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# A Hierarchical Multi-Label Classification Ant Colony Algorithm for Protein Function Prediction

Received: date / Accepted: date

**Abstract** This paper proposes a novel Ant Colony Optimisation algorithm (ACO) tailored for the hierarchical multi-label classification problem of protein function prediction. This problem is a very active research field, given the large increase in the number of uncharacterised proteins available for analysis and the importance of determining their functions in order to improve the current biological knowledge. Since it is known that a protein can perform more than one function and many protein functional-definition schemes are organised in a hierarchical structure, the classification problem in this case is an instance of a hierarchical multi-label problem. In this type of problem, each example may belong to multiple class labels and class labels are organised in a hierarchical structure—either a tree or a directed acyclic graph (DAG) structure. It presents a more complex problem than conventional flat classification, given that the classification algorithm has to take into account hierarchical relationships between class labels and be able to predict multiple class labels for the same example. The proposed ACO algorithm discovers an ordered list of hierarchical multi-label classification rules. It is evaluated on sixteen challenging bioinformatics data sets involving hundreds or thousands of class labels to be predicted and compared against state-of-the-art decision tree induction algorithms for hierarchical multi-label classification.

**Keywords** hierarchical multi-label classification · ant colony optimisation · protein function prediction

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## 1 Introduction

Classification is a well-known data mining task, where the goal is to learn a relationship between input values and a desired output [14]. In essence, a classification problem is defined by a set of examples, where each example is described by predictor attributes and associated with a class attribute. Generally, it involves two phases. In the first phase, given a labelled data set—i.e. a data set consisting of examples with a known class value (label)—as an input, a classification model that represents the relationship between predictor and class attribute values is built. In the second phase, the classification model is used to classify unknown examples—i.e. examples with unknown class value.

In the vast majority of classification problems addressed in the literature, each example is associated with only one class value or label and class values are unrelated—i.e. there are no relationships between different class values. This kind of classification problems are usually referred to as flat (non-hierarchical) single-label problems. On the other hand, in hierarchical multi-label classification problems, examples may be associated to multiple class values at the same time and the class values are organised in a hierarchical structure (e.g. a tree or a directed acyclic graph structure). From a data mining perspective, hierarchical multi-label classification is much more challenging than flat single-label classification. Firstly, it is generally more difficult to discriminate between classes represented by nodes at the bottom of the hierarchy than classes represented by nodes at the top of the hierarchy, since the number of examples per class tends to be smaller at lower levels of the hierarchy as opposed to top levels of the hierarchy. Secondly, class predictions must satisfy hierarchical parent-child relationships, since an example associated with a class is automatically associated with all its ancestors classes. Thirdly, multiple unrelated classes—i.e. classes which are not involved in ancestor/descendant relationship—may be predicted at the same time.

There has been an increasing interest in hierarchical classification, where in general early applications are found in text classification [7, 33, 36, 37, 39] and recently in protein

function prediction [2, 6, 9, 28, 38]. The latter is a very active research field, given the large increase in the number of uncharacterised proteins available for analysis and the importance of determining their functions in order to improve the current biological knowledge. It is important to emphasise that in this context, comprehensible classification models—which can be validated by the user—are preferred in order to provide useful insights about the correlation of protein features and their functions. Concerning the problem of protein function prediction, the focus of this paper, an example to be classified corresponds to a protein, predictor attributes correspond to different protein features and the classes correspond to different functions that a protein can perform. Since it is known that a protein can perform more than one function and function definitions are organised in a hierarchical structure (e.g. FunCat [34] and Gene Ontology [10] protein functional-definition schemes), the classification problem in this case is an instance of a hierarchical multi-label problem.

In this paper we propose a novel ant colony classification algorithm tailored for the hierarchical multi-label classification problem, extending the ideas of our previous *hAnt-Miner* (Hierarchical Classification Ant-Miner) [28] algorithm. *hAnt-Miner*—the first ant colony algorithm for hierarchical classification to the best of our knowledge—discovers a list of classification rules that can predict all classes from a class hierarchy, independently of their level, but has the limitation of not being able to cope with multi-label data. The proposed algorithm overcomes this limitation and it is evaluated on sixteen bioinformatics data sets, taking into account both the predictive accuracy and simplicity (size) of the discovered rule list. The evaluation consists in comparing the proposed algorithm against state-of-the-art decision tree induction algorithms for hierarchical multi-label classification. The data sets employed in this evaluation present challenging problems for any classification algorithm as the number of attributes range from 63 to 551, the number of class labels in the class hierarchy ranges from 456 to 4134 and each example is associated with more than one class label.

The remainder of this paper is organised as follows. Section 2 reviews the related work. Section 3 presents an overview of the Ant Colony Optimisation metaheuristic and its applications in data mining’s classification task. The details of the proposed hierarchical multi-label classification algorithm are presented in Section 4. In Section 5, the evaluation measure based on Precision-Recall curves used in our experiments is presented. Section 6 presents the computational results. Finally, Section 7 draws the conclusions of this paper and presents future research directions.

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## 2 Related Work on Hierarchical Multi-Label Protein Function Prediction

Much work on hierarchical classification of protein functions has been focused on training a classifier for each class label (function) independently, using the hierarchy to deter-

mine positive and negative examples associated with each classifier [2, 3, 20, 22]. As discussed in [6], predicting each class label individually has several disadvantages, as follows. Firstly, it is slow since a classifier needs to be trained  $n$  times (where  $n$  is the number of class labels in the hierarchy excluding the root label). Secondly, some class labels could potentially have few positive examples in contrast to a much greater number of negative examples, particularly class labels at deeper levels of the hierarchy. Many classification algorithms have problems with imbalanced class distributions [19]. Thirdly, individual predictions can lead to inconsistent hierarchical predictions, since parent-child relationships between class labels are not imposed automatically during the training. However, more elaborate approaches can correct the individual predictions in order to satisfy hierarchical relationships—e.g. a Bayesian network is used to correct the inconsistent predictions of a set of SVM classifiers in [2]. Fourthly, the discovered knowledge identifies relationships between predictor attributes and each class label individually, rather than relationships between predictor attributes and the class hierarchy as a whole, which could give more insights into the data.

In order to avoid the aforementioned disadvantages of dealing with each class label individually, a few authors have proposed classification algorithms that discover a single global model which is able to predict class labels at any level of the hierarchy. Kiritchenko et al. [21] present an approach where the hierarchical (possibly multi-label) classification problem is cast as a multi-label problem by expanding the class label set of an example with all their ancestor class labels. Then, a multi-label classification algorithm is applied to the modified data set. For some examples, there is still a need for a post-processing step to resolve inconsistencies in the class labels predicted. Rousu et al. [33] presents a kernel-based algorithm for hierarchical multi-label classification based on the maximum margin Markov networks framework, wherein a post-processing is not required in order to satisfy hierarchical class labels relationships.

In general all of the above approaches can be seen as a ‘black box’, since the produced classification model cannot be interpreted and validated by the user. As previously mentioned, comprehensibility plays an important role in protein function prediction. Clare et al. [9] present an adapted version of the well-known C4.5 decision tree algorithm, which is able to deal with all hierarchical class labels in the data set at hand at the same time. In their approach, a leaf of the decision tree predicts a vector of boolean values, indicating the presence/absence of a particular class label. A recent work by Vens et al. [38] presents three approaches for hierarchical multi-label classification using the concept of predictive clustering trees (PCT) to induce decision trees for hierarchical multi-label problems in the context of protein function prediction: (1) building a decision tree for each class individually; (2) building decision trees in a top-down fashion, where an example can only belong to a class  $c$  if it belongs to the  $c$ ’s parent class; (3) building a single decision tree that predicts all classes at once. They evaluated these approaches

on twenty-four bioinformatics data sets, from which we have selected sixteen to use in this paper, using as protein functional classification schemes the FunCat (tree structure) and Gene Ontology (directed acyclic graph structure). Alves et al. [1] proposes two versions of Artificial Immune Systems (AIS) algorithms for hierarchical multi-label classification using the Gene Ontology functional-definition scheme. AIS are computational systems based on the characteristics—mainly the capability of learning and memory—of biological immune systems.

Holden and Freitas [17] propose a method to improve the performance of top-down hierarchical classification, wherein a hybrid particle swarm optimisation (PSO) / ant colony optimisation (ACO) algorithm is used to select—out of a set of predefined candidate classification algorithms—the best (most accurate) classification algorithm to be used at each node of the class hierarchy. This ‘selective’ top-down approach is based on a previous work presented in [35], where the selection of the best algorithm at each node is done in a greedy fashion, rather than using the PSO/ACO algorithm. In Holden and Freitas [18], different ensembles of rules are built for each level of the class hierarchy—using the training examples at the level—and a PSO algorithm is used to optimise the weights used to combine the predictions of different rules in a top-down fashion. While both works are in the context of hierarchical classification, they have been applied to hierarchical single-label classification dealing with tree-structured class hierarchies. Therefore, they cannot be straightforwardly applied to the data sets used in this paper, which involves hierarchical multi-label classification dealing with both tree-structured and DAG-structured class hierarchies.

### 3 Ant Colony Optimisation

Inspired by the behaviour of natural ant colonies, Dorigo and Stützle [13] have defined an artificial ant colony metaheuristic that can be applied to solve optimisation problems, called Ant Colony Optimisation (ACO). The main idea for the definition of ACO came from the fact that many ant species, even with limited visual capabilities or completely blind, are able to find the shortest path between a food source and the nest. It was discovered that most of the communication among individual ants is based on the use of a chemical, called pheromone, that is dropped on the ground. As ants walk from a food source to the nest, pheromone is deposited on the ground, creating in this way a pheromone trail on the path used. Shorter paths will be traversed faster and, by consequence, will have stronger pheromone concentration than longer paths over a given period of time. The more pheromone a path contains, the more attractive it becomes to be followed by other ants. Hence, as time goes by, more and more ants will prefer the shorter path, which will have more and more pheromone. In the end, (almost) all ants will be following a single path, which usually will represent the shorter path between the food source and the nest.

