SYNTHETIC CHEMISTRY RESEARCH TRENDS REPORT

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American Chemical Society

Synopsis

Synthetic organic chemistry, although a well-established discipline, has continued to advance in the past decade with an aim to meet the needs of society in all aspects of life. The importance of organic synthesis to chemistry, technology, and perhaps to humanity justifies an understanding of its development. By studying the CAS Content Collection, we provide a view of the landscape of synthetic organic chemistry. Three key emerging organic synthesis research foci were selected from publication trend analysis and subject matter experts' evaluation: enzyme catalysis, photocatalysis, and green chemistry. We hope this report will place the current state of global research effort in this field into context and help researchers and decision makers to anticipate future opportunities and applications in organic synthesis.

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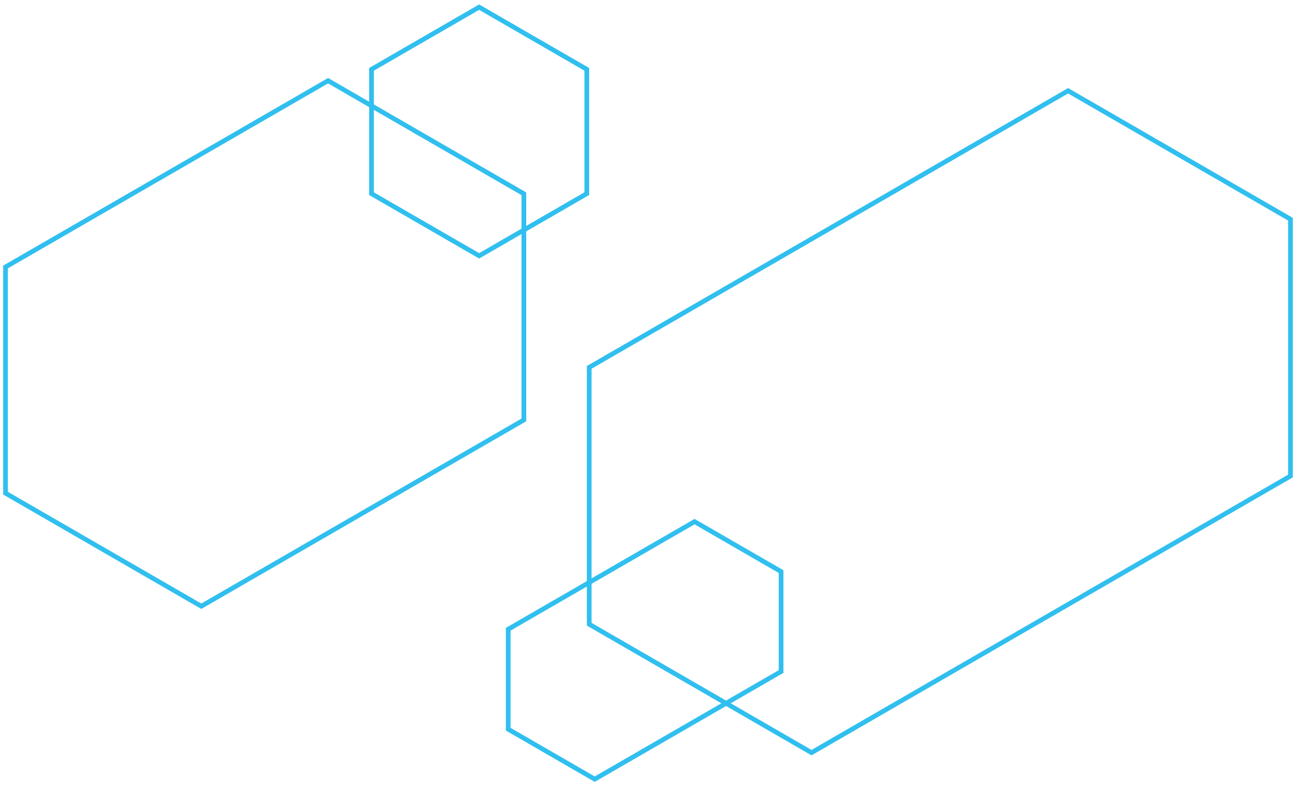
1. Introduction to organic synthesis

Organic synthesis is the assembly of organic molecules from simpler or more readily available precursors. Organic synthesis encompasses the set of methods and processes to make and modify carbon-containing molecules, and as such is an enabling and important technology in chemistry. Most of the substances used in everyday life, from plastic objects to pharmaceuticals, require making molecules that do not exist naturally or cannot be obtained in the necessary amounts. In addition, understanding the world requires the ability to create molecules with novel structures and functions. The importance of organic synthesis to chemistry, technology, and perhaps to humanity justifies an understanding of its development. Based on the CAS Content Collection™, this report intends to provide a view of the landscape of synthetic organic chemistry across time, geography, and research topic. We hope this report will be a useful resource for researchers and decision makers to appreciate the current state of global research efforts in synthetic organic chemistry and look forward to future opportunities in its development and applications.

Organic synthesis has incorporated a variety of new ideas and techniques to make molecules during last decade. The use of **organocatalysis**, particularly the use of catalysts such as secondary amines[1], ureas[2], thioureas[3], squaramides[4], and nonracemic Broensted acids[5], has significantly altered the practice of **enantioselective synthesis**. This was recognized in 2021 when David MacMillan and Benjamin List were awarded the Nobel Prize in Chemistry.[6] Another significant research topic is the use of base metal catalysts, particularly **nickel catalysts**[7], as alternatives to catalysts generated from more expensive and rarer metals such as palladium[8]. The use of **radical chemistry** to perform coupling reactions and alkene functionalization reactions[9] has increased substantially. Interest in the use of nickel and cobalt catalysts has increased in part because of their ability to accommodate single electron pathways and thus to be used in concert with radical chemistry.[10] **Photoredox chemistry**, the use of light in the presence of either metallic (iridium or ruthenium) or organic catalysts to generate highly oxidized or reduced intermediates from stable starting materials, has become a substantial topic of interest.[11, 12] The ability of light to provide energy to access reactive intermediates enables reactions such as cycloaddition, aromatic substitution and coupling reactions that would be difficult and likely nonselective when driven by heat. The ability to perform functionalization reactions at unactivated carbon-hydrogen bonds **(C-H activation)**, though a hot topic of research between 2001 and 2010, has further increased significantly in the most recent decade[13].While the use of auxiliaries such as aminoquinolines[14] to direct remote functionalization reactions have been common, the use of transient directing groups[15] and native functional groups such as amides for remote functionalization reactions[16, 17] have increased substantially. Electrochemical methods have become significantly more common, for example, the electrochemical Birch reduction, and the availability of synthetic electrochemical apparatus has facilitated the development of new electrochemical methods in organic synthesis. Finally, bioorthogonal chemistry (sets of reactions compatible with the conditions present in living cells and organisms)[18] enables synthesis in living organisms and has advanced biological understanding significantly[19, 20]. For a more comprehensive list of advances from 2011 to 2020 in this field, we selected 200 of the most notable research articles (20 per year) primarily based on citation numbers **(Appendix I)**.

