Ontology-aware neural network: a general framework for pattern mining from microbiome data

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Abstract

With the rapid accumulation of microbiome data around the world, numerous computational bioinformatics methods have been developed for pattern mining from such paramount microbiome data. Current microbiome data mining methods, such as gene and species mining, rely heavily on sequence comparison. Most of these methods, however, have a clear trade-off, particularly, when it comes to big-data analytical efficiency and accuracy. Microbiome entities are usually organized in ontology structures, and pattern mining methods that have considered ontology structures could offer advantages in mining efficiency and accuracy. Here, we have summarized the ontology-aware neural network (ONN) as a novel framework for microbiome data mining. We have discussed the applications of ONN in multiple contexts, including gene mining, species mining and microbial community dynamic pattern mining. We have then highlighted one of the most important characteristics of ONN, namely, novel knowledge discovery, which makes ONN a standout among all microbiome data mining methods. Finally, we have provided several applications to showcase the advantage of ONN over other methods in microbiome data mining. In summary, ONN represents a paradigm shift for pattern mining from microbiome data: from traditional machine learning approach to ontology-aware and model-based approach, which has found its broad application scenarios in microbiome data mining.

Keywords: microbiome, pattern mining, ontology-aware, neural network, knowledge discovery

Introduction

Pattern mining from microbiome data is a broad topic, which can include many types of knowledge to be discovered such as functional gene mining, novel species discovery, dynamic pattern mining and so on. Yet traditionally, microbiome data mining has heavily relied on sequence comparison for gene mining [1], species mining [2, 3] and taxonomic composition comparison for microbial community dynamic pattern discovery [4]. Machine learning methods have recently been used in a variety of microbiome data mining contexts whereas deep learning approaches are rarely developed in those contexts owing to the high heterogeneity of microbiome samples as well as the critical data involved in these pattern mining processes [5, 6].

Microbiome entities are usually organized in ontology structures (Figure 1). Functional genes are organized using general ontology such as Gene Ontology (GO) [7] or specialized ontology such as the antibiotic resistance ontology [8]. Species are organized using the phylogenetic tree of life [9, 10], and microbial community samples are organized using the biome ontology [11]. The structure of ontology can be described in terms of a directed graph, wherein each term is a node, and the relationships among the terms are directed edges between the nodes, representing the hierarchical relationships of two terms: usually the edge source term contains the edge target term. Specifically, all the defining terms are organized by a structured hierarchy, which is called the ontology structure. For example, in the antibiotic resistance ontology, the term ‘non–beta-lactam’ is parent of the term ‘aminoglycoside’. Therefore, there is a directed edge between ‘non–beta-lactam’ and ‘aminoglycoside’. Recently, pattern mining methods that have considered ontology structures have shown the advantages to be gained in mining efficiency and accuracy [12–15]. However, the neural network represents an advanced approach for microbiome data mining [16–19]. Therefore, building neural network models together with ontology structures of microbiome entities should facilitate pattern mining from microbiome data.

In this work, we have summarized the ontology-aware neural network (ONN) as a general framework for microbiome data mining. We first introduce the ONN
approach as a general framework for pattern mining from microbiome data, for a broad spectrum of microbiome data mining scenarios. Then, we discuss about applications of ONN in multiple contexts, including gene mining, species mining and dynamic pattern mining. We then highlighted one of the most important characteristics of ONN, namely novel knowledge discovery, which makes ONN a standout among all microbiome data mining methods. Taken together, ONN represents a paradigm shift for pattern mining from microbiome data: from traditional machine learning approach to ontology-aware and model-based approach, which has found its broad application scenarios in microbiome data mining.

Current methods and deep learning for microbiome data mining

There are already computational solutions for pattern mining from microbiome data [20–23] (Table 1). Most of these methods, however, have a clear trade-off, particularly when it comes to big-data analytical efficiency and accuracy.

