Cristian S. Calude
Michael J. Dinneen
Gheorghe Păun
Grzegorz Rozenberg
Susan Stepney (Eds.)

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Unconventional Computation

5th International Conference, UC 2006
York, UK, September 2006
Proceedings

Springer

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Volume Editors

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Preface

The 5th International Conference on Unconventional Computation, UC 2006, organized under the auspices of the EATCS by the Centre for Discrete Mathematics and Theoretical Computer Science of the University of Auckland, and the Department of Computer Science of the University of York, was held in York, UK, September 4–8, 2006.

York combines evidence of a history going back to Roman times with a bustling modern city center. The Minster, built on the foundations of the Roman city and an earlier Norman cathedral, is among the finest Gothic cathedrals, and dominates the city. Romans, Vikings, and more recent history are commemorated in a number of top-class museums, as well as being apparent in the architecture of the city.

The series of International Conferences on Unconventional Computation (UC), `https://www.cs.auckland.ac.nz/CDMTCS/conferences/uc/`, is devoted to all aspects of unconventional computation, theory as well as experiments and applications. Typical, but not exclusive, topics are: natural computing including quantum, cellular, molecular, neural and evolutionary computing; chaos and dynamical systems-based computing; and various proposals for computations that go beyond the Turing model.

The first venue of the Unconventional Computation Conference (formerly called Unconventional Models of Computation) was Auckland, New Zealand in 1998; subsequent sites of the conference were Brussels, Belgium in 2000, Kobe, Japan in 2002, and Seville, Spain in 2005.

The titles of volumes of the past UC conferences are the following:

1. C.S. Calude, J. Casti, M.J. Dinneen (eds.). *Unconventional Models of Computation*, Springer, Singapore, 1998, viii + 426 pp. ISBN: 981-3083-69-7.
2. I. Antoniou, C.S. Calude, M.J. Dinneen (eds.). *Unconventional Models of Computation, UMC'2K*, Springer, London, December 2000, xi + 301 pp. ISBN 1-85233-417-0.
3. C.S. Calude, M.J. Dinneen, F. Peper (eds.). *Third International Conference, UMC 2002*, Proceedings Lecture Notes in Computer Science, Vol. 2509, Springer, Heidelberg, 2002, vii + 331 pp. ISBN: 3-540-44311-8.
4. C.S. Calude, M.J. Dinneen, M.J. Pérez-Jiménez, Gh. Păun, G. Rozenberg (eds.). *Proc. 4th International Conference Unconventional Computation*, Lecture Notes in Computer Science, Vol. 3699, Springer, Heidelberg, 2005, xi + 267 pp. ISBN: 3-540-29100-8.

The Steering Committee of the series of International Conferences on Unconventional Computation includes T. Bäck (Leiden, The Netherlands), C.S. Calude (Auckland, New Zealand, Co-chair), L.K. Grover (Murray Hill, NJ, USA), J. van Leeuwen (Utrecht, The Netherlands), S. Lloyd (Cambridge, MA, USA), Gh. Păun

(Bucharest, Romania, and Seville, Spain), T. Toffoli (Boston, MA, USA), C. Torras (Barcelona, Spain), G. Rozenberg (Leiden, The Netherlands, and Boulder, Colorado, USA, Co-chair), A. Salomaa (Turku, Finland).

The five key-note speakers of the conference were:

1. Gerard Dreyfus (ESPCI, Paris, France): *Graph Machines and Their Applications to Computer-Aided Drug Design: A New Approach to Learning from Structured Data*
2. Michael C. Mozer (Department of Computer Science, and Institute of Cogntive Science, University of Colorado, USA): *Rational Models of Cognitive Control*
3. Reidun Twarock (University of York, UK): *Self-Assembly in Viruses*
4. Erik Winfree (Computer Science and Computation & Neural Systems, California Institute of Technology): *Fault-Tolerance in Biochemical Systems*
5. Damien Woods (University College Cork, Ireland): *Optical Computing and Computational Complexity*

UC 2006 included the following tutorials:

1. Andrew Adamatzky, Benjamin De Lacy Costello, Tetsuya Asai (Computing, Engineering and Mathematical Sciences, University of the West of England, Bristol, UK): *Reaction-Diffusion Computers*
2. Cristian S. Calude (University of Auckland, New Zealand): *Computing with Randomness*
3. Nataša Jonoska (University of South Florida, USA), and Darko Stefanovic (University of New Mexico, USA): *Biomolecular Automata*
4. Viv Kendon (University of Leeds, UK): *Quantum Computing*
5. Joseé del R. Millán (Institute for Systems, Informatics and Safety Joint Research Centre, Ispra, Italy): *Brain Signal Analysis*
6. Christof Teuscher (LANL, USA): *To Compute, or not to Compute*

The workshop “From Utopian to Genuine Unconventional Computers” was part of this year's conference.

The Programme Committee thanks the much appreciated work done by the paper reviewers for the conference. These experts were: Nevil Brownlee, Sam Braunstein, Douglas S. Bridges, Matteo Cavaliere, Cristian S. Calude, S. Barry Cooper, Jack Copeland, David Corne, Gabor Csardi, Erzsebet Csuhaj-Varjú, Michael J. Dinneen, Peter Erdi, Marian Gheorghe, Georgy Gimel'farb, James Goodman, Jozef Gruska, Oscar H. Ibarra, Mario de Jesus Pérez-Jiménez, Nataša Jonoska, Jarko Kari, Jan van Leeuwen, Chang Li, Rossella Lupacchini, Joseé del R. Millán, Pablo Moscato, Andrei Păun, Gheorghe Păun, Ion Petre, Vladimir Rogojin, Ulrich Speidel, Susan Stepney, Karl Svozil, Carme Torras, Christof Teuscher, Hiroshi Umeo.

The Programme Committee consisting of J.-P. Banâtre (Rennes, France), S. Braunstein (York, UK), C.S. Calude (Auckland, New Zealand, Co-chair), B. Cooper (Leeds, UK), D. Corne (Exeter, UK), M.J. Dinneen (Auckland, New Zealand, Secretary), P. Érdi (Kalamazoo, MI, USA), E. Goles (Santiago, Chile),

N. Jonoska (Tampa, FL, USA), J. Kari (Turku, Finland), J. van Leeuwen (Utrecht, Netherlands), R. Lupacchini (Bologna, Italy), J. del R. Millan (Ispra, Italy), Gh. Păun (Bucharest, Romania, and Seville, Spain, Co-chair), M.J. Pérez-Jiménez (Seville, Spain), I. Petre (Turku, Finland), P. Prusinkiewicz (Calgary, Canada), C. Teuscher (LANL, Los Alamos, USA), C. Torras (Barcelona, Spain), H. Umeo (Osaka, Japan), S. Stepney (York, UK), K. Svozil (Vienna, Austria), selected 17 papers (out of 36) to be presented as regular contributions.

We extend our thanks to all members of the Conference Committee, particularly to L. Caves, E. Clark, K. Clegg, G. Danks, O. Leyser (Co-chair), F. Polack, S. Stepney (Co-chair), J. Timmis, H. Turner, A. Weeks, J. Wright, for their invaluable organizational work.

We thank the University of York and the Centre for Discrete Mathematics of the University of Auckland for their technical support. The hospitality of our hosts, the Department of Computer Science of the University of York, is much appreciated.

The conference was partially supported by the Department of Biology of the University of York, the Enterprise and Innovation office of of the University of York, Microsoft Research, EPSRC, and the University consortium "White Rose"; we extend to all our gratitude.

It is a great pleasure to acknowledge the fine cooperation with the *Lecture Notes in Computer Science* team of Springer for producing this volume in time for the conference.

