Scientometric analysis and knowledge mapping of literature-based discovery (1986–2020)

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Abstract. Literature-based discovery (LBD) aims to discover valuable latent relationships between disparate sets of literatures. LBD research has undergone an evolution from being an emerging area to a mature research field. Hence it is timely and necessary to summarize the LBD literature and scrutinize general bibliographic characteristics, current and future publication trends, and its intellectual structure. This paper presents the first inclusive scientometric overview of LBD research. We utilize a comprehensive scientometric approach incorporating CiteSpace to systematically analyze the literature on LBD from the last four decades (1986–2020). After manual cleaning, we have retrieved a total of 409 documents from six bibliographic databases (Web of Science, Scopus, PubMed, IEEE Xplore, ACM Digital Library, and Springer Link) and two preprint servers (ArXiv and BiorXiv). The results have shown that Thomas C. Rindflesch published the highest number of LBD papers, followed by Don R. Swanson. The United States plays a leading role in LBD research with the University of Chicago as the dominant institution. To go deeper, we also perform science mapping including cascading citation expansion. The knowledge base of LBD research has changed significantly since its inception, with emerging topics including deep learning and explainable artificial intelligence. The results have indicated that LBD is still growing and evolving. Drawing on our insights, we now better understand the historical progress of LBD in the

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last 35 years and are able to improve publishing practices to contribute to the field in the future.

**Keywords** Literature-based discovery · Scientometrics · Information visualization · CiteSpace

1 Introduction

Research has shown that scientific output in terms of original articles, conference proceedings, and books has been increasing at an accelerated rate (Bornmann and Mutz 2015). For instance, the United States National Library of Medicine adds more than 2000 papers a day to MEDLINE, the world’s leading bibliographic database in the field of life sciences. Faced with information overload, scientists often miss valuable pieces of knowledge relevant to their research interests.

Given the massive amounts of scientific data generated every day, extracting and pinpointing relevant information becomes an important pursuit, albeit a challenging one. It is a challenging task to join disparate scientific pieces of information into a comprehensive body of knowledge. Nowadays, computational methods are used to complement manual knowledge discovery from textual data. Literature-based discovery (LBD) is an interesting yet highly challenging research paradigm that uses computational algorithms for mining scientific literature. In modern text mining, LBD research plays an important role. LBD has been successfully utilized in various application areas including life sciences (Pyysalo et al. 2019), humanities (Cory 1997), and counterterrorism (Jha and Jin 2016).

By definition, LBD is a text mining approach for automatically generating research hypotheses (Smalheiser 2017). The main aim of LBD is to stimulate and support human creativity to find important connections between disparate literatures by identifying hidden, previously unknown relationships from existing knowledge. The LBD approach was initiated by Swanson (1986a), who discovered that dietary fish oil might be used to treat Raynaud’s disease. This discovery was based on the observation that Raynaud’s disease lowers blood viscosity, reduces platelet aggregation and inhibits vascular reactivity. (Raynaud’s disease exhibits excessively reduced blood flow in response to cold or emotional stress, causing discoloration of the fingers, toes, and occasionally other areas.) Swanson’s hypothesis was later verified in vivo by DiGiacomo et al. (1989). Nowadays, LBD is an interdisciplinary research field and it is considered as a branch of both computer science and information science.

Swanson’s pioneering methodology is based on the presumption that there exist multiple complementary and non-intersecting knowledge domains in the scientific literature (Swanson 1986b). Knowledge in a given domain may be related to knowledge in another domain, but without the relationship being known. The Swanson’s LBD paradigm relies on the notion of concepts relevant to three literature domains: A, B, and C (Figure 1). For instance, let us suppose we have found a link between a disease A and a gene B. Next, suppose
that another research group has published the effect of a drug $C$ on the gene $B$. The use of LBD methodology may propose an $AC$ relation, suggesting that the drug $C$ may potentially treat the disease $A$. Such a latent link may represent a novel hypothesis for a potential, yet unconfirmed relationship.

Fig. 1 Swanson’s ABC discovery model. The model contains three concepts: start ($A$), intermediate ($B$), and target ($C$). The LBD process begins with retrieving $AB$ and $BC$ relationships. Next, we combine associations with the same intermediates. Finally, we get a list of $AC$ relationships. If there is no prior mention of a particular $AC$ connection, we formulate a hypothesis of a potential novel relationship between $A$ and $C$ concepts.

The ABC model could be used in two ways: open discovery and closed discovery (Weeber et al. 2001). The former is typically used as a hypothesis generation process, and the latter as a hypothesis testing process. In the open discovery (Figure 2a), we start with a concept $A$ (e.g., disease) and try to find intermediate concepts $B$ (e.g., molecular functions) that play a role in explaining the concept $A$. In the second step, we need to identify concepts $C$ (e.g., genes) that are directly connected to concepts $B$. Finally, we hypothesize that the concept $C$ is related to the concept $A$ through the intermediate $B$. On the other hand, a closed discovery (Figure 2b) starts with concepts $A$ and $C$ and tries to find intermediate $B$s. The more intermediates we find, the more plausible is the tested hypothesis. Although simple, Swanson’s ABC model is widely accepted in the LBD community. However, in the last decade, researchers have proposed several other discovery strategies, including discovery browsing (Wilkowski et al. 2011), outlier detection (Petrić et al. 2012), entityometrics (Ding et al. 2013), link prediction (Kastrin et al. 2016), analogical reasoning (Mower et al. 2017), heterogeneous bibliographic networks (Sebastian et al. 2017b), and neural networks (Crichton et al. 2018). All these approaches persuasively improve the performance of the basic ABC model (Smalheiser 2017).

LBD has found greatest utility in the biomedical domain. For instance, the LBD methodology has been applied to identify disease candidate genes for polymicrogyria (Hristovski et al. 2005) or to propose potential treatments for Parkinson’s disease (Kostoff and Briggs 2008). LBD is increasingly used for drug repurposing (Yang et al. 2017) and for better understanding and prediction of adverse drug events (Shang et al. 2014). Last but not least, LBD has been applied in a framework for cross-domain recommendation for biomedical research collaboration (Hristovski et al. 2015). The lack of comprehensive on-
Fig. 2 Closed (a) and open (b) discovery model. In closed discovery, we seek for intermediate concepts \(B_1, B_2, \ldots, B_n\) that connect a start concept \(A\) and a target concept \(C\). In open discovery mode, only the start concept \(A\) is given and the goal is to identify target concepts \(\{C_1, C_2, \ldots, C_m\}\) through intermediate concepts \(\{B_1, B_2, \ldots, B_n\}\).

tologies and tools (e.g., UMLS (Bodenreider 2004), SemRep (Rindflesch and Fiszman 2003), SemMedDB (Kilicoglu et al. 2012)) is the main reason why LBD has not been widely adopted outside the biomedical domain (Hui and Lau 2019).

Scientometric analysis has a critical role in strategic science planning, policy, and research performance evaluation. Scientometrics concerns a broad range of research methodologies and technologies including modern statistical analysis and visualization. The primary goal of the scientometric analysis is to assess the performance of a research unit of interest (e.g., scholar, journal, institution, discipline, country) and examine and summarize its knowledge structure and evolution. In recent decades, a scientometric review has been broadly adopted to quantitatively evaluate the previous research activities, track the transformative processes, understand knowledge landscapes, and predict emerging trends in various scientific fields (Chen and Song 2017). The roots of scientometrics could be traced back to the early 20th century (Godin 2006), however, the main methodological tools were developed in the 1960s (Price 1965; Pritchard 1969).

Contemporary scientometrics incorporates two different but methodologically complementary research approaches (Noyons et al. 1999): (i) performance analysis and (ii) science mapping. The former procedure includes, for instance, various counts (e.g., publications and citations by authors, countries, and institutions), burst detection (Kleinberg 2003), or \(h\)-index analysis (Hirsch 2005). On the other hand, science mapping employs different spatial and temporal representation techniques to examine the structural and dynamic properties of scientific research (Chen 2013; Chen and Song 2017). Frequently used tools are co-citation analysis (Small 1973) and co-word analysis (Callon et al. 1983). The development of scientometric software goes hand-in-hand with the advancement in information sciences and novel visualization approaches (Chen and Song 2017; Chen et al. 2009). The most popular software tools for bibliographic analysis are, among others, CiteSpace (Chen 2006), VOSviewer (van Eck and Waltman 2009), SciMAT (Cobo et al. 2012), and bibliometrix package for R (Aria and Cuccurullo 2017).
To the best of our knowledge, there is no detailed scientometric-based scientific review of the LBD research field currently, although—as we will see in the Related work section—at least two papers try to fill this gap (Chen and Song 2019; Thilakaratne et al. 2019a). However, the growth in LBD literature necessitates a detailed scientometric review. This study aims to extend previous traditional reviews of the LBD literature (Ahmed 2016; Bekhuis 2006; Davies 1989; Gopalakrishnan et al. 2019; Henry and McInnes 2017; Sebastian et al. 2017a; Smalheiser 2012, 2017; Thilakaratne et al. 2019a,b; Weeber et al. 2005); we conduct a quantitative scientometric analysis on publications retrieved from Web of Science (WoS), Scopus, PubMed, and other relevant bibliographic databases since the inception of LBD in 1986. We analyze bibliographic metadata from citation indexes (i.e., titles, abstracts, journal names, author names, author addresses) to infer production, impact, fields of interests, and general characteristics of the LBD literature and create a scientometric profile of LBD research. At the same time, we try to interpret the findings from the perspective of LBD experts. Specifically, to address the LBD field, this paper (i) provides a comprehensive overview of the research evidence using the scientometric analysis by summarizing the majority of the papers published in the last 35 years; (ii) identifies key authors, countries, institutions, and main describable keywords related to the research area; (iii) deduces the most noticeable end emerging research themes in the field of LBD; and (iv) compares the most influential works based on citation statistics. The findings of this study could be relevant to different stakeholders. Particularly, the presented analysis may be relevant to researchers new to LBD to orient in the field, to identify knowledge gaps, and to move the LBD field forward.

2 Related work

LBD is a complex, continually evolving, and collaborative research field. To the best of our knowledge, at least ten traditional literature reviews have been published to elucidate the extent of knowledge in the LBD research domain. Below we give a brief description of each of them.

Only three years after Swanson’s first paper on LBD, Davies (1989) published an interesting theoretical paper on the creation of new knowledge by information retrieval. This article provides an in-depth review of previous work on generating knowledge through information retrieval and presents methods to retrieve latent knowledge from the literature (e.g., serendipity browsing, proper search strategies, relational indexing, and artificial intelligence). Together with some recent theoretical papers (Chen et al. 2009; Uzzi et al. 2013), Davies’s paper is a must-read for all researchers who seek to deeply understand the formalistic foundations of LBD.

With the rise of various technologies (e.g., JavaScript) in the mid-1990s that stimulated the development of interactive Web applications, the LBD community started to build online LBD tools and services. Weeber et al. (2005) provided a review of methodology and LBD tools that had been developed
until 2005. The authors described Arrowsmith (Swanson and Smalheiser 1997), BITOLA (Hristovski et al. 2005), Manjal (Srinivasan 2004), LitLinker (Pratt and Yetisgen-Yildiz 2003), ACS (Eijk et al. 2004), IRIDESCENT (Wren et al. 2004), and Telemakus (Fuller et al. 2004). To our knowledge, only Arrowsmith and BITOLA are still available from that list to the broad research public.

Bekhuis (2006) described LBD in the context of conceptual biology and the broader domain of text mining. The author provided a general background for knowledge discovery, a brief review of Swanson’s ideas, and a short discussion of approaches for hypothesis discovery. Her review is complementary to the overviews published by Cohen (2005) and Jensen et al. (2006) around the same time.

As Swanson’s collaborator, Smalheiser wrote two review papers on LBD (Smalheiser 2012, 2017). In the first article Smalheiser provided a critical overview of the then prevalent ABC model. He concluded that the ABC paradigm was not wrong, however, it was only one of the many approaches to LBD that could stimulate the development of a new generation of LBD tools. Moreover, he advocated that we urgently needed some sort of objective function (i.e., interestingness measures) for filtering out the output of LBD systems. Smalheiser’s second review was written from a more personal perspective. The author discussed Swanson’s contributions to LBD and gave an outline of its future directions.

