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Magnetic nanoparticles research: a scientometric analysis of development trends and research fronts

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Abstract The research on magnetic nanoparticles attracts scientists from broad disciplines including chemistry, physics, and biomedical science. It is a great challenge for scientists from different background to discover the development trends and research fronts that are embodied in publications from different disciplines. This article aims to portray the global research profile and detect research fronts of magnetic nanoparticles by taking advantages of scientometric approaches. A total of 13,464 publications regarding magnetic nanoparticles indexed by Web of Science during 2000–2015 were used for a detailed analysis of the global magnetic nanoparticles research performance. The 500 most-cited publications on magnetic nanoparticles were analyzed for the temporal–spatial distribution characteristics as well as co-citation networks and co-word networks to identify research fronts and development trends. This study revealed that 'block-copolymers' attracted most attentions in high quality research of MNPs. Researches on yadh-bound MNPs were among the most hot MNPs topics. Recently, researches on catalysis characteristics emerged as the hot MNPs topics.

Keywords Magnetic nanoparticles (MNPs) · Co-citation network · Co-word network · Research fronts

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Introduction

Magnetic nanoparticles (MNPs) are a type of nanoparticles that allows manipulation under the control of a magnetic field (Ahn et al. 2004). MNPs commonly consist of magnetic elements such as iron, nickel and cobalt and their chemical compounds. Unique electrical, chemical, structural, and magnetic properties attract scientists from broad disciplines including chemistry, physics and biomedical science. Potential applications of MNPs include nanomaterial-based catalysts, biomedicine, magnetically tunable colloidal photonic crystals, microfluidics, magnetic resonance imaging, magnetic particle imaging, data storage, environmental remediation, nanofluids, optical filters, defect sensor and cation sensors (Elliott and Zhang 2001; Philip et al. 2003; Lu et al. 2004; Gleich and Weizenecker 2005; Gupta and Gupta 2005; Mornet et al. 2006; Philip and Raj 2006; Frey and Sun 2010; He et al. 2012; Mahendran 2012; Hyeon 2013; Philip and Felicia 2013; Kavre et al. 2014). According to information available on the Internet, major topics on MNPs are shown in Fig. 1. The visualization, known as form trees, was generated using Carrot software (http://search.carrotsearch.com/carrot2-webapp) based on the first 100 results of a web search. The crossing discipline researches on MNPs applications, MNPs materials (iron oxide, magnetic beads,…), synthesis (preparation, functionalization,…), biological systems (cells, blood, brain, peptide, cancer, antibody,…) are among the leading topics in MNPs research.

The earliest Web of Science-recorded MNPs article was written by Malaiya and Vyas (1988). Up to 26th August 2015, more than 13,500 articles, proceeding papers and reviews on the topic of “magnetic nanoparticle(s)” or “magnetic nano-particle(s)” have been indexed in Web of Science. More than ninety-nine percent of these articles are published in the new millennium (2000–2015). The fast growth of MNPs publications leads to at least two problems for MNPs researchers. One problem is that the number of MNPs publications is huge. It is difficult and takes time for researchers to make a complete literature survey. Some important or key literatures may be omitted. The other problem is that MNPs publications are written by experts from different disciplines. It is a huge burden for readers with less background knowledge to search, understand, and made judgment of