June 2006

C.S. Calude
M.J. Dinneen
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Graph Machines and Their Applications to Computer-Aided Drug Design: A New Approach to Learning from Structured Data

Aurélie Goulon[1], Arthur Duprat[1, 2], and Gérard Dreyfus[1]

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Abstract. The recent developments of statistical learning focused on *vector machines,* which learn from examples that are described by vectors of features. However, there are many fields where structured data must be handled; therefore, it would be desirable to learn from examples described by *graphs. Graph machines* learn real numbers from graphs. Basically, for each graph, a separate learning machine is built, whose algebraic structure contains the same information as the graph. We describe the training of such machines, and show that virtual leave-one-out, a powerful method for assessing the generalization capabilities of conventional vector machines, can be extended to graph machines. Academic examples are described, together with applications to the prediction of pharmaceutical activities of molecules and to the classification of properties; the potential of graph machines for computer-aided drug design are highlighted.

1 Introduction

Whether neural networks still fall in the category of "unconventional" computational methods is a debatable question, since that technique is well understood and widely used at present; its advantages over conventional regression methods are well documented and mathematically proven. Neural networks are indeed conventional in that they learn from *vector* data: typically, the variables of the neural model are in the form of a vector of numbers. Therefore, before applying learning techniques to neural networks, or any other conventional learning machine (Support Vector Machine, polynomial, multilinear model, etc.), the available data must be turned into a vector of variables; the learning machine then performs a mapping of a set of input vectors to a set of output vectors. In most cases, the output is actually a scalar, so that the mapping is from $\mathbb{R}^n$ to $\mathbb{R}$, where n is the dimension of the input vectors. When modeling a physical process for instance, the factors that have an influence on the quantity to be modeled are known from prior analysis, so that the construction of the vector of

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variables is straightforward, requiring simply normalization, and possibly variable selection by statistical methods.

In many cases of interest, however, encoding the data into a vector cannot be performed without information loss. Such is the case whenever the information to be learnt from is structured, i.e. is naturally encoded into a graph. In scene analysis for instance, a scene can be encoded into a graph that describes the relationships between the different parts of the scene. In computer-aided drug design, the purpose of learning is a mapping of the space of molecules to the space of pharmaceutical activities; in most cases, the structure of the molecule explains, to a large extent, its activity. Since molecular structures are readily described by graphs, QSAR (Quantitative Structure-Activity Relationships) aims at mapping the space of the graphs of molecular structures to the space of molecular activities or properties.

In the present paper, we describe an approach to learning that can be termed unconventional insofar as its purpose is a mapping of graphs to real numbers (or vectors) instead of a mapping of vectors to real numbers. The latter quantities may be either real-valued (graph regression) or binary (graph classification). The idea of learning from graphs (and generally structured data) can be traced back to the early days of machine learning, when Recursive Auto-Associative Memories (RAAMs) were designed for providing compact representations of trees [1]. It evolved subsequently to Labeled RAAMs [2], recursive networks [3], and graph machines (for a review of the development of numerical machine-learning from structured data, see [4]).

The first part of the paper is devoted to a description of graph machines and of some didactic, toy problems. It will also be shown that model selection methods that are proved to be efficient for conventional machine learning can be extended to graph machines. The second part of the paper will describe novel applications of graph machines to the prediction and classification of the properties or activities of molecules, a research area known as QSAR/QSPR (Quantitative Structure-Activity/Structure-Property Relationships). We show that graph machines are particularly powerful in that area, because they avoid a major problem of that field: the design, computation and selection of molecular descriptors.

2 Graph Machines

We first provide the definitions and notations for handling acyclic graphs, and the construction of graph machines from general graphs (possibly cyclic). Academic problems are described as illustrations. It is shown that the training and model selection methods developed for vector machines can be extended to graph machines.

2.1 Handling Directed Acyclic Graphs

Definitions: we consider the mapping from a set of acyclic graphs G to a set of real-valued numbers.