Ahmed (2016) provided the first attempt to systematically classify LBD methods and approaches. The author defined LBD exclusively through the lens of information retrieval. The paper identified three approaches that were most often used as a basis for LBD: vector space model, probabilistic methods, and inference network.

Nearly in the same year, Sebastian et al. (2017a) and Henry and McInnes (2017), published extensive papers on LBD. The first group of authors provided an in-depth discussion on a broad palette of existing LBD approaches and offered performance evaluations on some recent emerging LBD methodologies. The latter authors likewise introduced historical and modern LBD approaches and provided an overview of evaluation methodologies and current trends. Both papers provided a general unifying framework for the LBD paradigms, its methodologies, and tools. The next review was published recently by (Gopalakrishnan et al. 2019). Their paper provided a comprehensive analysis of the LBD field, and the paper served as a methodological introduction behind particular tools and techniques. The authors provided a detailed discussion of the key LBD systems through the critical analysis of selected influential papers. They also summarized recent research trends and identified future directions of LBD. Thilakaratne et al. (2019a) analyzed the methodologies used in LBD using a novel classification scheme (i.e., the main points of the review were computational techniques, central research topics, available tools, and applications) and provided a timeline with key milestones in LBD research. The authors also identified the current trends in LBD regarding publication over years, top cited papers, and top authors. However, they considered only journals and conference proceedings for the review. In
their second paper, Thilakaratne et al. (2019b) presented a large-scale systematic review of the LBD workflow by manually analyzing 176 LBD papers. Although these reviews successfully provide qualitative insight into the field of LBD through dissecting the research evidence and appropriate classification of research themes, their analysis was manual and did not offer quantitative examination. Recently, Chen and Song (2019) performed the first knowledge mapping of the LBD field. They use the LBD domain as a proxy to illustrate an intuitive method to compare multiple search strategies in order to identify the most representative body of scientific publications.

Although the aforementioned reviews are quite recent, an in-depth quantitative analysis in the LBD research field is urgently needed, to provide newcomers, researchers, and also clinicians with a state-of-the-art scientometric overview of the field. It is also important to keep researchers informed about emerging trends and essential turning points in the expansion of domain knowledge.

3 Methods

In this section, we first outline the data collection procedure. Then we proceed with computational methodology and techniques applied in scientometric analysis, and finally, we conclude with a description of tools that have been used.

3.1 Bibliographic data collection

We used the most authoritative bibliographic databases as the data sources for retrieving publications and related metadata in the LBD research domain, including WoS (https://clarivate.com/products/web-of-science; Clarivate Analytics, Philadelphia, Pennsylvania, USA), Scopus (https://www.scopus.com; Elsevier, Amsterdam, Netherlands), PubMed (https://www.ncbi.nlm.nih.gov/pubmed; National Library of Medicine, Bethesda, Maryland, USA), ACM Digital Library (https://dl.acm.org; Association for Computing Machinery, New York, New York, USA), IEEE Xplore (https://ieeexplore.ieee.org; Institute of Electrical and Electronics Engineers, Piscataway, New Jersey, USA), and SpringerLink (https://rd.springer.com; Berlin, Germany). In addition, we used two preprint servers, namely arXiv (https://arxiv.org) and bioRxiv (https://www.biorxiv.org). WoS and Scopus both offer more or less comprehensive synopsis of the world’s research evidence in science, technology, medicine, social science, and arts and humanities. Scopus indexes literature dating back to 1970, while WoS covers even older publications as its index goes back to 1900. Preliminary analysis and our own experiences indicated that the prevailing body of LBD literature originates from biomedicine. To this end, we also included PubMed which is a primary bibliographic database in the field of biomedicine. ACM Digital Library
and IEEE Xplore was used predominantly for retrieving conference proceedings. Due to the fact that more and more authors publish their manuscripts on preprint servers, we also included arXiv and bioRxiv. The former is an open-access repository of preprints for natural sciences and the latter for life sciences. Finally, to reduce the risk of losing important documents, we also collected all relevant references from recent LBD reviews (Gopalakrishnan et al. 2019; Henry and McInnes 2017; Sebastian et al. 2017a; Smalheiser 2012, 2017; Thilakaratne et al. 2019a,b).

Our objective was to include a complete univertum of publications on LBD. For this purpose, we designed a search strategy to identify records where LBD related terms were mentioned in the title, abstract, or among keywords of the bibliographic citations. The detailed search strategy for each database is shown in Table 1. The time span was set between the years 1986 and 2020, since Swanson’s first paper until now. We applied no language, geographic, or any other constraints on the database retrieval procedure. Each bibliographic record consists of metadata about the publication, including a list of authors, title, abstract, author keywords, author affiliation, as well as number of citations, and a list of references cited by the publication. We included publications of all source types including journals, conference proceedings, book series, and books. We included the following document types: article, article in press, review, letter, editorial, note, short survey, conference paper, book, book chapter, erratum, and conference review. For some bibliographic records a manual inspection of the underlying paper was needed to identify missing bibliographic details (e.g., author’s affiliation). Author names normalization and disambiguation was not necessary. We have collected and downloaded all full-texts in PDF format and imported them into the Zotero reference manager. We removed all duplicate records using the Jaro-Winkler distance between pairs of titles as implemented in the stringdist package in R.

The bibliographic records that satisfy the search strategy were included for further analysis. The first author (AK) conducted a manual verification to ensure that each publication was closely related to the LBD field. During this first check, based on screening titles, abstracts, and keywords of the publications, AK eliminated the irrelevant publications. In the second step, both authors have evaluated the remaining publications (the relevant ones). We discussed all discrepancies until consensus has been reached. If necessary, one of us read the full paper to understand the content and the background of the paper and decided whether to include it in the analysis. The detailed review framework is depicted in the Results section in Figure 3.

3.2 Data analysis

The bibliographic records from different databases were first merged into the core dataset. We have paid special attention to cross-checking to ensure consistency of the data. First, we identified the annual production of LBD literature. We statistically described the annual distribution of publications by
Price’s law (Price 1963), which postulates an exponential growth of scientific production in a given domain over a predefined survey period. Hence, we first plot publication frequency against year, and then we apply the best-fitting linear and exponential functions to the data. If the latter has a better fit then the former, than we can consider the distribution as fulfilling the Price’s law.

Next, we prepared and summarised the statistics on most prolific authors, countries, institutions, and journals. We identified the first author’s affiliation, corresponding institution name, and country from the author address information. In cases where the author address was missing, we identified proper affiliation using the “Author Search” function in WoS or Scopus. The impact factor of the journals was determined as a five-year impact factor from Journal Citation Reports (https://jcr.clarivate.com; Clarivate Analytics, Philadelphia, PA, USA). We identified the most prolific institutions based on the affiliation of the first author of a given publication. We evaluated the distribution of publications among journals regarding whether they followed Bradford’s law (Bradford 1934), which states that if we sort journals by the number of articles published and then assign them to three groups, with each group publishing one-third of all articles, then one should identify the number of journals in each zone as the ratio \(1:n:n^2\), where \(n\) is defined as the Bradford multiplier. In other words, a few core journals account for one-third of all papers published within a body of investigated literature, whereas many other journals publish only a few papers.

It is known from the early days of Gestalt psychology that the whole is usually more than the pure sum of its parts. In addition to studying individual scholars, it is important to study their interrelations, and how such relations evolve in time, respond to internal events and external perturbations (Chen 2013). Hence we covered the research characteristics both at the entity level (i.e., individual researcher, organization, or country) and at the complex network level. Besides simple counting, we used two scientometric techniques to elucidate the relationship structure and dynamics of LBD research: (i) co-authorship analysis (COA) that seeks author co-occurrences, and (ii) document co-citation analysis (DCA) that tries to summarize the citation structure and provide a glimpse of the relations between papers.

Empirical evidence shows that DCA can successfully reveal the latent scientific structure of an investigated research domain (Small 1973). Each scientific paper usually cites a number of other articles. In DCA we represent these references as nodes and the links between the nodes represent how often a pair of references are cited together. The underlying assumption of DCA is that the references are contextually related if they are frequently cited together (Chen et al. 2010). To facilitate the interpretation of the DCA network, we performed cluster analysis which partitions the co-citation network into non-overlapping clusters. Each cluster is characterized by the references that are tightly interconnected within a cluster and exhibit weak connections among different clusters. We measured the quality of the partitioning process using the cluster’s silhouette width, where greater width reflects higher homogeneity of the cluster.
In the next step, we extended the basic DCA approach with cascade citation expansion. The basic idea of this methodology is to select an initial seed article and automatically expand the initial set of references by adding new papers through citation links (Chen and Song 2019). We employed a 2-generation forward expansion process\(^1\) and utilized a procedure as implemented in CiteSpace with direct access to the Dimensions API (https://www.dimensions.ai; Digital Science & Research Solutions, London, England).

The nodes in a network play various roles. For instance, a node may be central in a localized region of nodes (i.e., hub) or act as a connector between disparate clusters of nodes (i.e., broker). The importance of a particular node in a network is measured by various centrality measures. In this regard, we measured two types of centrality: (i) betweenness, which identifies nodes that are tightly connected to each other in terms of hubs; and (ii) brokerage, which determines nodes that filter, control, and alter the flow of information among different groups of nodes. The procedure for computing betweenness centrality is already implemented in CiteSpace. To compute brokerage, we first exported the desired network to R and then used the `brokerage()` function from the `sna` package to perform the brokerage analysis of Gould and Fernandez (1989).

Next, we detected the burst strength of the authors, institutions, journals, countries, and keywords. The burst strength characterizes how great the change is in the item’s frequency that triggered the burst. In this study, we used the original Kleinberg’s (2003) burst detection algorithm, which can identify sudden increases in frequency over time. In the paper, we reported only statistically significant bursts, together with the burst start and end.

3.3 Software

Data preprocessing was performed using custom Bash and Python scripts. The main part of the data analysis and visualizations was performed in CiteSpace (ver. 5.6.R5) (Chen 2006) and R using the `bibliometrix` package (Aria and Cuccurullo 2017). We decided to use this package because it greatly facilitates reproducible analysis, although many other excellent software packages for scientometric analysis exist in the community (e.g., VOSviewer (van Eck and Waltman 2009) or SciMAT (Cobo et al. 2012)). The programming scripts to reproduce the results of our analysis are freely available in the GitHub repository https://github.com/akastrin/lbd-review. A comprehensive data archive is available at Zenodo (https://doi.org/10.5281/zenodo.3884423) and includes tabulated bibliographic data.

\(^1\) A 2-generation forward expansion collects all papers connecting to the seed paper with two-step citation paths.
4 Results

In this section, we present the results of the performed analysis. First, we analyze the authors’ contributions to the body of LBD and provide performance statistics for the LBD production across countries and institutions. In the second part of this section, we delve into science mapping and try to understand the intellectual base of LBD research through the analysis of keywords and co-citation patterns.

In Figure 3 we depict a four-phase flowchart based on the PRISMA recommendations (Liberati et al. 2009). Using the search strategy described previously in the Methods section, we first retrieve \( n = 8895 \) bibliographic records. Next, we remove duplicate publications \( (n = 3875) \) after which \( n = 5023 \) records remain. We manually screen the titles and abstracts and exclude \( n = 4596 \) records that are not relevant to LBD. The second screening is performed on full-text publications; in this phase, we exclude additional 18 non-relevant publications. Finally, 409 publications remain for further analysis.