Ant Colony Optimisation algorithms simulate the behaviour of real ants using a colony of artificial ants, which cooperate in finding good solutions to optimisation problems. Each artificial ant, representing a simple agent, builds candidate solutions to the problem at hand and communicates indirectly with other artificial ants by means of pheromone values. At the same time that ants perform a global search for new solutions, the search is guided to better regions of the search space based on the quality of solutions found so far. The algorithm converges to good solutions as a result of the collaborative interaction among the ants; an ant probabilistic chooses a trail to follow based on heuristic information and pheromone values, deposited by previous ants. The interactive process of building candidate solutions and updating pheromone values allows an ACO algorithm to converge to optimal or near-optimal solutions. The main aspects of an ACO algorithm are as follows:

- *problem representation*: the problem is mapped to a graph representation that is used by the artificial ants to build solutions. Ants perform randomized walks on a graph  $G_c = (C, L)$ , where the set  $C$  represents the vertices of the graph and the set  $L$  represent the edges between the vertices, in order to build solutions. The graph  $G_c$  represents the problem search space;
- *building solutions*: each ant incrementally builds a candidate solution by moving through neighbour vertices of the graph  $G_c$ . The vertices to be visited are chosen in a stochastic decision process, where the probability of choosing a particular vertex depends on both the amount of pheromone ( $\tau$ ) associated with the vertex (or the edge leading to the vertex) and a problem dependent heuristic information ( $\eta$ ). Hence, a candidate solution is represented by a trail in the graph  $G_c$ ;
- *indirect communication*: after building a candidate solution, an ant evaluates the solution in order to decide how much pheromone to deposit in the solution’s trail. In general, the amount of pheromone deposited is proportional to the quality of the candidate solution. The deposit of pheromone increases the probability that vertices/edges used in a solution will be used again by different ants.

ACO algorithms have been successfully applied to several different flat (non-hierarchical) classification problems, as reviewed in [15]. The first implementation of an ACO algorithm for discovering classification rules, named Ant-Miner, was presented in [29] and more recently variations were proposed in [25, 26, 27, 28]. Ant-Miner, and consequently its variations, combines a traditional machine learning’s sequential covering approach with an ACO-based classification rule induction procedure. The sequential covering approach consists of an iterative process of creating on-rule-at-a-time, removing examples from the training set until there are no uncovered training examples (i.e., training examples not classified by any of the created rules). Following the sequential covering approach, a rule is created using an ACO procedure at each iteration of the process in Ant-Miner.

Despite the Ant-Miner variations for flat classification proposed in the literature, extending Ant-Miner to hierarchical multi-label classification problems is a research topic that has not yet been explored by other authors, to the best of our knowledge. In the context of hierarchical and multi-label classification, there are two Ant-Miner variations which are worthy of mentioning.

Chan and Freitas [8] proposed a new ACO algorithm, named MuLAM (Multi-Label Ant-Miner), for discovering multi-label classification rules. In essence, MuLAM differs from the original Ant-Miner in three aspects, as follows. Firstly, a classification rule can predict one or more class attributes, as in multi-label classification problems an example can belong to more than one class. Secondly, each iteration of MuLAM creates a set of rules instead of a single rule as in the original Ant-Miner. Thirdly, it uses a pheromone matrix for each class value and pheromone updates only occur on the matrix of the class values that are present in the consequent of a rule. In order to cope with multi-label data, MuLAM employs a criterion to decide whether one or more class values should be predicted by the same rule.

Otero et al. [28] proposed an extension of the flat classification Ant-Miner algorithm tailored for hierarchical classification problems, named *hAnt-Miner* (Hierarchical Classification Ant-Miner), employing a hierarchical rule evaluation measure to guide pheromone updating, a heuristic information adapted for hierarchical classification, as well as an extended rule representation to allow hierarchically-related classes in the consequent of a rule. However, *hAnt-Miner* cannot cope with hierarchical multi-label problems, where an example can be assigned to multiple classes that are not ancestor/decendant of each other. Since in this paper we focus on extending the ideas of *hAnt-Miner* into the hierarchical multi-label classification problem, a more detailed overview is presented in Subsection 3.1.

### 3.1 An Overview of Hierarchical Classification Ant-Miner

The target problem of *hAnt-Miner* algorithm is the discovery of hierarchical classification rules in the form *IF antecedent THEN consequent*. The antecedent of a rule is composed by a conjunction of conditions based on predictor attribute values (e.g. *length > 25 AND IPR00023 = yes*) while the consequent of a rule is composed by a set of class labels in potentially different levels of the class hierarchy respecting ancestor/decendant class relationships (e.g., GO:0005216, GO:0005244—where GO:0005244 is a subclass of GO:0005216). *hAnt-Miner* divides the rule construction process into two different ant colonies, one colony for creating antecedent of rules and one colony for creating consequent of rules, and the two colonies work in a cooperative fashion.

In order to discover a list of classification rules, a sequential covering approach is employed to cover all (or almost all) training examples. Algorithm 1 presents a high-level pseudocode of the sequential covering procedure employed in *hAnt-Miner*. The procedure starts with an empty

rule list (*while* loop) and adds a new rule to the rule list while the number of uncovered training examples is greater than a user-specified maximum value. At each iteration, a rule is created by an ACO procedure (*repeat-until* loop). Given that a rule is represented by paths in two different construction graphs (illustrated in Fig. 1), antecedent and consequent, two separate colonies are involved in the rule construction procedure. Ants in the antecedent colony create paths on the antecedent construction graph while ants in the consequent colony create paths on the consequent construction graph. In order to create a rule, an ant from the antecedent colony is paired with an ant from the consequent colony (the first ant from the antecedent colony is paired with the first ant from the consequent colony, and so forth), so that the construction of a rule is synchronized between the two ant colonies. Therefore, it is a requirement that both colonies have the same number of ants. The antecedent and consequent paths are created by probabilistically choosing a vertex to be added to the current path (antecedent or consequent) based on the values of the amount of pheromone ( $\tau$ ) associated with edges and problem-dependent heuristic information ( $\eta$ ) associated with vertices. There is a restriction that the antecedent of the rule must cover at least a user-defined minimum number of examples, to avoid overfitting.

Once the rule construction procedure has finished, the rules constructed by the ants are pruned to remove irrelevant terms (attribute-value conditions) from their antecedent—which can be regarded as a local search operator—and class labels from their consequent. Then, pheromone levels are updated using the best rule (based on a quality measure  $Q$ ) of the current iteration and the best-so-far rule (across all iterations) is stored. The rule construction procedure is repeated until a user-specified number of iterations has been reached, or the best-so-far rule is exactly the same in a predefined number of previous iterations. The best-so-far rule found is added to the rule list and the covered training examples—i.e. examples that satisfy the rule’s antecedent conditions—are removed from the training set.

Overall, *hAnt-Miner* can be regarded as a memetic algorithm [23], in the sense that it combines conventional concepts and methods of the ACO metaheuristic with concepts and methods of conventional rule induction algorithms (e.g. the sequential covering and rule pruning procedures), as discussed earlier.

#### 3.1.1 Hierarchical Rule Evaluation

*hAnt-Miner* uses a variation of the hierarchical accuracy measure proposed by [21] in order to evaluate rules constructed by ants. Firstly, the set of predicted class labels  $P_r$  of rule  $r$  is extended with the corresponding ancestor labels ( $P_r'$ ) as

$$P_r' = P_r \cup \{\cup_{l_i \in P_r} \text{Ancestors}(l_i)\} - l_{root}, \quad (1)$$

where  $\text{Ancestors}(l_i)$  corresponds to all ancestor class labels of the class label  $l_i$  and  $l_{root}$  is the root class label of the

**Algorithm 1** High-level pseudocode of the sequential covering procedure employed in *hAnt-Miner*. The rule construction process in *hAnt-Miner* involves two separate colonies, one for the creation of the antecedent of a rule and one for the creation of the consequent of a rule.

**input** : *training examples*  
**output**: *discovered rule list*

```

1 begin
2   training_set ← all training examples;
3   rule_list ← 0;
4   while |training_set| > max_uncovered_examples do
5     rule_best ← 0;
6     i ← 1;
7     repeat
8       rule_current ← 0;
9       for j ← 1 to colony_size do
10        // use separate ant colonies for antecedent and consequent construction
11        rule_j ← CreateAntecedent() + CreateConsequent();
12        // applies a local search operator
13        Prune(rule_j);
14        // updates the reference to the best rule of the iteration
15        if Q(rule_j) > Q(rule_current) then
16          | rule_current ← rule_j;
17        end
18        j ← j + 1;
19      end
20      UpdatePheromones(rule_current);
21      if Q(rule_current) > Q(rule_best) then
22        | rule_best ← rule_current;
23      end
24      i ← i + 1;
25    until i ≥ max_number_iterations OR RuleConvergence();
26    rule_list ← rule_list + rule_best;
27    training_set ← training_set - Covered(rule_best, training_set);
28  end
29  return rule_list;
30 end

```

hierarchy. Then, the hierarchical measures of precision (*hP*) and recall (*hR*) are computed as

$$hP = \frac{\sum_{i \in S_r} \frac{|A_i \cap P_r'|}{|P_r'|}}{|S_r|} \quad hR = \frac{\sum_{i \in S_r} \frac{|A_i \cap P_r'|}{|A_i|}}{|S_r|}, \quad (2)$$

where  $S_r$  is the set of all examples covered by (satisfying the rule antecedent of) rule  $r$  and  $A_i$  is the set of actual (true) class labels of the  $i$ -th example. The hierarchical precision (*hP*) is the average number of true class labels that are predicted by rule  $r$  divided by the total number of predicted class labels across the examples covered by rule  $r$ ; the hierarchical recall (*hR*) is the average number of true class labels that are predicted by rule  $r$  divided by the total number of true class labels which should have been predicted across the examples covered by rule  $r$ . Finally, the rule quality measure  $Q$  is defined as a combination of the *hP* and *hR* measures, equivalent to the hierarchical F-measure, given by