Antibiotic resistance gene (ARG) is a major challenge for microbiome data mining, which aims to predict the presence of ARG from metagenomic data in livestock manure, compost, wastewater treatment plants, soil, water and other affected environments as well as within the human microbiome. Traditional methods for the identification of ARG are based on the computational
AI methods are suitable for detection of BGCs of known classes from bacterial genomes. Deep learning solutions, such as ONN4MST [14] and Strain-GeMS [2], have recently been proposed to solve this problem. Model-based methods, such as the neural network, are used in these deep learning solutions to help researchers quickly identify all possible sources of microbial source tracking among thousands to millions of samples in a fast and accurate manner.
learning models (i.e. neural network), and both accuracy and efficiency could be largely improved compared with traditional methods. For example, Kang et al. reported an ultrafast and interpretable source tracking method (i.e. ONN4MST), which utilizes a novel deep learning model to profile microbial community structures [14]. ONN4MST achieved the prediction accuracy of 0.97 when faced with millions of samples from thousands of biomes, while the running time of the entire source tracking procedure could be within 1 s per sample. Deep learning methods are advantageous in the generation of the models from a massive amount of samples, which are representative of the global profile of the context-dependent subjects [36]. Deep learning methods are therefore suitable for accurate and fast search when new samples (either a gene, species or community) are searched against models [37–39]. We summarized current methods and deep learning methods for microbiome data mining in Table 1.

In summary, deep learning methods are particularly suitable for solving the problem of source tracking, gene mining and other patterns mining. The advantages of deep learning methods for pattern mining from microbiome data are shown in Figure 2.

**Onn as a general framework for pattern mining from microbiome data**

Microbiome entities are usually organized in ontology structures (Figure 1), which inspires us to seek a general deep learning framework, that is compatible with the ontology structure of microbiome data. Here, we summarized ONN as a general framework for pattern mining from microbiome data. The advantages of ONN are established from several aspects (Figure 3). First, ONN is suitable for large-scale sample pattern mining from microbiome data. Second, ONN employs an advanced deep learning model (i.e. neural network), which has shown superiority in many fields of microbiome data mining. Third, ONN utilizes ontology information and thus can identify genes, species and patterns hierarchically, thus facilitating knowledge discovery from multiple dimensions. Moreover, ONN eliminates the trade-off between big-data’s analytical efficiency and accuracy of current methods for microbiome data mining.

The ontology structure of microbiome entities (e.g. gene ontology, biome ontology) and the neural network model adapted to specific problems are two key components of ONN. ONN was able to understand the hierarchy of microbiome entities by incorporating ontology structure into neural network models. ONN uses a novel ontology-aware layer to implement the model, which encodes the ontology information. As a result, ONN generates hierarchical annotations according to the ontology used. ONN can be easily applied to any microbiome data mining problem involving ontology structures, such as gene mining, species mining and dynamic pattern mining.

**Gene mining**

With the advanced sequencing technology and development of microbiome culture strategies, many microbiome projects focusing on different biomes have been proposed: for example, the Human Microbiome project for sequencing human gut microbiome [21], Tara Oceans project [40] for sequencing global ocean microbiome and Earth Microbiome project [22] for sequencing global soil microbiome. These projects have provided a large number of microbial genomes, which provide big reservoirs of functional genes. However, the functional diversity of microbiomes has not been fully explored, and about 40% of microbial gene functions remains to be discovered [41]. ARG represents one special category of functional genes, which is an urgent and growing threat to public health. The discovery of resistance genes in diverse environments offers possibilities for early surveillance, actions to reduce transmission, gene-based diagnostics and, ultimately, improved treatment. Currently, numerous ARG databases and ARG predictive tools have been established or proposed. For example, the comprehensive ARG database, i.e. CARD [8] is the most used ARG database. CARD is a rigorously curated collection of known resistance determinants and associated antibiotics, organized by the antibiotic resistance ontology that organizes ARGs according to their corresponding drug classes.

**Species mining**

Traditional microbiome studies have primarily focused on bacteria although bacteria only represent a small fraction of all microorganisms. In addition to bacteria, archaea, viruses, and protists are also often abundant in environments. Archaea are generally dominant in
Figure 3. The differences between traditional methods and ONN for microbiome data mining. ONN is suitable for large-scale samples pattern mining from microbiome data. The model used by traditional methods are usually machine learning models, including principle component analysis, random forest, supporting vector machine, Bayesian, and expectation–maximization. ONN employs advanced models such as neural network. ONN utilizes ontology information and thus are able to identify genes, species, and patterns hierarchically, facilitating knowledge discovery from multiple dimensions. The trade-off between big-data analytical efficiency and accuracy of current methods for microbiome data mining can be solved by ONN methods.