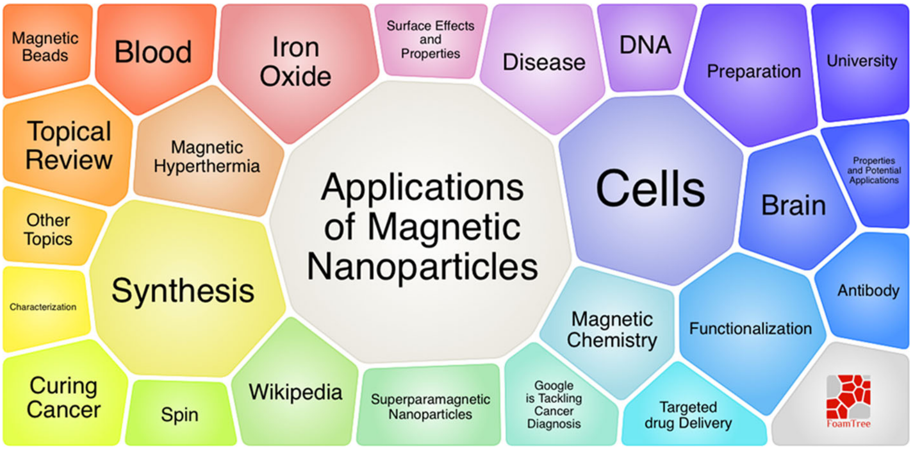

Fig. 1 A lightweight survey of major topics on the Internet on MNPs is shown. The visualization was generated by the Carrot system based on first 100 results of search on MNPs. (Color figure online)

literatures suiting their research. This situation calls for the need to portray MNPs research and development profile by using scientometrics approaches.

Scientometrics takes advantages of qualitative, quantitative and computational approaches to measure and analyze science, technology and innovation. Major research issues include the measurement of impact, reference sets of articles to investigate the impact of journals and institutions, understanding of scientific citations, mapping scientific fields and the production of indicators for use in policy and management contexts (Leydesdorff and Milojevic 2013). The use of quantitative performance indicators in scientometrics analysis is helpful in getting over the disadvantage of subjectivity in peer review and expert judgments (Smith 2006). It has been used to assess research performance in an increasing amount and variety of studies. Publications and citations are the two basic indicators in quantitative analysis of research performance. Research outcome is indicated by the number of publications. Research impact is reflected by the frequency of citations. In addition to publication number and citation frequency, the metadata of articles (e.g. title, author, publication year, keyword, and abstract) in a dataset can be analyzed and visualized to reveal the research fronts and development trends in a given subject or domain. This can be achieved by using scientometrics analysis software such as CiteSpace III or Sci 2 (Chen 2004, 2006; Chen et al. 2010; Sci2 Team 2009).

This article aims to portray MNPs research profile and detect MNPs research fronts. The bibliographic records of MNPs research during 2000–2015 were retrieved from Web of Science database. The quantitative analysis of the global MNPs research performance was based on the publication numbers and citation frequencies of MNPs articles. The 500 most-cited papers were selected and considered as representatives of MNPs frontier research. The co-citation network and co-word network of the 500 most-cited papers were constructed to detect and reveal the research fronts and development trends of MNPs research.

Data and methods

A Web of Science-based online retrieval (www.webofknowledge.com/) was performed to find research articles, proceeding papers or reviews published during 2000–2015 on the topic of "magnetic nanoparticle(s)" or "magnetic nano-particle(s)". Although researches in fields such as magnetic molecules, magnetic quantum wells, and magnetic nanodots may be relevant to MNPs, the focus of these researches is different to that of MNPs. Therefore, only publications with the term "magnetic nanoparticle(s)" or "magnetic nano-particle(s)" in the title, abstract, or author keywords have been considered. The document search was carried out on 26th August 2015. A total of 13,464 publications and 295,105 citations from these publications were analyzed for the global MNPs research productivity and impact as well as contributing countries, institutions and authors.

The 500 most-cited MNPs publications were detected with 120,312 citations that represented over 40 % of the total MNPs citations. These publications attracted most attention in the MNPs area and were considered as representatives of MNPs frontier research. Temporal–spatial distribution characteristics of these most-cited MNPs articles were analyzed including contributors (countries, institutions) and source journals. To reveal the intellectual structure of the 500 most-cited MNPs articles, the CiteSpace III software was used to construct the co-citation network and co-word network.

The global MNPs research productivity and impact during 2000–2015

A total of 13,933 publications on MNPs during 2000–2015 have been indexed by Web of Science. Among them, 13,464 publications (with a total of 295,105 citations) are articles, proceeding papers, or reviews. The reasons for including the three types of bibliography in the present study is that (1) original research articles and proceeding papers are representative of the state of the art of the field, although other types of documents such as letters may also represent the state of the art; and (2) review papers represent an additional layer of representative papers selected by domain experts (i.e., the authors of review papers) (Chen et al. 2014).