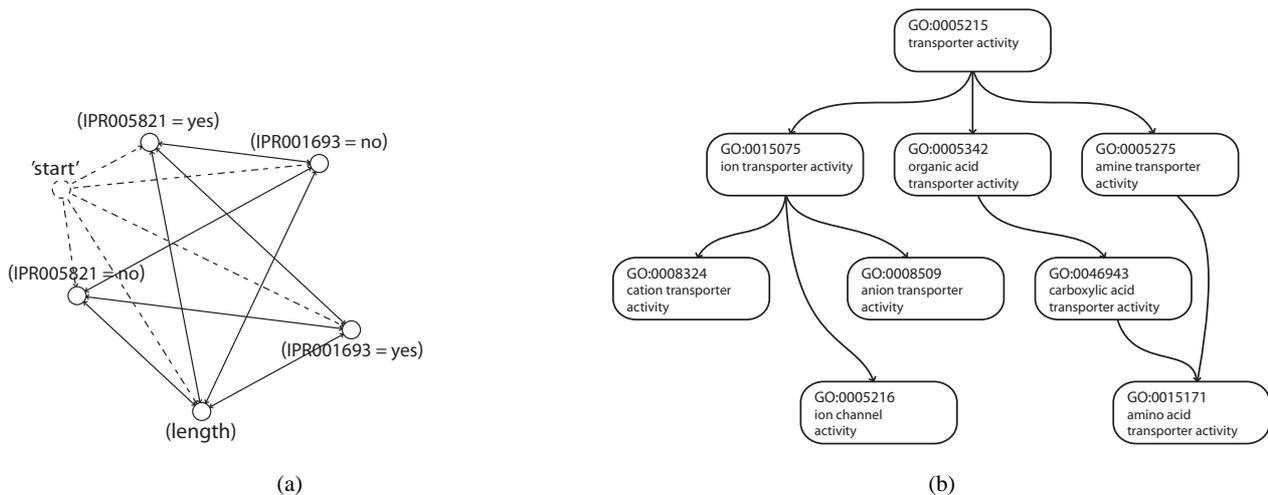
$$Q = hF = \frac{2 \cdot hP \cdot hR}{hP + hR}. \quad (3)$$

### 3.1.2 Heuristic Information

*Antecedent Heuristic Information* As in *Ant-Miner*, the heuristic information used in the antecedent construction graph is based on information theory, more specifically, it involves a measure of the entropy associated with each term (vertex) of the graph. The entropy for a term  $T$  is computed as

$$entropy(T; S) = \sum_{k=1}^{|L|} -p(l_k | S_T) \cdot \log_2 p(l_k | S_T), \quad (4)$$

where  $p(l_k | S_T)$  is the empirical probability of observing the class label  $l_k$  conditional on having observed term  $T$  in the set of training examples  $S$  and  $|L|$  is the total number of class labels. Equation (4) is a direct extension of the heuristic function of the original *Ant-Miner* [29] for flat classification into the problem of hierarchical classification. Since the entropy of a term  $T$  of the antecedent construction graph varies in the range  $0 \leq entropy(T) \leq \log_2(|L| - 1)$  (where  $|L| - 1$  is the number of class labels in the class hierarchy without considering the root class label) and lower entropy values are preferred over higher values, the heuristic information for a term  $T$  is computed as



**Fig. 1** Examples of the construction graphs employed in *hAnt-Miner*: in (a) the antecedent construction graph (*IPR005821* and *IPR001693* are binary attributes, and *length* is a continuous attribute), where the dummy *start* vertex is unidirectionally connected to all vertices to allow the association of pheromone values on the edge of the first term of the antecedent of a rule; (b) the consequent construction graph, which is defined by the class hierarchy of the problem at hand (in this case, the class hierarchy is represented by a subset of the Gene Ontology’s ion channel hierarchy).

$$\eta_T = \log_2(|L| - 1) - \text{entropy}(T; S), \quad (5)$$

where  $S$  is the set of training examples. Equation (5) will give a higher probability of being selected to terms with lower entropy values, which correspond to terms with higher predictive power.

*Consequent Heuristic Information* The heuristic information used in the consequent construction graph is based on the frequency of training examples for each class label of the hierarchy, given by

$$\eta_{l_k} = |TR_{l_k}|, \quad (6)$$

where  $|TR_{l_k}|$  is the number of training examples that belong to class label  $l_k$  and  $l_k$  is the  $k$ -th class label of the class hierarchy  $L$ .

### 3.1.3 Using a Rule List to Classify New Examples

In order to classify a test (unseen) example, rules in the discovered rule list are applied in a sequential order—i.e. the order in which they were discovered. Therefore, a test example is classified according to the consequent of the first rule that covers the example. More precisely, the example is assigned the class labels predicted by the rule’s consequent.

In the situation where no rule in the discovered rule list covers the test example, a default rule (a rule with an empty antecedent) predicting the set of class labels that occur in all uncovered training examples is used to classify the test example. For example, assuming that there are three uncovered examples  $e_1$ ,  $e_2$  and  $e_3$ , belonging to class labels

$\{1, 1.2, 1.2.1\}$ ,  $\{1, 1.2, 1.2.2\}$  and  $\{1, 1.2, 1.2.1, 1.2.1.3\}$ , respectively. The set of class labels occurring in all uncovered examples comprise the set  $\{1, 1.2\}$ , which would be the set of predicted class labels of the default rule.

## 4 A New Ant Colony Algorithm for Hierarchical Multi-Label Classification

While analysing *hAnt-Miner*, we have identified the following limitations. Firstly, the heuristic information, which involves a measure of entropy, used in *hAnt-Miner* is not very suitable for hierarchical classification—i.e. it does not take into account the hierarchical relationships between classes. Although *hAnt-Miner*’s entropy measure is calculated throughout all labels of the class hierarchy (apart from the root label), each class label is evaluated individually without considering parent-child relationships between class labels.

Secondly, the rule quality measure is prone to overfitting. Since only the examples covered by the rule are considered in the rule evaluation, rules with a small coverage are favoured over more generic rules. For example, considering the class label 1.2.1 with 20 examples and two rules that have class 1.2.1 as the most specific class label in their consequent:  $rule_1$  covering correctly 5 examples out of a total of 5 covered and  $rule_2$  covering correctly 19 examples out of a total of 20 covered. In this case,  $rule_1$  would have a higher quality, since all the examples covered by the rule are correctly classified, than  $rule_2$ , which misclassifies one example, though  $rule_2$  covers all but one examples belonging to class 1.2.1. One could argue that the rule quality measure of *hAnt-Miner* could be easily modified to avoid overfitting by evaluating a rule considering all the examples of its most specific class. The drawback of this approach is that

it favours rules predicting class labels at the top of the hierarchy, since the numbers of examples per class are greater at top class levels. This could potentially prevent the discovery of rules predicting more specific class labels given that the examples covered by a rule are removed from the training set—indeed, this problem was observed in some preliminary experiments.

Thirdly, *hAnt-Miner* does not support multi-label data since a single path in the consequent construction graph corresponds to the consequent of a rule. In the case of protein function prediction, where it is known that a protein can perform more than one function, this is an important limitation.

This section presents a new hierarchical multi-label ant colony classification algorithm, named *hmAnt-Miner* (Hierarchical Multi-Label Classification Ant-Miner), which is aimed at overcoming the aforementioned limitations. While *hmAnt-Miner* shares the same underlying procedure of the *hAnt-Miner* algorithm, presented in Algorithm 1, it differs from *hAnt-Miner* in the following aspects:

- the consequent of a rule is calculated using a deterministic procedure based on the examples covered by the rule, allowing the creation of rules that can predict more than one class label at the same time (multi-label rules). Therefore, *hmAnt-Miner* uses a single construction graph in order to create a rule—only the antecedent is represented in the construction graph;
- the heuristic function is based on the Euclidean distance, where each example is represented by a vector of class membership values in the Euclidean space. By using a distance measure, instead of entropy as in *hAnt-Miner*, it is possible to take into account the relationship between class labels given that examples belonging to related (ancestor/decendant) class labels will be more similar than examples belonging to unrelated class labels. The use of the Euclidean distance was inspired by a similar use in the CLUS-HMC algorithm for hierarchical multi-label classification [38], which is based on the paradigm of decision tree induction, rather than rule induction. Note that the Euclidean distance is used as the heuristic information, as well as in the dynamic discretisation procedure of continuous attributes;
- the rule quality is evaluated using a distance-based measure, which is a more suitable evaluation measure for hierarchical multi-label problems;
- the pruning procedure is not applied to the consequent of a rule. The consequent of a rule is (re-)calculated when its antecedent is modified during pruning, since the set of covered examples might have changed.

#### 4.1 Multi-Label Rule Consequent

Recall that the consequent of a rule in *hAnt-Miner* is represented as a path in the consequent construction graph, where a trail is a single path from the root class label towards a leaf class label in the class hierarchy. Although the consequent predicts multiple class labels in a hierarchical structure, it

has the limitation of not being able to predict unrelated class labels—i.e. multiple paths in the class hierarchy. One could argue that the consequent could be represented by multiple trails in order to be able to predict unrelated class labels, however it is not clear how to find the optimal combination and number of trails to consider without introducing yet another user-defined parameter.