For each acyclic graph G_i of G, a parameterized function g^i $\mathbb{R}^n \rightarrow \mathbb{R}$ is constructed, which is intended (i) to encode the structure of the graph [5], and (ii) to provide a prediction of the quantity of interest, e.g. a property or an activity of the molecule, from G_i. It is constructed as follows. A parameterized function $f_{\boldsymbol{\theta}}$ ("node function") is associated to each node. $\boldsymbol{\theta}$ denotes the vector of parameters of the node function. All nodes, except the root node, have the same node function $f_{\boldsymbol{\theta}}$; those functions are combined in such a way that g^i has the same structure as graph G_i: if an edge from node k to node l exists in the graph, then the value of the node function associated to node k is a variable of the node function associated to node l. The root node may be assigned a different function, denoted by $F_{\boldsymbol{\Theta}}$, where $\boldsymbol{\Theta}$ is the vector of parameters of $F_{\boldsymbol{\Theta}}$. If the node functions are neural networks, the g^i's are termed recursive neural networks [3].

Notations: the following notations are used throughout the paper.
We denote by $\mathbf{x}_j$ the (optional) vector of labels that provide information about node j of graph G_i. The size of the label vector is denoted by X_i; it is the same for all nodes of a given graph. Therefore, the parameterized function associated to G_i will be denoted as $g^i_{\boldsymbol{\theta},\boldsymbol{\Theta}}\left(\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_{\nu_i}\right)$, where ν_i is the number of nodes of graph G_i. If no specific information about the node is necessary, $g^i_{\boldsymbol{\theta},\boldsymbol{\Theta}}$ has no variable: its value depends only on the structure of graph G_i.

We denote by $\mathbf{z}_j$ the vector of variables of the node function $f_{\boldsymbol{\theta}}(\mathbf{z}_j)$ of the non-root node j of graph G_i. Denoting by d_j the in-degree of non-root node j, and defining $M_i = \arg\max_j d_j$, the size of vector $\mathbf{z}_j$ is equal to $D_i = M_i + X_i + 1$. The vectors of variables of the node functions $f_{\boldsymbol{\theta}}(\mathbf{z}_j)$ are constructed as follows: for all j, the first component z_j^0 is equal to 1 (the "bias" if $f_{\boldsymbol{\theta}}(\mathbf{z}_j)$ is a neural network, the constant term if $f_{\boldsymbol{\theta}}(\mathbf{z}_j)$ is an affine function); for node j, of in-degree d_j, components z_j^1 to $z_j^{d_j}$ are the values of the node functions assigned to the parent nodes of node j; if $d_j < M_i$, components $z_j^{d_j+1}$ to $z_j^{M_i}$ are equal to zero; if $X_i \neq 0$, components $z_j^{M_i+1}$ to $z_j^{M_i+X_i}$ are the labels of node j.

We denote by $\mathbf{y}_i$ the vector of variables of the node function $F_{\boldsymbol{\Theta}}\left(\mathbf{y}_i\right)$ of the root node of graph G_i. The size of $\mathbf{y}_i$ is $\Delta_i = d_r + X_r + 1$, where d_r denotes the in-degree of the root node and X_r the size of its vector of labels. y_i^0 is equal to 1 (bias), y_i^1 to $y_i^{d_r}$ are the values of the node functions assigned to the parent nodes of the root node, $y_i^{d_r+1}$ to $y_i^{d_r+X_r}$ are the labels assigned to the root node.