![PRISMA diagram](image)

**Fig. 3** PRISMA diagram

4.1 Retrieved literature

The number of publications indexed by different bibliographic databases (e.g., WoS, Scopus, and PubMed) on the same research subject tends to differ. Therefore, to extract a more reliable and valid set of data, we use eight databases. We include publications published between 1986 and 2020 that represent the complete active period of publication in LBD. A search of the databases was performed on 1st April 2020. Consequently, publications that
were indexed after this date might not have been captured in our study. The final set of bibliographic records covers a time period of 35 years (1986–2020) beginning with Swanson’s first paper on the LBD (Swanson 1986a). The majority of the records are original articles \((n = 236)\), followed by conference papers \((n = 127)\), review papers \((n = 24)\), book chapters \((n = 11)\), and other material \((n = 11)\); i.e., book review, letters to the editor, and reports). All documents were published in \(n = 224\) different sources. As of April 1, 2020, the complete set of publications had been cited \(n = 10198\) times.

| Query | WoS | Scopus | PubMed | ACM | IEEE | Springer | ArXiv | biorXiv | Total |
|-------|-----|--------|--------|-----|------|----------|-------|--------|-------|
| 1a    | 203 | 254    | 92     | 39  | 22   | 195      | 6     | 20     | 831   |
| 2b    | 14  | 23     | 109    | 10  | 3    | 0        | 2     | 0      | 161   |
| 3c    | 19  | 16     | 0      | 2   | 0    | 0        | 0     | 0      | 37    |
| 4d    | 1531| 2135   | 990    | 599 | 336  | 689      | 47    | 529    | 6856  |
| 5e    | 46  | 25     | 0      | 17  | 1    | 67       | 0     | 11     | 167   |

| Smalheiser (2012) | 53 |
| Henry and McNees (2017) | 96 |
| Smalheiser (2017) | 65 |
| Sebastian et al. (2017a) | 138 |
| Gopalakrishnan et al. (2019) | 129 |
| Thilakaratne et al. (2019a) | 224 |
| Thilakaratne et al. (2019b) | 138 |

Total 8895

4.2 Performance bibliometric analysis

4.2.1 Publication evolution over the years

The analysis of publication behavior over time might demonstrate the developmental trend from the macroscopic perspective. The maximum number of papers \((n = 34)\) were published in 2012. It is noteworthy that the term “Literature Based Discovery” was included in Medical Subject Headings (MeSH) vocabulary in 2013, indicating its high bibliographic importance. Figure 4 depicts the changing pattern of publications in our data set from 1986 until 2020. A reader can observe that the number of publications on LBD increased slowly from 1986 to mid-2000s, but since then it has been increasing significantly. This fact indicates that the field of LBD has acquired significant attention in the last decade.
The 35 years’ time span could be naturally clustered into three phases according to the published papers per year:

1. Incubation phase (1986–2003). In this phase, the number of publications was small, and the growing trend was more or less low. In the mid-1980s Swanson (1986a) published the seminal paper on LBD. In this period, first simple experiments for automating LBD were performed (Gordon and Lindsay 1996; Lindsay and Gordon 1999) and the basic terminology was refined (Weeber et al. 2001).

2. Developing phase (2004–2008). In this phase the empirical evidence gradually increased, however, the number of publications per year, with the exception of the year 2005, was still less than 20. In this phase, the foundational aspects of automated LBD were solidified and prepared the basis for more advanced investigations in the future. Also, the first book dedicated solely to LBD was published (Bruza and Weeber 2008).

3. Mature phase (2009–2020). The number of papers published in this period is significantly higher in comparison to the previous two phases. Research has entered a peak period and even demonstrated a booming tendency. In this period researchers developed a plethora of new methods and techniques for LBD. Additionally, the first two extensive review papers were published (Henry and McInnes 2017; Sebastian et al. 2017a).

We fit linear and exponential regression models to test whether the annual distribution of publications followed Price’s law. Both models were statistically significant ($p < 0.05$). The linear model achieved a coefficient of determination of $R^2 = 0.61$, while the exponential model fitted better with a coefficient of determination of $R^2 = 0.65$. Therefore, we could conclude that the annual
production of publications follows Price’s law. The annual growth rate was 8.66\%, where we omit the last year from the calculation.

4.2.2 Authors

The authors are the driving force in research. It is the task of every scientist to make a meaningful contribution to the body of knowledge and thus (co-)shape the development of the field in which (s)he works.

Our analysis identifies 802 distinct authors. The majority of the authors write in collaboration with colleagues \((n = 766)\). On average, we have detected 3.68 \((SD = 2.73)\) authors per document and 1.90 \((SD = 2.57)\) documents per author. The authors with the highest number of publications and citations have a tendency to be the scientists who drive the research field and have a casting vote for its development. The 10 most prolific authors are presented in Table 2. Rindflesch clearly holds the first position with 37 publications, although he is the first author in only one LBD paper. As stated above, Lotka’s law states that a small portion of researchers is responsible for most of the publications, whereas the majority contribute a very small number of papers. The discrepancy between the observed values and the expected frequencies according to Lotka’s law has been evaluated using the nonparametric Kolmogorov-Smirnov (KS) goodness-of-fit test. KS test reveals no statistically significant differences between the observed and the actual publication numbers \((D = 0.28, p = 0.491)\).

Table 2 Top 10 authors based on the total number of publications

| Rank | Author       | Institution                          | NP   | TC       | h   | h_s | b_i |
|------|--------------|--------------------------------------|------|----------|-----|-----|-----|
| 1    | Rindflesch TC| National Library of Medicine, USA    | 37   | 1617     | 24  | 16  | 0.04|
| 2    | Kostoff RN   | Georgia Institute of Technology, USA | 23   | 3016     | 29  | 15  | 0.00|
| 3    | Hristovski D | University of Ljubljana, Slovenia     | 23   | 429      | 10  | 11  | 0.01|
| 4    | Smalheiser NR| University of Illinois at Chicago, USA| 21   | 5453     | 41  | 14  | 0.00|
| 5    | Swanson DR   | University of Chicago, USA           | 20   | 2729     | 26  | 18  | 0.00|
| 6    | Cohen T      | University of Texas, USA             | 19   | 1048     | 19  | 10  | 0.01|
| 7    | Song M       | Yonsei University, South Korea       | 18   | 889      | 15  | 6   | 0.02|
| 8    | Cestnik B    | Jožef Stefan Institute, Slovenia      | 16   | 250      | 8   | 8   | 0.00|
| 9    | Peterlin B   | University Medical Center Ljubljana, Slovenia| 11   | 3438     | 28  | 7   | 0.00|
| 10   | Kastrin A    | University of Ljubljana, Slovenia     | 11   | 337      | 10  | 5   | 0.00|

Note: Rank = Ranking score based on number of publications, NP = number of publications, TC = total number of citations, \(h = h\)-index, \(h_s = h\)-index applied to LBD literature only, \(b_i = \) betweenness centrality

However, in terms of citations, Smalheiser scores far more than the rest of the researchers. As expected, the most cited is his paper in which he and Swanson as the first author described the Arrowsmith system (Swanson and Smalheiser 1997). Smalheiser and Peterlin also have the most significant difference between \(h\) and \(h_s\) scores, meaning that they are also highly productive outside the LBD area. The majority of authors are from the United States (Rindflesch, Kostoff, Smalheiser, Swanson, and Cohen), four authors come
from Slovenia (Hristovski, Cestnik, Peterlin, and Kastrin), and one from the Republic of Korea (Song). Kostoff prevails according to the authors’ dominance factor (data not shown), which is a ratio indicating the proportion of multi-authored papers in which a person appears as the first author. He authored 12 publications in which he appears as a first author.

The production over time was most prominent for Swanson. As stated previously, he wrote his first paper in 1986 (Swanson 1986a) and the final one in 2011 (Swanson 2011). Smalheiser, the researcher with the second-longest career path, joined Swanson in 1994 (Smalheiser and Swanson 1994). Smalheiser published his last paper on LBD in 2017 when he gave his personal perspective on Swanson’s contribution to science (Smalheiser 2017). In order to understand the temporal aspects of authors’ publishing patterns, we also perform burst analysis on authors’ career paths. A significant level of the burst is presented in five authors. As expected, the founding father of LBD had the longest burst; from 1986 until 2001. In this period Swanson published the majority of his papers. Rindflesch’s burst is significantly shorter; it ran for six years (2011–2016). Other authors (i.e., Smalheiser, Kostoff, and Jha) have very short bursts that last for only between one and five years.

Let us now consider co-authorship relations. The entire co-authorship network consists of 802 nodes and 5148 edges. Each node denotes an author and the edges among the authors represent academic partnership through the co-authorship on the publications. The average degree of the network was $c = 12.84$ neighbors. The network exhibits a relatively short average path length ($l = 4.94$ hops) and high clustering ($C = 0.72$). To draw the network, we filter out all nodes with degree $k_i < 2$ neighbors. The reduced co-authorship network is presented in Figure 5. The node size is proportional to the number of publications, and the edge width follows the strength of the collaboration. The colors of the nodes correspond to the different network communities as identified by the Louvain clustering algorithm (Blondel et al. 2008). The high clustering coefficient reflects the rich community structure of the network. The researchers inside the clusters establish strong partnerships with colleagues in the same research group and only weakly connect with other researchers. The biggest research community with robust collaboration among researchers include the highly productive research circuit of Rindflesch as the central author. The network exhibits low density ($\rho = 0.02$), which together with high modularity ($Q = 0.91$) indicates that research groups are dispersed. The author with the highest betweenness centrality is Wang; however, the average betweenness centrality is very low as well ($B = 0.001$), meaning that most authors’ influence is still at a low level. To sum up, the collaboration network exhibits many subnetworks, indicating that the LBD domain is composed of many small and medium-sized research groups with little communication among them.

### Countries

A total of 27 countries have contributed to the LBD literature, as depicted in the world map in Figure 6. First, it is worth noting that LBD production is
unevenly distributed across countries. The United States commits about half of the body of the literature to LBD research ($n = 167$ or 49% of all the documents). This indicates that the US is leading in LBD research. Interestingly, Slovenia, a small country in the heart of Europe, is the second most productive country with 34 publications (10%). Surprisingly, India has no researcher who published about LBD as the first author. We also report the productivity score for each country using the simple formula (production number / population $\times 1\,000\,000$). Slovenia has been found to be the most productive country (16.40) followed by the Netherlands (0.64) and the United States (0.51). Following the United Nations country classification schema, most countries are developed countries. Gross domestic product (GDP) measures goods and services produced in a country. We have found a moderate positive correlation between 2019 GDP values and number of publications of 27 countries ($r = 0.32$, $p = 0.099$). However, the United States is top-ranked according to total citations ($n = 6267$), followed by Germany ($n = 714$), and the Netherlands ($n = 520$).

The production concerning temporal evolution across countries reveals the primacy of the United States. Researchers from the United States have been publishing regularly since 1986 and they have significantly intensified the re-
search production since 2001. In the second place, we have identified the United Kingdom with the publication span 1989–2019. The early appearance of the United Kingdom on the LBD scene is due to two theoretical papers published at the end of the 1980s that discuss the creation of new knowledge by information retrieval (Davies 1989, 1990). However, the next paper originating from the UK was published only in 2006 (Song and Bruza 2006). We have detected no significant burst for countries.

4.2.4 Institutions

Next, we consider the institution level. Institution-based analysis might help to discover research organizations that deserve the researcher’s attention and provide a macro understanding of the spatial distribution of LBD efforts. Our analysis identifies 173 different organizations that contribute to the production of LBD publications. Please note that we only consider the affiliation of the first author in the analysis. The details for the top 10 institutions, ranked according to the number of publications, are summarised in Table 3. The University of Chicago stands out with the largest number of publications ($n = 17$), thanks to the work of Swanson, followed by the University of Illinois at Chicago ($n = 14$), and University of Ljubljana ($n = 14$). Actually, six of the top 10 institutions come from the United States and as many as three from Slovenia (University of Ljubljana, Jožef Stefan Institute, and University of Nova Gorica). Only the University of Chicago scores among the top 10 universities according to the Academic Ranking of World Universities in 2019.