The number of MNPs publications and citations significantly increased over the 16-year study period. Panel A in Fig. 2 gives a semi logarithmic presentation of the global publication numbers and citation frequencies during 2000–2015. Two stages of exponential growth of publications were observed during 2000–2007 (indicated by a green dash line) and 2008–2014 (indicated by a black dash line). It was also observed two stages of exponential growth in citation and indicated by a red dash line (2000–2007) and a blue dash line (2008–2014). The decrease of the slope from the black dash line to that of the green dash line indicates that the exponential growth of publications in the time window 2008–2014 is slower than that in 2000–2007. Similarly, the decrease of the slope from the red dash line to that of the blue dash line indicates that the exponential growth of citation in the time window 2008–2014 is slower than that in 2000–2007. The doubling time of

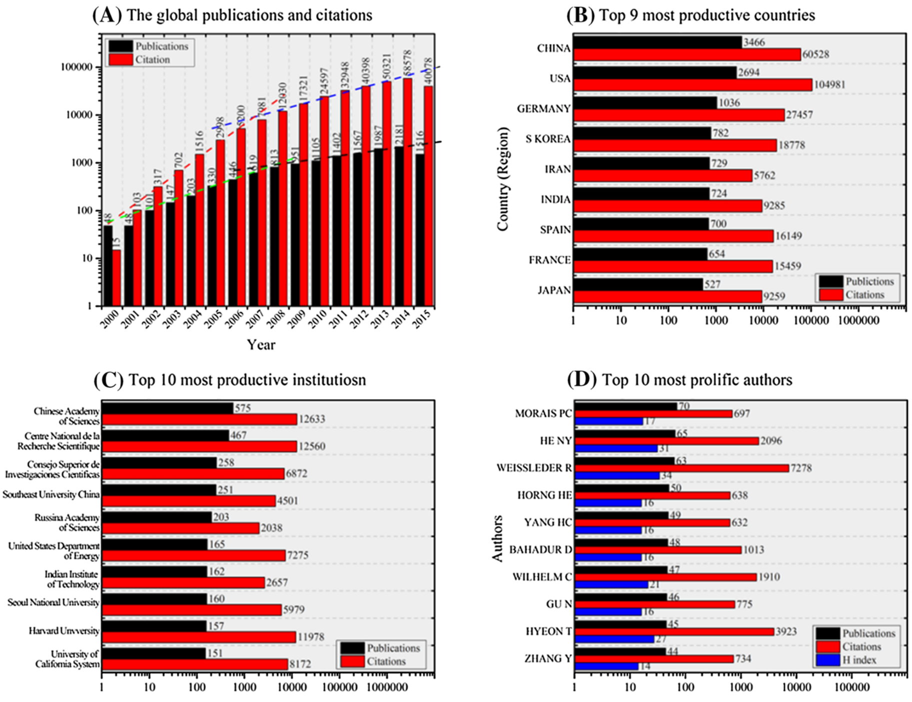

Fig. 2 The global growth of MNPs research (**a**) and top productive countries (**b**), top contributing institutions (**c**), top prolific authors (**a**). (Color figure online)

publication accumulation was calculated as 1.77 year ($R^2 = 0.9831$) during 2000–2007 and 4.06 year ($R^2 = 0.9928$) during 2008–2014. The doubling time of citation accumulation was calculated as 0.82 year ($R^2 = 0.9473$) during 2000–2007 and 2.63 year ($R^2 = 0.978$) during 2008–2014. The growing speed of citations is faster than that of publications. It indicates that the MNPs research is increasingly attractive.

Contributors to the global MNPs research were analyzed at national, institutional, and individual levels. There have been 100 countries or regions produced MNPs publications during 2000–2015. Among these countries, 28 countries (regions) published more than 100 articles (Table S1, see Supplementary Information). The top nine productive counties with over 500 publications are China, USA, Germany, South Korea, Iran, India, Spain, France, and Japan. The nine countries published 10,172 papers (75.5 % of total) with 238,882 citations (80.9 % of total). The publication numbers and citation frequencies of the top nine productive countries are presented in Panel B of Fig. 2. China with 3466 publications is the most productive country in the world. USA with a total of 104,981 citations is the highest impact country.