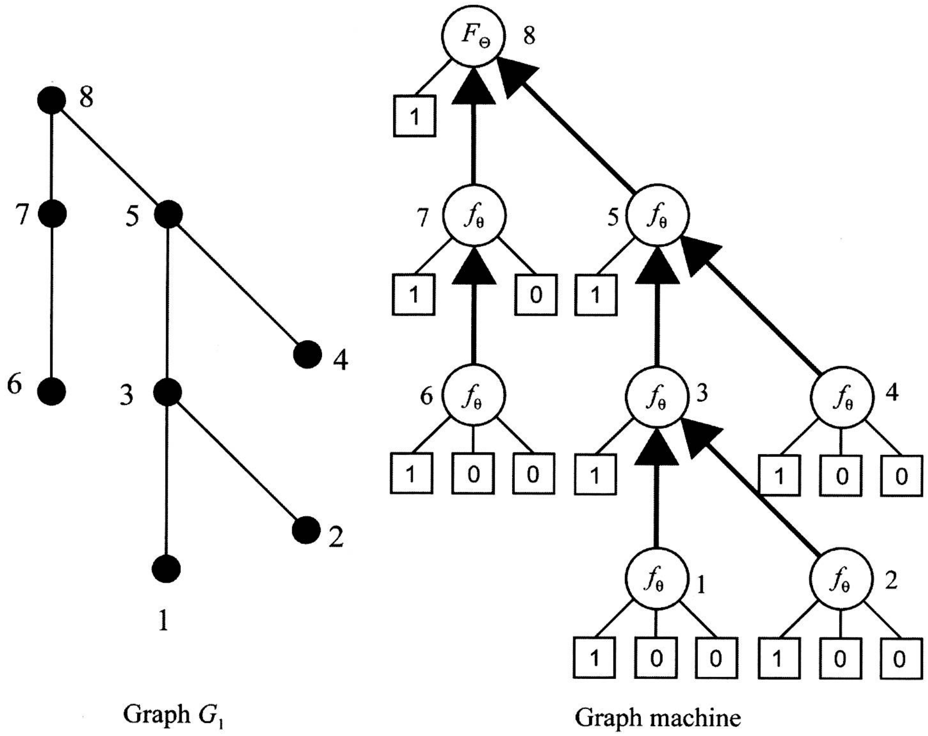
As an example, Fig. 1 shows an acyclic graph G_1 with maximum in-degree $M_1 = 2$; the corresponding graph machine is:

$$g^1_{\boldsymbol{\theta},\boldsymbol{\Theta}}\left(\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_8\right) = F_{\boldsymbol{\Theta}}\left(\mathbf{y}_1\right) = F_{\boldsymbol{\Theta}}\left(\mathbf{x}_8, f_{\boldsymbol{\theta}}\left(\mathbf{x}_7, f_{\boldsymbol{\theta}}\left(\mathbf{z}_6\right), 0\right), f_{\boldsymbol{\theta}}\left(\mathbf{x}_5, f_{\boldsymbol{\theta}}\left(\mathbf{z}_4\right), f_{\boldsymbol{\theta}}\left(\mathbf{x}_3, f_{\boldsymbol{\theta}}\left(\mathbf{z}_2\right), f_{\boldsymbol{\theta}}\left(\mathbf{z}_1\right)\right)\right)\right) \quad (1)$$

If no information about the nodes is required by the problem at hand ($X_1 = 0$), one has $D = 3$, and:

$$\mathbf{z}_1 = \mathbf{z}_2 = \mathbf{z}_4 = \mathbf{z}_6 = \begin{pmatrix} 1 & 0 & 0 \end{pmatrix}^{\mathrm{T}}, \ \mathbf{z}_3 = \begin{pmatrix} 1 & f_{\boldsymbol{\theta}}\left(\mathbf{z}_1\right) & f_{\boldsymbol{\theta}}\left(\mathbf{z}_2\right) \end{pmatrix}^{\mathrm{T}},$$

$$\mathbf{z}_5 = \begin{pmatrix} 1 & f_{\boldsymbol{\theta}}\left(\mathbf{z}_3\right) & f_{\boldsymbol{\theta}}\left(\mathbf{z}_4\right) \end{pmatrix}^{\mathrm{T}}, \ \mathbf{z}_7 = \begin{pmatrix} 1 & f_{\boldsymbol{\theta}}\left(\mathbf{z}_6\right) & 0 \end{pmatrix}^{\mathrm{T}}, \ \mathbf{y}_1 = \begin{pmatrix} 1 & f_{\boldsymbol{\theta}}\left(\mathbf{z}_5\right) & f_{\boldsymbol{\theta}}\left(\mathbf{z}_7\right) \end{pmatrix}^{\mathrm{T}}.$$



Graph G_1

Graph machine

Fig. 1. An acyclic graph and its graph machine

2.2 Cyclic Graphs

Graph machines handle cyclic graphs and parallel edges. To that effect, the initial graph is preprocessed by deleting a number of edges equal to the number of cycles, and all parallel edges but one; moreover, a label is assigned to each node: it is equal to the degree of the node, thereby retaining the information about the original graph structure. Finally, a root node is chosen and the edges are assigned orientations, according to an algorithm described in [6].

