Heliyon 10 (2024) e39329

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Research trends and hotspots in fundus image segmentation from 2007 to 2023: A bibliometric analysis

Hairui Deng [a,b,1], Yiren Wang [a,b,1], Venhui Cheng [c,1], Yongcheng He [d,1], Zhongjian Wen [a,b], Shouying Chen [a,b], Shengmin Guo [e,**], Ping Zhou [b,f,***], Yi Wang [g,*]

[a] School of Nursing, Southwest Medical University, Luzhou, 646000, China
[b] Wound Healing Basic Research and Clinical Application Key Laboratory of Luzhou, School of Nursing, Southwest Medical University, Luzhou, 646000, China
[c] Department of Ophthalmology, The Affiliated Hospital of Southwest Medical University, Luzhou, 646000, China
[d] Department of Pharmacy, Sichuan Agricultural University, Chengdu, 610000, China
[e] Department of Nursing, The Affiliated Hospital of Southwest Medical University, Luzhou, 646000, China
[f] Department of Radiology, The Affiliated Hospital of Southwest Medical University, Luzhou, 646000, China
[g] Department of Publicity, The Affiliated Hospital of Southwest Medical University, Luzhou, 646000, China

ARTICLE INFO

Keywords:
Automatic segmentation
CiteSpace
Frontier
Fundus lesions
Hotspots
Visual analysis
VOSviewer

ABSTRACT

Objective: To understand the current status, research hotspots, and trends of automatic segmentation of fundus lesion images worldwide, providing a reference for subsequent related studies.
Methods: The electronic database Web of Science Core Collection was searched for research in the field of automatic segmentation of fundus lesion images from 2007 to 2023. Visualization maps of countries, authors, institutions, journals, references, and keywords were generated and analyzed using the CiteSpace and VOSviewer software.
Results: After deduplication, 707 publications were sorted out, showing an overall increasing trend in publication volume. The countries with the highest publication counts were China, followed by India, the USA, the UK, Spain, Pakistan, and Singapore. A high degree of collaboration was observed among authors, and they cooperated widely. The keywords included "diabetic retinopathy," "deep learning," "vessel segmentation," "retinal images," "optic disc localization," and so forth, with keyword bursts starting in 2018 for "retinal images," "machine learning," "biomedical imaging," "deep learning," "convolutional neural networks," and "transfer learning." The most prolific author was U Rajendra Acharya from the University of Southern Queensland, and the journal with the most publications was *Computer Methods and Programs in Biomedicine*.
Conclusions: Compared with manual segmentation of fundus lesion images, the use of deep learning models for segmentation is more efficient and accurate, which is crucial for patients with eye diseases. Although the number of related publications globally is relatively small, a growing trend is still witnessed, with broad connections between countries and authors, mainly concentrated in East Asia and Europe. Research institutions in this field are limited, and hence, the

* Corresponding author.
** Corresponding author.
*** Corresponding author. Wound Healing Basic Research and Clinical Application Key Laboratory of Luzhou, School of Nursing, Southwest Medical University, Luzhou 646000, China.
E-mail address: wangyi3165026@swmu.edu.cn (Y. Wang).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2024.e39329
Received 16 April 2024; Received in revised form 23 September 2024; Accepted 11 October 2024
Available online 12 October 2024
2405-8440/

research on diabetic retinopathy and retinal vessel segmentation should be strengthened to promote the development of this area.

1. Introduction

Fundus features reflect the physical condition of the human body, including the status of the eyes, cardiovascular system, and cerebrovascular system [1,2]. More than 418 million people worldwide suffer from eye illnesses causing blindness, such as age-related macular degeneration (AMD), diabetic retinopathy (DR), and glaucoma [3]. Furthermore, fundus images allow for visualization of the retinal structures such as retinal vessels, optic disc (OD), optic cup (OC), and macula [4]. In clinical practice, the color fundus images captured using fundus cameras are commonly used for diagnosing various ophthalmic, cardiovascular, and cerebrovascular diseases due to their noninvasive acquisition and low cost [5]. Fundus images are projections of the fundus captured with a camera on a two-dimensional plane, which can be obtained in a noninvasive and cost-effective manner, making them more suitable for large-scale screening [6]. Fundus imaging may reveal lesions such microaneurysms, hemorrhages, hard exudates, soft exudates, OD, OC, and macula, as well as important biomarkers. Retinopathy of prematurity, DR, AMD, and diabetic macular edema can be diagnosed using these photos [7].

Deep learning (DL) has recently been used extensively for fundus image–based ocular disease detection. Without explicitly applying particular rules, DL methods enable computers to extract the most useful aspects from enormous datasets [8,9]. DL models can perform better via autonomous feature optimization compared with standard approaches relying on human feature area identification. Classification, segmentation, and synthesis problems comprise the bulk of DL applications in fundus images. Finding lesions and biomarkers is crucial for disease detection in segmentation tasks [10]. Bibliometric analyses are valuable in describing the current status of research disciplines, the scientific output of institutions and countries, and future research hotspots. Moreover, they are essential in guiding researchers to formulate research programs in the field [11]. Based on the collected data, we have generated several visualizations that showcase the countries with the most significant literary output, prominent authors, and other labels that indicate shifting trends and popular subjects in the area. The goal was to offer experts in the field with fresh perspectives on the present state, emerging trends, and key research points in fundus image segmentation.

2. Materials and methods

2.1. Search strategy

The Web of Science Core Collection (WoSCC, Clarivate Analytics), the world's leading citation database, was used as the data source. The WoSCC contains studies from the world's most influential journals (including open access journals), conference proceedings, and books. It covers a wide range of high-quality literature in areas such as agronomy, materials science, and computer science. In addition, the WoSCC is widely used in research for bibliometric analysis and visualization of scientific literature [12–14]. The search strategy was set as follows: ((((((TS=(fundus*)) OR TS=(Fundus Oculi)) OR TS=(Ocular Fundus)) OR TS=(Fundus of the Eye)) AND TS=(image*)) AND TS=(automatic*)) AND TS=(segment*), covering the period from January 1, 2007, to December 31, 2023.

2.2. Literature screening

This study established certain inclusion and exclusion criteria. The inclusion criteria were as follows: treatises and evaluations of the literature and publications in the English language only. Letters, reviews, editorials, conference abstracts, and studies published under similar or different journal titles were excluded. All records received (titles, authors, keywords, sources, abstracts, and references) were saved in plain text format (.txt). Two researchers used the abstracts and keywords to exclude irrelevant publications. The search was conducted on January 20, 2024, to prevent any alterations caused by database updates and was finished within 1 day. The data obtained from the WoSCC was downloaded by two researchers and integrated into Microsoft Excel 2016 for initial data processing. Subsequently, keywords, density maps, and other metrics were displayed and visualized using the VOSviewer software.

2.3. Visualization analysis

Visualization maps were generated using VOSviewer (Leiden University's Centre for Science and Technology Studies, version 1.6.20). Nodes represented countries and other elements, and could be related through citations, co-citations, and so forth. Node dimension was determined by the element's weight, which was influenced by criteria such as the number of documents or frequent occurrence of the element. Clusters were groupings of components in the structure with common characteristics. The connections among nodes illustrated the connections among items, and the width of the linkages indicated the intensity of these connections. The total link strength (TLS) was used to quantitatively evaluate links. Correlation studies were conducted to create visualization maps of extensively referenced literature, as well as publications from different nations and authors during each time, to highlight the evolution of these features [15].

CiteSpace (Chaomei Cheng, Version 6.3.R1) software was used for keyword clustering analysis, keyword burst detection, and dual-map overlay analysis, among others [16]. The parameter settings in CiteSpace were as follows: time slicing (2007–2023), per slice years (1), term source (Title, Abstract, Author Keywords, and Keywords plus), node types (one at a time), selection criteria (g-index.K = 10), and pruning (Cluster View-static and Show Merged Network). The specific process for evaluating literature and analyzing data is shown in Fig. 1.