A total of 4967 institutions have made MNPs publications during 2000–2015. Ten institutions published more than 150 articles (Fig. 2, Panel C). Chinese Academy of Sciences produced most publications (575) with the highest citation frequency (12,633).

It is difficult to estimate the actual author numbers in MNPs research although the Web of Science database showed 32,875 records of authors. This is due to the spelling variation of author names, especially for those authors from China and South Korea. In combination with address and e-mail, the top twenty most prolific authors were identified (Table S2, see Supplementary Information; Fig. 2, Panel D). The top three prolific authors are Morais PC (Universidade de Brasilia), He NY (Southeast University, China) and Weissleder R (Harvard University) and each has published more than 60 papers. The citation frequency

Table 1 Institutions that had more than ten top-cited MNPs publications during 2000–2015

Organizations-enhanced	Country (region)	Records	% of 500
Harvard University	USA	28	5.6
Massachusetts Institute of Technology	USA	24	4.8
Centre National de la Recherche Scientifique	France	24	4.8
Chinese Academy of Sciences	China	20	4
University of California System	USA	17	3.4
United States Department of Energy	USA	15	3
Brown University	USA	15	3
Stanford University	USA	13	2.6
Hong Kong University of Science Technology	Hong Kong	13	2.6
Yonsei University	Korea	12	2.4
Seoul National University	Korea	12	2.4
University System of Georgia	USA	11	2.2
University of Glasgow	UK	11	2.2
Georgia Institute of Technology	USA	11	2.2
University of Washington Seattle	USA	10	2
University of Washington	USA	10	2
National University of Singapore	Singapore	10	2

of three authors, Weissleder R (Harvard University), Sun SH (Brown University) and Hyeon T (Seoul National University) is significantly higher than other authors. Two authors, He NY (Southeast University, China) and Weissleder R (Harvard University), exhibit H index over 30 that are the highest scores among all authors.

Temporal–spatial distribution characteristics of the 500 most-cited MNPs publications during 2000–2015

Over the 16 year window 2000–2015, the 500 most-cited MNPs publications with 120,312 citations came from 38 countries (Table S3, see Supplementary Information). Among these countries, USA produced the highest number of publications (218 articles; 43.6 % of the total 500 articles), indicating that USA takes a leading position in MNPs research. China ranked second with 75 publications (15 %). Germany ranked third with 52 publications (10.4 %).

The 500 most-cited MNPs publications are contributed by 493 institutions. Table 1 shows the top 17 institutions with at least 10 of the 500 most-cited MNPs publications. Harvard University published 28 papers and ranked first, followed by Massachusetts Institute of Technology and Centre National de la Recherche Scientifique with 24 publications each, and Chinese Academy of Sciences with 20 publications.

The 500 most-cited MNPs articles were published in 154 journals. The distribution of these journals is shown in Table S4 (see supplementary information). *Journal of the*

Table 2 Five top-cited MNPs publications during 2000–2015

Authors	Title	Source	Published year	Total citations	Average citations per year
Medintz, IL; Uyeda, HT; Goldman, ER; et al.	Quantum dot bioconjugates for imaging, labelling and sensing	Nature Materials; 4(6): 435–446	2005	3011	273.73
Gupta, AK; Gupta, M	Synthesis and surface engineering of iron oxide nanoparticles for biomedical applications	Biomaterials; 26(18): 3995–4021	2005	2712	246.55
Gao, XH; Cui, YY; Levenson, RM; et al.	In vivo cancer targeting and imaging with semiconductor quantum dots	Nature Biotechnology; 22(8): 969–976	2004	2629	219.08
Pankhurst, QA; Connolly, J; Jones, SK; et al.	Applications of magnetic nanoparticles in biomedicine	Journal of Physics D-Applied Physics; 36(13): R167–R181	2003	2613	201.00
Lu, An-Hui; Salabas, E. L.; Schueth, Ferdi	Magnetic nanoparticles: Synthesis, protection, functionalization, and application	Angewandte Chemie-International Edition; 46(8): 1222–1244	2007	2314	257.11

American Chemical Society published 43 of the 500 most-cited articles and ranked first, followed by *Biomaterials* with 24 papers and *Langmuir* with 17 papers.