A sensible approach is to use the information available from the examples covered by the rule (i.e. examples that satisfy the rule antecedent) in order to determine the rule consequent. Therefore, the consequent of a rule in *hmAnt-Miner* is calculated using a deterministic procedure as follows. Given the set of examples  $S_r$  covered by a rule  $r$ , the consequent is a vector of length  $m$  (where  $m$  is equal to the number of class labels in the class hierarchy). The value for each  $i$ -th component of the consequent vector for rule  $r$  is given by

$$\text{consequent}_{r,i} = \frac{|S_r \ \& \ \text{label}_i|}{|S_r|}, \quad (7)$$

where  $|S_r \ \& \ \text{label}_i|$  is the number of examples covered by rule  $r$  that belong to the  $i$ -th class of the class hierarchy ( $\text{label}_i$ ). In other words, the consequent of a rule is a vector where each  $i$ -th component is the proportion of covered examples that belong to the  $i$ -th class label.

According to Equation (7), each position of the consequent vector is a continuous value between 0.0 and 1.0, rather than a presence/absence value of a particular class label. As a result, the value in the  $i$ -th component of the consequent of a rule represents the probability of an example that satisfies its antecedent to belong to the correspondent  $i$ -th class of the hierarchy. Figure 2 illustrates the consequent of a rule discovered by *hmAnt-Miner*; in this example, the predictor attributes in the antecedent of the rule correspond to amino acid ratios from the protein’s sequence and the class labels in the consequent of the rule are represented by Gene Ontology terms—the number following the colon of a class label in the consequent corresponds to the probability of predicting the associated class label.

In order to obtain class label predictions from a rule, it is necessary to select a classification threshold. If the value of the  $i$ -th component is greater than or equal to the classification threshold, the correspondent  $i$ -th class label is predicted. Note that the consequents of the rules fulfil the requirements for the hierarchical multi-label classification task: (1) the classes predicted are consistent with the class hierarchy, since the probability of a parent class label is always equal to or greater than the probability of its children class labels; (2) multiple unrelated classes can be predicted according to the examples covered by the rule.

The same deterministic procedure is applied to compute the consequent of the default rule when classifying an unseen example, as described in Subsection 3.1.3, with the difference that the uncovered set of examples (i.e., the set of examples which is not covered by any rule) is taken into account in Equation (7).

```

IF
    aa_rat_pair_a_h >= 0.053
    AND aa_rat_pair_t_c >= 0.1055
    AND aa_rat_pair_c_w < 0.0695
    AND aa_rat_pair_a_e < 0.2960
    AND aa_rat_pair_t_h >= 0.0275
THEN
    GO0000226:0.10,GO0000943:0.50,
    GO0001302:0.10,GO0003674:1.00,
    GO0003676:0.50,GO0003723:0.50,
    GO0003824:0.50,GO0003887:0.50,
    ...
    GO0044464:1.00,GO0045053:0.10,
    GO0045185:0.10,GO0046907:0.20,
    GO0051234:0.20,GO0051235:0.10,
    GO0051649:0.20,GO0051651:0.10

```

**Fig. 2** Example of the consequent of a rule discovered by *hmAnt-Miner*; in this example, the predictor attributes in the antecedent of the rule correspond to amino acid ratios from the protein’s sequence and the class labels in the consequent of the rule are represented by Gene Ontology terms—the number following the colon of a class label in the consequent corresponds to the probability of predicting the associated class label. Only a subset of the class labels predicted by the rule are shown.

#### 4.2 Distance-based Heuristic Information

According to Subsection 3.1.2, the heuristic information in *hAnt-Miner* involves a measure of entropy, as in the original *Ant-Miner*. The entropy characterizes the homogeneity of a collection of examples related to the class attribute values, giving a notion of (im-)purity of the class values’ distribution. The more examples of the same class the lower the value of entropy will be and the ‘purest’ is the collection of examples. It should be noted that in all calculations involving entropy, the different class labels (values) are independently evaluated—i.e. no relationship between class labels is taken into account. In the case of *Ant-Miner*, which is applied to flat classification problems, the use of the entropy measure does not present a limitation, since there is no relationship between class labels. On the other hand, the same cannot be said for *hAnt-Miner*, which aims at extracting hierarchical classification rules, derived from data where the class labels are organised in a hierarchical structure.

To illustrate the limitation of the entropy measure when used in hierarchical problems, let us consider the following example. Given a tree-structured class hierarchy, where labels  $\{1, 2, 3\}$  are children of the root label and labels  $\{2.1, 2.2\}$  are children of the ‘2’ label and each class label has 10 examples. Although the entropy is calculated—according to Equation (4)—across all class labels, the hierarchical relationships are not taken into account. Therefore, the entropy of a hypothetical term ‘*IPR00023 = yes*’ which is present in 10 examples of class ‘1’ and in 10 examples of class ‘3’ would be the same as of a hypothetical term ‘*IPR00023 = no*’ which is present in 10 examples of class ‘2’ and in 10 examples of class ‘2.1’. The drawback in this

case is that it is known that class labels ‘2’ and ‘2.1’ are more similar than class labels ‘1’ and ‘3’. Hence, it would be expected/desired that the entropy measure (or an alternative heuristic information) exploit hierarchical relationships in order to better reflect the quality of each term in the case of hierarchical classification problems. Intuitively this becomes even more important when dealing with bigger (in terms of number of class labels and depth) hierarchical structures. It should be noted that several *Ant-Miner* variations—as discussed in [15]—have used a heuristic information based on the relatively frequency of the class predicted by the rule (or the majority class) among all the examples that have a particular term, which would also present the above limitation.

*hmAnt-Miner* employs a distance-based heuristic information, which directly incorporates information from the class hierarchy. More precisely, the heuristic information of a term corresponds to the variance of the set of examples covered by the term (the set of examples that satisfy the condition represented by the term). In order to calculate the variance, the class labels of each example are represented by a numeric vector of length  $m$  (where  $m$  is the number of class labels of the hierarchy without considering the root label). The  $i$ -th component of the class label vector of an example is equal to 0 or 1 if the correspondent class label is absent or present, respectively. The distance between class label vectors is defined as the weighted Euclidean distance, given by

$$distance(\mathbf{v}_1, \mathbf{v}_2) = \sqrt{\sum_{i=1}^m w(l_i) \cdot (\mathbf{v}_{1,i} - \mathbf{v}_{2,i})^2}, \quad (8)$$

where  $w(l_i)$  is the weight associated with the  $i$ -th class label,  $\mathbf{v}_{1,i}$  and  $\mathbf{v}_{2,i}$  are the values of the  $i$ -th component of the class label vectors  $\mathbf{v}_1$  and  $\mathbf{v}_2$ , respectively. Then, the variance of a set of examples is defined as the averaged squared distance between each example’s class label vector and the set’s mean class vector, given by

$$variance(S_T) = \frac{\sum_{k=1}^{|S_T|} distance(\mathbf{v}_k, \bar{\mathbf{v}})^2}{|S_T|}, \quad (9)$$

where  $S_T$  is the set of examples covered by a term  $T$  and  $\bar{\mathbf{v}}$  is the set’s mean class label vector. Finally, the heuristic information of a term  $T$  is given by

$$\eta_T = \frac{variance_{max} - variance(S_T)}{variance_{max}}, \quad (10)$$

where  $variance_{max}$  is defined as the sum of the worst and best variance values observed across all terms in order to assign values greater than zero to the worst terms, which otherwise would avoid them to be selected by an ant. Note that the heuristic value is normalised so the smaller the value of the variance of a term  $T$  the greater its heuristic value becomes. This is analogous to the use of the entropy measure in *Ant-Miner* and *hAnt-Miner*, where smaller values are preferred

over bigger values since they correspond to a more homogeneous partition (where the great majority of examples belong to the same class).

Recall that the distance function in Equation (8) requires the definition of a class-specific weight. In Vens et al. [38], where the proposed CLUS-HMC algorithm also uses a variance measure based on a weighted Euclidean distance, several weighting schemes have been evaluated in the context of hierarchical multi-label classification. As a result of their findings, the preferred weighting scheme—and the one used in *hmAnt-Miner*—is defined as

$$w(l) = w_0 \cdot \frac{\sum_{i=1}^{|P_l|} w(p_i)}{|P_l|}, \quad (11)$$

where  $w_0$  is set to 0.75 (based on [38]),  $P_l$  is the parent class label set of the class label  $l$  and  $w(p_i)$  is the weight associated with the  $i$ -th parent class label of the class label  $l$ . In other words, the weight of a class label  $l$  is the multiplication of the  $w_0$  weight and the average weight of its parent class labels. For class labels at the top of the hierarchy (children of the root label), their weights are set to  $w_0$ . According to Equation (11), class labels appearing higher in the hierarchy will have greater weights than class labels appearing lower in the hierarchy. Therefore, concerning the weighted distance function in Equation (8), similarities at higher levels of the hierarchy are more important than similarities at lower levels.

#### 4.3 Distance-based Discretisation of Continuous Values

As discussed in Subsection 4.2, the entropy measure is not very suitable for hierarchical multi-label classification problems. Therefore, the entropy-based discretisation procedure employed by *hAnt-Miner* (derived from *cAnt-Miner* [26]) presents the same limitation of evaluating each of the class labels individually, not taking into account their relationships. Consequently, the quality of continuous attributes threshold values are compromised, which can lead to poor discovered rules.

Using the variance measure previously defined in Equation (9), *hmAnt-Miner* employs a distance-based discretisation procedure of continuous attributes values in its rule construction process. Given a continuous attribute  $y_i$ , the basic idea is to find a threshold value  $v$  (where  $v$  is a value in the domain of attribute  $y_i$ ) that maximises the variance gain of both  $(y_i < v)$  and  $(y_i \geq v)$  generated partitions of examples—i.e. the set of examples which have the value of attribute  $y_i$  less than  $v$  and the set of examples which have the value of the attribute  $y_i$  greater than or equal to  $v$ —relative to a set of examples  $S$ . The distance-based discretisation procedure, dubbed variance-gain discretisation, is divided into two steps as follows.