There has been some emphasis (particularly at large scale) on developing organic reactions under mild and eco-friendly conditions, also known as green synthesis. For example, enzyme catalysis is particularly relevant because of its use of aqueous solvents and its ability to facilitate selective reactions. Both the commercial availability of enzymes and the ability to readily generate and optimize enzymes via directed evolution (a technique which won Professor Frances Arnold a share of the 2018 Nobel Prize in Chemistry) make enzyme catalysis a useful tool for organic synthesis. To date, enzymes are used to manufacture a variety of pharmaceutical intermediates and products[21, 22] and thus to reduce their environmental costs. Routes to the COVID-19 treatment molnupiravir and the anti-HIV agent islatravir have been devised using enzymes in key steps for large scale production. Flow chemistry and microflow chemistry are another set of approaches to minimize environmental costs of organic synthesis. [23] These methods can be used to generate highly reactive intermediates such as Grignard reagents[24] and can improve mass transfer and thus facilitate photochemical and electrochemical methods[25]. Solvent use is a significant contributor to the environmental costs of organic synthesis, and a variety of attempts have been made to minimize it; in particular, surfactants have been used to perform a variety of organic reactions in water with little or no organic solvent.[26, 27, 28] Finally, methods using retrosynthesis software such as SciFinder^{n} (https://www.cas.org/solutions/cas-scifinder-discovery-platform/cas-scifinder/retrosynthesis-planning) in conjunction with automation and flow methods[29, 30] have been developed and assessed for their potential in general use.

Organic synthesis is continuing evolving to develop new drugs, chemicals, and materials in an economical and responsible manner. In this report, we first provide a high-level overview of the publication trends and distributions by studying the publication data from CAS Content Collection. We then analyze the concepts based on CAS index frequencies to illustrate the emerging concepts and connections between them. Finally, three emerging topics — green chemistry, enzyme catalysis and photocatalysis — are discussed with analyses of publication trends, concept connections, and substance functions and categories. In general, organic synthesis has become more cost effective, environmentally friendly and capable of synthesizing new substances during the last decade.



2. Overall publication trends in organic synthesis research

2.1 Trends of journal and patent publications in organic synthesis

The CAS Content Collection represents the largest collection of published scientific knowledge in chemistry. It is particularly useful for quantitative analysis of global scientific publications against variables such as time, research area, formulation, application, and chemical composition. The analysis in this report focused on organic synthesis research for the ten-year period between 2011 and 2020. Organic synthesis-related publications and their derived data were extracted from the CAS Content Collection with defined search criteria (see Method Section). Journal publication data excluding reviews were extracted from a selection of chemistry-related journals from the CAS Content Collection (**Appendix II**). Patents were selected from the 64 patent offices in the full CAS Content Collection. To minimize the effect of variance between years, biennial data were used for the trend analysis.

The global output of journal and patent publications related to organic synthesis from 2011 to 2020 is shown in **Figure 1**. As shown in the left panel, the number of organic synthesis papers published in 2011-2012 was around 63,000, which increased around 25% to 80,000 in 2019-2020. This rate of increase is slightly higher than that for overall chemistry-related journal publications (20%) in the CAS Content Collection during the same period. The trend of global output of organic synthesis patents in this decade is displayed in the right panel of **Figure 1**. 78,000 organic synthesis patents were published in 2011-2012, while 124,000 were published in 2019-2020, a 60% increase in publication volume. However, during the same period, the number of total patents in the CAS Content Collection increased by about 85%.

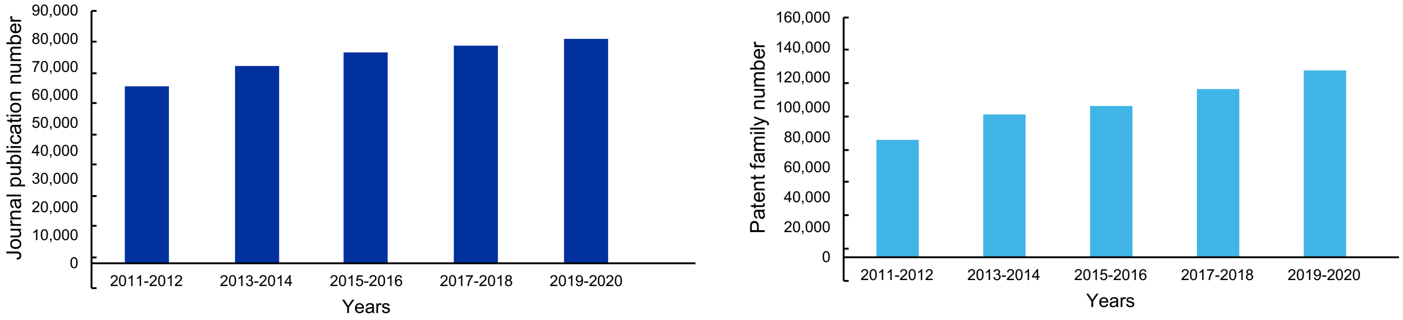


Figure 1. Trends of journal and patent publications in organic synthesis from the CAS Content Collection during 2011-2020. Left panel: journal publications in organic synthesis from a selection of chemistry-related journals; right panel: patent family applications in organic synthesis.

2.2 The distribution of publications among countries/regions in organic synthesis research

To understand where active organic synthesis research is occurring, we identified the 10 countries/regions producing the largest number of journal or patent publications in organic synthesis, as shown in **Figure 2**. A total of 11 countries/regions appeared in these two lists. China contributed 30% of journal papers and 55% of patents in organic synthesis during the past ten years. It is noteworthy that the ratio of patent publications to journal publications varies significantly among the 11 countries/regions. South Korea, China and Japan publish roughly three times as many patents as journals, while United States, Germany, and France publish similar numbers of patents and journals, and Russia, United Kingdom, and India publish significantly larger numbers of journals than patents.

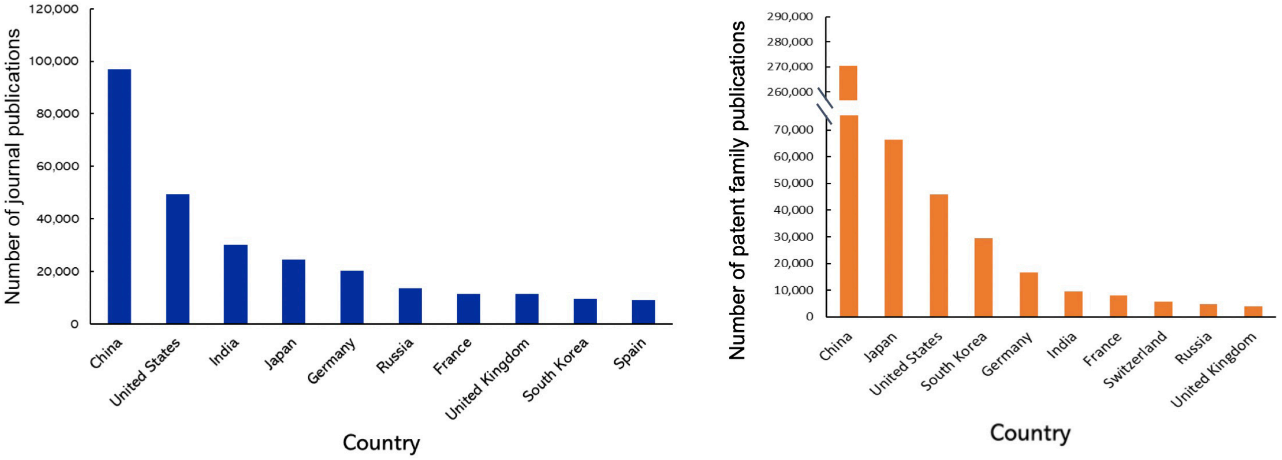


Figure 2. Top 10 countries/regions in numbers of journal (left) or patent (right) publications (2011-2020) in organic synthesis.

To further study the publication trends of the top 5 countries/regions, biennial data of their journal or patent publications were analyzed and their trends are displayed in **Figure 3**. China is the only country with consistent growth in both journal and patent publications. Publications from other countries/regions either stayed constant or decreased over the past ten years. The volume of publications from China nearly tripled over this span.