3. Results

3.1. Publication volume and trends

Based on the growth trend displayed in Fig. 2, we separated the research history into three phases: (1) 2007–2010: the initial phase,

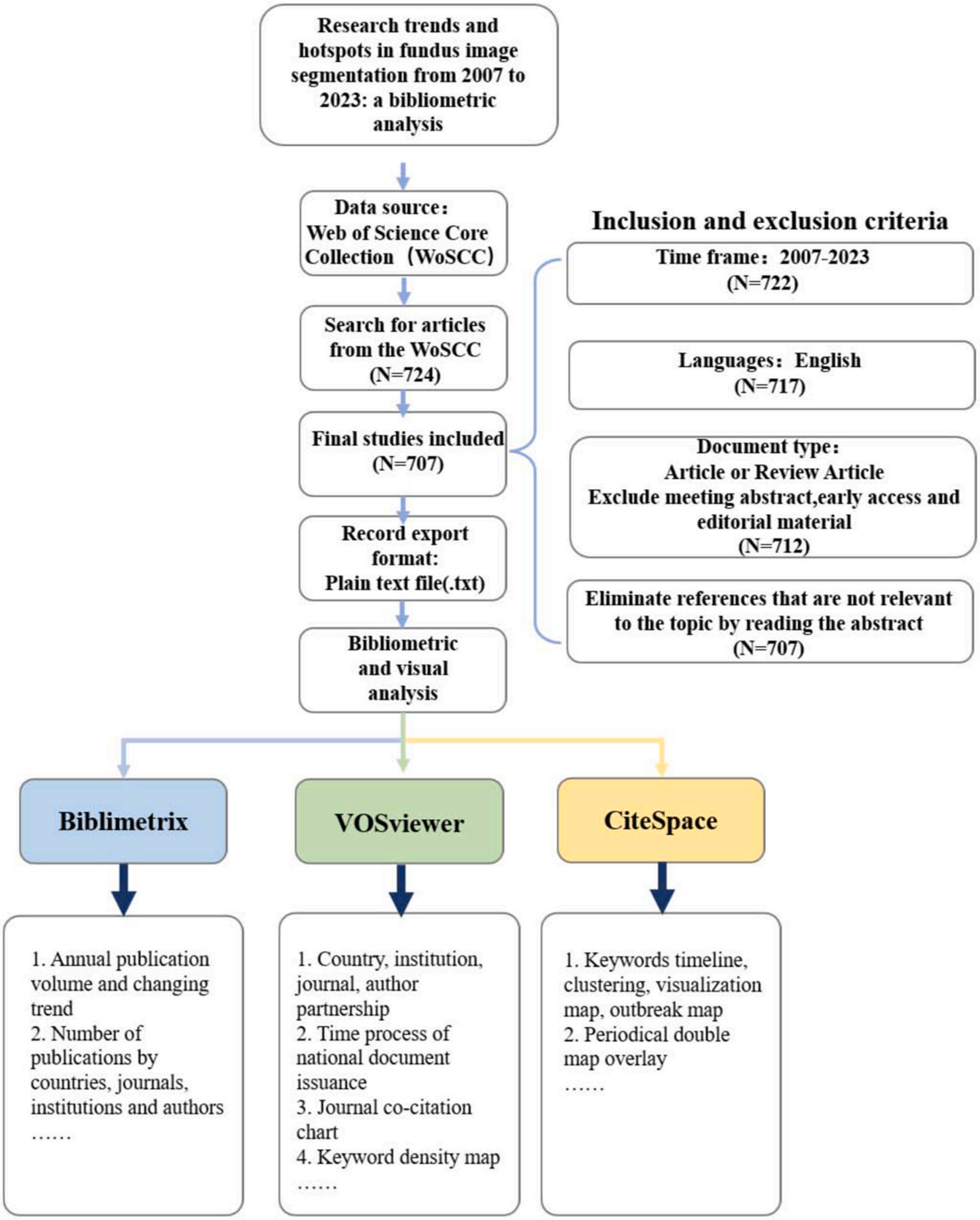

Fig. 1. Workflow of literature screening and data analysis.

with less than 10 publications annually and a slow increase in citations; (2) 2011–2019: the rapid growth phase, with annual publications ranging between 10 and 73, and a steady growth rate; and (3) 2019–2023: the stable development phase, with more than 80 publications on fundus automatic segmentation in 2022. The relationship between cumulative publication numbers and publication years was evaluated using an exponential growth function, which matched the trend of cumulative publications ($R^2 = 0.9612$). The number of citations showed an overall increasing trend from 2007, reaching a high of 2463 in 2017 and then gradually declining to 143 in 2023.

3.2. *Contributions by country/region*

A total of 707 studies were published by 73 countries or regions. From 2010 to 2023, the top five countries accounted for 74.68 % of global publications. A majority of publications originated from China (212, 29.9 %) and India (148, 20.9 %), followed by the USA (78, 11.0 %), Spain (48, 6.7 %), and the UK (42, 5.9 %). The map of transnational collaboration showed the intensity of collaboration between countries/regions (Fig. 3B and **C**). Setting the VOSviewer parameter to a country with at least 5 publications yielded 36 countries that satisfied the threshold. China was the country with the highest number of publications and had close cooperation with the USA and UK. The United States had the highest TLS (18) due to its strong connections with China (Fig. 3A). Also, India and Singapore were closely linked, with a TLS of 16.

3.3. *Institutional contributions*

A total of 1069 institutions contributed to the aforementioned 707 publications. The 10 most prominent institutions in regard to the number of publications are listed in Fig. 4A. Among these, the Chinese Academy of Sciences (China) was the most productive institution, followed by the National Institute of Technology (NIT System, India) and Central South University (China). The visual map (obtained through VOSviewer) of the network of institutions with 3 and more publications contained 166 institutions, forming 6 clusters of different colors. Fig. 4B illustrates the collaboration between institutions, with Ngee Ann Polytechnic ranking first with a TLS of 307, followed by Universiti Malaya (TLS = 286) and Kasturba Medical College (TLS = 238). We next examined the time course of fundus lesion segmentation according to the institution's start of the study; the bluer the color, the earlier the institution appeared, and the redder the color, the later the institution appeared. As shown in Fig. 4C, the University of Iowa was a pioneer in the field.

3.4. *Authors and co-cited authors*

An aggregate of 2513 authors participated in the research, of which 2047 had just one publication. The top 10 authors in the publication company are shown in Table 1, and the bar chart is shown in Fig. 5A. U Rajendra Acharya ranked first with 13 publications, followed by Augustinus LAUDE and Jen Hong TAN with 10 publications each. An author co-citation network mapping with 69 nodes, 328 linkages, and 5 clusters was created by setting the minimum number of publications to 3 and the minimum citation criterion to 45

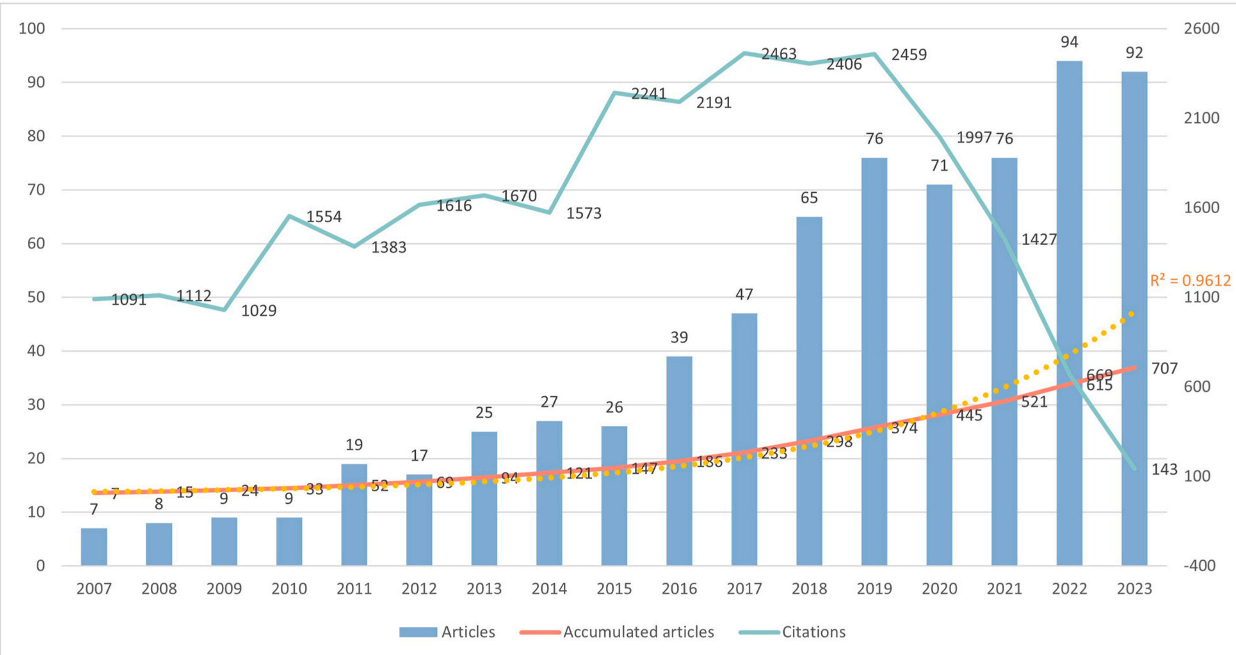

Fig. 2. Number of publications and citations per year and trends.