Let  $y_i$  be a continuous attribute to undergo the discretisation process and  $v$  a value in the domain of  $y_i$ . The best

threshold value for attribute  $y_i$  is the value  $v$  which minimises the variance of both  $(y_i < v)$  and  $(y_i \geq v)$  generated partitions of examples from  $S$ , maximising the variance gain relative to  $S$  as a result, given by

$$\begin{aligned} \text{variance\_gain}(y_i, v) = & \text{variance}(S) \\ & - \frac{|S_{y_i < v}|}{|S|} \cdot \text{variance}(S_{y_i < v}) \\ & - \frac{|S_{y_i \geq v}|}{|S|} \cdot \text{variance}(S_{y_i \geq v}), \end{aligned} \quad (12)$$

where  $|S_{y_i < v}|$  is the total number of examples in the partition  $y_i < v$  (partition of training examples where the attribute  $y_i$  has a value less than  $v$ ),  $|S_{y_i \geq v}|$  is the total number of training examples in the partition  $y_i \geq v$  (partition of training examples where the attribute  $y_i$  has a value greater than or equal to  $v$ ) and  $|S|$  is the total number of training examples. The values of  $\text{variance}(S)$ ,  $\text{variance}(S_{y_i < v})$  and  $\text{variance}(S_{y_i \geq v})$  are calculated according to Equation (9). The variance gain measure is calculated for all values  $v$ , which comprises the average value of each pair of adjacent values  $v_t$  and  $v_{t+1}$  in the domain of the attribute  $y_i$ —computed as  $(v_t + v_{t+1})/2$ —and the value  $v$  with the highest variance gain associated is then selected as the best threshold value.

Note that the set of training examples  $S$  varies according to the context of the rule construction process, that is to say, the set of training examples  $S$  is restricted to the set of training examples covered by the current partial rule being constructed. The only exception to this restriction is when the current partial rule is empty, thus all training examples are used on the evaluation of threshold values. As a result of this restriction, the choice of a threshold value during the rule construction process is tailored to the current candidate rule.

After the selection of the best threshold value  $v$ , a relational operator is selected based on the individual variance values of the generated partitions, given by

$$\text{operator} = \begin{cases} < & \text{if } \text{variance}(S_{y_i < v}) < \text{variance}(S_{y_i \geq v}) \\ \geq & \text{if } \text{variance}(S_{y_i < v}) > \text{variance}(S_{y_i \geq v}) \end{cases}. \quad (13)$$

According to Equation (13), if the partition of examples  $y_i < v$  has a lower variance, then the operator ‘<’ (less-than operator) is selected; if the partition of examples  $y_i \geq v$  has a lower variance, then the operator ‘≥’ (greater-than-or-equal-to operator) is selected; ties are broken at random. As can be noticed, the operator selection has a bias of selecting the more homogeneous partition, given that lower variance values are preferred over higher values. This is analogous to the bias of the entropy-based discretisation of *hAnt-Miner*, where lower entropy values are preferred since they are associated with the ‘purest’ partition (the partition with more examples belonging to the same class).

At the end of the discretisation process, a term (a triple *attribute, operator, value*) is created to be added to the current partial rule (e.g.  $y_i < 20$ ) and the rule continues to undergo the rule construction process.

Concerning the computational time complexity of the entropy-based discretisation used in *hAnt-Miner* and the proposed distance-based discretisation in *hmAnt-Miner*, the process of finding a threshold value can be divided into two steps. First, both discretisation procedures require the sorting of continuous attribute values in order to facilitate the partition of examples. The time complexity of this step is  $O(n \cdot \log n)$ , where  $n$  is the number of training examples under consideration.

In the case of the entropy-based discretisation, the second step involves the evaluation of potentially  $n$  candidate threshold values—assuming that each training example has a different value for the continuous attribute undergoing discretisation<sup>1</sup>—over  $k$  different class labels. The complexity of this step is  $O(n \cdot k)$ , and the total complexity of the entropy-based discretisation is  $O(n \cdot \log n) + O(n \cdot k)$ .

In the case of the distance-based discretisation, the second step involves the calculation of the mean class label vector for each partition of training examples. This calculation has time complexity of  $O(n \cdot k)$ . Furthermore, it involves the calculation of the distance between each example's class label vector and the partition mean's class label vector in order to determine the variance of the partitions. Since each class label vector has  $k$  positions and there are potentially  $n$  candidate threshold values, the time complexity of the variance calculation is  $O(n \cdot k)$ . Given that for each candidate threshold value, the mean class label vectors of the partitions must be recalculated because a partition's example distribution varies according to the threshold value, the total time complexity of the distance-based discretisation is  $O(n \cdot \log n) + O([n \cdot k]^2)$ .

Intuitively, if both complexity notations are simplified by dropping the common element  $O(n \cdot \log n)$ , the entropy-based discretisation growing factor is linear in relation to  $n \cdot k$ , while the distance-based discretisation growing factor is quadratic in relation to  $n \cdot k$ . Therefore, the distance-based discretisation is more computationally complex than the entropy-based discretisation. It should be noted that the number of training examples  $n$  covered by a rule, and consequently the potential number of candidate threshold values, tends to decrease in relation to the number of terms in the antecedent of a rule. Hence, the efficiency of the discretisation procedure is increased at later stages of the rule construction process, since less candidate threshold values have to be evaluated.

<sup>1</sup> This represents the worse case scenario for the discretisation procedure, and in general, the number of candidate threshold values is smaller than the number of training examples.

#### 4.4 Hierarchical Multi-Label Rule Evaluation

Following a similar approach of using a distance-based measure for the discretisation of continuous values, the variance gain can be applied to compute a rule quality measure. The basic idea to evaluate a rule  $r$  using the variance gain measure is to virtually divide the training set  $S$  (where  $S$  corresponds to the set of all training examples) into two partitions: the set of examples covered by the rule  $r$  ( $S_r$ ) and the set of examples not covered by the rule  $r$  ( $S_{-r}$ ). Then, the variance gain of rule  $r$  relative to  $S$  can be computed as

$$\begin{aligned} \text{variance\_gain}(r, S) = & \text{variance}(S) \\ & - \frac{|S_r|}{|S|} \cdot \text{variance}(S_r) \\ & - \frac{|S_{-r}|}{|S|} \cdot \text{variance}(S_{-r}). \end{aligned} \quad (14)$$

The motivation of using the variance as a rule quality measure is as follows. Firstly, it can naturally cope with hierarchical multi-label data, taking into account the relationships and similarities between class labels. Secondly, it favours rules that partition the training set into a more homogeneous sets of examples. As a result, rules that cover a more homogeneous set of examples, as well as leaving uncovered a more homogeneous set of examples (which should facilitate the discovery of other rules in the future), are preferred.

#### 4.5 Simplified Rule Pruning

Since the consequent of a rule is determined as detailed in Subsection 4.1, *hmAnt-Miner* does not employ a second colony in order to construct the consequent of rules. Therefore, the rule pruning procedure is simplified as follows. The rule is submitted to a removal process of its antecedent's last term and has its consequent re-calculated, since the set of covered examples could change after the removal of the term. The removal process is repeated until the quality of the rule decreases when its last term is removed or the rule has only one term left in the antecedent.

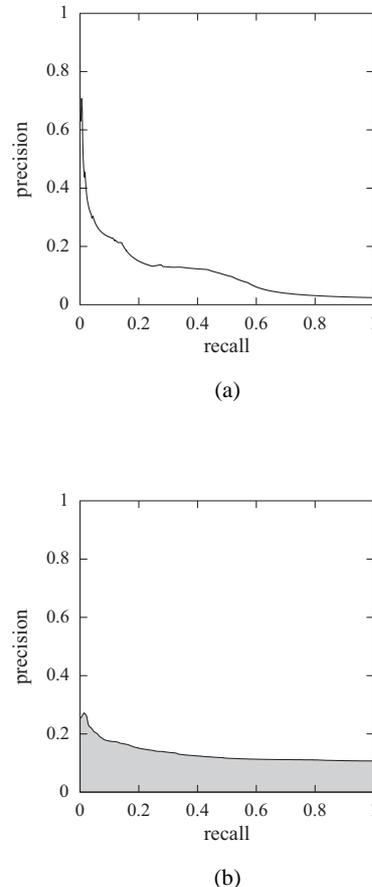
Let  $rule_{current}$  be the rule undergoing the pruning, which is considered the best rule at the beginning of the pruning procedure. At each iteration of the pruning procedure, a candidate rule  $rule_i$  is created by removing the last term of the antecedent of the current best  $rule_{best}$  and the consequent of  $rule_i$  is computed according to Subsection 4.1. Then, the quality measure  $q_i$  for  $rule_i$  is computed. If the quality measure  $q_i$  is higher than the current best quality  $q_{best}$ ,  $rule_i$  substitutes  $rule_{best}$ , completing an iteration of the pruning procedure. This procedure is repeated until  $rule_{best}$  has just one term left on its antecedent or a candidate rule  $rule_i$  does not improve the quality over  $rule_{best}$  (i.e.  $q_{best} > q_i$ ).

## 5 Evaluation Measure based on Precision-Recall Curves

As mentioned in Subsection 4.1, the consequent of a rule in *hmAnt-Miner* is a numeric vector, where each component of the vector is the probability associated with predicting a particular class label. If the  $i$ -th component value is above a specified classification threshold, then the  $i$ -th class label is predicted; otherwise it is not predicted. Instead of arbitrarily selecting a classification threshold value—or a set of threshold values—to evaluate a rule list, *hmAnt-Miner* employs a threshold-independent measure. As discussed by [38], a motivation for employing an evaluation measure independently from a classification threshold is that different contexts may require different threshold settings.