The five top-cited MNPs publications are shown in Table 2. The most cited MNPs article was written by Medintz et al. (2005) and published in *Nature Materials*. This article mentioned the use of MNPs in quantum dots biotechnology. Gupta and Gupta (2005) published an article in *Biomaterials* and ranked second in the number of total citations. This article focused on synthesis and surface engineering of iron oxide nanoparticles for biomedical applications. Gao et al. (2004) published an article in *Nature Biotechnology*

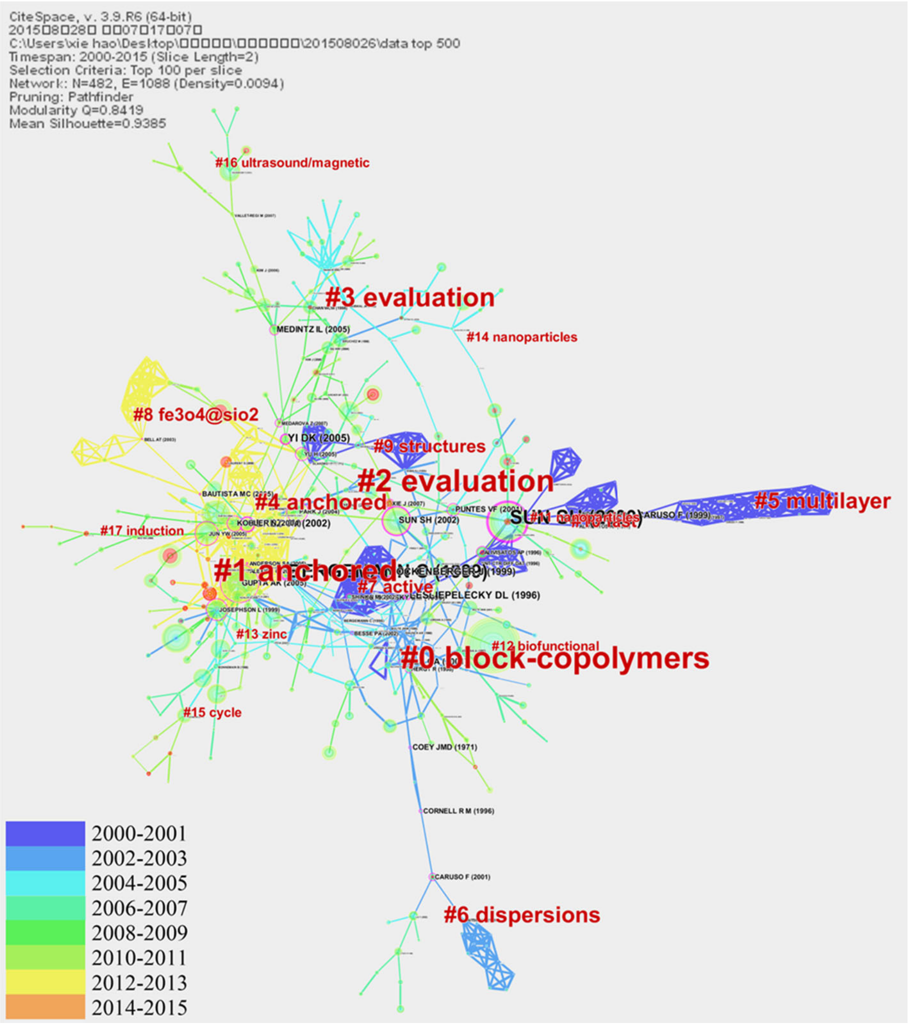

Fig. 3 A network of 482 co-cited references representing citation patterns of the 500 most-cited MNPs articles between 2000 and 2015. Nodes in the network represent cited references. *Lines* that connect nodes are co-citation links. The *colors* of these *lines* show when a connection was made for the first time. Clusters are *numbered* and labeled in *red color*. The font size of the labels is proportional to the cluster size. (Color figure online)