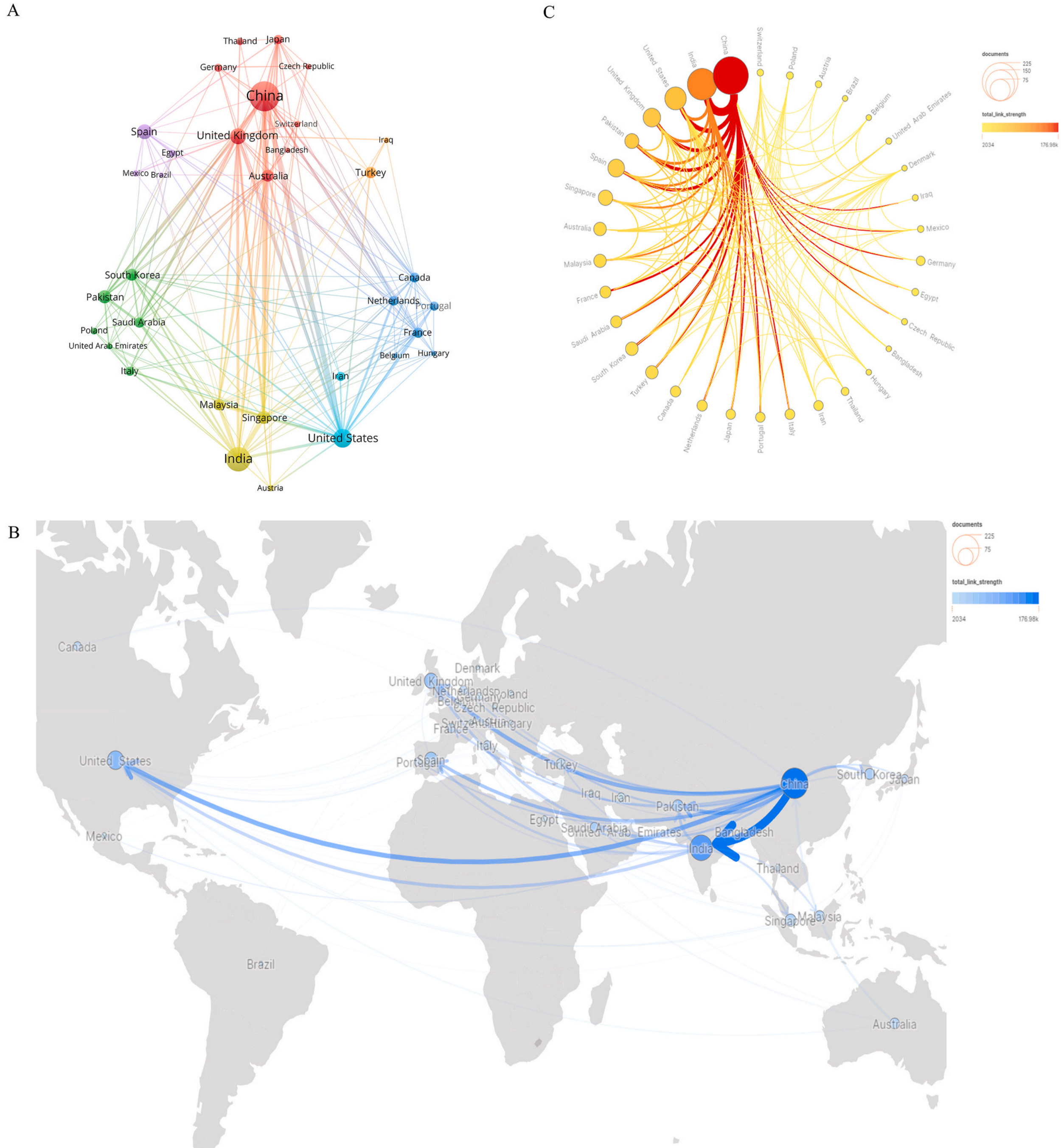

Fig. 3. (A) Network map of countries with VOSviewer threshold set to five publications. (B and C) Country presentation of the number of publications and the cross-map collaboration map.

in VOSviewer (Fig. 5B).

3.5. Journals and co-cited journals

A total of 201 journals had 707 publications on automatic fundus segmentation. In addition, we evaluated the quality of scientific material using Journal Citation Report (JCR) categories and impact factor (IF). An essential indicator of the influence of academic journals was the IF of the journal, which was the frequency with which the publications in the journal were referenced in a particular year or period [17]. Each scientific journal was given an impact factor by the JCR, based on which the journals were ranked in each

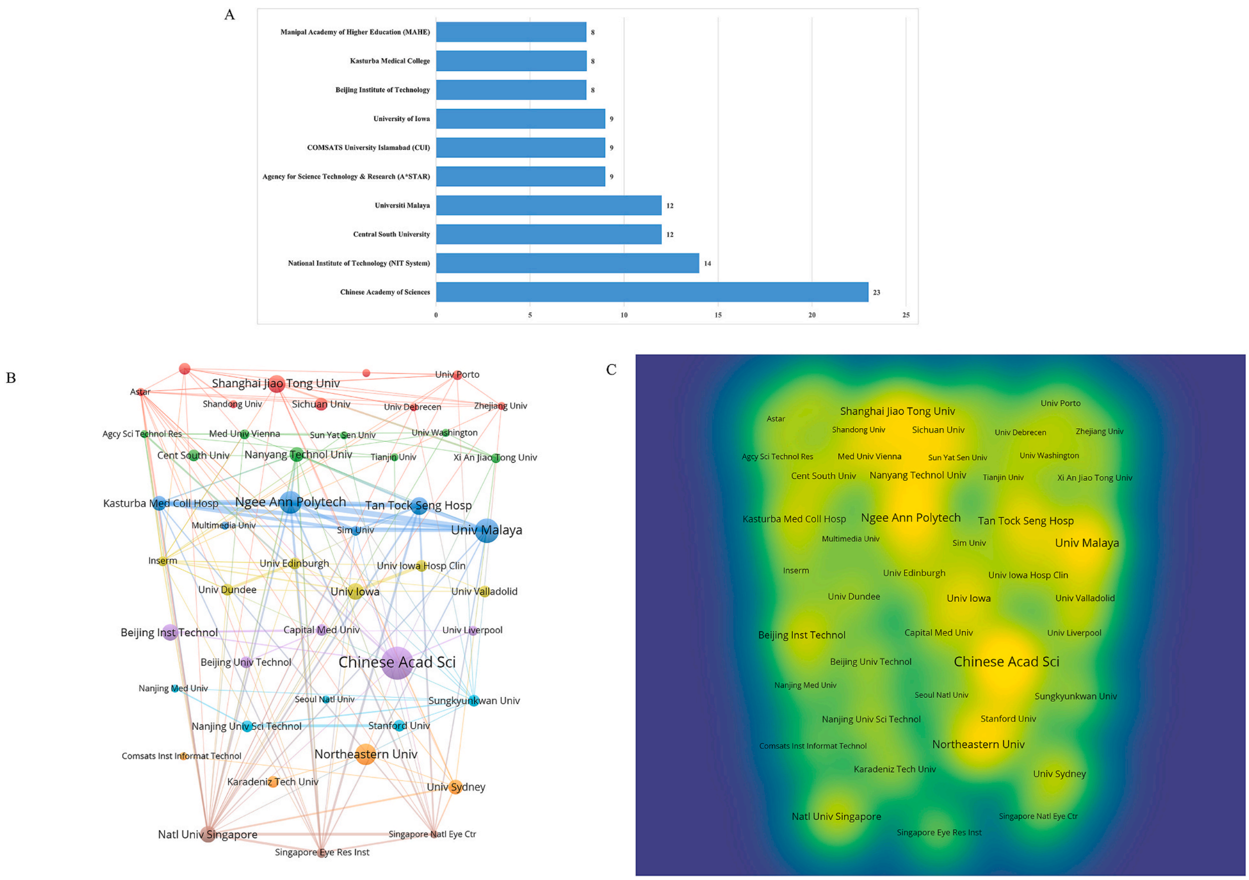

Fig. 4. (A) Top 10 organizations in terms of number of publications. (B) Clustering of issuing organizations. (C) Time course of organizations with publications.

Table 1
Top 10 authors in terms of the number of publications.

Rank	Author	Article	Citations	Total Link Strength
1	U Rajendra Acharya	13	903	75
2	Augustinus LAUDE	10	314	51
3	Jen Hong TAN	10	662	67
4	Sulatha V Bhandary	9	634	59
5	Bram van Ginneken	9	1083	40
6	Jun Wu	9	70	28
7	Michael D. Abràmoff	8	1070	30
8	Lei Geng	8	61	28
9	Muthu Rama Krishnan Mookiah	8	439	47
10	Fang Zhang	8	61	28

field. We used the JCR 2023 IF and categories in this study (Q1, Q2, Q3, and Q4) [18]. Another statistic used in this study was the H-index, which indicates that an investigator has published H articles, and every single article has been cited at least H times. The H-index is also used to assess the number and level of scholarly outputs of researchers [19]. A total of 226 publications appeared in the highest-ranking 10 journals, making up around 31.9 % of all publications (Table 2 and Fig. 6A). The journal *Computer Methods and Programs in Biomedicine* ranked first in terms of the total number of publications and has become an indispensable scientific resource for the automated segmentation of fundus diseases. The journal *IEEE Transactions on Medical Imaging* had the highest citation frequency (Total Link = 3928). The eighth most published journal, the *Journal of Medical Imaging and Health Informatics*, was not included in the most recent JCR, and hence no related information could be derived.