4.2.5 Journals

When analyzing research productivity, it is essential to study the journals in which papers are published. LBD is a narrow and specific research field that has no specialized journal. Instead, the LBD research is published mainly

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2 The Journal of Biomedical Discovery and Collaborations (DISCO) was an open access online journal that encompassed all aspects of scientific information management and studies of scientific practice. The journal connected disparate perspectives (e.g., informatics,
Table 3 Top 10 research institutions based on the total number of publications

| Rank | Institution                        | Country   | NP  | TC        | ARWU |
|------|------------------------------------|-----------|-----|-----------|------|
| 1    | University of Chicago              | USA       | 17  | 1847      | 10   |
| 2    | University of Illinois at Chicago  | USA       | 14  | 299       | 201-300 |
| 3    | University of Ljubljana            | Slovenia  | 14  | 451       | 401-500 |
| 4    | University of Texas                | USA       | 13  | 229       | 201-300 |
| 5    | Office of Naval Research           | USA       | 12  | 480       | –    |
| 6    | Drexel University                  | USA       | 11  | 254       | 301-400 |
| 7    | University of Tokyo                | Japan     | 11  | 78        | 25   |
| 8    | Jožef Stefan Institute             | Slovenia  | 10  | 54        | –    |
| 9    | National Library of Medicine       | USA       | 9   | 279       | –    |
| 10   | University of Nova Gorica          | Slovenia  | 9   | 93        | –    |

Note: Rank = Ranking score based on number of publications, NP = number of publications, TC = total number of citations, ARWU = Academic Ranking of World Universities

Table 4 Top 10 journals based on the total number of publications

| Rank | Journal title                        | Country   | NP  | TC        | IF       |
|------|--------------------------------------|-----------|-----|-----------|----------|
| 1    | Lecture Notes in Computer Science    | Germany   | 21  | 186       | –        |
| 2    | Journal of Biomedical Informatics    | USA       | 20  | 522       | 3.724    |
| 3    | Technological Forecasting and Social Change | USA | 14  | 484       | 4.040    |
| 4    | BMC Bioinformatics                   | UK        | 13  | 423       | 2.970    |
| 5    | Information Science and Knowledge Management | USA | 11  | 70        | –        |
| 6    | PLOS ONE                             | USA       | 9   | 122       | 3.337    |
| 7    | AMIA Annual Symposium Proceedings    | USA       | 7   | 218       | –        |
| 8    | Bioinformatics                       | UK        | 7   | 346       | 8.860    |
| 9    | Journal of the American Society for Information Science and Technology | USA | 7   | 405       | 2.762    |
| 10   | Briefings in Bioinformatics          | UK        | 6   | 709       | 8.265    |

Note: NP = number of publications, TC = total number of citations, IF = 5 year impact factor

To study journal distribution and to identify “core” journals, we have also employed Bradford’s law of scattering (Bradford 1934). In Figure 7 we have plotted the Bradford plot where the cumulative frequency of LBD literature in journals related to (biomedical) informatics and bioinformatics. Table 4 summarizes details about the top 10 journals. Interestingly, with respect to the number of publications, Lecture Notes in Computer Science has published 21 papers on LBD research, followed by the Journal of Biomedical Informatics with a similar number of papers. Bioinformatics, which has the highest impact factor in our list, has published only 7 papers on LBD. Out of 10 journals, six are published in the United States.
has been plotted against the logarithm of the journal rank. The journals are grouped into three zones, comprising a similar number of publications. The core journals are those whose data points lie in Zone 1 ($n = 14$). The middle third (i.e., Zone 2) has 75 journals, and the last zone has 134 journals. The relationship of each zone (14:75:134) does not fit well into the expected Bradford's distribution (26:88:294) ($\chi^2(2) = 11.17, p = 0.004$). Thus, we cannot confirm Bradford’s assumption that a few core journals account for one-third of all papers published within the body of LBD literature. It is also important to note that the curve does not take a typical “S” shape and there is no “gross drop” at the end of the curve. In our case, the Bradford plot has taken more or less a linear shape after the initial rise.

The main body of knowledge on LBD is ingrained in journal papers. The first coherent book on LBD was published in 2008 by Springer and edited by Bruza and Weeber (2008). The book contains 11 chapters by prominent authors in the LBD field and offers the reader a comprehensive overview of LBD research.

4.2.6 Publications

Employing the processed bibliometric data, we can identify the most important hallmarks of LBD research. In total, we have extracted 13026 references from 409 papers related to LBD research. The top 10 most cited papers are listed in Table 5, including their first author, year of publication, title, the total number of citations, and the number of citations per year. The data are ranked by the number of citations. Swanson is the author of four listed publications.
First on the rank list is Swanson’s seminal paper on fish oil and Raynaud’s disease (Swanson 1986a), which has 409 citations and is cited about 12 times annually. This paper is categorically the first hallmark of LBD research. The second and the third rank are reserved for two review papers, written by Cohen (2005) and Jensen et al. (2006). Both articles are of interest to the broader domain of researchers because they provide an in-depth review of methods and techniques used in text mining and especially in biomedical informatics and bioinformatics. The most recent of highly cited papers is an interesting article published by (Uzzi et al. 2013) in which authors discuss balancing conventional and atypical knowledge which may be critical to link innovativeness and scientific impact. However, it is important to note that Uzzi’s paper has considerably more citations per year in comparison to other papers on the list. This is probably due to the high impact factor of the Science journal in which the paper was published. A paper written by Chen and Sharp (2004) is the first serious attempt of applying a complex network approach to LBD and is relatively highly cited among researchers who utilize network analysis for bioinformatics. These ten publications cover the theoretical research as well as practical applications of LBD. However, all these papers were published before 2013, yet important scientific achievements in LBD have also been published more recently. For example, one key achievement that we can identify and is not on the list is a novel LBD system called LION LBD which offers a broad range of metrics for evaluating the strength of entity associations, and allows fast real-time discovery of indirect associations among biomedical concepts (Pyysalo et al. 2019). This and other important publications are not among the current top 10 due to their relatively recent publication date.

To gain a deeper understanding of the citation structure, we have also conducted a burst analysis. In total, 46 documents have citation bursts. Table 6 summarizes the top 10 papers with the strongest citation burst. The top paper with the strongest burst (11.39) is the paper written by Swanson and Smallheiser (1997) in which they describe the Arrowsmith discovery support system and evaluate various LBD search strategies. The paper’s burst began in 1998 and ended in 2005. The second paper with the strongest citation burst (9.61) was written by Weeber et al. (2001). This paper is one of the methodological hallmarks in the pioneering era of LBD. First, it formally describes a two-step model of the discovery process in which research hypotheses are generated (i.e., open discovery mode) and subsequently tested (i.e., closed discovery mode). Second, for LBD analysis authors employ UMLS concepts and use semantics with these concepts to filter out unmeaningful information. Third on the list is the article by Lindsay and Gordon (1999) on lexical statistics, which initiated the era of statistically-based LBD applications (Sebastian et al. 2017a).

4.3 Science mapping

Science mapping is the next logical step in our analysis. In this section we provide keywords analysis and DCA.
Table 5  Top 10 references based on the total number of citations

| Rank | Author       | Year | Title                                                                 | Journal                       | TC  | TC/Y  |
|------|--------------|------|----------------------------------------------------------------------|-------------------------------|-----|-------|
| 1    | Swanson      | 1986 | Fish oil, Raynaud’s syndrome, and undiscovered public knowledge       | Perspectives in Biology and Medicine | 409 | 11.69 |
| 2    | Jensen et al.| 2006 | Literature mining for the biologist: From information retrieval to biological discovery | Nature Reviews Genetics       | 389 | 25.93 |
| 3    | Cohen et al. | 2005 | A survey of current work in biomedical text mining                   | Briefings in Bioinformatics   | 367 | 22.94 |
| 4    | Kell         | 2009 | Iron behaving badly: inappropriate iron chelation as a major contributor to the etiology of vascular and other progressive inflammatory and degenerative diseases | BMC Medical Genomics         | 312 | 26.00 |
| 5    | Uzzi et al.  | 2013 | Atypical combinations and scientific impact                          | Science                       | 286 | 35.75 |
| 6    | Perez-Iratxeta et al. | 2002 | Association of genes to genetically inherited diseases using data mining | Nature Genetics               | 246 | 12.95 |
| 7    | Swanson et al.| 1997 | An interactive system for finding complementary literatures: A stimulus to scientific discovery | Artificial Intelligence      | 232 | 9.67  |
| 8    | Swanson      | 1988 | Migraine and magnesium: Eleven neglected connections                  | Perspectives in Biology and Medicine | 231 | 7.45  |
| 9    | Chen et al.  | 2004 | Content-rich biological network constructed by mining PubMed abstracts | BMC Bioinformatics            | 204 | 12.00 |
| 10   | Swanson      | 1986 | Undiscovered public knowledge                                        | The Library Quarterly          | 171 | 4.89  |

Note: TC = total number of citations, TC/Y = total number of citations per year

Table 6  Top 10 references with the strongest citation bursts

| Rank | Author       | Year | Title                                                                 | Strength | Begin | End |
|------|--------------|------|----------------------------------------------------------------------|----------|-------|-----|
| 1    | Swanson      | 1989 | Online search for logically-related noninteractive medical literatures: A systematic trial-and-error strategy | 3.67     | 1990  | 1997|
| 2    | Gordon et al.| 1996 | Toward discovery support systems: A replication, re-examination, and extension of Swanson’s work on literature-based discovery of a connection between Raynaud’s and fish oil | 5.27     | 1997  | 2004|
| 3    | Smalheiser et al. | 1996 | Indomethacin and Alzheimer’s disease                                  | 3.82     | 1998  | 2004|
| 4    | Swanson et al.| 1997 | An interactive system for finding complementary literatures: A stimulus to scientific discovery | 11.39    | 1998  | 2005|
| 5    | Gordon et al.| 1998 | Using latent semantic indexing for literature based discovery        | 4.20     | 1999  | 2006|
| 6    | Lindsay et al.| 1999 | Literature-based discovery by lexical statistics                      | 8.15     | 2000  | 2007|
| 7    | Smalheiser   | 1998 | Using ARROWSMITH: a computer-assisted approach to formulating and assessing scientific hypotheses | 4.94     | 2001  | 2006|
| 8    | Weeber et al.| 2001 | Using concepts in literature-based discovery: Simulating Swanson’s Raynaud-fish oil and migraine-magnesium discoveries | 9.61     | 2003  | 2006|
| 9    | Weeber et al.| 2000 | Text-based discovery in biomedicine: The architecture of the DAD-system | 5.56     | 2003  | 2005|
| 10   | Swanson et al.| 1999 | Implicit text linkages between Medline records: Using Arrowsmith as an aid to scientific discovery | 4.16     | 2003  | 2006|

Note: Strength = strength of burst, Begin = begin of burst, End = end of burst
4.3.1 Keyword analysis

The research topics studied in LBD research can be characterized by the keywords assigned to each bibliographic record. The keywords enable us to summarise, qualify, and explain the entire scientific document within the boundaries of a particular research domain. The keywords provide a plausible summarization of research hotspots, for example, burst keywords represent research frontiers and indicate possible emerging trends. The word cloud in Figure 8 reflects the frequency distribution of keywords in the core set of 409 documents. The five most frequent keywords are knowledge discovery, information retrieval, data mining, natural language processing, and literature mining. It is important to note that we detect no significant burst among the keywords.

Fig. 8 Word cloud of keywords extracted from documents on LBD research. Please note that the term literature-based discovery is omitted.

The timeline view of the keywords is presented in Figure 9. The timeline starts with the year 1996 because keywords were rarely assigned to bibliographic records before this early period. The research until the year 2001 is topical and domain-specific; the timeline is loaded with keywords such as fish oil, information retrieval, raynaud, magnesium, and migraine. Entering the new millennium, the richness of keywords increases, and terms evolve rapidly. In the 2010s we can observe two main directions of research: one is interweaving of LBD ideas with genetics; the other concerns application of semantics in LBD. Prevailing keywords are text mining, knowledge discovery, data mining, disease, information, system, gene, and natural language processing. This indicates that LBD research in this decade was developing from baseline
Swanson’s approach and its replications (e.g., Gordon and Lindsay (1996)) towards systematic development of knowledge discovery methods and data mining tools for LBD. In terms of LBD reviews from this era we can observe a shift from statistical-based approaches (e.g., pure co-occurrence) to rule-based (e.g., association rules) and semantic approaches. For example, in 2005 Hristovski et al. (2005) introduced the BITOLA system, which utilizes association rule mining to reveal (gene-disease) relations between biomedical concepts by observing frequent patterns among data objects. Roughly at the same time, researchers introduced a semantic-based discovery pattern approach (Ahlers et al. 2007; Hristovski et al. 2006), which significantly increases the precision and enhances the interpretability of LBD systems. A plethora of other Web tools and services were also developed within this decade (e.g., DAD (Weeber et al. 2001), LitLinker (Pratt and Yetisgen-Yildiz 2003), Manjal (Srinivasan 2004), IRIDESCENT (Wren 2004), and RaJoLink (Petrič et al. 2009)). The fourth decade of LBD (i.e., 2011–2020) has been the decade of network science in the LBD community. Important keywords in this time period are network, link discovery, link prediction, network analysis, knowledge graph, drug discovery, and pharmacovigilance. According to Sebastian et al. (2017a) this decade coincides with the stage of emerging LBD approaches which could be characterized by two directions. First, traditional co-occurrence-based and knowledge-driven approaches culminate in solutions that integrate both. Second, LBD becomes more interdisciplinary, incorporating methods and tools from information sciences (Chen et al. 2009), scientometrics (Kostoff 2014), and machine learning (Sebastian et al. 2017b).