extreme environments and define the limits of life on Earth in many cases [42]. Archaea were originally discovered and described in extreme environments including in high salinity [43], extremely acidic [44] and anaerobic environments [45]. Viruses, as very small infectious agents, rely on living cells to multiply and are the smallest and most abundant of all microorganisms [46]. Protists are unicellular eukaryotic microorganisms that exhibit less complex physiological structures than other eukaryotes. Although microorganisms harbor very important functional genes, most of their genomic contents remains poorly understood. For example, over 60 000 protist species have been identified in the NCBI (National Center for Biotechnology Information) taxonomy system, while many have also yet to be identified [47].
Dynamic pattern mining
Niche-specific spatiotemporal dynamics within microbial communities in addition to the consequences of these spatiotemporal dynamics on species evolution are key determinants for the formation, development, stability and dynamics of microbial communities [48]. However, many microbial ecological and evolutionary patterns remain to be discovered; for example, the temporal dynamics of human gut microbial communities. Human gut microbiota rapidly respond to changes in diet [49, 50], and the composition of an individual’s gut microbiota is predominantly determined by dietary habits over the long term (i.e. >1 year) [51, 52]. However, these dynamics are highly variable among individuals [53]. Over short-term time scales (i.e. <1 month), human gut microbiota can drastically change during dietary shifts, while such changes can also be quickly reversed after shifts in diet [4]. In addition, strong plastic patterns can be observed over mid-term time scales (i.e. between a month and a year). Overall, investigations into these problems could help develop a better understanding of the ecological and evolutionary patterns ranging from small to large scales.

Disease pattern mining
Increasing evidence suggests that the human microbiome, not just the gut microbiome, is tightly related to a variety of diseases, including chronic diseases [54], inflammation diseases [55] and cancer [30]. Revealing the relationships between human diseases and microbes can not only promote our understanding of the disease pathogenesis but also provide new strategies for the diagnosis and treatment of diseases. Multiple computational models have been developed in recent years to predict microbes that are linked to diseases. These computational models include a wide range of algorithms and models for analyzing microbiome data, such as score-function-based models, network algorithm-based models, machine learning-based models and experimental analysis-based models [56]. The relationship between the human microbiome and specific diseases, however, is far from clear, let alone the intricate patterns that could be used to differentiate these diseases [57]. Bottlenecks can occur as a result of batch effects between multiple cohorts [58], the dynamic nature of diseases [59] and so forth. Traditional machine learning methods are unable to distinguish diseases based on the human microbiome despite the fact that some diseases, such as inflammatory bowel disease, may share a high proportion of microbes [60].

Applications of onn in microbiome data mining contexts
Recently, a series of ONN methods have been developed for pattern mining from microbiome data. Those ONN methods have achieved robust performance compared with traditional machine learning methods or other deep learning methods that do not consider biological ontology. In this section, we summarize several major applications of ONN in microbiome data mining contexts (Table 2).

Gene function predicting and ARG mining
A large number of protein sequences are becoming available through the application of novel high-throughput sequencing technologies. Experimental functional characterization of these proteins is time consuming and expensive and is often only done rigorously for a few selected model organisms. Computational function prediction approaches have been suggested to fill this gap. The functions of proteins are classified using the GO, which contains over 40,000 classes. To address the problem in protein function prediction, DeepGO [12] utilizes the dependencies between GO classes as background information to construct an ONN model and specifically outputs information in the hierarchical structure of the GO. Developers compared DeepGO with the other two top-performing methods on a standard benchmark data set, and results show DeepGO achieved the highest area under the curve (AUC) of 88%.