The visualization map displayed the citation trends for 38 journals, broken down into 7 clusters with 392 linkages, when the minimum publication volume was set to 5 (Fig. 6B). The co-citation relationships between different journals revealed that the journal *IEEE Transactions on Medical Imaging* had the most co-citations (2995), followed by the journals *Lecture Notes in Computer Science* (913),

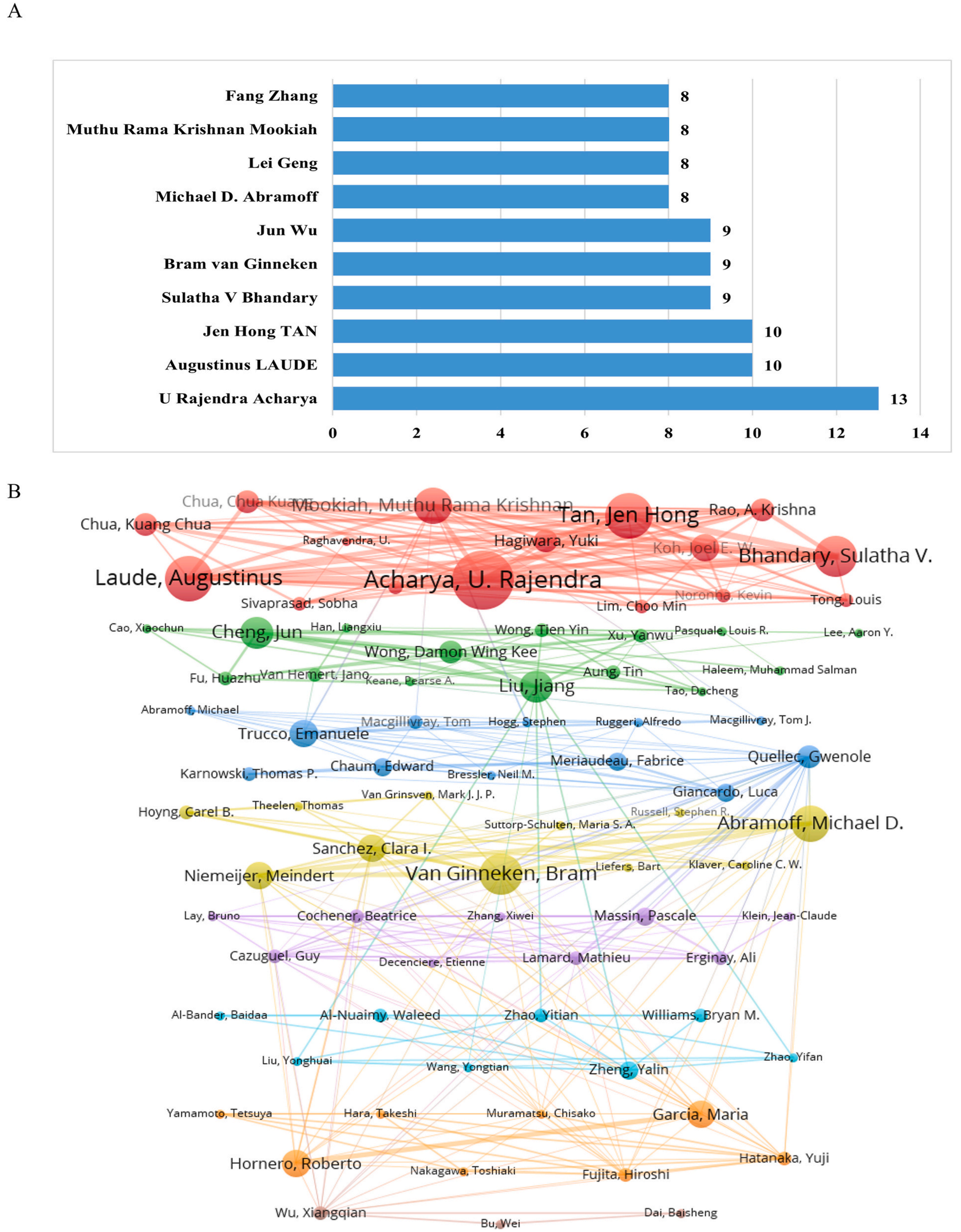

Fig. 5. (A) Top 10 authors in terms of publications. (B) Connection map of authors with a citation threshold of 45 and minimum number of publications of 3.

Table 2
Top 10 journals in terms of the number of publications.

Rank	Source	Article	JCR	IF	H-index	Citations	Total Link Strength
1	*Computer Methods and Programs in Biomedicine*	34	Q1	6.1	124	2106	316
2	*Multimedia Tools and Applications*	29	Q2	3.6	52	184	165
3	*IEEE Transactions on Medical Imaging*	28	Q1	10.6	195	4022	430
4	*Computers in Biology and Medicine*	27	Q1	7.7	75	711	229
5	*IEEE Access*	25	Q3	3.9	56	645	154
6	*Biomedical Signal Processing and Control*	21	Q2	5.1	51	499	157
7	*Biomedical Optics Express*	17	Q2	3.4	67	386	50
8	*Journal of Medical Imaging and Health Informatics*	16	/	/	/	114	61
9	*IEEE Journal of Biomedical and Health Informatics*	15	Q1	7.1	104	596	103
10	*Investigative Ophthalmology & Visual Science*	14	Q1	4.4	196	666	36

Computer Methods and Programs in Biomedicine (770), and *Investigative Ophthalmology & Visual Science* (764) (Fig. 6C).

Fig. 6D shows the dual-map overlay mapping of journals. On the left and right are citing and cited journals, respectively. Most of the publications on the left were in the knowledge frontiers of "Medicine, Medical, Clinical" and "Ophthalmology, Ophthalmic," which were mainly influenced by the "Systems, Computing, Computer" and "Molecular, Biology, Computer Science" journals shown on the right. These were mainly influenced by the knowledge base areas of "Systems, Computing, Computer" and "Molecular, Biology, Genetics" displayed on the right. The two primary citation pathways in the current map are shown by colored curves representing the citation associations.

3.6. References and co-cited references

We examined the 10 most often cited publications (TC = 83–243) to thoroughly understand the developing scenario (Table 3). Fig. 7 shows the visual timeline of the top 10 co-citations for fundus disease automatically segmented by CiteSpace according to the loglikelihood ratio (LLR) algorithm based on the co-citation analysis. The 10 clustered labels representing the hot topics were selected and arranged on the right side of Fig. 7, which can reflect the temporal characteristics of the research hotspots in this field. On the dotted lines connected to each label, circles with larger radii indicate higher citation frequency and lines with warmer colors indicate later publication date. Among them, cluster #1 (anatomic structure) occurs the earliest. Further, cluster #0 (retinal blood vessel segmentation), cluster #2 (optic cup segmentation), cluster #3 (DR), cluster #4 (using DL technique) are hot topics of current research, indicating that retinal vascularization, OC, and diabetic retinopathy are areas that have received a great deal of attention. It is worth noting that deep learning methods are also a popular tool in the aforementioned areas. Fig. 8 shows the top five clusters filtered based on co-cited article topics, most of which are similar to what is shown in the timeline graph. However, cluster #1 shows that the application of convolutional neural networks (CNNs) for fundus image segmentation is still a hot area.

Fig. 9 shows the emergent graph of the top 25 co-cited references. In this study, the time of emergence of these 25 co-cited references was divided into 3 categories, and then the highest intensity literature in each category was selected for analysis: the 7 references that started between 2009 and 2013 were the earlier and more popular co-cited literature. Among these, Youssif developed a method for automatic detection of optic disc position in retinal fundus images and proposed a simple matched filter that captured the retinal blood vessel's vertical longitudinal structure to roughly match the direction of blood vessels near the OD to localize the optic disc position [30]. Thirteen references from 2014 to 2020 were the top co-cited papers in the midterm. Among these, Ronneberger proposed U-Net, a CNN for medical imaging, which effectively used annotated text and enabled fast segmentation of 512*512 pixel images on the latest graphics processing units won the ISBI Challenge. The co-cited literature from 2021 to the present year is studied in an area currently receiving significant attention [31]. Yan proposed a segmentation-level loss method emphasizing the thickness consistency of thin blood vessels during training. This method balances the importance of thick and thin blood vessels in the loss calculation, enabling the learning of effective features for blood vessel segmentation without increasing model complexity [32].

