education, and traditional bioinformatics research (see Figure 1). When applied to information retrieval, MeSH and its indexing results have been used to build "tag clouds" for improving the visualization of search results [5, 6] and to help distinguish between publication authors with identical names [7, 8]. Another major use of MeSH indexing is in biomedical text mining, where it has been applied to problems such as document summarization [9], document clustering [10], and word sense disambiguation [11]. MeSH indexing also serves several key roles in citation analysis, from identifying emerging research trends [12, 13] to measuring similar journals [14] and characterizing research profiles for an individual researcher, institute or journal [15]. In the era of evidence-based practice. MeSH becomes increasingly important in assessing and training the literature search skills of healthcare professionals [16, 17], as well as in assisting undergraduate education in biological sciences [18]. Finally, much bioinformatics research, such as gene expression data analysis [19, 20], greatly benefits from MeSH indexing [21-25].

Like many manual annotation projects [26-30], MeSH indexing is a labour-intensive process. As shown in 13, 311, it can take an average of 2 to 3 months for an article to be manually indexed with relevant MeSH terms after it first enters PubMed. In response, many automated systems for assisting McSH indexing have been previously proposed. In general, most existing methods are based on the following techniques: i) pattern matching, ii) text classification, iii) k-Nearest Neighbours, iv) learning-torank, or v) combination of multiple techniques. Pattern-matching methods [32] search for exact or approximate matches of MeSH terms in free text. Automatic MeSH indexing can also be regarded as a multi-class text classification problem where each MeSH term represents a distinct class label. Thus many multilabel text classification methods have been proposed, such as neural networks [33]. Support Vector Machines (SVM) [34, 35]. Inductive Logic Programming [36], naïve Bayes with optimal training set [37], Stochastic Gradient Descent [38], and metalearning [39]. While the pattern matching and text classification methods use only the information in the MeSH thesaurus and document itself, the k-Nearest Neighbours (k-NN) approach takes advantage of the manual annotations of documents similar to the target document, e.g. [40]. Additional information, such as citations, can also be utilized for automatic McSH indexing. For example, Delbecque and Zweigenbaum [41] investigated computing neighbour documents based on the cited articles and cited authors. More recently, Huang et al. [3] reported a novel approach based on learning-to-rank algorithms [42]. This approach has been shown to be highly successful in the recent BioASO challenge evaluations 143-451 and has also been adopted by many others [46, 47]. Finally, many methods attempt to combine results of different approaches [48, 49]. For instance, the current production system in MeSH indexing at the NLM is called Medical Text Indexer (MTI), which is a hybrid system that combines both pattern matching and k-NN results [50] via

manually-developed rules and continues to be improved over the years [51, 52]. The proposed method in this work is also a hybrid system but unlike MTL, which only uses machine learning to predict a small set of MeSH terms, it combines individual results and ranks the entire set of recommendations through machine learning instead of bearistic rules.

Despite these efforts, automatic MeSH indexing remains a challenging task: the current state-of-the-art performance remains at about 0.6 in F-measure [53]. Several factors contribute to this performance bottleneck: First, since each PubMed article can be assigned with multiple MeSH terms, i.e. class labels, the task of automatic MeSH indexing can be seen as a multi-class classification problem. In this regard, the size of the MeSH vocabulary makes automatic classification challenging: 2014 MeSH includes more than 27,000 main subject headings and they are not equally used in indexing [31]. Second, MeSH indexing is a highly complex cognitive task. It has been reported that the consistency between human indexers is only 48.2% for main heading assignment [54]. Lastly, both the MeSH vocabulary and indexing principles keep evolving over time. For instance, in response to emerging new concepts in the biomedical research, MeSH 2014 includes almost five times more concepts than the edition of MeSH in 1963 that only contains 5,700 descriptors. On the other hand, the articles in PubMed are not re-indexed when MeSH gets updated. Thus, it is not always obvious in selecting benchmarking data sets for system development and comparison.

In this paper, we propose a new method, MeSH Now, to the automatic MeSH indexing task. MeSH Now is built on our previous research [3] but has a number of significant advancements: First, MeSH Now combines different methods through machine learning. Second, new post-processing and list-pruning steps are now added in MeSH Now for improved performance. Third, from a technical perspective. MeSH Now is optimized using the latest MeSH lexicon and recent indexed articles for system training and development. Finally, MeSH Now is implemented to operate in a parallel computing environment, making it possible for largescale processing needs (e.g., providing computer results of new PubMed articles for assisting human indexing). For evaluation, we first test MeSH Now on a previous dataset that was widely used in benchmarking. Furthermore, we created a new benchmarking dataset based on the recent BioASQ 2014 challenge task data. Our experimental results show that MeSH Now achieves state-of-the-art performance on both data sets.

### Methods

#### Approach overview

Our approach reformulates the MeSH indexing task as a ranking problem. Figure 2 shows the three main steps: First, given a target article, we obtain an initial list of candidate MeSH terms from three unique sources. Next, we apply a learning-torank algorithm to sort the candidate MeSH terms based on the

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