ARG represents a specific class of functional genes, which enable bacteria to survive under extremely antibiotic environments. The discovery of resistance genes in diverse environments offers possibilities for early surveillance, actions to reduce transmission, gene-based diagnostics, and, ultimately, improved treatment. Recently, ONN4ARG [13] has been proposed to solve problems in novel ARG identification and make efforts for comprehensive profiling of ARGs in diverse environments. ONN4ARG is an ONN model that employs a novel ontology-aware layer and generates multilevel annotations of antibiotic resistance types. Systematic evaluations show that the ONN4ARG model has profound performance improvement over state-of-the-art models such as DeepARG [16], especially for the detection of remotely homologous ARGs. Experiments based on more than 200 million candidate microbial genes collected from thousands of samples from various environments have resulted in submillon candidate ARGs and more than 40,000 putative novel ARGs, which have greatly expanded existing ARG repositories [16]. Furthermore, we compared the ONN method (i.e. ONN4ARG) with current standard methods for ARG predicting. The ONN model of ONN4ARG is built based on CARD version 3.0.3. When we compared the latest CARD version 3.1.4 with the previous version 3.0.3, we discovered 2281 new ARGs. The 2281 ARGs were then clustered into 312 clusters with a 90% sequence identity, and the 312 representative ARGs were used as the testing data set. For Diamond, we searched CARD version 3.0.3 with the testing data set. For DeepARG, we used the DeepARG program (default parameters) to predict the testing data set. For ONN4ARG, we used the ONN4ARG program (default parameters) to predict
the testing data set. The ONN4ARG method outperformed current ARG prediction methods (Diamond and DeepARG) in terms of accuracy and efficiency, i.e. high accuracy and less time required given that the memory usage is acceptable for a regular laptop computer. (Supplementary Table S1 available online at http://bib.oxfordjournals.org/). ONN4ARG achieved better performance than DeepARG largely because it was able to identify remote homologous ARGs. For example, ONN4ARG predicted one representative ARG (WP_122630831.1) in the testing data set to be an ARG, but DeepARG predicted it to be non-ARG. Notably, the representative ARG (WP_122630831.1) shares a remotely sequence identity of 48.9% with its closest homologous ARG (CAQ53840.1) in DeepARG database (i.e. ARGminer v1.1.1). We also searched WP_122630831.1 against the CARD version 3.0.3, and the closest homologous ARG in CARD version 3.0.3 is also CAQ53840.1. Therefore, results on this representative ARG (WP_122630831.1) have confirmed that ONN4ARG could be superior than other methods in the discovery of novel ARGs.

### Species mining, including bacteria, virus and protist mining

Despite the fact that microorganisms contain many important functional genes, the majority of their genomic content is still unknown. In the NCBI taxonomy system, for example, over 60 000 protist species have been identified, with many more yet to be identified [46]. Numerous bioinformatics tools have taken advantage of the growing amount of genomic data to identify new species. For example, StrainPhlAn [33], ConStrains [34] and Strain-GeMS [2] are proposed for bacterial identification at the strain level based on genomic information and ArboTyping [61] for the identification of virus species and genotypes. By considering that species are organized according to the phylogenetic tree of life, the latter can be considered an ontology structure, and the identification of novel species is an ontology-related problem. As a result, ONN is appropriate for species mining.

### Microbial source tracking

With the rapid accumulation of microbial community samples from various niches (also referred to as biomes) around the world, knowledge about microbial communities and their influence on the environment and human health has grown rapidly. The rapid accumulation of microbial community samples has provided the opportunity to investigate the interactions among microbes, human health and the environment. These community samples have created an enormous hurdle for characterizing the potential inputs from other associated biomes, thus calling for fast and accurate microbial source tracking. Considerable attention has been paid to exploring the interactions on small scales, such as disease diagnosis, early development, pregnancy and immigration whereas integrative, large-scale and scalable investigations are understudied. Such investigations are challenging for a few reasons. First, the number of samples easily exceeds millions whereas the number of niches exceeds hundreds, and microbial source tracking becomes a very complex task. Second, the noises that exist in the rich-sourced data might hire important patterns invisible for traditional methods. To address these limitations, ONN4MST was proposed for microbial source tracking. The ONN4MST model employs a novel ontology-aware approach that encourages prediction satisfying the ‘biome ontology’. In other words, the ONN model can utilize the biome ontology information to model the dependencies between biomes and estimate the proportion of various biomes in a community sample. ONN4MST has provided an ultrafast (<0.1 s) and accurate (AUC >0.97 in most cases) solution for searching a sample against the data set containing hundreds of potential biomes and millions of samples, and also outperformed state-of-the-art methods in scalability and stability. Furthermore, we compared ONN method (i.e. ONN4MST) with current standard methods for microbial source tracking. The data set used for evaluation consists of 10 270 microbial community samples selected from the data sets used in published study by Shenhav et al.

| Method   | Category                        | Description                                                                 | Reference |
|----------|---------------------------------|-----------------------------------------------------------------------------|-----------|
| DeepGO   | Gene function prediction        | DeepGO utilizes the dependencies between GO classes as background information to construct an ONN model and specifically outputs information in the hierarchical structure of the GO | [12]      |
| ONN4ARG  | Functional gene prediction      | ONN4ARG was proposed to solve problems in novel ARG identification and make efforts for comprehensive profiling of ARGs in diverse environments. ONN4ARG is an ONN model that employs a novel ontology-aware layer and generates multilevel annotations of antibiotic resistance types | [13]      |
| ONN4MST  | Dynamic pattern mining          | ONN4MST was proposed for microbial source tracking. The ONN model can utilize the biome ontology information to model the dependencies between biomes, and estimate the proportion of various biomes in a community sample | [14]      |
| EXPERT   | Disease prediction              | EXPERT is an exact and pervasive expert model for source tracking microbial communities based on transfer learning. EXPERT could easily expand the supervised model’s search scope to include the context-dependent community samples and understudied biomes (e.g. samples from different disease stages) | [15]      |
Disease prediction