3.7. Keyword hotspot analysis

A dependable technique for examining advancements in an area is keyword co-occurrence, which is frequently used to identify a cutting-edge hotspot in specific research. A total of 2006 keywords were taken out of 707 publications. Table 4 and Fig. 10A display the top 20 keywords among these based on co-occurrence frequency. First, we selected keywords with a frequency of occurrence greater than 3 to create a visualization map using CiteSpace (Fig. 10B). Then, we created a density map (Fig. 10D) using 58 terms with more than 20 occurrences to see how items were distributed across the domain. As shown in Fig. 10B, "Diabetic Retinopathy," "Segmentation," "Blood Vessels," and "Retinal Images" had a central position in the density map, suggesting that these were the most occurring topics in the study. The selected keywords were analyzed for clustering. All clusters were labeled with index terms extracted from the keywords. Five clusters were calculated (Fig. 10C), representing the five main research directions in the field. Cluster 0 is the largest cluster, focusing on DR, with keywords such as "boundary," "feature extraction," and "optic disc detection." Cluster 1 focuses on CNNs, with keywords such as "retinal image," "blood vessel segmentation," and "matched filter." Cluster 2 is shown as a yellow circle and focuses on DR. Keywords include "retinal image," "diabetes," and "atherosclerosis risk." Cluster 3 focuses on optical tomography and includes "microaneurysm," "diagnosis," and "exudate detection". Cluster 4 shows keywords in green circles, focusing on retinal

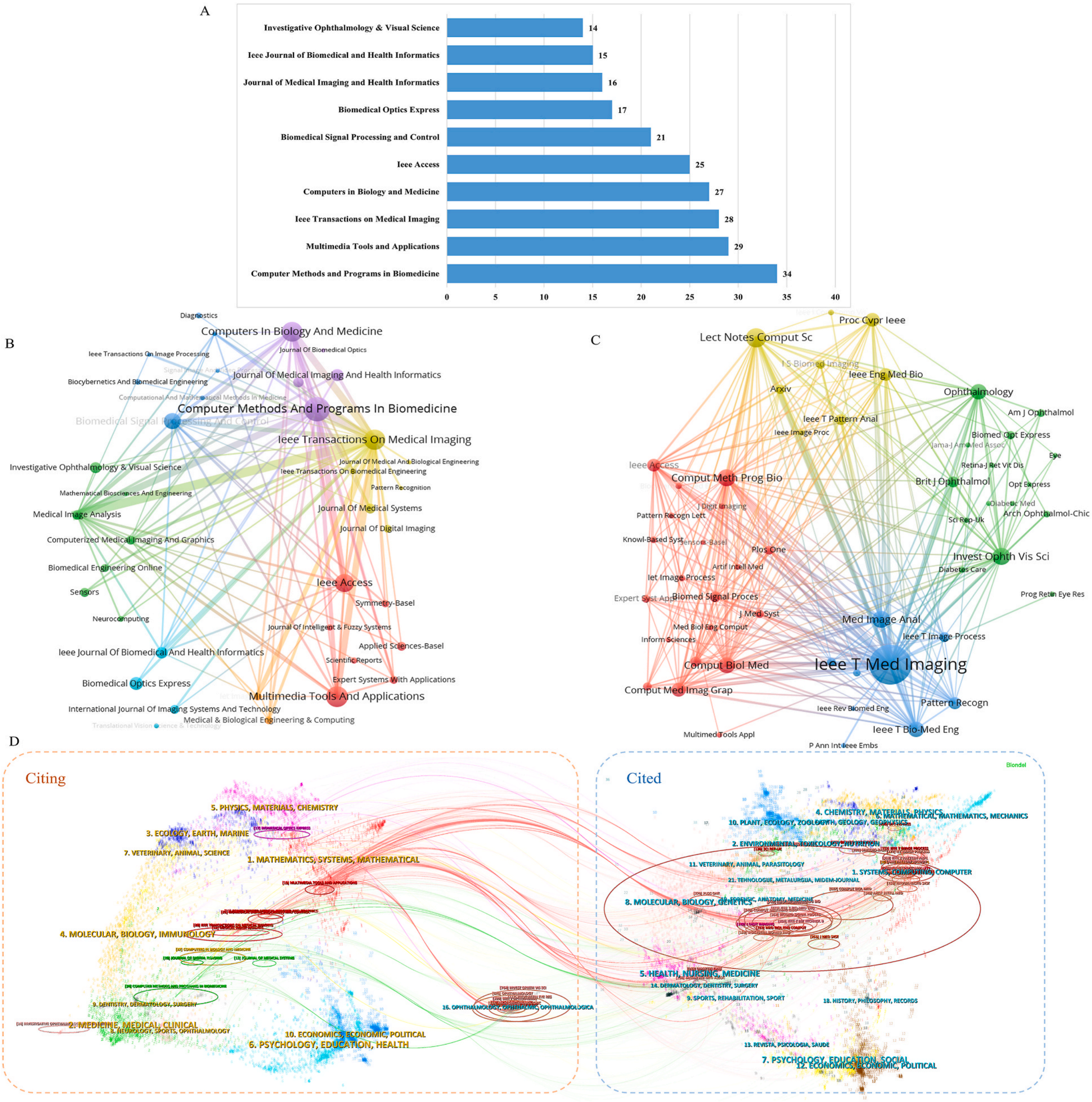

Fig. 6. (A) Top 10 journals in terms of the number of publications. (B) Linkage map of issuing journals. (C) Co-citation map of journals. (D) Dual-map overlay of issuing journals.

images. Keywords include "macular degeneration" and "choroidal neovascularization." Finally, we identified the 20 most cited keywords, which are considered indicators of research frontiers or emerging trends. As shown in Fig. 11, the citation explosion of keywords after 2020 are biomedical imaging (3.62), deep learning (17.68), network (8.67), retinal vessel segmentation (5.23), convolutional neural network (4.04), transfer learning (3.64).

4. Discussion

Our bibliometric analysis of 707 documents related to the automatic segmentation of fundus diseases from the WoSCC database between 2007 and 2023 revealed several valuable insights. First, this was an active area of investigation. The number of global publications on the automatic segmentation of fundus diseases steadily increased during the study period. We reported 92 publications as of 2023, whereas the growth pattern pointed to a rise in publications by 2024.

Another valuable aspect of bibliometric analysis was that it reflected global trends, including changes over time in elements such as

Table 3
Top 10 most frequently co-cited references.

Rank	Count	Year	Title	Author	Journal	DOI	Citation Number
1	47	2019	DUNet: A deformable network for retinal vessel segmentation	Jin QG et al.	*Knowledge-Based Systems*	DOI 10.1016/j.knosys.2019.04.025	[20]
2	44	2018	Joint Optic Disc and Cup Segmentation Based on Multi-Label Deep Network and Polar Transformation	Fu HZ et al.	*IEEE Transactions on Medical Imaging*	DOI 10.1109/TMI.2018.2791488	[21]
3	44	2018	Joint Segment-Level and Pixel-Wise Losses for Deep Learning Based Retinal Vessel Segmentation	Yan ZQ et al.	*IEEE Transactions on Biomedical Engineering*	DOI 10.1109/TBME.2018.2828137	[22]
4	43	2016	Segmenting Retinal Blood Vessels With Deep Neural Networks	Liskowski P et al.	*IEEE Transactions on Medical Imaging*	DOI 10.1109/TMI.2016.2546227	[23]
5	40	2015	U-Net: Convolutional Networks for Biomedical Image Segmentation	Ronneberger O et al.	*Medical Image Computing and Computer-Assisted Intervention – MICCAI 2015*	DOI 10.1007/978-3-319-24574-4, 28	[24]
6	39	2015	THP-1 cell line: an in vitro cell model for immune modulation approach	Azzopardi G et al.	*International Immunopharmacology*	DOI 10.1016/j.media.2014.08.002	[25]
7	39	2017	A Discriminatively Trained Fully Connected Conditional Random Field Model for Blood Vessel Segmentation in Fundus Images	Orlando JI et al.	*IEEE Transactions on Biomedical Engineering*	DOI 10.1109/TBME.2016.2535311	[26]
8	39	2016	A Cross-Modality Learning Approach for Vessel Segmentation in Retinal Images	Li QL et al.	*IEEE Transactions on Medical Imaging*	DOI 10.1109/TMI.2015.2457891	[27]
9	37	2019	CE-Net: Context Encoder Network for 2D Medical Image Segmentation	Gu ZW et al.	*IEEE Transactions on Medical Imaging*	DOI 10.1109/TMI.2019.2903562	[28]
10	34	2017	ImageNet classification with deep convolutional neural networks	Krizhevsky Alex et al.	*Communications Of The ACM*	DOI 10.1145/3065386	[29]

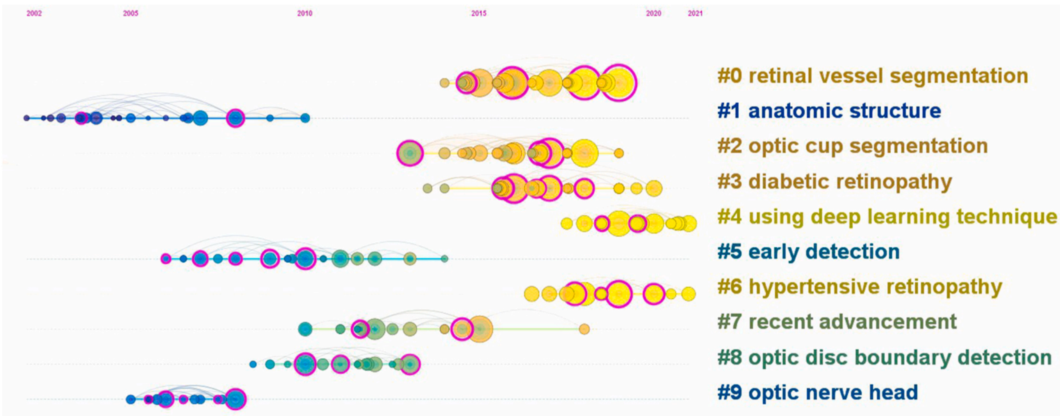

Fig. 7. Visualized timeline of the top 10 co-cited references per year.

countries and journals. The Netherlands had an earlier interest in relevant research compared with the rest of the world, with US scientists being the main driving force. Recent manufacturing expansions in China, Singapore, and India were indicative of significant advancements in the scientific capacities of these nations. Spain, South Korea, and Pakistan were 3 of the top 10 publishing nations with the least amount of international cooperation, highlighting the need for more global collaboration in fundus research. The output of countries was naturally reflected in their institutions. As mentioned, the USA was a major producer and source of cited publications. In line with this, 5 of the top 10 prolific institutions were located in the USA, with the remaining 5 from the UK, the Netherlands, and Ireland. Moreover, 9 of these 10 institutions were universities, and 1 was a research center. In terms of co-authorship analysis, U Rajendra Acharya from the University of Southern Queensland published the most, with 13 publications, playing a significant leadership role in the field. He was followed by Augustinus LAUDE from the National Healthcare Group and Jen Hong TAN from the National University of Singapore. Many scholars collaborated actively, maximizing regional advantages and further enhancing academic influence.