and ranked third in the number of total citations. This article described the development of multifunctional nanoparticle probes based on semiconductor quantum dots (QDs) for cancer targeting and imaging in living animals. Pankhurst et al. (2003) published an article in *Journal of Physics D-Applied Physics* and ranked fourth in the number of total citations. This article reviewed the physical principles underlying some current biomedical applications of magnetic nanoparticles. Lu et al. (2007) published an article in *Angewandte Chemie-International Edition* and ranked fifth in the number of total citations. This review focused on the synthesis, protection, functionalization, and application of magnetic nanoparticles, as well as the magnetic properties of nanostructured systems.

Quantitative analysis on the 500 most-cited MNPs publications

Co-citation network reflects research fronts in a series of co-cited publication clusters. Publications locating in the center represent the core achievement in this research field. Appearance of new trends and bursts of scientific publications normally results from either proposing a new finding or major scientific breakthrough in a publication or enlightening scientists to study issues from a new prospective (Chen 2004, 2006).

In the present study, the co-citation network of the 500 most-cited MNPs publications was built by taking advantages of Citespace III. With a Time Slicing value of 2 year, the dataset covering the period 2000–2015 was divided into 8 parts. The 100 most-cited references in each part were selected with node type of “cited-reference” and pathfinder network scaling selection. The visualized network for co-cited references was created (Fig. 3). A total of 482 co-cited references were detected and divided into 19 clusters (Table S5, see Supplementary Information). The earliest structure consists of clusters such as ‘#9 structures’ and ‘#18 magnetic’. The most recent structure consists of ‘#4 anchored’ and ‘#8 fe3o4@sio2’. The largest cluster ‘#0 block-copolymers’ has 55 references as its members with an average year of publication of 1995. The article ‘Sun2008’ (Sun et al. 2008) is with the strongest citation burst. This article reviewed MNPs in MR imaging and drug delivery. The article ‘Pankhurst2003’ (Pankhurst et al. 2003) is with the highest citation frequency. This review about MNPs is also one of the five top-cited articles of the 500 most-cited MNPs articles.

The betweenness centrality of a node in a network measures the extent to which the node is part of paths that connect an arbitrary pair of nodes in the network (Chen 2004; Brandes 2001; Freeman 1977). In the present study, ‘Sun2000’ (Sun et al. 2000) and ‘Bergemann1999’ (Bergemann et al. 1999) were detected with the highest centrality and located in the center of the co-citation network. The two articles are potentially revolutionary publications that attracted more attentions than other literatures in the network. The article ‘Sun2000’ reported synthesis of monodisperse iron-platinum (FePt) nanoparticles by reduction of platinum acetylacetonate and decomposition of iron pentacarbonyl in the presence of oleic acid and oleyl amine stabilizers. It is in Cluster #10 and cited by 68 articles. The article ‘Bergemann1999’ reviewed studies of magnetic ion-exchange nano- and microparticles for medical, biochemical and molecular biological applications. It is in Cluster #1 and cited by 15 articles.

The largest cluster formed by more recently published articles is ‘#4’ that has 35 members with an average year of publication of 2007 (Table S6, see Supplementary Information). In this cluster, ‘Dobson2006’ (Dobson 2006) is with the highest citation frequency. This review focused on technical aspects of magnetic targeting as well as nanoparticle design and animal and clinical trials. Articles ‘Berry2003’(Berry et al. 2003), ‘Duran2008’(Durán et al. 2008) and ‘Chorny2010’ (Chorny et al. 2010) are with the highest centrality. The article ‘Berry2003’ reported the use of magnetic nanoparticles synthesized and derivatised with either dextran or albumin. The article ‘Duran2008’ is a review on magnetic drug delivery systems. The article ‘Chorny2010’ demonstrated the feasibility of site-specific drug delivery to implanted magnetizable stents by uniform field-controlled targeting of MNPs with efficacy for in-stent restenosis. The common theme in terms of the citing articles to this cluster is the iron oxide nanoparticles, drug delivery, and oxide nanoparticles (Table S7, see Supplementary Information). In terms of the silhouette