Microorganisms have been discovered to be closely related to a variety of important human diseases. The growing number of human microbe-disease associations provides important insights into the underlying disease mechanism from the perspective of human microbes, which is extremely useful for pathogenesis research, early diagnosis and precision medicine [62, 63]. EXPERT [15] is an exact and pervasive expert model for source tracking microbial communities based on transfer learning. Built on the ontology information and transfer learning techniques, EXPERT has acquired the context-aware flexibility and could easily expand the supervised model’s search scope to include the context-dependent community samples and understudied biomes. EXPERT considers gut communities at different disease stages as context-dependent biomes and estimates the contribution from different disease stages for a given microbial community sample. EXPERT’s utility in characterizing human gut microbial communities associated with different types of diseases is superior to current standard methods. The superiority of EXPERT has been demonstrated in disease pattern mining. For example, when dealing with 635 samples from a recent study of colorectal cancer, EXPERT could achieve an AUROC of 98% when predicting the host’s phenotypical status [15].

To sum up, we have demonstrated that ONN could be applied on a broad spectrum of applications, including functional gene mining, novel species mining and microbial community dynamic pattern mining. Of note, ONN is especially suitable for disease pattern mining, which is very robust against batch effects and other confounding factors.

Onn modeling tells us more about unknown than known

The deep learning approach could best utilize the ontology information hidden from the biological big data. At the lowest ontology level, the deep learning approach should be comparable with other methods. However, on the higher ontology levels, the deep learning approach could identify remote similarities among genes, species and patterns of interest.

Microbiome samples could be collected from diverse niches around the world, and genes, species and communities represent the three levels of microbiome knowledge. The ontological organization of the knowledge about microbiomes, whether on gene, species or community levels, could naturally lead us to the discovery of new knowledge about microbiomes (Figure 4). Currently, we know little at all of the gene, species and community levels, and we can only obtain more knowledge if the expanding of our knowledge could keep pace with the increasing changes at these levels.

Compared with traditional methods, ONN is not advantageous for the identification of genes, species and communities in existing databases as numerous methods already exist for database searches, sequence comparisons and structure comparisons. However, ONN’s performance is equally good compared with existing methods proving the power of neural network models on such data mining processes.

ONN demonstrated its advantages in the discovery of novel genes, species and communities owing to its ability to sense the ontology structure and lead to discovery at higher levels of the ontology structure (Figure 5). ONN outputs hierarchical predictions with predicted probability scores. In most cases, ONN makes confident predictions at higher levels and less confirmatory predictions at lower levels. Those less confirmatory predictions are potential candidates for novel genes, species and patterns. ONN can give information about ancestors (or categories at higher levels) of those potential candidates, which is impracticable for methods without considering ontology. One example is on functional gene discovery: GAR is a newly discovered non–beta-lactam aminoglycoside resistance gene (e.g. gentamicin, micromycin), that is not found in any existing databases [13]. With both DeepARG and HMD-ARG models, search results show that the GAR is not an actual ARG. ONN4ARG, however, correctly identified GAR as an ARG resistant to non–beta-lactam antibiotics. Despite the fact that ONN4ARG could only predict GAR as a non–beta-lactam rather than a subtype of aminoglycoside, it was the only method used in this study that could predict GAR as an ARG demonstrating ONN4ARG’s capability for knowledge discovery [13]. Another example is on microbial community sample source tracking: a microbial source tracking investigation that involved 11 microbial community samples from groundwater biome also showed the capability of ONN4MST for knowledge discovery [14]. ONN4MST could identify a large proportion of these groundwater samples from aquatic biomes coupled with a considerable proportion from terrestrial biome, thus suggesting that the samples might be collected from terrestrial water (i.e. river, lake and groundwater) or its sediment. In contrast, FEAST assigned a large proportion of unknowns for these groundwater samples.