Based on the JCR 2023 requirements, 2 of the top 10 journals in terms of publishing volume belonged to the ophthalmology JCR category, with the rest related to biomedical, computer science, artificial intelligence, and radiology and nuclear medicine imaging. Notably, the journal *Computer Methods and Programs in Biomedicine* had the highest publication volume in this study. Founded in 1985,

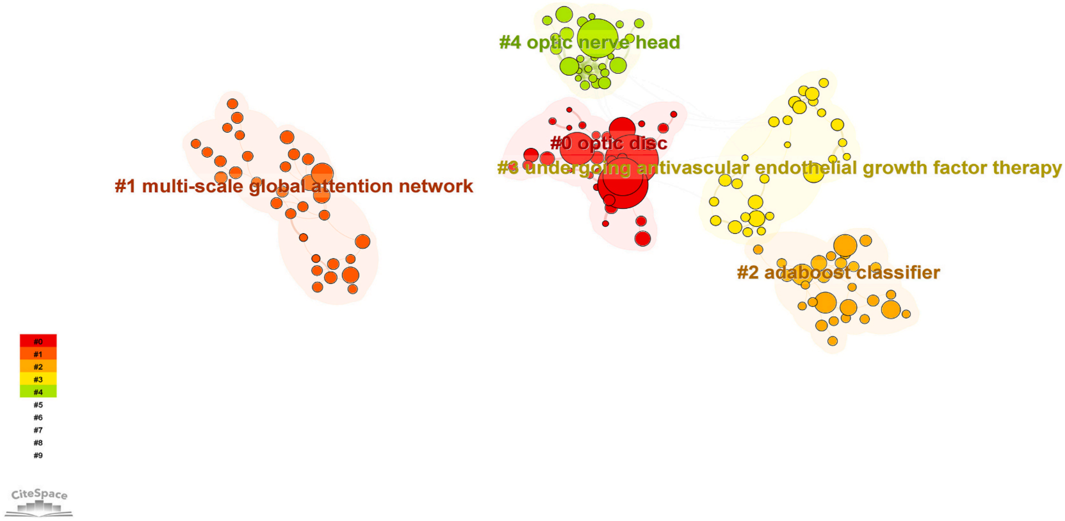

Fig. 8. Clusters of the top five co-cited references classified according to article title.

Top 25 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2007 - 2023
Niemeijer M, 2007, IEEE T MED IMAGING, V26, P116, DOI 10.1109/TMI.2006.885336, DOI	2007	8.14	**2009**	2012	
Youssif AAHAR, 2008, IEEE T MED IMAGING, V27, P11, DOI 10.1109/TMI.2007.900326, DOI	2008	11.59	**2010**	2013	
Niemeijer M, 2010, IEEE T MED IMAGING, V29, P185, DOI 10.1109/TMI.2009.2033909, DOI	2010	8.38	**2011**	2014	
Marín D, 2011, IEEE T MED IMAGING, V30, P146, DOI 10.1109/TMI.2010.2064333, DOI	2011	10.93	**2012**	2016	
Aquino A, 2010, IEEE T MED IMAGING, V29, P1860, DOI 10.1109/TMI.2010.2053042, DOI	2010	9.5	**2012**	2015	
Joshi GD, 2011, IEEE T MED IMAGING, V30, P1192, DOI 10.1109/TMI.2011.2106509, DOI	2011	8.5	**2013**	2016	
Abramoff Michael D, 2010, IEEE REV BIOMED ENG, V3, P169, DOI 10.1109/RBME.2010.2084567, DOI	2010	7.37	**2013**	2015	
Fraz MM, 2012, COMPUT METH PROG BIO, V108, P407, DOI 10.1016/j.cmpb.2012.03.009, DOI	2012	14.63	**2014**	2017	
Cheng J, 2013, IEEE T MED IMAGING, V32, P1019, DOI 10.1109/TMI.2013.2247770, DOI	2013	12.76	**2015**	2018	
Morales S, 2013, IEEE T MED IMAGING, V32, P786, DOI 10.1109/TMI.2013.2238244, DOI	2013	8.42	**2015**	2017	
Lu SJ, 2011, IEEE T MED IMAGING, V30, P2126, DOI 10.1109/TMI.2011.2164261, DOI	2011	7.43	**2015**	2016	
Decencière E, 2014, IMAGE ANAL STEREOL, V33, P231, DOI 10.5566/ias.1155, DOI	2014	9.88	**2016**	2019	
Yu H, 2012, IEEE T INF TECHNOL B, V16, P644, DOI 10.1109/TITB.2012.2198668, DOI	2012	7.68	**2016**	2017	
Azzopardi G, 2015, MED IMAGE ANAL, V19, P46, DOI 10.1016/j.media.2014.08.002, DOI	2015	13.84	**2017**	2020	
Liskowski P, 2016, IEEE T MED IMAGING, V35, P2369, DOI 10.1109/TMI.2016.2546227, DOI	2016	10.21	**2017**	2021	
Li QL, 2016, IEEE T MED IMAGING, V35, P109, DOI 10.1109/TMI.2015.2457891, DOI	2016	9.24	**2017**	2021	
Ronneberger O, 2015, LECT NOTES COMPUT SC, V9351, P234, DOI 10.1007/978-3-319-24574-4, 28, DOI	2015	16.61	**2018**	2020	
Gulshan V, 2016, JAMA-J AM MED ASSOC, V316, P2402, DOI 10.1001/jama.2016.17216, DOI	2016	9.77	**2018**	2021	
Zhao YT, 2015, IEEE T MED IMAGING, V34, P1797, DOI 10.1109/TMI.2015.2409024, DOI	2015	9.03	**2018**	2020	
He KM, 2016, PROC CVPR IEEE, V0, PP770, DOI 10.1109/CVPR.2016.90, DOI	2016	8.11	**2019**	2021	
Maninis Kevis-Kokitsi, 2016, M ...... CEEDINGS: LNCS 9901, V0, PP140, DOI	2016	9.14	**2020**	2021	
Yan ZQ, 2018, IEEE T BIO-MED ENG, V65, P1912, DOI 10.1109/TBME.2018.2828137, DOI	2018	10.62	**2021**	2023	
Gu ZW, 2019, IEEE T MED IMAGING, V38, P2281, DOI 10.1109/TMI.2019.2903562, DOI	2019	10.06	**2021**	2023	
Jin QG, 2019, KNOWL-BASED SYST, V178, P149, DOI 10.1016/j.knosys.2019.04.025, DOI	2019	9.29	**2021**	2023	
Oliveira A, 2018, EXPERT SYST APPL, V112, P229, DOI 10.1016/j.eswa.2018.06.034, DOI	2018	7.57	**2021**	2023	

Fig. 9. Top 25 references with the strongest citation bursts.

it is a journal that applies computational science methods to biomedical research and medical practice, with key research directions including (1) biomedical simulation and modeling, (2) medical decision support systems, (3) medical data mining and knowledge discovery, and (4) medical image segmentation and registration. The publications on these topics have played an essential role in promoting research in retinal vessel segmentation, OD segmentation, driving related research and providing valuable references for scholars in these research directions.

The publication by Jin et al. in 2019, which has become the most cited during a certain period with 47 citations [20], could be considered a milestone in developing a specific area in this field. Their work presented the Deformable U-Net (DUNet), using the local properties of retinal vasculature with the U-Net architecture for end-to-end retinal vascular segmentation. Inspired by the newly

Table 4
Top 20 keywords in co-occurrence frequency ranking.