Fig. 9 A timeline view of keywords extracted from documents on LBD for the period 1986–2020. We have built a list of keywords from author keywords and keywords assigned by database curators. For the description of the clusters please see the text.
4.3.2 Document co-citation analysis

DCA allows us to examine a network of co-cited references. The body of cited references provides the knowledge base of the selected documents. Figure 10 depicts the subset of the DCA network as pruned with the Pathfinder algorithm (Chen 2006). The network exhibits 399 nodes and 891 edges. Each node in the network refers to a document that is labeled with the first author name and the year of publication. Each edge represents a co-citation relation among the pair of documents. The size of the nodes is proportional to the co-citation frequency. The most highly cited documents were written by Srinivasan (2004) and Wren et al. (2004). As we have said previously in the Methods section, we have computed two types of node importance, namely betweenness centrality, and brokerage. The aforementioned Wren’s paper is the document with the highest betweenness centrality (0.34), followed by Jensen et al. (2006) (0.27). Together with Frijters et al. (2010), both papers also exhibit the highest brokerage score. These references are not only important as hubs in the DCA network but also as bridging nodes among contextually different groups of nodes.

Using cluster analysis of the cited references we obtain a set of 44 co-citation clusters that may provide us the main research topics of the intellectual base. Figure 10 depicts the DCA network with the embedded clusters. In total we have identified 13 clusters that are worth further consideration. Table 7 summarizes the basic statistics for each cluster sorted by its size: ID number, size, silhouette width, mean year, and first cluster label as identified by the log-likelihood ratio extraction method. The silhouette width ranges from 0.72 to 0.99 indicating adequate consistency of derived clusters. The clusters could be summarized as follows.

1. Cluster \#0 (finding linkage) has the largest number of members. Cluster’s mean age is 2003 and is relatively old. This cluster is to be interpreted as a general LBD cluster while it contains generic phrases such as life science, online tool, biomedical text mining, vector space model, and discovery approach. Representative references in this cluster are Lindsay and Gordon (1999), Weeber et al. (2003), and Hristovski et al. (2005) which also exhibit the highest citation burst. The paper written by Hristovski et al. demonstrated high Sigma\(^3\) value, indicating a high degree of scientific novelty. Two typical citing papers are for example Cohen’s (2005) review on text mining with a special section on LBD and Weeber et al.’s (2005) paper, in which the authors review Web-based tools for LBD.

2. Cluster \#1 (link prediction) is much younger; its mean age is 2011 and it assembles 42 references. The main theme of this cluster is on the prediction of future discoveries using link prediction methods. The cluster is loaded with terms reflecting its affinity to complex networks science (e.g., semantic

\(^3\) Sigma (\(\Sigma\)) index is used to characterize scientific novelty according to centrality and burstness as criteria of transformative discovery Chen et al. (2009). Sigma is defined as \((\text{centrality} + 1)^{\text{burstness}}\).
Fig. 10 Document co-citation network of the core dataset based on documents published between 1986 and 2020. Cluster labels in red text are taken from the titles of the cited documents using the log-likelihood ratio algorithm. Red nodes refer to documents with high citation burst. For the description of the clusters please see the text. CiteSpace configuration: LRF = 3, LBY = 8, e = 2.0, Top N = 50.

medline network, mesh co-occurrence network, supervised link discovery). The three top-cited references are Cameron et al. (2015), Hristovski et al. (2013), and Wilkowski et al. (2011). Representative citing papers include seminal work by Katukuri et al. (2012) on supervised link discovery and Kastrin et al.’s (2016) generalization of link prediction for LBD.

3. Cluster #2 (literature mining) contains 35 members and refers to gene prioritization and drug repurposing using LBD methods. It contains phrases such as high-throughput literature analysis, disease candidate gene, and gene prioritization. The three most representative references for this cluster are Wren et al. (2004), Frijters et al. (2010), and Jensen et al. (2006). The latter is a highly cited review paper on biomedical text mining and exhibits high Sigma value, reflecting its novelty in the field. Two typical citing articles are for instance Andronis’s (2011) paper on literature mining for drug repositioning and Deftereos’s (2011) review on adverse event prediction using literature analysis.
4. Cluster #3 (side-effect relationship) consists of 32 members. The representative phrases in this cluster are both technical (e.g., learning predictive models, literature-derived semantic predication) as well as applied (e.g., large clinical dataset, identifying plausible adverse drug reactions, adverse event prediction). Some representative cited references with the highest citation bursts are Cohen et al. (2012), Shang et al. (2014), and Cameron et al. (2013). The citing papers include for example Cohen’s papers in which he discusses and elaborates the methodology of embedding of semantic predications (Cohen and Widdows 2017; Widdows and Cohen 2015).

5. Cluster #4 (emerging approaches) consists of 28 members. The average mean year of 2013 reflects its relative recentness. This cluster is mainly related to the description of novel and emerging approaches in LBD, which is reflected in phrases and terms such as new approach, heterogeneous bibliographic information network, or convolutional neural network method. The most cited reference with the highest citation burst is Smalheiser (2012). The citing articles include recent reviews by Sebastian et al. (2017a), Smalheiser (2017), and Thilakaratne et al. (2019b).

6. Cluster #5 (using arrowsmith) is the oldest extracted cluster (with a mean age of 1998). It reflects early pioneering days of LBD. Some representative phrases are for instance lexical statistics, human-computer collaboration, and medline record. In this cluster, the most representative cited references with the highest burst are Swanson and Smalheiser (1997), Weeber et al. (2001), and Gordon and Dumais (1998). The representative citing articles include Swanson and Smalheiser’s (1999) paper on using Arrowsmith for biomedical relation discovery and Lindsay and Gordon’s (1999) article in which they applied lexical statistics to extend and replicate original Swanson’s discoveries.

7. Cluster #6 (artificial intelligence) contains 22 members and is represented with terms such as emerging in-silico scientist, bridging biology, and content-rich biological network. The most cited and highly burst references in this cluster are Jenssen et al. (2001), Stapley and Benoit (2000), and Hristovski et al. (2001). Citing papers include for instance Chen and Sharp’s (2004) paper on building biological networks beyond pure co-occurrence approach.

8. Cluster #7 (literature-related discovery) may be referred to as Kostoff’s cluster. Its mean year is 2006 and is loaded with terms like potential treatment or future research directions. This cluster contains mainly Kostoff’s references that were part of the special issue of the journal Technological Forecasting and Social Change in 2008.

9. Cluster #8 (large-scale validation) is the youngest cluster in this list (mean year = 2014). It contains 20 members and is loaded with phrases such as hypothesis generation system, candidate ranking, and automated literature mining. One and only reference with a significant burst in this cluster is Kilicoglu et al.’s (2012) paper on SemMedDB, a large scale repository of semantic predication extracted from MEDLINE. The citing papers reflect the recent work on large-scale LBD by Sybrandt et al. (2018a,b).
10. Clusters #9, #13, #16, and #17 are the smallest ones. Each of them consists of less than 20 members and are thus unstable to interpret.

### Table 7  Co-citation clusters of LBD research 1986–2020

| ID | Size | Width | Year | Label                                      |
|----|------|-------|------|--------------------------------------------|
| 0  | 43   | 0.72  | 2003 | finding linkage                            |
| 1  | 42   | 0.83  | 2011 | link prediction                            |
| 2  | 35   | 0.82  | 2008 | literature mining                          |
| 3  | 32   | 0.87  | 2011 | side-effect relationship                   |
| 4  | 28   | 0.86  | 2013 | emerging approaches                        |
| 5  | 24   | 0.96  | 1998 | using arrowsmith                           |
| 6  | 22   | 0.92  | 2001 | artificial intelligence                     |
| 7  | 21   | 0.97  | 2006 | literature-related discovery               |
| 8  | 20   | 0.99  | 2014 | large-scale validation                     |
| 9  | 17   | 0.99  | 2003 | contemporary scientific practice           |
| 13 | 9    | 0.97  | 2002 | validating discovery                       |
| 16 | 7    | 0.96  | 2005 | pubmed abstract                            |
| 17 | 7    | 0.95  | 2011 | identifying evidence                       |

Note: ID = cluster ID, Size = number of references in a cluster, Width = silhouette width of a cluster, Year = mean year, Label = cluster label as identified by a LLR algorithm

#### 4.3.3 Cascading citation expansion

For the citation expansion process we use Swanson’s ground-breaking paper on fish oil and Raynaud’s disease [Swanson 1986a] as the seed article. The 2-generation forward expansion procedure collects a total of 86,927 distinct references. After pruning with the Pathfinder algorithm, we obtain the merged network with 622 nodes and 1267 edges. The extracted network contains 478 nodes, which is 76% of the full network we have obtained using the expansion procedure. Figure 11 depicts the largest connected component of the co-citation network.

Most cited is the paper by Kozomara and Griffiths-Jones (2011) which introduced the miRBase, a primary Web repository for microRNA sequences and annotations. Our inspection reveals that RNA research and LBD are related through Smalheiser’s clinical work. For a deeper understanding of this connection, we refer the reader to the paper by Chen and Song (2019), who deduce similar conclusions. A citation burst has been detected in 227 papers. Among the top 25 papers with the strongest citation burst we identify three of Swanson’s works including his seminal paper on fish oil and Raynaud’s disease [Swanson 1986a] and a subsequent paper on migraine and magnesium [99].

The modularity of the network is high ($Q = 0.91$). Clustering reveals 68 coherent groups of nodes, out of which 20 significant clusters are labeled in Figure 11. All silhouette widths are in the range 0.87–0.99 indicating high
homogeneity of clusters. The oldest cluster is #10 (natural language) with 1990 as a mean year of publication. Most interesting are the youngest clusters that might indicate the new trends and topics which are worth addressing in LBD research. The youngest (mean age = 2014) are clusters #14 (deep learning) and #15 (artificial intelligence). The former includes terms like convolutional neural network, reinforcement learning, and machine learning, while the latter contains keywords such as big data analytics, computational intelligence, and precision medicine.

Until recently, neural network models have been rarely used in LBD applications (Crichton et al. 2018, 2020; Sang et al. 2018). Although they have great potential to achieve better prediction performance and more stable results than ABC-based methods, their output suffers from low explainability and interpretability, due to their black-box nature (Zitnik et al. 2019). But on the other hand, this is also a great opportunity for artificial intelligence. Developing prediction models with the ability to explain the statistical learning process is currently a hot topic trend under the umbrella of the so-called Explainable Artificial Intelligence (XAI) (Barredo Arrieta et al. 2020). Thus, the
combination of both deep learning models and XAI presents fundamentally new frontiers for LBD research.

5 Discussion

LBD research is more than thirty years old. In this work, we have conducted a scientometric analysis that provides a detailed overview of the LBD literature, its intellectual structure, and dynamics. The present work demonstrates that the publication trend is increasing in the LBD community. Our investigations show a colorful palette of authors and topics in the various nuances of LBD research. The findings offer insights on the current state of the LBD research and provide future research directions such as deep learning and XAI. The current study also extends the current classical reviews on LBD. To the best of our knowledge, this is the first inclusive scientometric analysis of the body of research evidence in LBD.