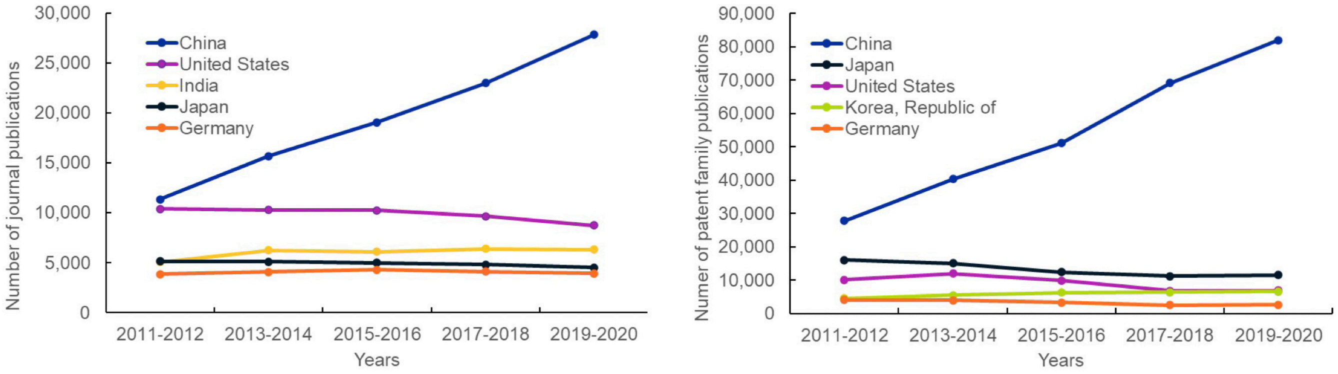


Figure 3. Journal (left) and patent (right) publication trends in organic synthesis for the top 5 countries/regions between 2011 and 2020.

To get insight on the overall quality of journal publications from each country/region, pp-index is introduced[31]. The relative impact of a country's organic synthesis research can be compared through the representation of its articles among the world's top 1% of cited articles. For a specific year, a given country/region's pp-index = (counts of top 1% most cited journal publications/total counts of journal publications) ×100. Based on the total citation counts, the top 1% of most cited journal publications are selected from the organic synthesis journal publications described previously for the overall publication trends. In general, publications receiving higher citation counts have more impact on its research field. By using this normalized index, the overall journal publications quality from different countries/regions can be compared without publication volume effects.

The biennial pp-index of the top 5 countries/regions is presented in **Figure 4**. In 2011-2012, United States achieved pp-index of 2.2, which means its share of top 1% of cited papers is more than twice the size of its share of organic synthesis papers. During the same time frame, Germany's pp-index is 1.7 and pp-indexes of China and Japan are around 1. On the other hand, India's pp-index in 2011-2012 is 0.16, which is significantly lower than the other four countries/regions. In 2019-2020, China surpassed United States by achieving pp-index 1.6, while Germany and United States had similar pp-indexes of about 1.3. Japan's pp-index dropped to 0.6 by the end of 2020 and India's pp-index stayed roughly the same at 0.17. From this point, it can be concluded that the overall quality of organic synthetic journal papers from China has increased steadily over the past ten years, while the impact of organic synthesis publication from United States, Germany and Japan decreased.

As comparison, top 5% and top 10% pp-indexes are also presented in **Figure 4**. Similar trends can be seen in top 5% pp-index chart; however, it is not as significant as shown in top 1% pp-index chart. pp-index from China, United States and Germany are higher than 5, which means their share of top 5% cited papers are much more than their shares of total publications in organic synthesis. Different from top 1% and 5% pp-index, the top 10% pp-index trend from all five countries/regions decreased during the past ten years, which indicates more and more journal papers from other countries/regions involved in the top 10% publications.

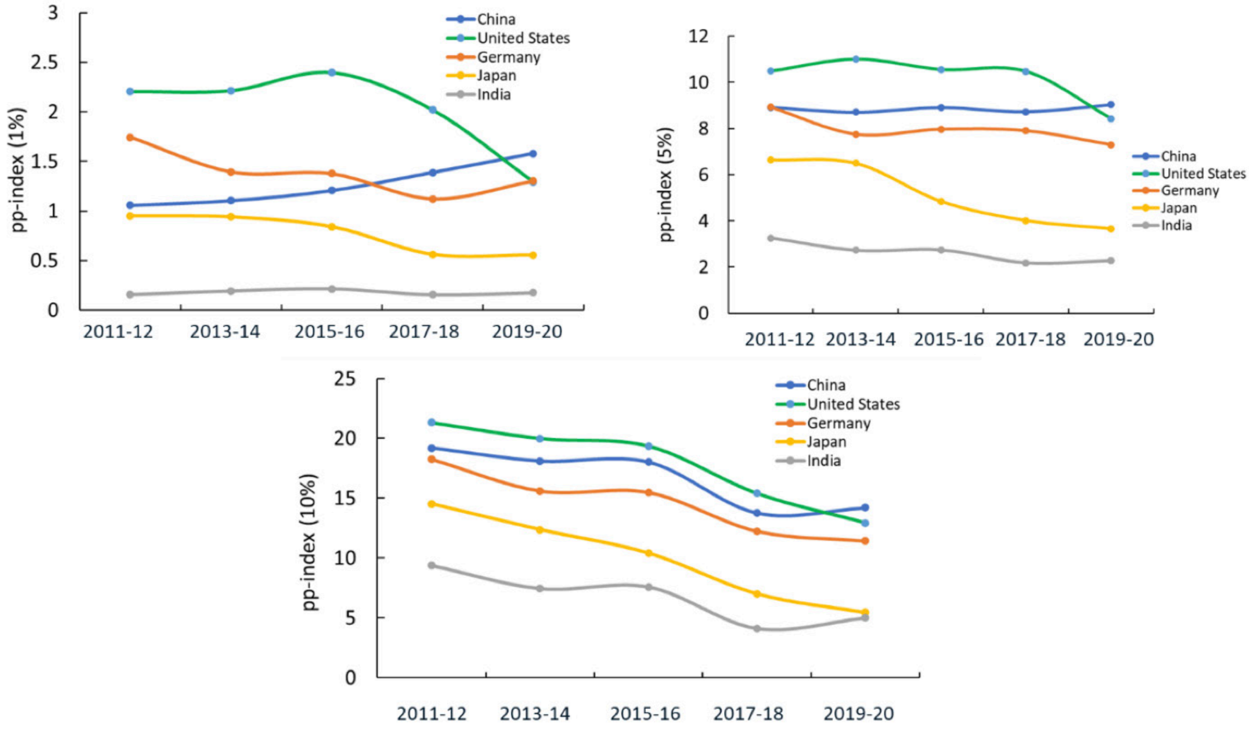


Figure 4. Top 5 countries' pp-index in organic synthesis journal publications during 2011-2020. pp-index = (country-specific number of papers in the top 1%, 5% or 10% most cited papers worldwide)/(the total number of papers produced in the same country) ×100

2.3 Top organizations in organic synthesis journal and patent publications

To understand more finely the source of organic synthesis research, we identified the 20 research organizations producing the largest number of journal publications in organic synthesis as shown in **Figure 5**. Organizations from China constitute 15 out of the 20 entities on the list. The Russian Academy of Sciences, the University of California system, Kyoto University, Osaka University, and the University of Tokyo make up the remainder of the list. The Chinese Academy of Sciences is made up of over 100 research institutions, of which the top contributors are depicted in the inset. Similarly, the Russian Academy of Sciences and the University of California are also groups of affiliated institutions. Among independent research institutes, Sichuan University published the greatest number of journal papers in this ten-year period.

