, X_r) . The graph suggests that cognitive deficits at school-age, Y_8 , are directly dependent on all of the remaining variables when the more recent information on the motoric risks are unrecorded. There are direct and indirect pathways from H and from E to Y_8 . They involve nonlinear dependences of cognitive deficits on previous motoric deficits or risks. These are recognized in the fitted equations but not directly in the graph alone.

What the graph also cannot show is that with X_8, X_4 unrecorded, the early risks, Y_r, H are less important as predictors when Y_4, X_r, X_r^2, E are available as regressors of Y_8 . This effect is due to the strong partial dependences of Y_r, E^2 given E, X_r, H and of X_r, H given E, E^2, Y_r . Such implications, due to the special parametric constellations are not reflected in the graph alone.

Many more conclusions may be drawn by using just graphs like in Figures 2 to 6. The substantive research questions and the special conditions of a given study are important; for some different types of study analyzed with graphical Markov models see, for instance, Klein, Keiding and Kreiner (1995), Gather, Imhoff and Fried (2002), Hardt et al (2004), Wermuth, Marchetti and Byrnes (2012).

One major attraction of sequences of regressions in joint responses is that they may model longitudinal data from observational as well as from intervention studies. For instance, with fully randomized allocation of persons to a treatment, all arrows that may point to the treatment in an observational study, are removed from the regression graph. This removal reflects such a successful randomization: independence is assured for the treatment variable of all regressors or background variables, no matter whether they are observed or hidden.

5 Conclusions

The paper combines two main themes. One is the notion of traceable regressions. These are sequences of joint response regressions together with a set of background variables for which an associated regression graph not only captures an independence structure but permits the tracing of pathways of dependence. Study of such structures has both a long history and at the same time is the focus for much current development.

Joint responses are needed when causes or risk factors are expected to affect several responses simultaneously. Such situations occur frequently and cannot be adequately modeled with distributions generated over directed acyclic graph or such a graph with added dashed lines between responses and variables in their past to permit unmeasured confounders or endogenous responses.

A regression graph shows, in particular, conditional independences by missing edges and conditional dependences by edges present. The independences simplify the underlying data-generating process and emphasize the important dependences via the remaining edges. The dependences form the basis for interpretation, for the planning of or comparison with further studies and for possible policy action. Propagation of independencies is now reasonably well understood. There is scope for complementary further study that focuses on pathways of dependence.

The second theme concerns specific applications. Among the important issues here are an appropriate definition of population under study, especially when relatively rare events and conditions are to be investigated, appropriate sampling strategies, and the importance of building an understanding on step-by-step local analyses. The data of the Mannheim study happen to satisfy all properties needed for tracing pathways of dependence. This permits discussion of the advantages and limitations for some illustrated path tracings.

In the near future, more results on estimation and goodness of fit tests are to be expected, for instance by extending the fitting procedures for regression graph models of Marchetti and Lupparelli (2010) to mixtures of discrete and continuous variables, more results on the identification of models that include hidden variables such as those by Stanghellini and Vantaggi (2012) and those by Foygel, Draisma and Drton (2012), and further evaluations of properties of different types of parameters; see Xie, Ma and Geng (2008) for an excellent starting discussion.

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