Rank	Keyword	Occurrences	Total Link Strength
1	Segmentation	277	2280
2	Fundus Images	147	1357
3	Retinal Images	133	1128
4	Diabetic Retinopathy	127	1087
5	Blood-Vessels	116	1024
6	Deep Learning	110	978
7	Images	108	801
8	Classification	106	1034
9	Optic Disc	106	990
10	Automatic Detection	99	1042
11	Vessel Segmentation	84	669
12	Diagnosis	80	780
13	Glaucoma	74	684
14	Model	67	625
15	Fundus Image	63	525
16	Extraction	62	600
17	Image Segmentation	52	513
18	Microaneurysms	51	459
19	Retina	50	566
20	Optical Coherence Tomography	48	442

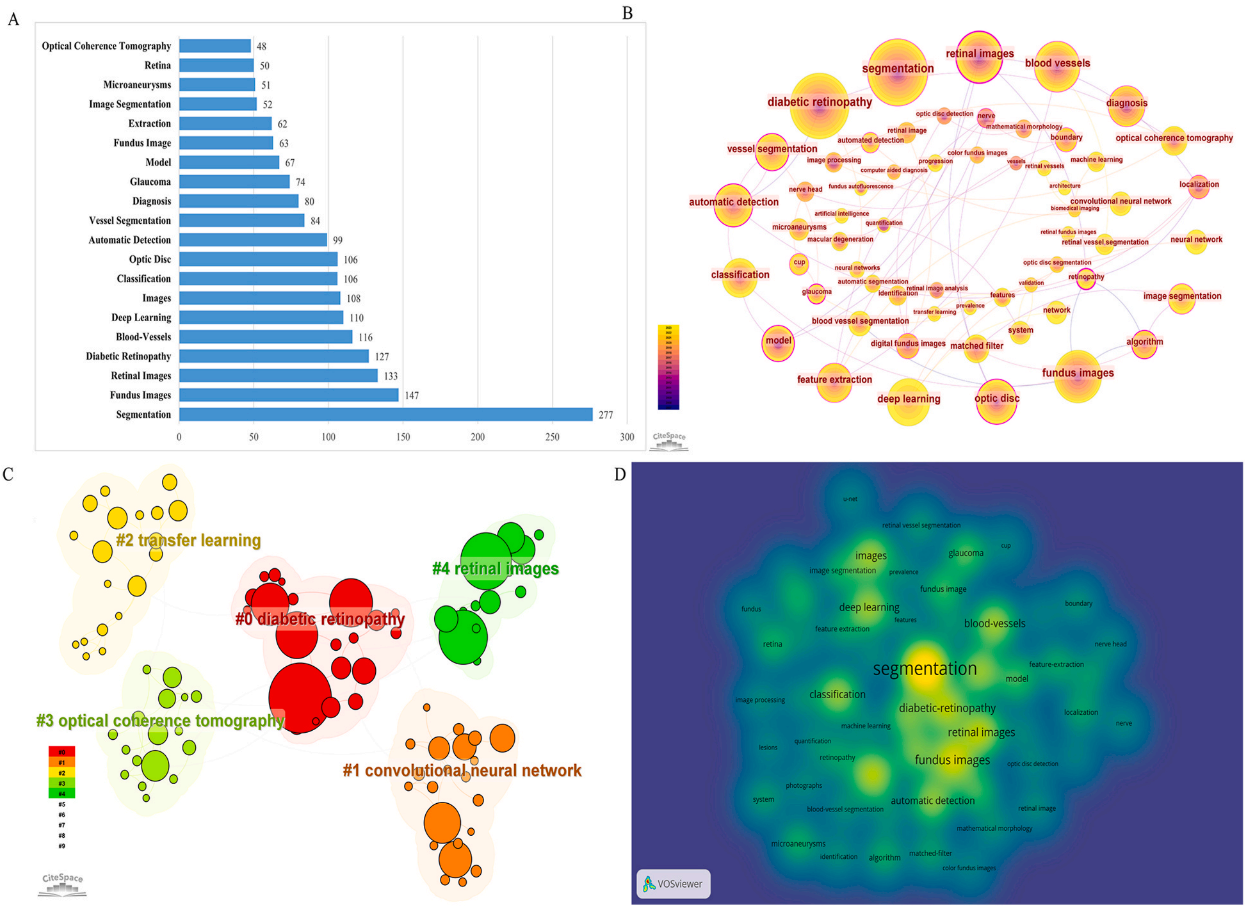

Fig. 10. (A) 20 ranked keywords in terms of co-occurrence frequency. (B) Visualization map created using CiteSpace selecting keywords with frequency of occurrence greater than 3. (C). Five clusters of keywords. (D) Density map of selected keywords.

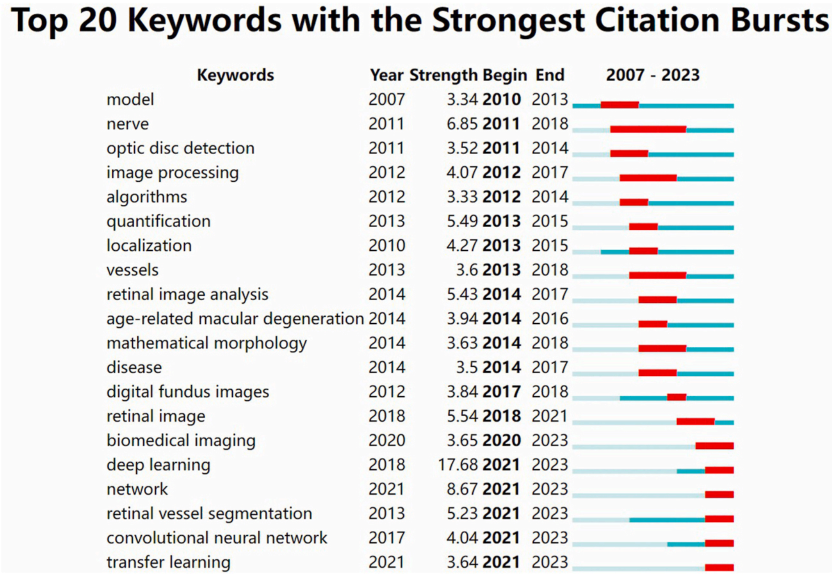

Fig. 11. Keyword burst map.

announced deformable convolutional networks, deformable convolutions were added to the suggested network. DUNet employed upsampling operators to boost output resolution, intending to capture context information and achieve exact localization by integrating low-level characteristics with high-level features. Furthermore, DUNet might adaptively modify the receptive fields depending on the scale and form of vessels, effectively catching retinal vessels of varied shapes and sizes. This study offers much reference information for ongoing studies on the topic. The frequent hot themes in studying the automated segmentation of fundus illnesses have altered in recent years, similar to most other research domains. Particularly, since 2020, extensive research has been conducted on segmenting fundus images using DL algorithms, with CNNs and transfer learning being the most common applications.

In the resulting keyword co-occurrence maps, excluding descriptive keywords such as “fundus images,” “segmentation,” and “automatic,” the remaining high-frequency keywords included “diabetic retinopathy,” “retinal images,” “boundary,” “automatic localization,” “deep learning,” “classification,” “macular diseases,” and “optic disc localization.” The first set of high-frequency keywords described disease types, such as “diabetic retinopathy” and “macular diseases.” The retinal vascular system is considered a distinct entity for investigating anatomical and pathological alterations related to ocular conditions such as glaucoma, hypertension, and AMD. The retinal vasculature system may be measured and analyzed to provide biomarkers for diagnosing cardiovascular disorders [33]. DR can result in blindness, so retinal vascular segmentation is essential for an early diagnosis. The second set of high-frequency keywords was related to methodological aspects, such as “deep learning,” “convolutional neural networks,” and “optic disc localization."

Manual identification and segmentation of disease-related regions is a time-consuming and labor-intensive operation. Applying ML or DL may considerably boost the quality and efficiency of segmentation. For instance, adopting Vess-Net, a dual-stream feature-enriching network for retinal vascular segmentation, allows for segmenting tiny features with only a few layers. Direct connections from the encoder to the decoder offer edge information, allowing the network to converge swiftly and execute the exact segmentation of vessels while drastically lowering the number of trainable parameters. This is critical for determining the number of vascular pixels needed to diagnose diabetic or hypertensive retinopathy [34]. Among various ML techniques, DL models, particularly those in the form of CNNs, have been at the forefront of ophthalmic image analysis [35]. The multilayer structure of CNNs enables these deep neural networks to extract local features, detect hidden patterns, and classify images in a data-efficient and self-learning manner. Leopold and colleagues suggested a PixelCNN with batch normalization (PixelBNN) based on U-Net and PixelCNN, where preprocessing was employed for scaling, dimensionality reduction, and picture improvement [36]. Feng et al. presented a cross-connected CNN (CcNet) for retinal vascular segmentation. CcNet is trained purely on the green channel of fundus images; cross-connection and fusing of multiscale characteristics boost the performance of the network [37].

The output of research in this domain has significantly increased with the introduction of artificial intelligence, especially after the introduction of large models such as CNNs in recent years. A new DL architecture called “Vision Transformer (ViT)" has recently attracted significant attention. It consists of a series of transformer blocks, each comprising a self-attention layer and a feed-forward layer. ViT allows for variable-sized image inputs and excels at handling multimodal data [38].