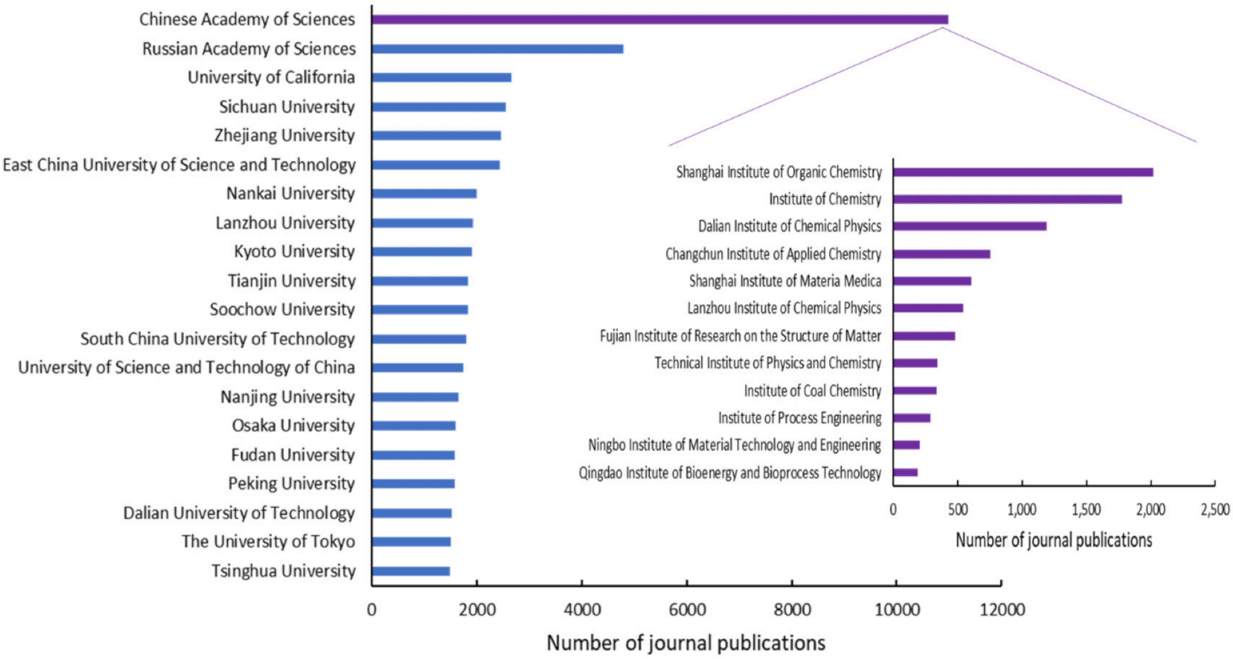


Figure 5. Top 20 research organizations on journal publications in organic synthesis research from 2011-2020 in the CAS Content Collection. Insert shows separate data from regional institutes of the Chinese Academy of Sciences.

The top 20 patent assignees in organic synthesis from 2011 to 2020 are shown in **Figure 6**. This list consists of 7 chemical companies and 13 universities or research institutions. The top 4 assignees in this list are all chemical companies, which indicate strong commercial interest in organic synthesis. In the years 2011-2020, China Petroleum & Chemical Corp. published more than 11,900 patents, which surpassed the sum of patents filed by LG Chemical Ltd., Sumitomo Chemical Co., Ltd. and BASF SE. Meanwhile, universities and research institutions on this list, all from China, also actively published patents in this area. Among them, Zhejiang University of Technology published the highest volume of patents from 2011 to 2020.

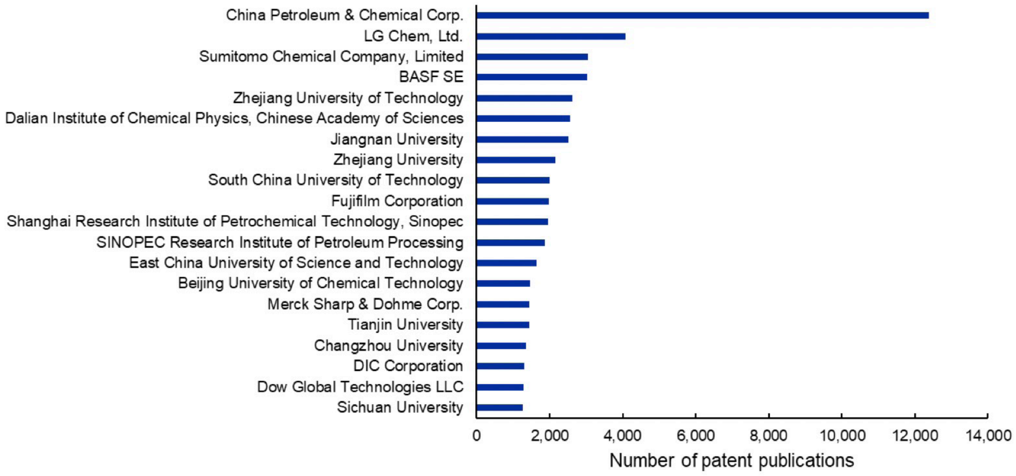


Figure 6. Top 20 patent assignees in patent publications on organic synthesis from 2011-2020 in the CAS Content Collection.

2.4 Overview of the most prominent concepts and their interconnections in the field of organic synthesis in the years 2018-2020

To have an overview of how concepts interact with each other in the field of organic synthesis in the recent years of 2018-2020, the most frequently indexed concepts in journal articles were identified and concepts occurring together in the same document were determined. Pairs of concepts commonly associated are visualized based on their frequencies of co-occurrences using VOSviewer software (**Figure 7**). The synthetic concepts can be grouped into three clusters. One cluster (red) is composed of synthetic methods and targets. Of the topics in this cluster, the most comsa a a ca a a amon concepts are those for regioselective synthesis, diastereoselective synthesis, enantioselective synthesis, green chemistry, tandem reactions, cyclizations, reaction mechanisms, and C-H bond activation. Control of the selectivity between two reacting groups at different positions in the same molecule (regioselectivity) or of the selective formation of stereoisomers (diastereoselectivity or enantioselectivity) is crucial for a useful synthetic method. The selective activation of C-H bonds has been a topic of interest in organic synthesis during the last decade; control of selectivity in C-H activation is crucial to its use in generating complex molecules from simpler, less-functionalized starting materials. Cyclization reactions are an effective method to generate complexity in organic synthesis. Green chemistry has received greater research emphasis because of the concerns of global warming and the desire to sustain chemistry at reduced costs to society and the environment. Enzyme-mediated synthesis is an important class of methods to this end because of its use of water as solvent and its ability to perform chemistry without requiring highly reactive or toxic reactants under mild conditions. Tandem reactions are combinations of reactions performed at once or in close sequence; they can generate structures with both less waste and better yields than the corresponding separate reactions, and so help chemistry to generate products economically and with improved environmental impact.

A second cluster is made up of two smaller clusters (blue and green) which include concepts for the chemical and physical characteristics of synthetic products and their uses. Advances in X-ray sources and in computers have made X-ray crystallography more affordable, more available, and easier to perform than ever before. The spectral and physical characterization of molecules by UV/visible spectra and fluorescence are commonly used to characterize dyes, optoelectronic materials, and nanoparticles and their stabilities. Finally, a red cluster contains concepts for the uses of synthetic compounds potentially relevant to human medicine, including molecular docking and structure-activity relationships for pharmaceutical agents. The most common pharmaceutical targets indexed are antibacterial and antitumor agents; fluorescent dyes for biological use are also commonly seen. The prevalence of antitumor agents as a concept is consistent with the increased interest in developing cancer treatments, while antibacterial agents have been noted as an important public health need. The initial testing and discovery of antitumor and antibacterial agents are amenable to both academic and industrial laboratories.