Precision-Recall (PR) curves have been frequently used in information retrieval [24, 32] and more recently in the context of hierarchical multi-label classification [38]. A PR curve plots a precision value against its recall value. The precision value corresponds to the number of correct predictions divided by the total number of predictions; the recall value corresponds to the number of correct predictions divided by the total number of positive examples—i.e., examples belonging to the predicted class label. One of the advantages of using PR curves as a performance measure is its suitability to cope with highly skewed data sets (data sets with a larger amount of negative examples in contrast to a smaller amount of positive examples) given that the number of negative examples is not involved to calculate precision and recall values—i.e. precision and recall measures only take into account the number of correct positive predictions (true positives), the number of incorrect positive predictions (false positives) and the number of incorrect negative predictions (false negative). Therefore, the number of correct negative predictions (true negatives) does not influence the evaluation. This is an important characteristic concerning hierarchical classification since, as previously mentioned, classes at the lower levels of the hierarchy have fewer (positive) examples. Therefore, it is more important to measure how well a rule predicts the presence of a particular class label (true positive examples) rather than its absence (true negative examples)—independent of whether the positive examples correspond to the majority class or not for the given class label.

A PR curve, illustrated in Figure 3, is defined by a set of points, where each point corresponds to a pair of precision and recall values for a particular classification threshold. Given a classification threshold  $t$ , decreasing the value of  $t$  from 1.0 to 0.0, different pairs of precision and recall values are obtained. With higher classification threshold values, fewer class labels are predicted (lower recall value) while the proportion of correct predictions tends to be greater (higher precision value). As the classification threshold is decreased, more class labels are predicted (higher recall values) while the proportion of correct prediction tends to decrease (lower precision values). Hence, the goal in PR curves is to be on the upper-right-corner, which corresponds to high precision and recall values.



**Fig. 3** Examples of precision-recall curves: (a) a PR curve showing that higher precision values are generally associated with lower recall values; (b) the shaded area of a PR curve corresponds to the area under the curve measure.

In order to compute the points of a PR curve, and thus calculate the area under the curve, we follow an approach described in [38]. This approach consists in creating an overall PR curve by micro-averaging precision and recall values across all class labels for a range of classification thresholds. The averaged precision ( $\overline{Prec}$ ) and recall ( $\overline{Rec}$ ) values for a classification threshold  $t$  is given by

$$\overline{Prec}_t = \frac{\sum_i TP_{t,i}}{\sum_i TP_{t,i} + \sum_i FP_{t,i}} \quad (15)$$

$$\overline{Rec}_t = \frac{\sum_i TP_{t,i}}{\sum_i TP_{t,i} + \sum_i FN_{t,i}},$$

where  $i$  ranges over all class labels (excluding the root label, since it is present in all examples),  $t$  ranges over all different probability values found in the vector of class labels probabilities, and  $TP_{t,i}$ ,  $FP_{t,i}$  and  $FN_{t,i}$  are the number of true positives, false positives and false negatives for the  $i$ -th class

label at the classification threshold  $t$ , respectively. The value of  $\overline{Prec}_t$  corresponds to the number of correct class labels predictions divided by the number of class labels predicted across all class labels for the given classification threshold  $t$ —i.e.,  $\overline{Prec}_t$  is the proportion of predicted class labels that are correct. The value of  $\overline{Rec}_t$  corresponds to the number of correct class labels predictions divided by the total number of class labels should have been predicted across all class labels for the given classification threshold  $t$ —i.e.,  $\overline{Rec}_t$  is the proportion of the available class labels that are correctly predicted. A pair of  $\overline{Prec}_t$  and  $\overline{Rec}_t$  values corresponds to a point of the PR curve.

Note that points of the PR curve must be interpolated in order to approximate the area under the curve, as discussed in [11]. After determining the points of the PR curve, the area under the PR curve can be approximated by calculating the trapezoidal areas created between each point. Finally, the evaluation measure is defined as the area under the averaged PR curve, denoted as  $AU(\overline{PRC})$ .

## 6 Computational Results

The proposed *hmAnt-Miner* algorithm was compared against three decision tree induction algorithms for hierarchical multi-label classification proposed in [38]: CLUS-SC, which consists in inducing a decision tree for each class label individually; CLUS-HSC, which consists in inducing decision trees in a top-down fashion; CLUS-HMC, which consists in inducing a single decision tree that predicts all class labels at once.

We have selected sixteen bioinformatics data sets from Vens et al. [38], which use two different class hierarchy structures: tree structure (FunCat data sets) and directed acyclic graph structure (Gene Ontology data sets). The directed acyclic graph (DAG) structure represents a complex hierarchical organisation, where a particular node of the hierarchy can have more than one parent, in contrast to only one parent in tree structures. Table 1 and 2 present details of the data sets used in our experiments. In the experiments conducted by Vens et al. [38], 2/3 of each data set was used for training and the remaining 1/3 for testing. We have used the same training and testing partitions in our experiments.

A summary of the user-defined parameters, their descriptions and correspondent values, used by *hmAnt-Miner* is shown in Table 3. We have used the same set of user-defined parameter values in all data sets, which are also considered a standard in the literature [29]; no attempt was made to tune either parameter value for individual data sets. The *hmAnt-Miner* experiments were performed on a Pentium 4 3.2GHz processor with 1GB of RAM running Linux. Each run of *hmAnt-Miner* took on average 2.62 hours (in the range of 0.32 to 6.24 hours, excluding ‘pheno’ data set which took 21 seconds) for FunCat data sets and 12.90 hours (in the range of 1.90 to 21.80 hours, excluding ‘pheno’ data set

**Table 1** Summary of the data sets used in our experiments. The first column (‘data set’) gives the data set name, the second column (‘|training|’) gives the number of training examples, the third column (‘|test|’) gives the number of test examples, the fourth column (‘|attributes|’) gives the number of attributes and the fifth column (‘|classes|’) gives the number of classes in the class hierarchy.

| FunCat        |          |      |            |         |
|---------------|----------|------|------------|---------|
| data set      | training | test | attributes | classes |
| celcycle      | 2476     | 1281 | 77         | 500     |
| derisi        | 2450     | 1275 | 63         | 500     |
| eisen         | 1587     | 837  | 79         | 462     |
| expr          | 2488     | 1291 | 551        | 500     |
| gasch1        | 2480     | 1284 | 173        | 500     |
| pheno         | 1009     | 582  | 69         | 456     |
| seq           | 2580     | 1339 | 478        | 500     |
| spo           | 2437     | 1266 | 80         | 500     |
| Gene Ontology |          |      |            |         |
| data set      | training | test | attributes | classes |
| celcycle      | 2473     | 1278 | 77         | 4126    |
| derisi        | 2447     | 1272 | 63         | 4120    |
| eisen         | 1583     | 835  | 79         | 3574    |
| expr          | 2485     | 1288 | 551        | 4132    |
| gasch1        | 2477     | 1281 | 173        | 4126    |
| pheno         | 1005     | 581  | 69         | 3128    |
| seq           | 2568     | 1332 | 478        | 4134    |
| spo           | 2434     | 1263 | 80         | 4120    |

**Table 2** The average number of class labels in the hierarchy and the average number of class labels per example of both FunCat and Gene Ontology data sets.

|                            | FunCat | Gene Ontology |
|----------------------------|--------|---------------|
| average number of classes  | 489    | 3932          |
| average labels per example | 8.5    | 34.2          |

which took 151 seconds) for Gene Ontology data sets.<sup>2</sup> The data sets with a large number of attributes, namely ‘expr’ and ‘seq’, are the most time consuming in both FunCat and Gene Ontology data sets.

We compared all algorithms in terms of predictive accuracy using a measure derived from precision-recall (PR) curves, more specifically the area under the averaged PR curve, denoted as  $AU(\overline{PRC})$ —discussed in Section 5. Since *hmAnt-Miner* is a stochastic algorithm, *hmAnt-Miner* was run 15 times—using a different random seed to initialise the search each time—for each data set. Therefore, the value of  $AU(\overline{PRC})$  reported for each data set corresponds to the average value obtained over 15 runs of the algorithm, followed

<sup>2</sup> The time taken by CLUS decision tree induction algorithms is reported in [38], but in that work a cluster was used, so the time reported in that work cannot be meaningfully compared with the time reported for our experiments in a single processor.

by the standard deviation (*average  $\pm$  standard deviation*). For CLUS-SC, CLUS-HSC and CLUS-HMC, the  $AU(\overline{PRC})$  value for each data set corresponds to the value obtained with a single run of the algorithm, since they are deterministic algorithms.

Table 4 shows the  $AU(\overline{PRC})$  value obtained on the test set by each algorithm and the induced classification model size across all data sets used in our experiments, using FunCat and Gene Ontology, respectively. Figure 4 illustrates a sample of precision-recall curves of *hmAnt-Miner*, CLUS-HMC, CLUS-HSC and CLUS-SC for ‘cellycycle’, ‘pheno’ and ‘seq’ FunCat data sets and ‘seq’, ‘eisen’ and ‘pheno’ Gene Ontology data sets. As discussed in Section 5, the closest to the upper-right corner, the better (more accurate) the curve. For *hmAnt-Miner*, the classification model size is defined as the number of rules discovered; for CLUS-HMC, CLUS-HSC and CLUS-SC the model size is defined as the number of leaf nodes in the induced decision tree, since each path from the root node to a leaf node can be viewed as a rule. In this way, the classification model size for both types of algorithms represents an overall measure of the complexity of the model. It should be noted that *hmAnt-Miner* discovers a rule list and the order in which rules are organised is relevant when classifying new examples. Given a new example, the prediction of its class labels is made by the first rule that covers the example, following the order of the rule list—as detailed in Subsection 3.1.3. Therefore, a particular rule is used only if its previous rules do not cover the example—i.e. if its previous rules have not been used. On the other hand, a decision tree can be converted into a set of rules [30], where the order of rules is not relevant, and therefore each rule can be individually analysed.