Understanding the past and the current body of publications is a sine qua non for growing the LBD research in the future. In the recent decade, there have been a plethora of studies examining knowledge structure and evolution through the scientometric lens of particular scientific fields. The lack of similar studies in the LBD area makes it difficult if not impossible to compare LBD with other research fields. However, LBD leans to biomedicine and medical informatics in particular. There are two reasons for this fact. First, historically, LBD originates from medical applications (Swanson 1986a, 1988). Second, in a practical sense, the MEDLINE distribution is freely available to researchers, which is not the case with WoS or Scopus. Due to its availability, a number of open-source Web applications that use MEDLINE and text mining for the purpose of LBD have been developed (Gopalakrishnan et al. 2019). A review of empirical evidence reveals that several bibliometric studies have been performed in the domain of biomedical informatics. For example, DeShazo et al. (2009) characterized the field of medical informatics in general over a 20 year period (1987–2006). Schuemie et al. (2009) identified three main subdomains of medical informatics including health information systems, knowledge representation, and data analysis. Last but not least, Nadri et al. (2017) performed bibliometrics analysis on the top 100 most cited papers in medical informatics and demonstrated the dominance of statistics and artificial intelligence sub-areas.

Relative to other research fields, LBD can be considered young. However, from its beginnings in the mid-1980’s it has grown into a mature scientific discipline, even with its own entry in the MeSH vocabulary. We have demonstrated that LBD interacts with various research fields, so it is needless to say that LBD stands on the shoulders of many giants, including information science, text mining, and natural language processing. Even more, our hypothesis is that LBD effectively adopts and recycles the ideas and research trends from other research fields, such as natural language processing and statistics. The first such example was the research conducted by Gordon and Dumais (1998),
who borrowed latent semantic analysis (Deerwester et al. 1990) to compute the semantic similarity between a source term and a target term in the LBD discovery process. Recently, Lever et al. (2017) showed that singular-value decomposition, a well-known factorization method from linear algebra, provides the best scoring approach for predicting future co-occurrences in comparison to the leading methods in LBD. This behavior is in line with the theory of transformative discoveries proposed by Chen et al. (2009). The central postulate of this theory is that connecting otherwise divergent pieces of knowledge is an important mechanism of creative thinking in science. In addition, Uzzi et al. (2013) empirically demonstrated that the highest-impact science is based on unusual combinations of existing patches of knowledge.

A conspicuous change in the number of papers published per year suggests that a major turning point is occurring in the field. We have found that the number of publications has been increasing over the last 20 years, particularly since 2008. The development of the LBD field is associated with great progress in computer science and natural language processing in particular. It is important to note that there are some general factors promoting the development of the field, such as knowledge fragmentation, overspecialization, and information overload. On the other hand, availability of text mining resources (e.g., SemMedDB (Kilicoglu et al. 2012), PubTator Central (Wei et al. 2019)) has allowed more people to work on the LBD problem. The total citations accumulate over the years and consequently, the recent papers do not have enough time to acquire more citations. The growth of publications and citations in the last decade indicates a promising future of LBD. According to Shneider’s (2009) four-stage theory of scientific evolution, the research process is classified into four phases: (i) the first phase introduces new subject matters into the realm of science; (ii) the second phase develops domain methodology, enabling the language to describe a broad spectrum of phenomena; (iii) the third phase applies known research methods to new research subject matters; and (iv) the last, fourth, phase records existing knowledge and puts it into practical use. In line with the above categorization, LBD could be placed in the second, tool-construction, stage. In the first stage, pioneers such as Swanson and Smalheiser conceived the field, identified central research questions, and built first applications. In the second stage, the LBD community built and improved computation tools to systematically study original problems. However, we are still far away from the fourth stage. In our opinion, we need to bring together efforts from both the computer science community and biomedical literature mining groups. While the former is oriented towards developing new algorithms, the latter tends more to solve applied problems (Zhao et al. 2020).

Scientific productivity is strongly correlated with international collaboration among researchers, countries, and institutions (Lee and Bozeman 2005). Studies investigating the scientific impact of cross-institution groups confirm that their papers have a higher citation rate in comparison to papers produced by a single research group. Papers with international co-authorship have an even higher impact (Thonon et al. 2015). However, we have demonstrated
that there is a lack of collaboration among research groups in the field of LBD. Most of the research produced in the field of LBD is generated by small cliques of researchers. Even though the collaboration and internationalization among researchers have certain, mainly societal, downsides, it provides great benefits. Abramo et al. (2011) demonstrated an increasing trend in collaboration among institutions could be attributed to different policies stimulating research collaboration (e.g., the EU Framework Programme for Research and Innovation). We are aware of at least one successful EU FP7 funded project from the broad domain of LBD named BISON (2008–2011) that investigates novel methods for discovering new, domain-bridging connections and patterns from heterogeneous data sources (Berthold 2012).

Although the number of publications has grown over the years, scientific production in LBD is still very limited and evolves much slower than comparable research fields (e.g., scientometrics (Hou et al. 2018)). It is worth noting that the scientific production in the LBD field across countries is far from uniform. Among the 10 countries with the greatest contribution to the field, the United States have contributed most papers, far exceeding other countries. This is not surprising as they have more established research backgrounds and research funding.

It is known that today’s science stimulates the growth of large teams in all areas of research, whereas small teams and solitary researchers diminish (Wu et al. 2019). Small groups disrupt science with new ideas, concepts, and theories, while large teams tend to further develop existing ones. Our results have demonstrated that LBD research is distinctively partitioned into small groups. This is somehow surprising, since modern LBD problems are highly complex and require interdisciplinary work (i.e., a team of information scientists, computer scientists, statisticians, natural language processing experts, etc.). On the other hand, Li et al. (2019) show that exceptional scientific achievement comes from small teams. However, we agree with Wu et al. (2019) that to further strengthen the science and LBD, in particular, it is necessary to amplify both (i) science disruption by exploring older and lesser known but promising work (such research was for example demonstrated by Lever et al. (2017), who combined LBD and singular value decomposition) and (ii) solving already known problems and refining common designs (such research was for instance demonstrated recently by Crichton et al. (2018), who used neural link prediction for LBD). A possible solution might be to organize an international scientific conference (or some other sort of capacity building) dedicated solely to LBD, which is needed to facilitate networking among LBD researchers. Such an event might significantly contribute to the further development of top-level

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4 To our knowledge two LBD events have been organized in the past decade. The First International Workshop on the role of Semantic Web in Literature-Based Discovery (SWLBD 2012) was co-organized with The IEEE International Conference on Bioinformatics and Biomedicine in Philadelphia, USA (http://www.ischool.drexel.edu/iseebibm/bibm12). At the time of this writing, Smalheiser and Sebastian organized the First International Workshop on Literature-Based Discovery (LBD2020) co-located with the 24-th Pacific-Asia Conference on Knowledge Discovery and Data Mining in Singapore (http://scientificar bitrage.com/lbd-2020).
research and foster collaboration, especially between researchers from different countries.

A keyword analysis is a frequently used technique in scientometrics to outline preferences, trends, and emerging tendencies in a set of publications. Our exploration reveals the tight integration of LBD research with information retrieval and natural language processing themes. On a higher semantic level, LBD relates to computer science and computational biology in particular. Through the whole keyword network, we can observe the intertwining of technical (e.g., artificial intelligence, text mining) and biomedical (e.g., gene, genetics) terms. This network is constructed using the authors’ keywords and terms attributed by the database curators. For presentation purposes, we need to greatly reduce the network. This way we lose low-frequency terms which may indicate new, emerging trends in LBD. However, manual exploration of the LBD literature has identified deep learning as a possible future direction in LBD. Two main contributions were published about LBD and deep learning at the end of 2018: an article written by Korhonen’s lab (Crichton et al. 2018) and a short, only two-page long conference paper by Sang et al. (2018).

Despite its contributions, this study also has certain limitations. First, although our review is based on deliberate search queries in eight most comprehensive databases, it may be that other search strategies have yielded (slightly) different results. However, it is very difficult to define a search query that covers all the relevant papers in the scientific literature while simultaneously excluding irrelevant papers. Second, employed databases preferably list English-language publications. To this end, some papers in other languages might not have been included. Third, the presented approach uses solely quantitative methods, without in-depth qualitative interpretation of the content. Despite these limitations, we believe that we properly present a worldwide view on LBD in the last four decades. Additional future work should also consider combining quantitative and qualitative analysis to further extend this analysis.

6 Conclusions

In this study, we have performed a comprehensive study of the worldwide scientific output of LBD research from 1986 to 2020. During this time span, the number of LBD publications increased. Rindflesch published the highest number of publications on LBD, followed by Swanson. Swanson was also the most cited author in the field. The United States was the most dominant country according to the number of published papers. The University of Chicago was the most influential institution, both with the largest number of publications on LBD, as well as with the largest number of citations.

5 At the time of the submission of this paper we came across a new paper (Crichton et al. 2020) from Korhonen’s group which discussed implementation of graph-based neural network methodology for open and closed LBD.
In the future, we anticipate that studies in LBD extend in two directions, namely deep learning and XAI. Both fields are strongly connected to advanced machine learning techniques and next-generation network science including network embeddings. For example, graph neural networks provide a very powerful toolbox, achieving excellent performance on a wide scope of tasks including node classification and link prediction (Ying et al. 2019). On the other hand, we need to ensure strong interpretability and explainability of prediction models, while black-box nature of the current deep learning models often limits their adoption in practical applications.

To sum up, this study could significantly augment the traditional literature reviews and provide helpful information to determine new research directions and perspectives of LBD research. More collaboration is needed among research groups to further stimulate LBD research. LBD is still an important research theme; deep learning for improving results of LBD systems could be a scientific frontier in the next few years.

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Declarations

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Conflicts of interest

The authors declare that they have no conflict of interest.

Availability of data and material

The data set discussed in this paper has been deposited in the public repository Zenodo (https://doi.org/10.5281/zenodo.3884423) and is freely available to the research community.

Code availability

R code to replicate the results of the study is accessible on the author’s GitHub page (https://github.com/akastrin/lbd-review).
Authors’ contributions

AK conceived the study, collected the data, performed data analysis, and wrote the manuscript. DH contributed with critical revisions of the manuscript. Both authors read and approved the final version of the manuscript.

References

Abramo G, D’Angelo CA, Solazzi M (2011) The relationship between scientists’ research performance and the degree of internationalization of their research. Scientometrics 86(3):629–643, DOI 10.1007/s11192-010-0284-7

Ahlers CB, Hristovski D, Kilicoglu H, Rindflesch TC (2007) Using the literature-based discovery paradigm to investigate drug mechanisms. In: AMIA Annual Symposium Proceedings, pp 6–10

Ahmed A (2016) Literature-based discovery: Critical analysis and future directions. International Journal of Computer Science and Network Security 16(7):11–26

Andronis C, Sharma A, Virvilis V, Deftereos S, Persidis A (2011) Literature mining, ontologies and information visualization for drug repurposing. Briefings in Bioinformatics12(4):357–368, DOI 10.1093/bib/bbr005

Aria M, Cucurullo C (2017) bibliometrix: An R-tool for comprehensive science mapping analysis. Journal of Informetrics 11(4):959–975, DOI 10.1016/j.joi.2017.08.007

Barredo Arrieta A, Díaz-Rodríguez N, Del Ser J, Bennetot A, Tabik S, Barbara A, García S, Gil-Lopez S, Molina D, Benjaminis R, Chatila R, Herrera F (2020) Explainable Artificial Intelligence (XAI): Concepts, taxonomies, opportunities and challenges toward responsible AI. Information Fusion 58:82–115, DOI 10.1016/j.inffus.2019.12.012

Bekhuis T (2006) Conceptual biology, hypothesis discovery, and text mining: Swanson’s legacy. Biomedical Digital Libraries 3(1), DOI 10.1186/1742-5581-3-2

Berthold MR (ed) (2012) Bisociative knowledge discovery: An introduction to concept, algorithms, tools, and applications. Lecture Notes in Artificial Intelligence, Springer, Berlin, DOI 10.1007/978-3-642-31830-6

Blondel VD, Guillaume JL, Lambiotte R, Lefebvre E (2008) Fast unfolding of communities in large networks. Journal of Statistical Mechanics: Theory and Experiment 2008(10):P10008, DOI 10.1088/1742-5468/2008/10/P10008

Bodenreider O (2004) The Unified Medical Language System (UMLS): Integrating biomedical terminology. Nucleic Acids Research 32(Database issue):D267–270, DOI 10.1093/nar/gkh061