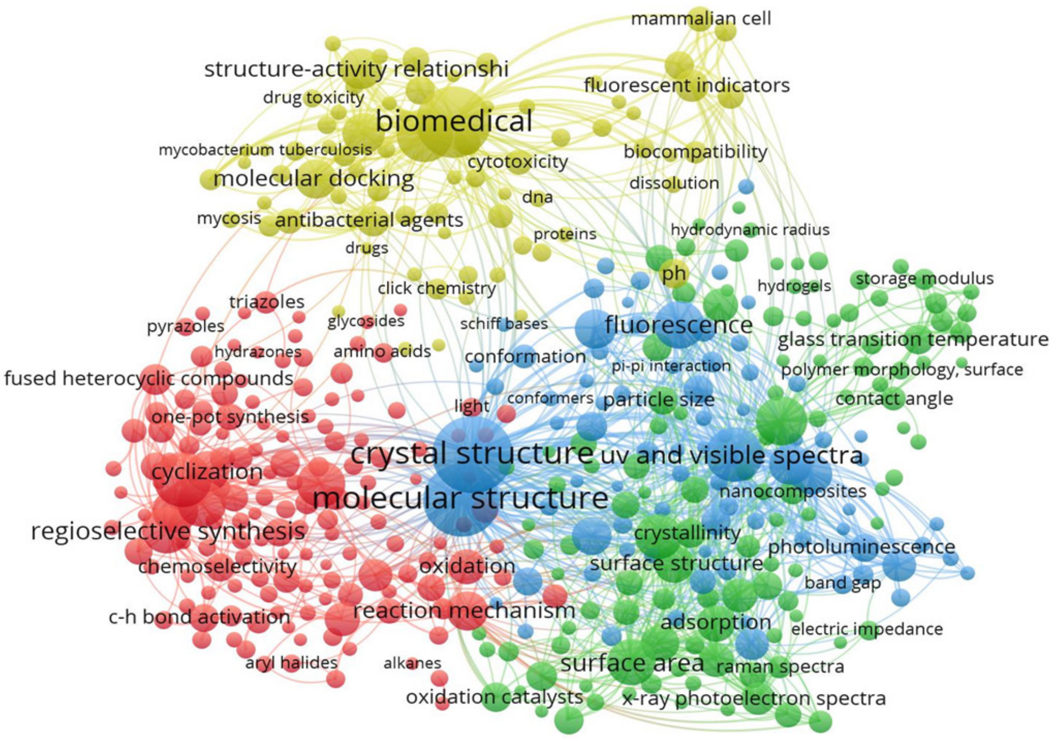


Figure 7. Concepts and co-occurrence in journal publications of organic synthesis in the years 2018-2020. Due to space limitations, only selected concepts are shown in this figure. **Appendix III** gives a more complete list of concepts and their frequencies of links and occurrences.

The same analysis was performed to determine the most frequently indexed concepts in patent publications. **Figure 8** shows that these concepts are clustered roughly into three major groups more widely separated than those in journal articles. There are many polymer-related concepts in the red cluster, such as polyoxyalkylenes, polymerization catalysts, and crosslinking agents. The most indexed polymer types are polyoxyalkylenes and polysiloxanes, with organosilicon compounds also indexed; the frequency of indexing is much greater in patents than in journal articles. Polymers are common materials with strong commercial interest. Furthermore, methods for recycling plastics and for creating polymers with new properties have been studied intensively, and the subject frequencies are consistent with increasing interest in synthetic methods for polymers. The red cluster includes a variety of synthetic methods and products, with hydrogenation and oxidation being the most common reactions. Reduction and oxidation reactions are used frequently in organic synthesis and their improvement in commercial processes is important to reduce waste and cost. Physical processes that are involved in preparing substances are also associated with this cluster. Organic luminescent devices and the associated substances are commercially important and rely on synthesis to prepare their components. A connected smaller cluster includes concepts for biological methods, with fermentation and biosequences being the most prevalent. The yellow and green clusters encompass biological uses for synthesis in treating diseases; diseases and their treatments often appear together in one document. One of the most indexed concepts is antitumor agents, indicating that cancer continues to be a widely held concern among the population and so development of antitumor agents attracts strong commercial interest. Breast cancer, lung cancer, prostate cancer, pancreatic cancer, and liver cancer are the most prevalent types of cancer that have been indexed in the patent literature. Other highly indexed concepts related to pharmaceutical agents are those for treatment of inflammation, viral infection, diabetes, autoimmune diseases, and Alzheimer's disease.

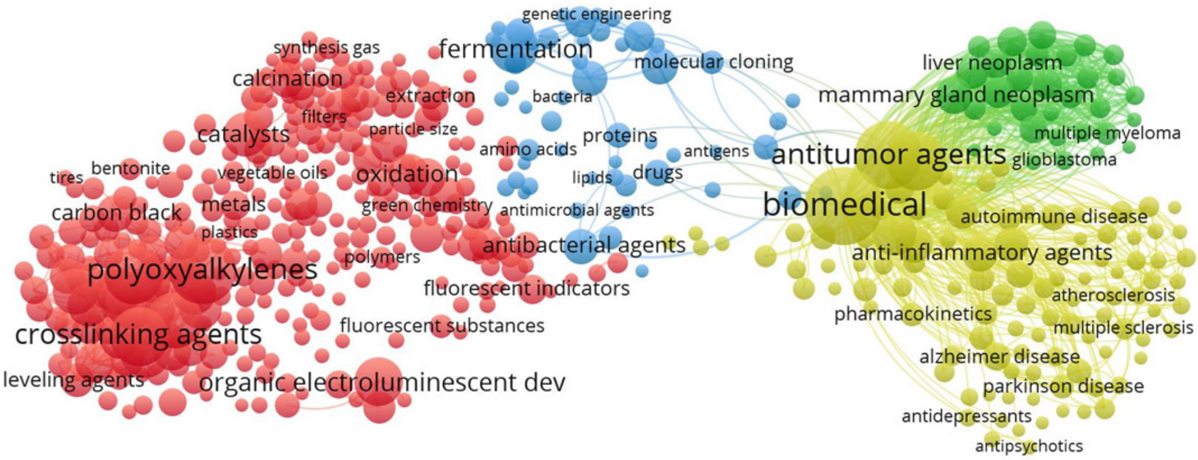


Figure 8. Concepts and co-occurrence in patent publications of organic synthesis in the years 2018-2020. For a more complete list of concepts and their frequencies of links and occurrences, please see **Appendix IV**.

2.5 Rising concepts in the field of organic synthesis in the years 2001-2020

To identify current research topics of interest, related concepts from journal publications in organic synthesis from 2001-2020 were assessed. Briefly, concepts were identified when they were indexed more than 400 times in 2020 and have increased more than 50 times from 2001-2020 (**Figure 9**). Four classes of organic substances, fused heterocyclic compounds, metal-organic frameworks, ionic liquids and triazoles, are the frequently indexed classes of organic compounds with fastest growing rate in CAS Content Collection in the last two decades. Journal publications on fused heterocyclic compounds, metal-organic frameworks and triazoles significantly increased, especially in the last ten years. Starting from 2013, research related to ionic liquids has reached a plateau. Four organic reaction types - regioselective synthesis, C-H activation, three-component reaction, and click chemistry - are the most indexed organic reaction types from the CAS Content Collection. Recent progress in regioselective synthesis mainly focused on regioselective construction of heterocycles. The direct formation of a C-C bond from C-H bonds, instead of using a pre-synthesized functional group, has the potential to significantly reduce the synthetic steps and thus increase the efficiency of chemical production.

From 2011 to 2020, enormous success has been made in the direct functionalization of C-H bonds for synthetic purposes. The term "click chemistry" was first introduced by K. B. Sharpless in 2001 to describe reactions that are high yielding, wide in scope, stereospecific, and simple to perform in easily removable or benign solvents, which with bioorthogonal was just awarded the Nobel Prize in Chemistry in 2022. Molecular docking can be used to predict the binding-conformation of small molecule ligands to the appropriate target binding site of biologically relevant molecules such as proteins, peptides, nucleic acids, carbohydrates, and lipids, to reveal their relative orientation of the two interacting partners. Benefiting from the development of molecular docking software, silicon-technology improvement, and cumulation of various biological databases, molecular docking has recently become a valuable tool in structural molecular biology and computer-assisted drug design. From the analysis, it can be concluded that current organic synthesis research is focusing on pursuing more concise, precise, efficient and energy-saving synthetic methods. Reducing reaction steps, directly functionalizing unactivated positions of organic molecules, and utilizing environmentally friendly solvents have been emphasized in recent years.