2.3 The Training of Graph Machines

Graph machines are trained in the usual framework of empirical risk minimization. A cost function $J(\boldsymbol{\Theta},\boldsymbol{\theta})$ is defined, and its minimum with respect to the parameters is sought, given the available training data. The cost function takes into account the discrepancy between the predictions of the models and the observations present in the training set, and may include regularization terms, e.g.:

$$J\left(\boldsymbol{\theta},\boldsymbol{\Theta}\right)=\sum_{i=1}^{N}\left(y^i-g^i_{\boldsymbol{\theta},\boldsymbol{\Theta}}\right)^2+\lambda_1\left\|\boldsymbol{\theta}\right\|+\lambda_2\left\|\boldsymbol{\Theta}\right\|, \tag{2}$$

where N is the size of the training set, y^i is the value of the i-th observation of the quantity to be modeled, and λ_1 and λ_2 are suitably chosen regularization constants.

Since the parameter vectors $\boldsymbol{\theta}$ and $\boldsymbol{\Theta}$ must be identical within each function g^i and across all those functions, one must resort to the so-called *shared weight* trick; the k-th component of the gradient of the cost function can be written as

$$\frac{\partial J(\boldsymbol{\theta},\boldsymbol{\Theta})}{\partial \theta_k} = \sum_{i=1}^{N} \frac{\partial J^i}{\partial \theta_k}, \tag{3}$$

where J^i is the contribution of example i to the cost function. We denote by $n^i_{\theta_k}$ the number of occurrences of parameter θ_k in acyclic graph G_i; if the root is assigned the same parameterized function as the other nodes, then $n^i_{\theta_k}$ is equal to the number of nodes in graph G_i. The shared weight trick consists in setting

$$\frac{\partial J^i}{\partial \theta_k} = \sum_{j=1}^{n^i_{\theta_k}} \frac{\partial J^i}{\partial \theta_{k_j}}, \tag{4}$$

so that one has finally:

$$\frac{\partial J(\boldsymbol{\theta},\boldsymbol{\Theta})}{\partial \theta_k} = \sum_{i=1}^{N} \sum_{j=1}^{n^i_{\theta_k}} \frac{\partial J^i}{\partial \theta_{k_j}}. \tag{5}$$

Relation (5) is subsequently used for minimizing cost function (2) by any suitable gradient descent algorithm (Levenberg-Marquardt, BFGS, conjugate gradient, ...).

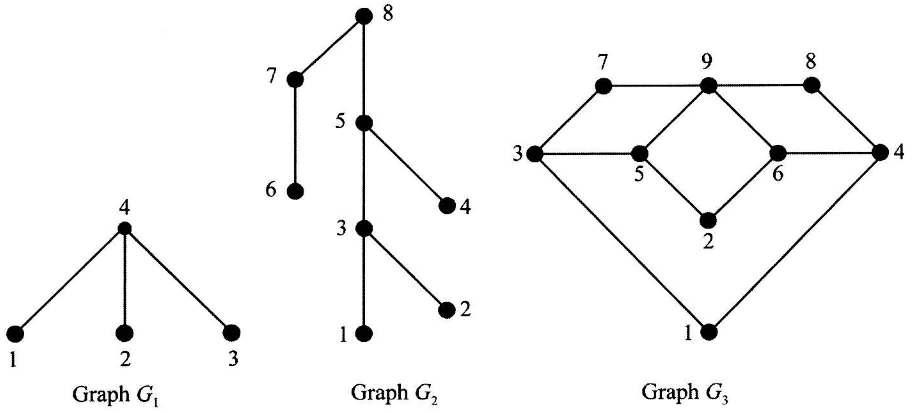
If functions $f_{\boldsymbol{\theta}}$ and $F_{\boldsymbol{\Theta}}$ are neural networks, the usual backpropagation algorithm may be conveniently used for computing the gradient; otherwise, one resorts to numerical estimations thereof.