Bornmann L, Mutz R (2015) Growth rates of modern science: A bibliometric analysis based on the number of publications and cited references. Journal of the Association for Information Science and Technology 66(11):2215–2222, DOI 10.1002/asi.23329
Bradford SC (1934) Sources of information on specific subjects. Engineering 137:85–86
Bruza P, Weeber M (eds) (2008) Literature-based discovery. Springer, Berlin, DOI 10.1007/978-3-540-68690-3
Callon M, Courtial JP, Turner WA, Bauin S (1983) From translations to problematic networks: An introduction to co-word analysis. Information (International Social Science Council) 22(2):191–235, DOI 10.1177/053901883022002003
Cameron D, Bodenreider O, Yalamanchili H, Danh T, Vallabhaneni S, Thirunarayan K, Sheth AP, Rindflesch TC (2013) A graph-based recovery and decomposition of Swanson’s hypothesis using semantic predications. Journal of Biomedical Informatics 46(2):238–251, DOI 10.1016/j.jbi.2012.09.004
Cameron D, Kavuluru R, Rindflesch TC, Sheth AP, Thirunarayan K, Bodenreider O (2015) Context-driven automatic subgraph creation for literature-based discovery. Journal of Biomedical Informatics 54:141–157, DOI 10.1016/j.jbi.2015.01.014
Chen C (2006) CiteSpace II: Detecting and visualizing emerging trends and transient patterns in scientific literature. Journal of the American Society for information Science and Technology 57(3):359–377, DOI 10.1002/asi.20317
Chen C (2013) Mapping scientific frontiers: The quest for knowledge visualization. Springer, London, DOI 10.1007/978-1-4471-5128-9
Chen C, Song M (2017) Representing scientific knowledge: The role of uncertainty. Springer, New York, NY, DOI 10.1007/978-3-319-62543-0
Chen C, Song M (2019) Visualizing a field of research: A methodology of systematic scientometric reviews. PLOS ONE 14(10):e0223994, DOI 10.1371/journal.pone.0223994
Chen C, Chen Y, Horowitz M, Hou H, Liu Z, Pellegrino D (2009) Towards an explanatory and computational theory of scientific discovery. Journal of Informetrics 3(3):191–209, DOI 10.1016/j.joi.2009.03.004
Chen C, Ibekwe-SanJuan F, Hou J (2010) The structure and dynamics of cocitation clusters: A multiple-perspective cocitation analysis. Journal of the American Society for Information Science and Technology 61(7):1386–1409, DOI 10.1002/asi.21309
Chen H, Sharp BM (2004) Content-rich biological network constructed by mining PubMed abstracts. BMC Bioinformatics 5(1):147, DOI 10.1186/1471-2105-5-147
Cobo MJ, Lopez-Herrera AG, Herrera-Viedma E, Herrera F (2012) SciMAT: A new science mapping analysis software tool. Journal of the American Society for Information Science and Technology 63(8):1609–1630, DOI 10.1002/asi.22688
Cohen AM (2005) A survey of current work in biomedical text mining. Briefings in Bioinformatics 6(1):57–71, DOI 10.1093/bib/6.1.57
Cohen T, Widdows D (2017) Embedding of semantic predications. Journal of Biomedical Informatics 68:150–166, DOI 10.1016/j.jbi.2017.03.003
Cohen T, Widdows D, Schvaneveldt RW, Davies P, Rindflesch TC (2012) Discovering discovery patterns with predication-based semantic indexing. Journal of Biomedical Informatics 45(6):1049–1065, DOI 10.1016/j.jbi.2012.07.003

Cory KA (1997) Discovering hidden analogies in an online humanities database. Computers and the Humanities 31(1):1–12, DOI 10.1023/A:100042220677

Crichton G, Guo Y, Pyysalo S, Korhonen A (2018) Neural networks for link prediction in realistic biomedical graphs: A multi-dimensional evaluation of graph embedding-based approaches. BMC Bioinformatics 19(1), DOI 10.1186/s12859-018-2163-9

Crichton G, Baker S, Guo Y, Korhonen A (2020) Neural networks for open and closed literature-based discovery. PLOS ONE 15(5):e0232891, DOI 10.1371/journal.pone.0232891

Davies R (1989) The creation of new knowledge by information retrieval and classification. Journal of Documentation 45(4):273–301, DOI 10.1108/eb026868

Davies R (1990) Generating new knowledge by retrieving information. Journal of Documentation 46(4):368–372, DOI 10.1108/eb026868

Deerwester S, Dumais ST, Furnas GW, Landauer TK, Harshman R (1990) Indexing by latent semantic analysis. Journal of the American Society for Information Science 41(6):391–407, DOI 10.1002/(SICI)1097-4571(199009)41:6<391::AID-ASI1>3.0.CO;2-9

Deftereos SN, Andronis C, Friedla EJ, Persidis A, Persidis A (2011) Drug repurposing and adverse event prediction using high-throughput literature analysis. WIREs Systems Biology and Medicine 3(3):323–334, DOI 10.1002/wsbm.147

DeShazo JP, LaVallie DL, Wolf FM (2009) Publication trends in the medical informatics literature: 20 years of “Medical Informatics” in MeSH. BMC Medical Informatics and Decision Making 9(1):7, DOI 10.1186/1472-6947-9-7

DiGiacomo RA, Kremer JM, Shah DM (1989) Fish-oil dietary supplementation in patients with Raynaud’s phenomenon: A double-blind, controlled, prospective study. The American Journal of Medicine 86(2):158–164, DOI 10.1016/0002-9343(89)90261-1

Ding Y, Song M, Han J, Yu Q, Yan E, Lin L, Chambers T (2013) Entitymetrics: Measuring the impact of entities. PLOS ONE 8(8):e71416, DOI 10.1371/journal.pone.0071416

van Eck N, Waltman L (2009) Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics 84(2):523–538, DOI 10.1007/s11192-009-0146-3

Eijk CCvd, Mulgigen EMv, Kors JA, Mons B, Berg Jvd (2004) Constructing an associative concept space for literature-based discovery. Journal of the American Society for Information Science and Technology 55(5):436–444, DOI 10.1002/asi.10392
Frijters R, van Vugt M, Smeets R, van Schaik R, de Vlieg J, Alkema W (2010) Literature mining for the discovery of hidden connections between drugs, genes and diseases. PLOS Computational Biology 6(9), DOI 10.1371/journal.pcbi.1000943

Fuller SS, Revere D, Bugni PF, Martin GM (2004) A knowledgebase system to enhance scientific discovery: Telemakus. Biomedical Digital Libraries 1(1):2, DOI 10.1186/1742-5581-1-2

Godin B (2006) On the origins of bibliometrics. Scientometrics 68(1):109–133, DOI 10.1007/s11192-006-0086-0

Gopalakrishnan V, Jha K, Jin W, Zhang A (2019) A survey on literature based discovery approaches in biomedical domain. Journal of Biomedical Informatics 93:103141, DOI 10.1016/j.jbi.2019.103141

Gordon MD, Dumais S (1998) Using latent semantic indexing for literature based discovery. Journal of the American Society for Information Science 49(8):674–685, DOI 10.1002/(SICI)1097-4571(199806)49:8<674::AID-ASI213.0.CO;2-T

Gordon MD, Lindsay RK (1996) Toward discovery support systems: A replication, re-examination, and extension of Swanson’s work on literature-based discovery of a connection between Raynaud’s and fish oil. Journal of the American Society for Information Science 47(2):116–128, DOI 10.1002/(SICI)1097-4571(199602)47:2<116::AID-ASI31.0.CO;2-1

Gould RV, Fernandez RM (1989) Structures of mediation: A formal approach to brokerage in transaction networks. Sociological Methodology 19:89–126, DOI 10.2307/270949

Henry S, McInnes BT (2017) Literature based discovery: Models, methods, and trends. Journal of Biomedical Informatics 74:20–32, DOI 10.1016/j.jbi.2017.08.011

Hirsch JE (2005) An index to quantify an individual’s scientific research output. Proceedings of the National Academy of Sciences 102(46):16569–16572, DOI 10.1073/pnas.0507655102

Hou J, Yang X, Chen C (2018) Emerging trends and new developments in information science: A document co-citation analysis (2009–2016). Scientometrics 115(2):869–892, DOI 10.1007/s11192-018-2695-9

Hristovski D, Stare J, Peterlin B, Džeroski S (2001) Supporting discovery in medicine by association rule mining in Medline and UMLS. Studies in Health Technology and Informatics 84(Pt 2):1344–1348

Hristovski D, Peterlin B, Mitchell JA, Humphrey SM (2005) Using literature-based discovery to identify disease candidate genes. International Journal of Medical Informatics 74(2):289–298, DOI 10.1016/j.ijmedinf.2004.04.024

Hristovski D, Friedman C, Rindflesch TC, Peterlin B (2006) Exploiting semantic relations for literature-based discovery. In: AMIA Annual Symposium Proceedings, pp 349–353

Hristovski D, Rindflesch T, Peterlin B (2013) Using literature-based discovery to identify novel therapeutic approaches. Cardiovascular & Hematological Agents in Medicinal Chemistry 11(1):14–24
Hristovski D, Kastrin A, Rindflesch TC (2015) Semantics-based cross-domain collaboration recommendation in the life sciences: Preliminary results. In: Pei J, Silvestri F, Tang J (eds) Proceedings of the 2015 IEEE/ACM International Conference on Advances in Social Networks Analysis and Mining 2015, Association for Computing Machinery, Paris, France, ASONAM ’15, pp 805–806, DOI 10.1145/2808797.2809300

Hui W, Lau WK (2019) Application of literature-based discovery in nonmedical disciplines: A survey. In: Proceedings of the 2nd International Conference on Computing and Big Data, Association for Computing Machinery, Taichung, Taiwan, ICCBD 2019, pp 7–11, DOI 10.1145/3366650.3366660

Jensen LJ, Saric J, Bork P (2006) Literature mining for the biologist: From information retrieval to biological discovery. Nature Reviews Genetics 7(2):119–129, DOI 10.1038/nrg1768

Jennsen TK, Lægreid A, Komorowski J, Hovig E (2001) A literature network of human genes for high-throughput analysis of gene expression. Nature Genetics 28(1):21–28, DOI 10.1038/ng0501-21

Jha K, Jin W (2016) Mining hidden knowledge from the counterterrorism dataset using graph-based approach. In: Métair E, Meziane F, Sarace M, Sugumaran V, Vadera S (eds) Natural language processing and information systems, Springer, Cham, pp 310–317, DOI 10.1007/978-3-319-41754-7_29

Kastrin A, Rindflesch TC, Hristovski D (2016) Link prediction on a network of co-occurring MeSH terms: Towards literature-based discovery. Methods of Information in Medicine 55(4):340–346, DOI 10.3414/ME15-01-0108

Katukuri JR, Xie Y, Raghavan VV, Gupta A (2012) Hypotheses generation as supervised link discovery with automated class labeling on large-scale biomedical concept networks. BMC Genomics 13(3):S5, DOI 10.1186/1471-2164-13-S3-S5

Kiliçoglu H, Shin D, Fiszman M, Rosemblat G, Rindflesch TC (2012) SemMedDB: A PubMed-scale repository of biomedical semantic predications. Bioinformatics 28(23):3158–3160, DOI 10.1093/bioinformatics/bts591

Kleinberg J (2003) Bursty and hierarchical structure in streams. Data Mining and Knowledge Discovery 7(4):373–397, DOI 10.1023/A:1024940629314

Kostoff RN (2014) Literature-related discovery: Common factors for Parkinson’s disease and Crohn’s disease. Scientometrics 100(3):623–657, DOI 10.1007/s11192-014-1298-3

Kostoff RN, Briggs MB (2008) Literature-related discovery (LRD): Potential treatments for Parkinson’s disease. Technological Forecasting and Social Change 75(2):226–238, DOI 10.1016/j.techfore.2007.11.007

Kozomara A, Griffiths-Jones S (2011) miRBase: Integrating microRNA annotation and deep-sequencing data. Nucleic Acids Research 39(suppl_1):D152–D157, DOI 10.1093/nar/gkq1027

Lee S, Bozeman B (2005) The impact of research collaboration on scientific productivity. Social Studies of Science 35(5):673–702, DOI 10.1177/0306312705052359