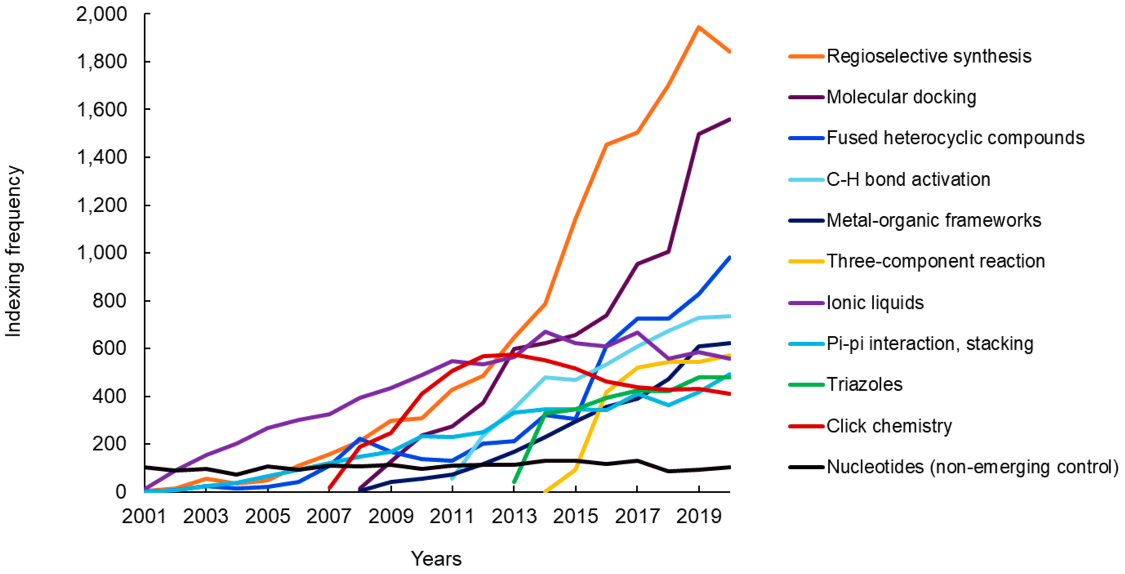


Figure 9. Emerging concepts related to organic compounds or reactions in journal publications of organic synthesis in years 2001-2020. Concept "Nucleotides" was included as a non-emerging topic control.

Organic synthesis can find good applications in developing functional materials, such as small molecules for pharmaceutical use, nanomaterial and nanoparticles, and OLED materials, etc. The trends of functional material related concepts in organic synthesis are summarized and displayed in **Figure 10**. These concepts are grouped into five categories, green chemistry (including, green chemistry, recycling, and biomass); drug developing (including neoplasm, pharmacokinetics, fluorescence imaging, and enzyme inhibitors); organic electroluminescent (including LUMO, and photoluminescence); property (including electric current-potential relationship, X-ray photoelectron spectra, and pore size distribution); and reaction catalysts (including photocatalysts and electrochemical reduction catalysts). Nanoparticles, as a special topic, received the most attention in 2020.

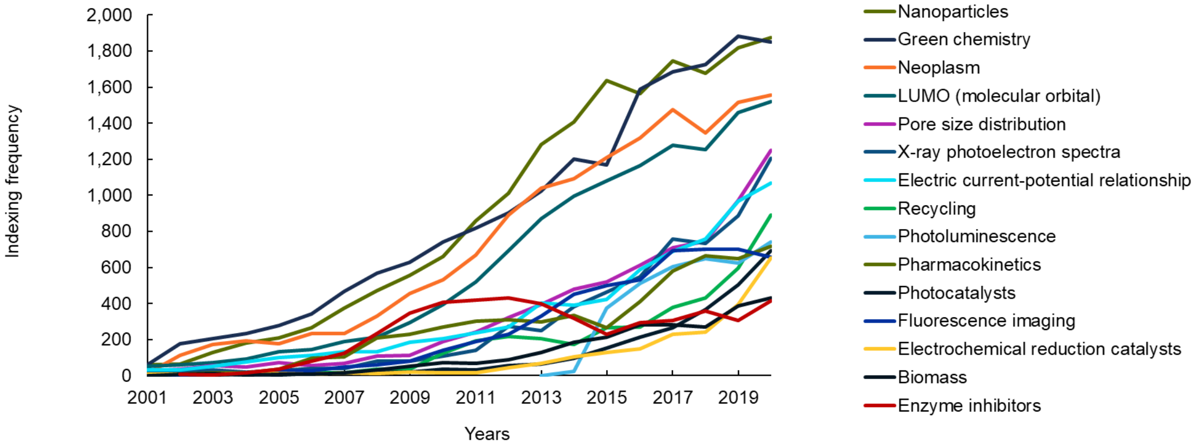


Figure 10. Emerging concepts related to functional materials in journal publications of organic synthesis in years 2001-2020

In patent publications, a similar analysis was performed to identify those concepts that have been indexed more than 400 times in 2020 and increased more than 25 times from 2001 to 2020. The trends of functional material related concepts for the past two decades are shown in **Figure 11**, which is quite different from those concepts indexed in journal publications. Pharmaceutical formulation (see the insert) is a major motivation for functional material-related research; its indexing frequency is much higher than that of other concepts. From another aspect, the direct utility of pharmaceutical formulations makes their protection through intellectual property laws more important. Antifoaming agents, leveling agents, electroluminescent substances, thickening agents, fluorescent indicators, wetting agents, photocatalysts and coloring materials are the most indexed concepts, which emphasize the application of the patented substances/materials. Isocyanates is the only class of substances appeared in this list. Isocyanates are a group of chemicals that are widely used in the manufacture of foams, fibers, and coatings.

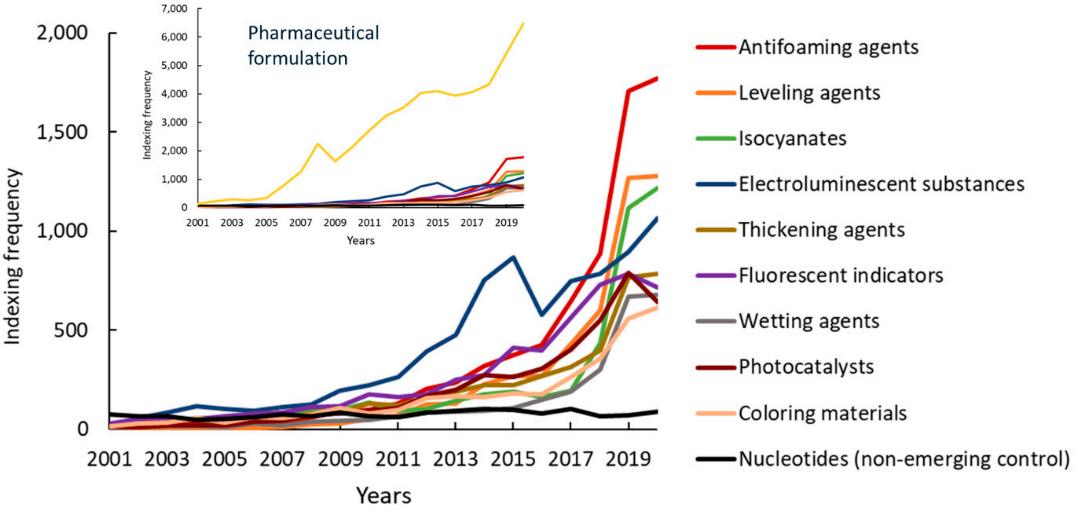


Figure 11. Emerging concepts related to functional materials in patent publications of organic synthesis in years 2001-2020.