*Comparison of hmAnt-Miner and CLUS-HSC/SC to CLUS-HMC:* Table 5 presents the summary of the comparisons of the CLUS-HMC algorithm—the algorithm with the best average rank—with the remaining algorithms used in our experiments according to the non-parametric Friedman test with the Holm’s post-hoc test [12, 16] in terms of predictive accuracy and classification model size. For each algorithm, the average rank and the adjusted  $p$ -value obtained by Holm’s post-hoc test are reported using both FunCat and Gene Ontology data sets (‘Combined’ column), using only FunCat data sets (‘FunCat’ column) and using only Gene Ontology data sets (‘Gene Ontology’ column)—the lower the averaged rank, the better the algorithm’s performance.

According to Table 5, there are no statistically significant differences at the 0.01 significance level between *hmAnt-Miner* and CLUS-HMC, in terms of both predictive accuracy and classification model size in all of the experiments; CLUS-HMC performs significantly better than CLUS-HSC in terms of predictive accuracy on the FunCat data sets and in terms of both predictive accuracy and classification model size on the combined (both FunCat and Gene Ontology) data sets; CLUS-HMC performs significantly better than CLUS-SC in terms of both predictive accuracy and classification model size in all of the experiments.

*Pairwise comparisons between CLUS-HMC/HSC/SC and hmAnt-Miner:* Table 6 presents the summary of all pairwise comparisons according to the non-parametric Friedman test with the Holm’s post-hoc test [12, 16] in terms of predictive accuracy and classification model size. For each hypothesis (pair of algorithms) tested, the adjusted  $p$ -value obtained by Holm’s post-hoc test is reported using both FunCat and Gene Ontology data sets (‘Combined’ column), using only FunCat data sets (‘FunCat’ column) and using only Gene Ontology data sets (‘Gene Ontology’ column).

According to Table 6, the pairwise comparisons do not show statistically significant differences at the 0.01 significance level between *hmAnt-Miner* and CLUS-HMC, neither between *hmAnt-Miner* and CLUS-HSC, in terms of both predictive accuracy and classification model size; *hmAnt-Miner* is significantly better than CLUS-SC in terms of predictive accuracy in the combined data sets, and in terms of classification model size in all of the experiments; CLUS-HMC is significantly better than CLUS-HSC in terms of predictive accuracy on the FunCat data sets and in terms of classification model size on the combined data sets; CLUS-HMC is significantly better than CLUS-SC in terms of both predictive accuracy and classification model size in all of the experiments.

*Summary:* The experiments have shown that the proposed *hmAnt-Miner* algorithm is competitive with CLUS-HMC—the most accurate of the CLUS algorithms—in terms of both predictive accuracy and classification model size. Additionally, *hmAnt-Miner* outperformed CLUS-SC in terms of predictive accuracy on the combined (both FunCat and Gene Ontology) data sets and it has discovered a much simpler classification model than CLUS-SC in all of the experiments. We regard our results as promising, especially considering that the method of inducing decision trees using predictive clustering trees (PCT)—which is employed by all variations of CLUS algorithms—has been evolving for more than one decade, with early applications in [4, 31] and more recently in the context of hierarchical multi-label classification [5, 6, 38]. On the other hand, the proposed *hmAnt-Miner* is the first ACO algorithm tailored for hierarchical multi-label classification—to the best of our knowledge—and the application of ACO algorithms for classification is relatively recent [29].

## 7 Conclusions

This paper has proposed a novel ant colony algorithm tailored for hierarchical multi-label classification, named *hmAnt-Miner* (Hierarchical Multi-Label Classification Ant-Miner). Extending on the ideas of our previous hierarchical classification *hAnt-Miner* algorithm, *hmAnt-Miner* discovers a single global classification model, in the form of an ordered list of *IF-THEN* classification rules, which can predict all class labels from a class hierarchy at once, and examples may be assigned to multiple unrelated class labels. In order

**Table 3** Summary of the user-defined parameter values used by *hmAnt-Miner* for all data sets; no attempt was made to tune either parameter value for individual data sets. The first column ('parameter') gives the parameter name, the second column ('description') gives a short description and the third column ('value') gives the value used in our experiments.

| parameter                     | description  | value |
|-------------------------------|--|-------|
| <i>max_uncovered_examples</i> | maximum number of uncovered examples                   | 10    |
| <i>max_number_iterations</i>  | maximum number of iterations                           | 1500  |
| <i>rule_convergence</i>       | number of iterations used to test the rule convergence | 10    |
| <i>min_examples_per_rule</i>  | minimum number of covered examples per rule            | 10    |
| <i>colony_size</i>            | number of ants per iteration                           | 30    |

**Table 4** The  $AU(\overline{PRC})$  value obtained on the test set by each algorithm and the induced classification model size across all data sets used in our experiments. For *hmAnt-Miner*, the model size is defined as the number of rules discovered; for *CLUS-HMC*, *CLUS-HSC* and *CLUS-SC* the model size is defined as the number of leaf nodes in the decision tree, since each path from the root node to a leaf node can be viewed as a rule. In the case of *hmAnt-Miner*, the value of each row represents the average value obtained over 15 runs of the algorithm, followed by the standard deviation (*average*  $\pm$  *standard deviation*).

| data set  | <i>hmAnt-Miner</i>   |                    | FunCat               |      | <i>CLUS-HSC</i>      |      | <i>CLUS-SC</i>       |       |
|-----------|----------------------|--------------------|----------------------|------|----------------------|------|----------------------|-------|
|           | $AU(\overline{PRC})$ | size               | $AU(\overline{PRC})$ | size | $AU(\overline{PRC})$ | size | $AU(\overline{PRC})$ | size  |
| cellcycle | $0.154 \pm 0.001$    | $28.667 \pm 1.623$ | 0.172                | 24   | 0.111                | 4037 | 0.106                | 9671  |
| derisi    | $0.161 \pm 0.002$    | $19.333 \pm 1.661$ | 0.175                | 4    | 0.094                | 3520 | 0.089                | 7807  |
| eisen     | $0.180 \pm 0.003$    | $19.000 \pm 0.981$ | 0.204                | 29   | 0.127                | 2995 | 0.132                | 6311  |
| expr      | $0.175 \pm 0.002$    | $30.600 \pm 1.466$ | 0.210                | 12   | 0.127                | 4711 | 0.123                | 10262 |
| gasch1    | $0.175 \pm 0.003$    | $24.867 \pm 1.701$ | 0.205                | 10   | 0.106                | 4761 | 0.104                | 10447 |
| pheno     | $0.162 \pm 0.001$    | $7.400 \pm 0.767$  | 0.160                | 8    | 0.152                | 777  | 0.149                | 1238  |
| seq       | $0.181 \pm 0.002$    | $20.067 \pm 1.152$ | 0.211                | 14   | 0.091                | 4923 | 0.095                | 10443 |
| spo       | $0.174 \pm 0.002$    | $15.800 \pm 1.172$ | 0.186                | 6    | 0.103                | 3623 | 0.098                | 8527  |

| data set  | <i>hmAnt-Miner</i>   |                    | Gene Ontology        |      | <i>CLUS-HSC</i>      |       | <i>CLUS-SC</i>       |       |
|-----------|----------------------|--------------------|----------------------|------|----------------------|-------|----------------------|-------|
|           | $AU(\overline{PRC})$ | size               | $AU(\overline{PRC})$ | size | $AU(\overline{PRC})$ | size  | $AU(\overline{PRC})$ | size  |
| cellcycle | $0.332 \pm 0.002$    | $35.400 \pm 1.594$ | 0.357                | 21   | 0.371                | 19085 | 0.252                | 36260 |
| derisi    | $0.334 \pm 0.003$    | $22.533 \pm 1.939$ | 0.355                | 10   | 0.349                | 16693 | 0.218                | 31175 |
| eisen     | $0.376 \pm 0.002$    | $18.200 \pm 0.823$ | 0.380                | 37   | 0.365                | 14384 | 0.270                | 24844 |
| expr      | $0.351 \pm 0.003$    | $28.600 \pm 1.778$ | 0.368                | 35   | 0.351                | 20812 | 0.249                | 38313 |
| gasch1    | $0.356 \pm 0.002$    | $27.933 \pm 0.918$ | 0.371                | 30   | 0.351                | 20070 | 0.239                | 37838 |
| pheno     | $0.337 \pm 0.001$    | $7.133 \pm 0.792$  | 0.337                | 6    | 0.416                | 5691  | 0.316                | 6213  |
| seq       | $0.366 \pm 0.003$    | $18.067 \pm 1.016$ | 0.386                | 15   | 0.282                | 21703 | 0.197                | 38969 |
| spo       | $0.341 \pm 0.003$    | $26.333 \pm 2.520$ | 0.352                | 14   | 0.371                | 15552 | 0.213                | 35400 |

to take into account the information from the class hierarchy, *hmAnt-Miner* employs a distance-based measure in the dynamic discretisation procedure of continuous attributes and as a heuristic information in the ACO construction graph. Thus, the entropy measure used in *hAnt-Miner* is replaced by the distance measure in *hmAnt-Miner*, which is a more suitable measure for hierarchical multi-label classification.