In summary, ONN could enable novel knowledge discovery from microbiome data at multiple levels: gene, species, communities and so forth. These can deepen our understanding of how microbial communities are assembled and functioned, leading to better utilization.
Figure 4. The hierarchical organization of knowledge about microbiome. Microbiome samples could be collected from diverse niches around the world, including environment (e.g. soil, water and air), host associated (e.g. human gut, oral and skin), and engineered (e.g. fermentation). Genes, species and communities represent the three level of microbiome knowledge. The ontological organization of the knowledge about microbiome, whether on gene, species or community levels, could naturally lead us to the discovery of new knowledge about microbiome.

Knowledge about microbiome on different level

Figure 5. Rationale on ‘why’ ONN could discover novel knowledge from microbiome data. Left: ONN outputs hierarchical predictions with predicted probability scores. In most cases, ONN makes highly confident predictions at higher levels (e.g. L1, L2 and L3 in the figure) and low confirmatory predictions at lower levels (e.g. L4 in the figure). Those low confirmatory predictions are potential candidates of novel genes, species and patterns. ONN can give information about ancestors (or categories at higher levels) of those potential candidates and provide clues about novel knowledge. Right: In contrast, traditional methods without considering ontology treat all terms as equal, so that no candidate (at lower levels of the hierarchical structure) has highly confident prediction, resulting in no clue about the potentially novel knowledge. ONN showed its advantages on the discovery of novel genes, species and communities, largely due to its ability to sense the ontology structure, and leads to the discovery at higher levels of the ontology structure.
of microbiome data in environmental and clinical applications.

Conclusions

ONN is a general framework that can be used for a broad spectrum of microbiome data mining applications. On the one hand, in many contexts, the biological data are organized in the hierarchical or ontological manner; therefore, ONN is naturally suitable for these types of data. On the other hand, neural network methods could generate models that always outperform traditional methods in gene mining, species mining and dynamic pattern discovery. Therefore, ONN, which combines ontology awareness and neural network models, could greatly facilitate pattern mining from microbiome data.

ONN has revealed an excellent pool of knowledge about microbiome patterns at gene, species and community levels, and it would lead to broader and deeper knowledge about microbiomes. The power of ONN on knowledge discovery has been exemplified in many contexts: whether novel genes, new species or novel dynamic patterns of communities, ONNs have already led us to the discovery of new knowledge about microbiomes whereas there might still be a large space toward the full picture about the microbial world.

It should be noted that the ONN method could be powerful but might not be a general and all-purpose method. Its usefulness in the context of functional gene mining and microbial source tracking have been proved in previous work and benchmarked in this work, yet its applicability in novel species mining has not been proved yet. Thus, though ONN could be a general framework for pattern mining from microbiome data, its utility in the broad spectrum of microbiome data mining applications should be worthy of further investigation.

There is no doubt that ONN has limitations. First of all, a good ontology structure is always dependent on domain knowledge, which is not readily available in numerous contextualized applications. The ONN model is also limited by the interpretability of its results: the quantitative classification results could be used for gene mining or sample source tracking whereas the exact accuracy of such pattern mining remains to be determined. Furthermore, ONN’s robustness against batch effects, as well as its applicability in contextualized applications that have very few samples, remains to be examined. Despite these limitations which remain to be overcome, ONN represents a paradigm shift for pattern mining from microbiome data: from traditional machine learning approach to ontology-aware and model-based approach, which has found its broad application scenarios in microbiome data mining.

Finally, we should admit that currently we know little at all of the gene, species and community levels, and we can only obtain more knowledge if the expanding of our knowledge could keep pace with the increasing changes at these levels. ONN is a powerful tool toward this end, and we hope similar ideas and methods could be used in the broad spectrum to speed up the knowledge discovery in the microbial world.

Key Points

- Microbiome entities are usually organized in ontology structure, and pattern mining methods consider ontology structures.
- ONN, which has considered ontology structures, could offer advantages in mining efficiency and accuracy for microbiome data mining.
- ONN could be used in multiple contexts, including gene mining, species mining and microbial community dynamic pattern mining.
- ONN could discover novel knowledge from microbiome data, thus making it a standout among all microbiome data mining methods.

Supplementary data

Supplementary data are available online at https://academic.oup.com/bib.

Author contributions

K.N. conceived of and proposed the idea and designed the study. K.N. and Y.Z. performed the review. All the authors edited and proofread the manuscript. All the authors have read and approved the final manuscript.

Funding

National Natural Science Foundation of China (Grant Nos. 32071465, 31871394 and 31671374); National Key R&D Program (Grant No. 2018YFC0910502).

Ethics approval and consent to participate

Not applicable.

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