Figure 12 shows polymer-related emerging concepts in patents whose frequencies have increased most rapidly between 2001 and 2020. Photopolymerization catalysts have increased significantly. This observation is consistent with the increase in interest in photochemistry in organic synthesis in the early 2010s.[32] The application of photochemistry to macromolecular synthesis was likely inspired by its use in small molecule synthesis. In addition, the ability to precisely control the position of light makes photochemistry a useful method for 3D-printing, and the development of photopolymerization catalysts may be useful to improve the ease and resolution of 3D-printing. Finally, photopolymerization catalysts are likely to be useful for photocurable inks, coatings, and adhesives. Hydroxy-containing polyethers and hydroxy-terminated polyesters are likely useful in the manufacture of novel polyurethanes. As noted earlier, the volume of Chinese patents published has increased dramatically in the last decade, and the Chinese economy has grown as well.[33] Polyurethanes are ubiquitous in durable consumer products such as automobiles and furniture and the use of polyurethanes has increased and the trend is likely to continue.[34, 35] Polyurethanes themselves have been used in products for many years, and so the overall rate of increase in their patent volume is not as significant as for novel monomer components in their manufacture. Hydroxy-containing components may also be derivable from plants or other renewable sources, and so interest in them may be driven by the need for improvements in sustainability and reductions in the environmental costs of consumer products. Finally, polyether polysiloxanes are used in antifoaming and leveling agents, functional materials with significant patent interest, and increases in the market for consumer products may have driven the development of novel materials for these applications.

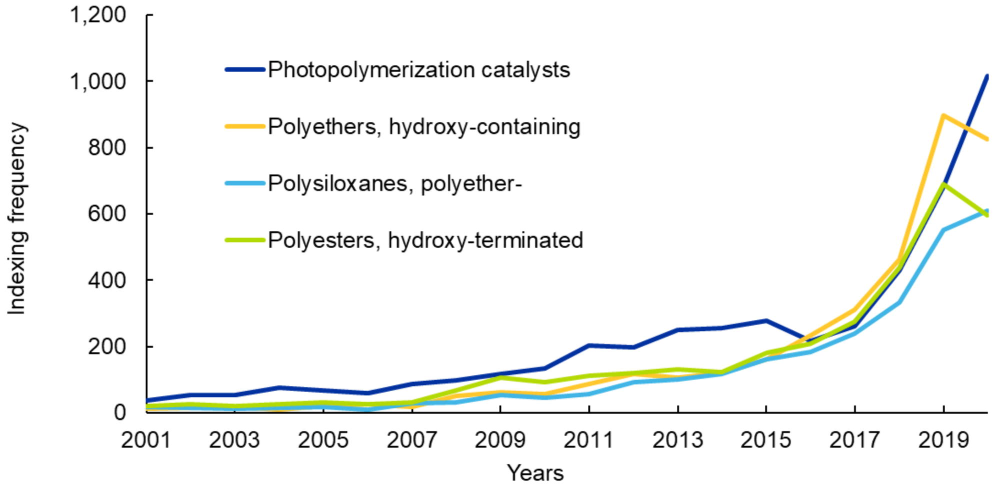


Figure 12. Emerging concepts related to polymer materials or reactions in patent publications of organic synthesis in years 2001-2020

3. Emerging topic: Enzyme Catalysis

One important topic in organic synthesis research is the use of enzymes as catalysts. As noted previously[22, 21], enzymes provide a variety of benefits to organic synthesis. Enzymes can allow reactions to be performed in water or mostly aqueous solvents, though enzymes can also be modified to function in organic solvents as well[36], reducing the costs of organic synthesis to industry and the environment. Besides the sustainability and environmental benefits, enzyme catalysis also offers higher efficiency and selectivity benefits, both enticing chemists to consider this route to complement or even supplant more traditional synthetic routes.[37] Enzyme-catalyzed reactions benefit from rapidly growing sequencing technology to determine DNA, RNA, and protein sequences. Information from nucleic acid sequencing and protein profiling allows biologists to assign functions and identify modules in previously unknown proteins, expanding the spectrum of reactions amenable to enzymic catalysis. To date, a large variety of enzymes are commercially available, allowing chemists to rapidly scan for useful catalytic activity. Biochemical tools such as directed evolution allow scientists to modify natural enzymes for even better catalytic performance, expand the substrate scope and working conditions, and improve reaction efficiency and catalyst stability and selectivity. These technologies allow scientists to purchase or rapidly develop enzymes to perform known or novel reactions, accelerating reaction development and synthesis. Finally, the combination of chemical and enzymic catalysts allows dynamic kinetic resolutions, which might further increase the yield and atom economy of enzyme-catalyzed reactions.[38] Enzymic synthesis can thus allow chemists to perform reactions which cannot be performed in sufficient selectivity or under useful conditions, or to perform reactions under conditions that help to mitigate their economic or environmental costs.[39, 40]

3.1 Trends of journal and patent publications in enzyme catalysis in the field of organic synthesis

To study the global trends of research on enzymic catalysis, the number of journal and patent publications were summarized biennially to minimize the effect of variance between years. **Figure 13** shows the global output of journal and patent publications related to enzymic catalysis from 2011 to 2020. As a relative new research area, journal publications are the majority output on enzymic catalysis. The volume of global journal publications on enzymic catalysis increased from 1400 in 2011-2012 to over 1800 in 2019-2020, which is around 30% growth over the past ten years. Compared with journal output, patent applications in this area are still at the very early stage. The increase from 2011 to 2016 was fast (around 50% increase), however, increasing slowed down from 2017-2020 (around 15% increase). The ratio between journal and patent publications decreased from 7:1 in 2011-2012 to 5:1 in 2019-2020. This perhaps reflects a situation that many cutting-edge research discoveries have not led to industrial applications yet.

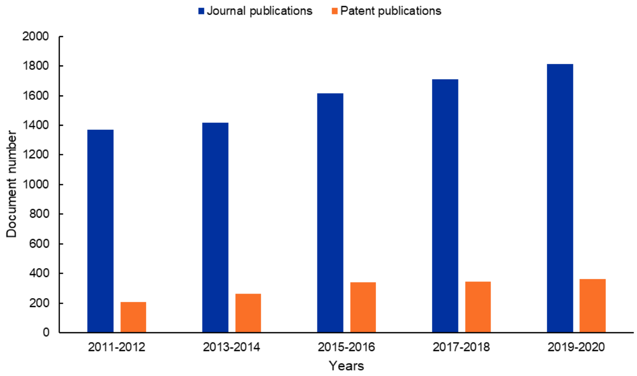


Figure 13. Trends of journal and patent publications in enzyme catalysis in the field of organic synthesis from the CAS Content Collection during 2011-2020.

3.2 The distribution of publications among countries in enzyme catalysis of organic synthesis

The top 10 countries/regions with the most journal publications on enzymic catalysis are shown in **Figure 14**, as a comparison, the corresponding patent output from these countries/regions are displayed (in orange) as well. China is the leading country on both journal and patent publications in enzymic catalysis. United States, Germany, India and United Kingdom are also strong contributors in journal publications on this topic, while United States, Germany and South Korea ranked second to forth on patent publications in this list.

To further investigate the publication trends of the top 5 countries/regions, biennial data of their journal or patent publications were collected and displayed in **Figure 15**. China is the only country with consistent growth in both journal and patent publications in enzymic catalysis. Publications from other countries/regions either stayed constant or decreased over the past ten years. The volume of journal publications from China doubled over the past ten years, and the volume of patent publications from China increased more than 4 times during the same time frame.