Lever J, Gakkhar S, Gottlieb M, Rashnavadi T, Lin S, Sin C, Smith M, Jones MR, Krzywinski M, Jones SJ (2017) A collaborative filtering-based approach
to biomedical knowledge discovery. Bioinformatics 34(4):652–659, DOI 10.1093/bioinformatics/btx613
Li J, Yin Y, Fortunato S, Wang D (2019) Nobel laureates are almost the same as us. Nature Reviews Physics 1:301–303, DOI 10.1038/s42254-019-0057-z
Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. PLOS Medicine 6(7):e1000100, DOI 10.1371/journal.pmed.1000100
Lindsay RK, Gordon MD (1999) Literature-based discovery by lexical statistics. Journal of the American Society for Information Science 50(7):574–587, DOI 10.1002/(SICI)1097-4571(1999)50:7<574::AID-ASI3>3.0.CO;2-Q
Mower J, Subramanian D, Shang N, Cohen T (2017) Classification-by-analogy: Using vector representations of implicit relationships to identify plausibly causal drug/side-effect relationships. In: AMIA Annual Symposium Proceedings, pp 1940–1949
Nadri H, Rahimi B, Timpka T, Sedghi S (2017) The top 100 articles in the medical informatics: A bibliometric analysis. Journal of Medical Systems 41(10):150, DOI 10.1007/s10916-017-0794-4
Noyons EC, Moed HF, Luwel M (1999) Combining mapping and citation analysis for evaluative bibliometric purposes: A bibliometric study. Journal of the American Society for Information Science 50(2):115–131, DOI 10.1002/(SICI)1097-4571(1999)50:2<115::AID-ASI3>3.0.CO;2-J
Petrič I, Urbančič T, Cestnik B, Macedoni-Lukšič M (2009) Literature mining method RaJoLink for uncovering relations between biomedical concepts. Journal of Biomedical Informatics 42(2):219–227, DOI 10.1016/j.jbi.2008.08.004
Petrič I, Cestnik B, Lavrač N, Urbančič T (2012) Outlier detection in cross-context link discovery for creative literature mining. The Computer Journal 55(1):47–61, DOI 10.1093/comjnl/bxq074
Pratt W, Yetisgen-Yildiz M (2003) LitLinker: Capturing connections across the biomedical literature. In: Proceedings of the 2nd international conference on Knowledge capture, Association for Computing Machinery, Sanibel Island, FL, USA, K-CAP ’03, pp 105–112, DOI 10.1145/945645.945662
Price DJDS (1963) Little science, big science. Columbia University Press, New York, NY
Price DJDS (1965) Networks of scientific papers. Science 149(3683):510–515
Pritchard A (1969) Statistical bibliography or bibliometrics. Journal of Documentation 25(4):348–349
Pyysalo S, Baker S, Ali I, Haselwimmer S, Shah T, Young A, Guo Y, Högberg J, Stenius U, Narita M, Korhonen A (2019) LION LBD: A literature-based discovery system for cancer biology. Bioinformatics 35(9):1553–1561, DOI 10.1093/bioinformatics/bty845
Rindflesch TC, Fiszman M (2003) The interaction of domain knowledge and linguistic structure in natural language processing: Interpreting hypernymic propositions in biomedical text. Journal of Biomedical Informatics
Sang S, Yang Z, Liu X, Wang L, Zhang Y, Lin H, Wang J, Yang L, Xu K, Zhang Y (2018) A knowledge graph based bidirectional recurrent neural network method for literature-based discovery. In: Zheng HJ, Callejas Z, Griol D, Wang H, Hu X, Schmidt H, Baumbach J, Dickerson J, Zhang L (eds) 2018 IEEE International Conference on Bioinformatics and Biomedicine (BIBM), IEEE, pp 751–752, DOI 10.1109/BIBM.2018.8621423

Schuemie M, Talmon J, Moorman P, Kors J (2009) Mapping the domain of medical informatics. Methods of Information in Medicine 48(01):76–83, DOI 10.3414/ME0576

Sebastian Y, Siew EG, Orimaye SO (2017a) Emerging approaches in literature-based discovery: Techniques and performance review. The Knowledge Engineering Review 32, DOI 10.1017/S0269888917000042

Sebastian Y, Siew EG, Orimaye SO (2017b) Learning the heterogeneous bibliographic information network for literature-based discovery. Knowledge-Based Systems 115:66–79, DOI 10.1016/j.knosys.2016.10.015

Shang N, Xu H, Rindflesch TC, Cohen T (2014) Identifying plausible adverse drug reactions using knowledge extracted from the literature. Journal of Biomedical Informatics 52:293–310, DOI 10.1016/j.jbi.2014.07.011

Shneider AM (2009) Four stages of a scientific discipline; four types of scientist. Trends in Biochemical Sciences 34(5):217–223, DOI 10.1016/j.tibs.2009.02 .002

Smallheiser N, Swanson D (1994) Assessing a gap in the biomedical literature: Magnesium deficiency and neurologic disease. Neuroscience Research Communications 15(1):1–9

Smallheiser NR (2012) Literature-based discovery: Beyond the ABCs. Journal of the American Society for Information Science and Technology 63(2):218–224, DOI 10.1002/asi.21599

Smallheiser NR (2017) Rediscovering Don Swanson: The past, present and future of literature-based discovery. Journal of Data and Information Science 2(4):43–64, DOI 10.1515/jdis-2017-0019

Small H (1973) Co-citation in the scientific literature: A new measure of the relationship between two documents. Journal of the American Society for Information Science 24(4):205–269, DOI 10.1002/asi.4630240406

Song D, Bruza P (2006) Text based knowledge discovery with information flow analysis. In: Hutchison D, Kanade T, Kittler J, Kleinberg JM, Mattern F, Mitchell JC, Naor M, Nierstras O, Pandu Rangan C, Steffen B, Sudan M, Terzopoulos D, Tygar D, Vardi MY, Weikum G, Zhou X, Li J, Shen HT, Kitsuregawa M, Zhang Y (eds) Frontiers of WWW Research and Development - APWeb 2006, vol 3841, Springer, Berlin, pp 692–701, DOI 10.1007/11610113_60

Srinivasan P (2004) Text mining: Generating hypotheses from MEDLINE. Journal of the American Society for Information Science and Technology 55(5):396–413, DOI 10.1002/asi.10389

Stapley BJ, Benoit G (2000) Biobibliometrics: Information retrieval and visualization from co-occurrences of gene names in Medline abstracts. Pacific Sym-
Swanson DR (1986a) Fish oil, Raynaud’s syndrome, and undiscovered public knowledge. Perspectives in Biology and Medicine 30(1):7–18, DOI 10.1353/pbm.1986.0087

Swanson DR (1986b) Undiscovered public knowledge. The Library Quarterly 56(2):103–118, DOI 10.1086/601720

Swanson DR (1988) Migraine and magnesium: Eleven neglected connections. Perspectives in Biology and Medicine 31(4):526–557, DOI 10.1353/pbm.1988.0009

Swanson DR (2011) Literature-based resurrection of neglected medical discoveries. Journal of Biomedical Discovery and Collaboration 6:34–47, DOI 10.5210/disco.v6i0.3515

Swanson DR, Smalheiser NR (1997) An interactive system for finding complementary literatures: A stimulus to scientific discovery. Artificial Intelligence 91(2):183–203, DOI 10.1016/S0004-3702(97)00008-8

Swanson DR, Smalheiser NR (1999) Implicit text linkages between Medline records: Using Arrowsmith as an aid to scientific discovery. Library Trends 48(1):48–59

Sybrandt J, Carrabba A, Herzog A, Safro I (2018a) Are abstracts enough for hypothesis generation? In: Abe N, Liu H, Pu C, Hu X, Ahmed N, Qiao M, Song Y, Kossmann D, Liu B, Lee K, Tang J, He J, Saltz J (eds) 2018 IEEE International Conference on Big Data (Big Data), pp 1504–1513, DOI 10.1109/BigData.2018.8621974

Sybrandt J, Shtutman M, Safro I (2018b) Large-scale validation of hypothesis generation systems via candidate ranking. In: Abe N, Liu H, Pu C, Hu X, Ahmed N, Qiao M, Song Y, Kossmann D, Liu B, Lee K, Tang J, He J, Saltz J (eds) 2018 IEEE International Conference on Big Data (Big Data), pp 1494–1503, DOI 10.1109/BigData.2018.8622637

Thilakaratne M, Falkner K, Atapattu T (2019a) A systematic review on literature-based discovery: General overview, methodology, & statistical analysis. ACM Computing Surveys 52(6):129:1–129:34, DOI 10.1145/3365756

Thilakaratne M, Falkner K, Atapattu T (2019b) A systematic review on literature-based discovery workflow. PeerJ Computer Science 5:e235, DOI 10.7717/peerj-cs.235

Thonon F, Boulkedid R, Delory T, Rousseau S, Saghatelian M, Harten Wv, O’Neill C, Alberti C (2015) Measuring the outcome of biomedical research: A systematic literature review. PLOS ONE 10(4):e0122239, DOI 10.1371/journal.pone.0122239

Uzzi B, Mukherjee S, Stringer M, Jones B (2013) Atypical combinations and scientific impact. Science 342(6157):468–472, DOI 10.1126/science.1240474

Weeber M, Klein H, de Jong-van den Berg LT, Vos R (2001) Using concepts in literature-based discovery: Simulating Swanson’s Raynaud-fish oil and migraine-magnesium discoveries. Journal of the American Society for Information Science and Technology 52(7):548–557, DOI 10.1002/asi.1104
Weeber M, Vos R, Klein H, de Jong-van den Berg LTW, Aronson AR, Molema G (2003) Generating hypotheses by discovering implicit associations in the literature: A case report of a search for new potential therapeutic uses for thalidomide. Journal of the American Medical Informatics Association 10(3):252–259, DOI 10.1197/jamia.M1158
Weeber M, Kors JA, Mons B (2005) Online tools to support literature-based discovery in the life sciences. Briefings in Bioinformatics 6(3):277–286, DOI 10.1093/bib/6.3.277
Wei CH, Allot A, Leaman R, Lu Z (2019) PubTator central: Automated concept annotation for biomedical full text articles. Nucleic Acids Research 47(W1):W587–W593, DOI 10.1093/nar/gkz389
Widdows D, Cohen T (2015) Reasoning with vectors: A continuous model for fast robust inference. Logic Journal of the IGPL 23(2):141–173, DOI 10.1093/jigpal/jzu028
Wilkowski B, Fiszman M, Miller CM, Hristovski D, Arabandi S, Rosenblat G, Rindflesch TC (2011) Graph-based methods for discovery browsing with semantic predications. In: AMIA Annual Symposium Proceedings, pp 1514–1523
Wren JD (2004) Extending the mutual information measure to rank inferred literature relationships. BMC Bioinformatics 5(1):145, DOI 10.1186/1471-2105-5-145
Wren JD, Bekeredjian R, Stewart JA, Shohet RV, Garner HR (2004) Knowledge discovery by automated identification and ranking of implicit relationships. Bioinformatics 20(3):389–398, DOI 10.1093/bioinformatics/btg421
Wu L, Wang D, Evans JA (2019) Large teams develop and small teams disrupt science and technology. Nature 566(7744):378, DOI 10.1038/s41586-019-0941-9
Yang HT, Ju JH, Wong YT, Shmulevich I, Chiang JH (2017) Literature-based discovery of new candidates for drug repurposing. Briefings in Bioinformatics 18(3):488–497, DOI 10.1093/bib/bbw030
Ying R, Bourgeois D, You J, Zitnik M, Leskovec J (2019) GNNExplainer: Generating explanations for graph neural networks. Advances in neural information processing systems 32:9240–9251
Zhao S, Su C, Lu Z, Wang P (2020) Recent advances in biomedical literature mining. Briefings in Bioinformatics p bbaa057, DOI 10.1093/bib/bbaa057
Zitnik M, Nguyen F, Wang B, Leskovec J, Goldenberg A, Hoffman MM (2019) Machine learning for integrating data in biology and medicine: Principles, practice, and opportunities. Information Fusion 50:71–91, DOI 10.1016/j.inffus.2018.09.012