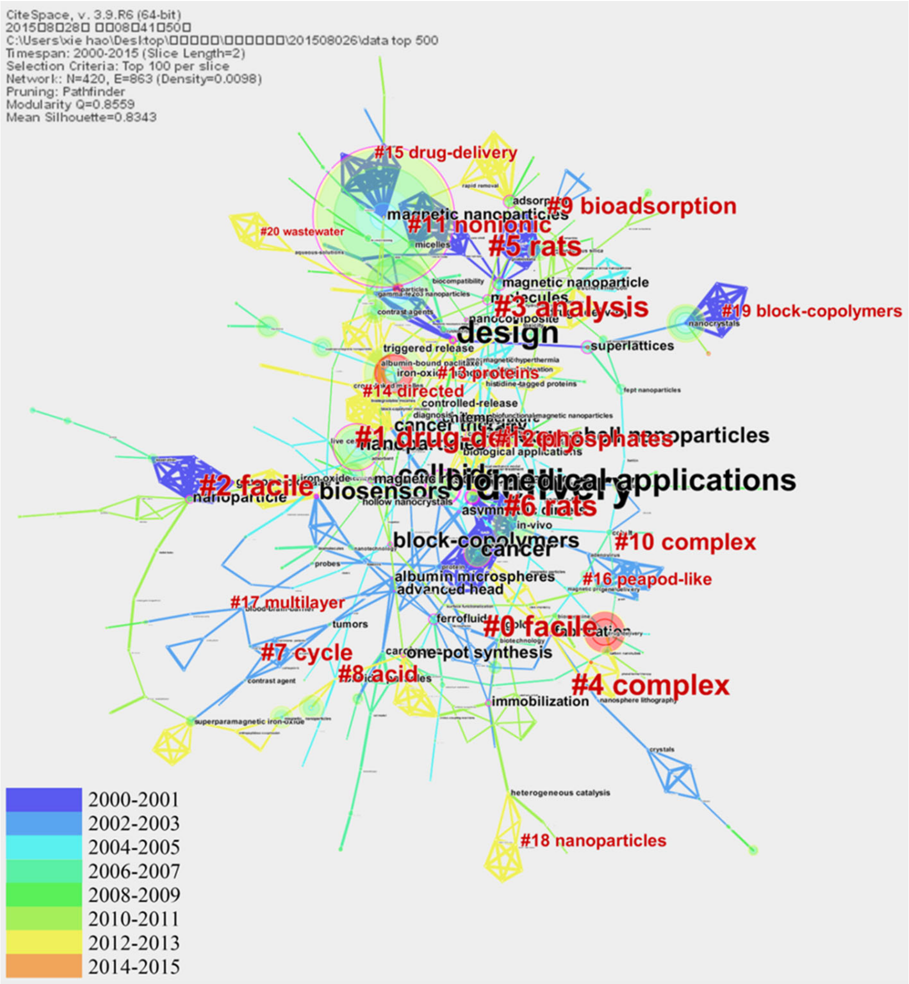

Fig. 4 A network of 420 co-occurred keywords of the 500 most-cited MNPs articles between 2000 and 2015. Nodes in the network represent co-occurred keywords. *Lines* that connect nodes are co-occurred links. The *colors* of these *lines* show when a connection was made for the first time. Clusters are *numbered* and labeled in *red color*. The font size of the labels is proportional to the cluster size. (Color figure online)

values, the homogeneity of clusters #4 is generally considered very high at 0.899, implying the high quality of the grouping.