Bowd et al. [39] used fundus images from the Ocular Hypertension Treatment Study (OHTS) and five external datasets to detect primary open-angle glaucoma so as to compare the accuracy and generalizability of the new DL technology ViT model (data-efficient image transformer, DeiT) with traditional CNN (ResNet-50). The DeiT model performed with ResNet-50 on the OHTS dataset and consistently had higher diagnostic accuracy on external datasets not part of the training data, making ViT a potential key tool for detecting glaucoma from fundus images. Training transformers typically requires large amounts of data. Hence, Yu et al. [40]

presented an “MIL head” to employ a vision transformer for tasks related to classifying retinal diseases. It was based on multiple instance learning (MIL). The transformer model was pre-trained on a large fundus image library and then fine-tuned for subsequent tasks related to the categorization of retinal diseases. The MIL–ViT system, which is plug-and-play compatible with ViT, uses an MIL-based head. Experiments on the APTOS2019 and RFMiD2020 datasets showed that the performance of MIL–ViT surpassed that of CNN models. Overall, the application of ViT in retinal image analysis has shown tremendous potential, performing well across various computer vision tasks, including image classification, object detection, and segmentation. Recently, it has been used for retinal imaging issues such as lesion detection, vessel segmentation, and OD and fovea localization, emerging as a new force in ophthalmic diseases. Attention should also be paid to the ethical and clinical deployment issues of related technologies in this field. In the future, it is anticipated that the field of fundus image segmentation will continue to focus on the application of DL technologies, particularly on the study of diabetic fundus diseases, with a special emphasis on emerging technologies such as ViT. Concurrently, relevant medical institutions should expand their sample collection efforts, enhance international cooperation, and conduct multicenter and large-sample studies on fundus image processing. This approach would better meet the substantial data requirements for training large models such as transformers, ultimately facilitating their application in clinical practice to provide assistance and reference for clinicians’ diagnoses.

Although these techniques are widely used in detecting clinical ocular and systemic diseases, the large amount of data acquired, the cost of feature extraction and training, and the time required for detection and diagnosis may limit their use [41]. The use of DL methods in fundus diseases requires a large amount of image support [42]. Adding different sources with high-quality data can significantly increase the effectiveness of the network.

The various machine learning methods currently used in the field of fundus image segmentation are not a substitute for clinical experts. Because of factors such as their high cost and difficulty in clinical deployment, applying these new technologies to a wide range of clinical applications is a long-term and challenging endeavor. In the future, it will be an important task to reduce the amount of data required for DL techniques, improve the data quality, and minimize the time and computational cost required for functions such as prediction, diagnosis, and classification.

In addition, the ethical implications of these new technologies should be considered before they are applied to the general public. Currently, machine learning technology lacks ethical and legal regulations, and ethical issues may arise in all aspects of product development, testing, and deployment [43].

Multi-Reader Multi-Case (MRMC) studies are commonly used to assess improvements in study accuracy through the assistance of computer-aided equipment [44]. Specifically, the design of a multi-reader multi-case study is based on the following idea: an appropriate number of representative patients and investigators are selected as samples, and each patient is subjected to two or more diagnostic tests, followed by an independent interpretation of the patient’s imaging test results by the investigator. Hu et al. recruited 36 radiologists and 12 neurosurgeons from 6 hospitals to conduct a study with/without AI-assisted detection of intracranial aneurysms by the MRMC method [45]. The experimental results showed that the constructed AI model had high acceptance and application potential, and could significantly improve the diagnosis of aneurysms, with a sensitivity of up to 94.3 % for detecting aneurysms and 95.3 % and 95.9 % for detecting subarachnoid hemorrhage and non-subarachnoid hemorrhage, respectively, which were higher than that of the physician’s diagnosis. Multi-reader, multi-case studies are still lacking in the field of automated segmentation of fundus images. Hence, more similar studies are needed in this field to assess whether experimental methods can significantly impact clinical applications to obtain better segmentation schemes.

This was the first bibliometric analysis to examine research trends and hotspots in fundus image segmentation in the last 15 years. It was not without limits. First, several publications were unavoidably left out because we only gathered data from the WoSCC database and excluded additional databases such as print publications and video resources. However, the WoSCC is one of the mainstream literature databases recognized by researchers worldwide, so we chose the WoSCC as the data source for this study. Second, the bibliometric method has its limitations because the producer’s design and the user’s settings may lead to results that do not accurately reflect the true situation. Finally, the results of this study are dynamic and can change over time. Despite this, we tried to analyze the development and research content of the automatic segmentation of fundus lesion images as comprehensively as possible to summarize the findings in this discipline during rapid development and provide references for future research in this field.

In the future, the field of fundus image segmentation will continue to focus on the following aspects. (1) Diabetic fundopathy: diabetic retinopathy is one of the most common causes of blindness in adults, and therefore the detection of DR is extremely important for slowing down the deterioration of the disease and preserving vision [46]. Most of the current studies can only distinguish whether a patient has DR or not, and cannot accurately determine the developmental stage of DR [47]. Abràmoff et al. used AlexNet-based CNNs to classify different types of DR, including referable DR (rDR), vision-threatening DR (vtDR), and proliferative DR (pDR) [48]. In developing relevant DL networks, the primary goal was to create more refined and diverse DR detection systems capable of staging and classifying individual diseases. (2) Retinal vessel segmentation: Retinal vessel segmentation is extremely important for diagnosing fundus diseases and is one of the most urgent tasks at present. Singh et al. [49] combined machine learning with feature extraction techniques using five different feature sets and used the data to train four machine learning classifiers with DRIVE public data as test data. They performed performance evaluations for each classifier, focusing on the time required to segment blood vessels for each classifier. The experimental results showed that both the KNN and decision tree algorithms had considerable accuracy with AUC values of more than 97 % and that the decision tree classifier outperformed the other three classifiers in terms of the short time it took. In another study, five improved deep learning networks and a customized deep neural network were used to segment the retinal vascular tree by patch extraction approach. The results of the deep evaluation of the six neural networks showed that the proposed LadderNet performed well, with a high accuracy of 0.971 and an AUC value of 0.980. It was also proposed that the edge features would be used to segment the blood vessels to build a more lightweight CNN in the future [50]. By analyzing the existing research, we can identify future directions in retinal segmentation. (1) Currently available public databases have a small amount of data. Image enhancement techniques, such as flipping, mirroring, cropping, can be used to increase the dataset. (2) Cross-validation of multiple databases is more conducive to assessing the generalization ability of the model, and the remaining samples can also be used for testing [51]. (3) Although CNNs have achieved excellent results in deep learning, challenges such as their high data requirements, the need for high-quality data, long computation times, and ethical concerns still need to be addressed. Healthcare organizations should not only ensure the high quality of data but also always pay attention to protect the privacy of collected data in the future while expanding the scope of data collection. To address the ethical issues involved with data collection, Yang et al. proposed a federated learning approach focusing on solving data siloing and privacy issues. Federated learning can be categorized into horizontal federated learning that is secure to trusted servers; vertical federated learning that applies to two datasets sharing the same samples but with different feature spaces; and migrated federated learning for two datasets with different samples and also with different feature spaces. Implementing the aforementioned architecture considers not only privacy protection and the effectiveness of collaborative modeling among multiple organizations, but also how to reward organizations contributing more data to motivate improved data collection, thereby achieving a closed conscience loop learning mechanism [52].

5. Conclusions

This study collected 707 publications related to fundus lesion segmentation from 2007 to 2023 from the WoSCC database and used CiteSpace and VOSviewer software for visual processing. This included visual analysis of total publications, publications by country, connections between countries, co-cited authors, journals and institutions, and keywords through maps, clusters, tables, and bar graphs. We identified the most influential authors and journals and focused on analyzing keywords and frontier hotspots. One of the leading countries for relevant research is the Netherlands, with researchers in the United States being the main driving force. The increase in production in China, Singapore, and India in recent years reflects the considerable progress made by researchers in these countries. US institutions are major producers and sources of cited publications, working closely with institutions in the UK, China, and France. Our study provides insights into collaboration between institutions and countries. This will help researchers in the field to identify possible collaborators for their research. A large number of co-cited papers have research areas and keywords focusing on DR, localization and detection of optic discs, retinal vascular segmentation, and application of CNNs in deep learning. These research areas will continue to evolve in the future to provide a better experience for clinicians and patients.

CRediT authorship contribution statement

Hairui Deng: Writing – original draft. **Yiren Wang:** Writing – original draft. **Venhui Cheng:** Writing – original draft. **Yongcheng He:** Writing – original draft. **Zhongjian Wen:** Data curation. **Shouying Chen:** Data curation. **Shengmin Guo:** Writing – review & editing. **Ping Zhou:** Writing – review & editing. **Yi Wang:** Writing – review & editing.

Ethics approval and consent to participate

This study does not report or involve the use of any animal or human data or tissues, and hence ethical approval and consent to participate do not apply.

Availability of data and materials

- All data reported in this study are available from the corresponding author upon request.
- This study does not report the original code.
- Any additional information required to re-analyze the data reported in this study is available from the corresponding author upon request.

Additional information

No additional information is available for this study.

Funding

This study was supported by the Key-funded Project of the National College Student Innovation and Entrepreneurship Training Program (No. 202310632001), the National College Student Innovation and Entrepreneurship Training Program (No. 202310632028), the National College Student Innovation and Entrepreneurship Training Program (No. 202310632036), the National College Student and Entrepreneurship Training Program (No. S202410632165X), the University-level Research Program of Southwest Medical University (No. 2021KPZP03), and the Hejiang County People's Hospital–Southwest Medical University Science and Technology strategic cooperation project funding plan (No. 2023HIXNYD11).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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