We conducted experiments comparing *hmAnt-Miner* against state-of-the-art decision tree induction algorithms for

hierarchical multi-label classification in sixteen bioinformatics data sets involving the prediction of protein function, with large numbers of predictor attributes and large numbers of class labels to be predicted. The class hierarchies used in the experiments were structured in a tree (where a class label has a single parent, apart from the root label) or in a directed acyclic graph (where a class label can have multiple parents, apart from the root label) forms. *hmAnt-Miner* was competitive in term of both predictive accuracy and simplic-

**Table 5** Summary of the comparisons of the CLUS-HMC (control) algorithm with the remaining algorithms according to the non-parametric Friedman test with the Holm’s post-hoc test [12, 16] in terms of (i) predictive accuracy and (ii) classification model size. For each algorithm, the average rank and the adjusted  $p$ -value obtained by Holm’s post-hoc test are reported using both FunCat and Gene Ontology data sets (‘Combined’ column), using only FunCat data sets (‘FunCat’ column) and using only Gene Ontology data sets (‘Gene Ontology’ column). A  $p$ -value is shown in bold when the difference in the average ranks of the algorithms is statistically significant at the 0.01 significance level ( $p_{Holm} \leq 0.01$ ), which in this case represents that the particular algorithm is significantly worse than the CLUS-HMC (control) algorithm.

| Algorithm                      | Combined  |                  | FunCat    |                  | Gene Ontology |                  |
|--------------------------------|-----------|------------------|-----------|------------------|---------------|------------------|
|                                | avg. rank | $p_{Holm}$       | avg. rank | $p_{Holm}$       | avg. rank     | $p_{Holm}$       |
| <i>(i) Predictive Accuracy</i> |           |                  |           |                  |               |                  |
| CLUS-HMC (control)             | 1.2812    | -                | 1.1250    | -                | 1.4375        | -                |
| hmAnt-Miner                    | 2.1875    | 0.0471           | 1.8750    | 0.2453           | 2.5000        | 0.1995           |
| CLUS-HSC                       | 2.6562    | <b>0.0052</b>    | 3.2500    | <b>0.0020</b>    | 2.0625        | 0.3329           |
| CLUS-SC                        | 3.8750    | <b>3.9794E-8</b> | 3.7500    | <b>1.4309E-4</b> | 4.0000        | <b>2.1579E-4</b> |
| <i>(ii) Model Size</i>         |           |                  |           |                  |               |                  |
| CLUS-HMC (control)             | 1.3125    | -                | 1.2500    | -                | 1.3750        | -                |
| hmAnt-Miner                    | 1.6875    | 0.4113           | 1.7500    | 0.4386           | 1.6250        | 0.6985           |
| CLUS-HSC                       | 3.0000    | <b>4.3611E-4</b> | 3.0000    | 0.0134           | 3.0000        | 0.0236           |
| CLUS-SC                        | 4.0000    | <b>1.1726E-8</b> | 4.0000    | <b>6.1251E-5</b> | 4.0000        | <b>1.4309E-4</b> |

**Table 6** Summary of all pairwise comparisons according to the non-parametric Friedman test with the Holm’s post-hoc test [12, 16] in terms of (i) predictive accuracy and (ii) classification model size. For each hypothesis tested, the adjusted  $p$ -value obtained by Holm’s post-hoc test is reported using both FunCat and Gene Ontology data sets (‘Combined’ column), using only FunCat data sets (‘FunCat’ column) and using only Gene Ontology data sets (‘Gene Ontology’ column). A  $p$ -value is shown in bold when the difference in the average ranks of the first algorithm and the second algorithm—reported in Table 5—is statistically significant at the 0.01 significance level ( $p_{Holm} \leq 0.01$ ), which in this case represents that the first algorithm outperforms the second algorithm.

| Hypothesis                     | Combined         | FunCat           | Gene Ontology    |
|--------------------------------|------------------|------------------|------------------|
|                                | $p_{Holm}$       | $p_{Holm}$       | $p_{Holm}$       |
| <i>(i) Predictive Accuracy</i> |                  |                  |                  |
| hmAnt-Miner vs. CLUS-HMC       | 0.0942           | 0.4906           | 0.2993           |
| hmAnt-Miner vs. CLUS-HSC       | 0.3044           | 0.0995           | 0.6658           |
| hmAnt-Miner vs. CLUS-SC        | <b>0.0011</b>    | 0.0147           | 0.0805           |
| CLUS-HMC vs. CLUS-HSC          | 0.0104           | <b>0.0050</b>    | 0.6658           |
| CLUS-HMC vs. CLUS-SC           | <b>7.9587E-8</b> | <b>2.8618E-4</b> | <b>4.3158E-4</b> |
| CLUS-HSC vs. CLUS-SC           | 0.0227           | 0.4906           | 0.0134           |
| <i>(ii) Model Size</i>         |                  |                  |                  |
| hmAnt-Miner vs. CLUS-HMC       | 0.4113           | 0.4386           | 0.6985           |
| hmAnt-Miner vs. CLUS-HSC       | 0.0121           | 0.1584           | 0.0995           |
| hmAnt-Miner vs. CLUS-SC        | <b>2.0267E-6</b> | <b>0.0024</b>    | <b>0.0012</b>    |
| CLUS-HMC vs. CLUS-HSC          | <b>8.7221E-4</b> | 0.0268           | 0.0473           |
| CLUS-HMC vs. CLUS-SC           | <b>2.3451E-8</b> | <b>1.2250E-4</b> | <b>2.8618E-4</b> |
| CLUS-HSC vs. CLUS-SC           | 0.0569           | 0.2427           | 0.2427           |

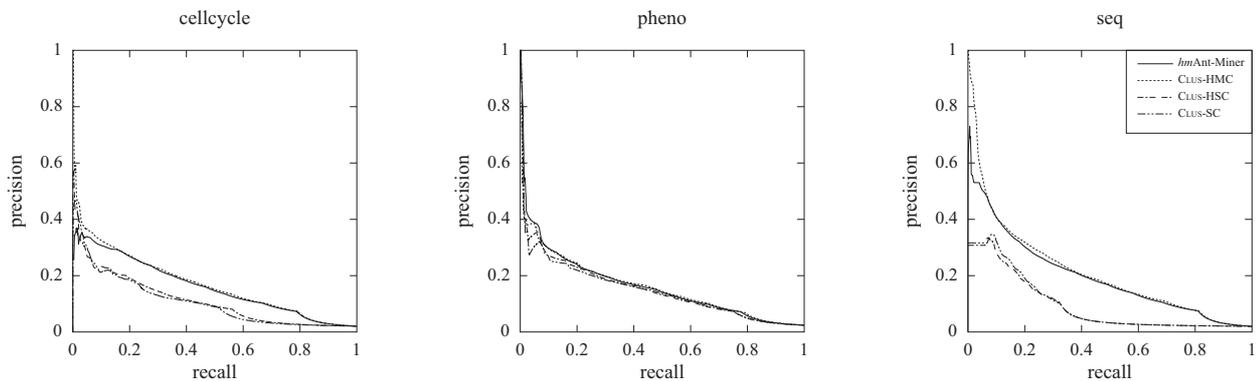
ity (measured as size of the discovered model). We regard these results promising, given that *hmAnt-Miner* is the first ACO algorithm tailored for hierarchical multi-label classification, to the best of our knowledge.

There are several potential avenues for future research. Since having a deterministic procedure to determine the consequent of rules led to a simplified rule pruning procedure, where the consequent is not pruned, different variations of the rule pruning procedure could prove to be more effective. In addition, it would be interesting to investigate differ-

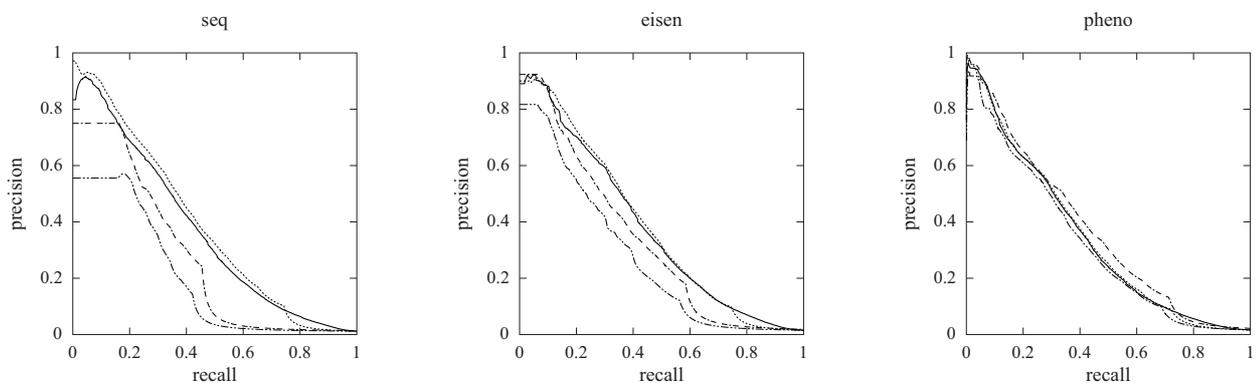
ent rule evaluation measures in order to optimise the quality of the discovered rules. Finally, evaluating other kinds of pheromone update strategies—e.g. updating the pheromone based on the quality of a rule list instead of a single rule—is also a direction worth further exploration.

**Acknowledgements** The authors gratefully acknowledge the financial support from an European Union’s INTERREG project (Ref. No. 162/025/361). Fernando E. B. Otero also acknowledges further financial support from the School of Computing, University of Kent.

## (a) FunCat



## (b) Gene Ontology



**Fig. 4** A sample of precision-recall curves of *hmAnt-Miner*, *CLUS-HMC*, *CLUS-HSC* and *CLUS-SC* for (a) ‘cellcycle’, ‘pheno’ and ‘seq’ FunCat data sets and (b) ‘seq’, ‘eisen’ and ‘pheno’ Gene Ontology data sets—the closest to the upper-right-corner, the better (more accurate) the curve.

The authors would like to thank Jan Struyf, Celine Vens and Leander Schietgat for providing support for running the *CLUS* algorithms and the data sets used in the experiments.

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