To analyze hot topics in MNPs research, visualized network of co-occurred keywords was created using the pathfinder method. With a Time Slicing value of 2 year, the dataset selected during 2000–2015 was divided into 8 parts. The top 100 co-occurred keywords in each part were selected with node type of “keyword”. The visualized network of co-occurred keywords was created (Fig. 4) to reveal the overall structure of MNPs research in a broader context. A total of 420 co-occurred keywords were detected and divided into 21 clusters (Table S8, see Supplementary Information). Keywords with the highest centrality include ‘delivery’, ‘immobilization’ and ‘in-vivo’. Keywords with the highest frequency include ‘magnetic nanoparticles’, ‘particles’, “iron-oxide nanoparticles’, ‘nanoparticles’, ‘drug-delivery’, ‘in-vivo’, and ‘nanocrystals’. Keywords with the highest bursting strength include ‘particles’, ‘drug-delivery’, ‘superlattices’, and ‘iron-oxide nanoparticles’.

The earliest structure consists of clusters such as ‘#6 rats’, ‘#11 nonionic’ and ‘#15 drug-delivery’. The most recent structure consists of ‘#18 nanoparticles’ and ‘#20 wastewater’. The largest cluster ‘#0 facile’ has 33 keywords as its members with an average year of occurrence of 2005. Its high silhouette value of 0.831 indicates a high homogeneity of the cluster. The keyword ‘immobilization’ is with the highest frequency in the cluster. Keywords ‘biotechnology’, ‘gamma-fe2o3’ and ‘biofunctional magnetic nanoparticles’ exhibit the highest centrality. The main topic of this cluster is on yadh-bound MNPs.

The largest cluster formed by more recently occurred keywords is ‘#18 nanoparticles’. This cluster has 9 members and an average year of occurrence of 2012. In this cluster, the phrase ‘heterogeneous catalysis’ shows the highest centrality and frequency. Other phrases with high centrality include ‘homogeneous catalysis’, ‘assisted organic-synthesis’ and ‘aqueous micellar media’.

Conclusion

A total of 13,464 publications in MNPs research were indexed in Web of Science during 2000–2015. Two stages of exponential growth were observed on MNPs publications and citations during 2000–2014. The number of publications in 2014 is nearly fifty times that in 2000. These findings suggest that the field of MNPs research was in a stage of fast development in the new millennium.

The top nine productive countries (China, USA, Germany, South Korea, Iran, India, Spain, France, and Japan) contributed more than three quarter of total global MNPs publications and citations. With the highest number of MNPs publications, China is the most productive country. With the highest citation frequency, USA is the highest impact country in MNPs research. With the most publications and the highest citation frequency than other institutions, Chinese Academy of Sciences is the leading institution in the global MNPs research. ‘Morais PC’, ‘He NY’ and ‘Weissleder R’ are the most prolific authors in MNPs research.

The 500 most-cited publications (3.7 % of total publications) in MNPs research were further analyzed. With an accumulated citation frequency of 120,312 (40.7 % of total citations), these articles attracted most MNPs researchers. The article with the highest citation frequency (3011, a mean of 273.7 times per year) was written by Medintz et al. (2005). The 500 most-cited publications on MNPs research originate from 38 countries.

With 218 articles (43.6 % of the total 500 articles), USA is ranked first and takes the leading position in this area. Among the included institutions, Harvard University published 28 papers each and ranked first. Among the journals publishing the 500 most-cited MNPs articles, *Journal of the American Chemical Society* had 43 publications and ranked first.

The present study detected emerging trends and new developments of MNPs research during 2000–2015 based on structural and temporal properties derived from the 500 most-cited MNPs publications. The co-citation network analysis of the 500 most cited MNPs articles revealed that ‘block-copolymers’ attracts most attentions in high quality research of MNPs. Two articles, one on iron-platinum (FePt) nanoparticles and the other on magnetic ion-exchange nano- and microparticles for medical, biochemical and molecular biological applications are potentially revolutionary publications that attracted more attentions than other literatures. The co-word network analysis revealed that researches relating to yadh-bound MNPs are among the most hot MNPs topics and keywords ‘biotechnology’, ‘gamma-fe2o3’ and ‘biofunctional magnetic nanoparticles’ exhibit the highest centrality in the topic. Recently, researches on catalysis characteristics emerged as the hot MNPs topics.

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