2.4 Didactic Examples: Learning the Number of Nodes and the Number of Cycles of a Graph

In the present section, two simple examples are provided, whose solutions can be worked out analytically because they are linear. In both cases, we consider the training set made of three graphs, shown on Fig. 2.

Learning the number of nodes of a graph: first, assume that it is desired to learn, from examples, the number of nodes of a graph. Then the desired mapping is: $G_1 \to 4$; $G_2 \to 8$; $G_3 \to 9$. Moreover, generalization should be performed by using the node functions thus obtained in any other graph machine, i.e. to compute the number of nodes of any graph.

The first step consists in constructing directed acyclic graphs (DAGs) from the initial graphs. The construction of the DAGs is obvious for G_1 and G_2. Since graph G_3 has four cycles, four edges must be deleted. Fig. 3 shows the directed acyclic graphs on which the graph machines will be based.



Graph G_1 Graph G_2 Graph G_3

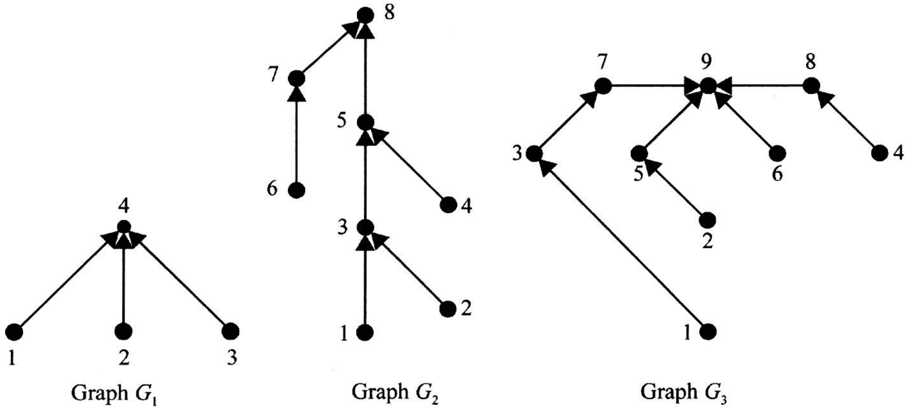
Fig. 2. A training set

The node function $f_\boldsymbol{\theta}$ is sought in the family of affine functions $f_\boldsymbol{\theta}(\mathbf{z}) = \sum_{j=0}^{D-1} \theta_j z_j$, and $F_\boldsymbol{\Theta}$ is taken identical to $f_\boldsymbol{\theta}$. Since the presence or absence of an edge is irrelevant for the computation of the number of nodes, no label is necessary: $X_1 = X_2 = X_3 = 0$. The node functions being the same for all graphs of the training set, we take $D = \max_i M_i + 1 = 5$. Since all edges are equivalent, one has $\theta_1 = \theta_2 = \theta_3 = \theta_4 = \theta$. Therefore, there are actually two independent parameters only.

The obvious solution is $\theta_0 = \theta = 1$. For graph G_1 for instance, one has:

$$g^1_{\boldsymbol{\theta},\boldsymbol{\Theta}}(\mathbf{x}_1,\mathbf{x}_2,\mathbf{x}_3,\mathbf{x}_4) = f_\boldsymbol{\theta}\left(1, f_\boldsymbol{\theta}(\mathbf{z}_1), f_\boldsymbol{\theta}(\mathbf{z}_2), f_\boldsymbol{\theta}(\mathbf{z}_3), 0\right) = \theta_0 + 3\theta\theta_0 = 4,$$

where $\mathbf{z}_1 = \mathbf{z}_2 = \mathbf{z}_3 = \begin{pmatrix}1 & 0 & 0 & 0 & 0\end{pmatrix}^\mathrm{T}$.



Graph G_1 Graph G_2 Graph G_3

Fig. 3. The acyclic graphs derived from the training set shown on Fig. 2