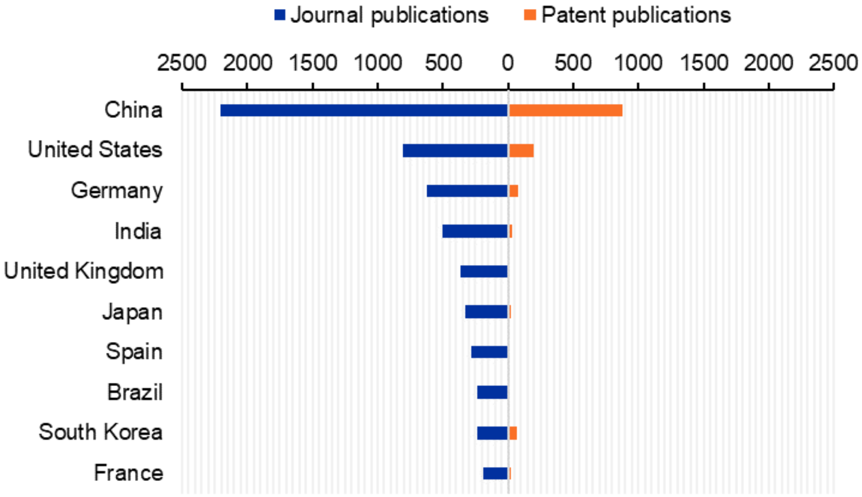


Figure 14. The distribution of journal publications among top countries/regions and their patent publications in enzyme catalysis of organic synthesis

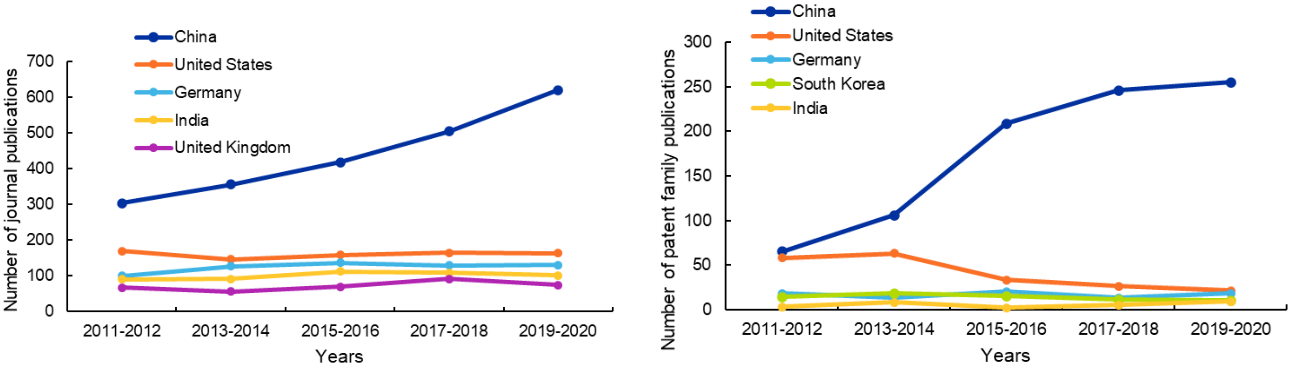


Figure 15. Journal (left) and patent (right) publication trends in enzyme catalysis for the top 5 countries/regions between 2011 and 2020.

3.3 Research organizations with a focus on enzyme catalysis in organic synthesis and their publications

To identify the most active organizations in enzymic catalysis research, the top 20 most productive organizations are summarized in **Figure 16**. Chinese Academy of Sciences, Zhenjiang University of Technology and Jiangnan University are the three most productive organizations in enzymic catalysis. It is worth noting that most research institutes/organizations in this list had more than 30% of their total publications produced in the last three years, which indicated consistent research efforts were put on this topic from these organizations.

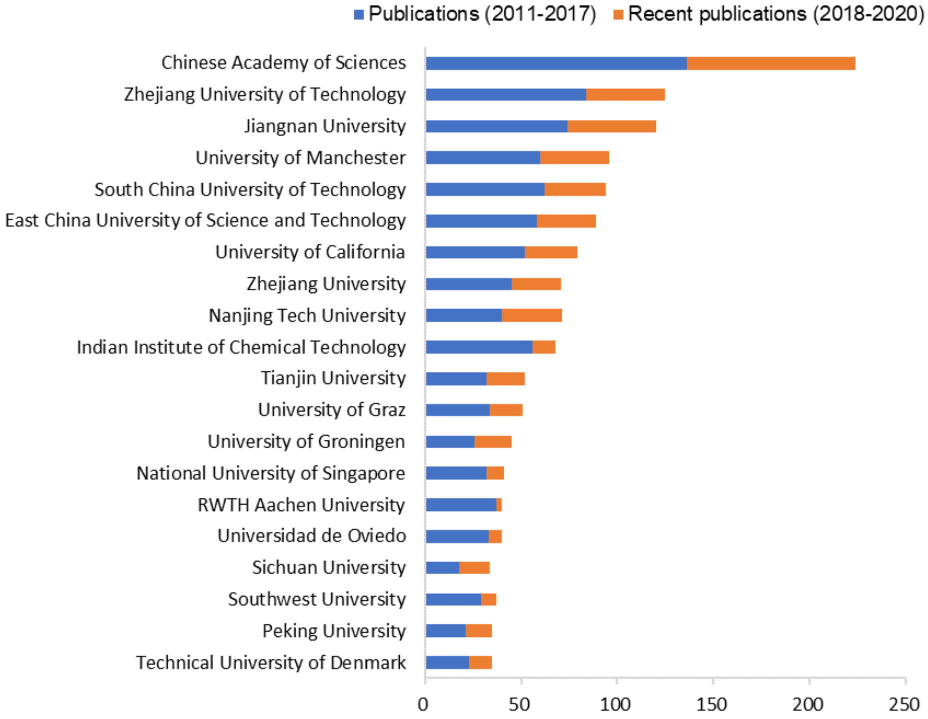


Figure 16. Top research organizations in publication volumes on enzyme catalysis

3.4 Concept analysis of journal and patent publications on enzyme catalysis

Figure 17 shows the relationship between concepts indexed in enzyme catalysis-related journal documents. Four major clusters can be identified from this network diagram: biomimetic synthesis-related concepts, nanoparticle and polymer-related concepts, temperature effect-related concepts and enzyme/protein structure-related concepts. Concepts like natural product, oxidation, rearrangement, and Michael reaction are frequently used reactions in biomimetic synthesis (green area). Meanwhile, diastereo- and enantioselective synthesis, and regioselective synthesis reflect the advantages of published methods in enzyme catalysis over previously known methods, while an understanding of transition state structure is important for the development of effective enzymic methods. The occurrence of nanoparticle- and polymer-related concepts (red area) implies that nanoparticle- or polymer-supported enzymes or catalysts are salient topics in enzyme catalysis research. Enzyme/protein structure (blue/yellow area), including secondary, quaternary structure, active site and molecular orientation are also studied in enzyme catalysis because the structure of enzymes controls their stability and chemical behavior, and the structure of enzymes can help scientists to understand the mechanisms of enzyme-catalyzed reactions. Finally, temperature is an important variable in enzyme catalysis and optimization; it affects the kinetics of reactions and is important to enzyme optimization and genetic engineering and so has been thoroughly investigated. The heavy connections between concepts among four clusters indicate strong correlations between interest in reactions, reaction optimization, enzyme structure or reaction mechanism, and reaction output (stereoselectivity) in enzyme research.

Figure 17. Network diagram of concepts in enzyme catalysis in the years 2011-2020 of journal publications

Figure 18 shows the relationship between concepts indexed in enzyme catalysis-related patent documents. Fermentation is enzyme catalysis performed in living organisms; it is performed on a large scale in industry for the manufacture of food and ethanol. In addition, culture media, extraction, catalysis, stereoselective reduction and drug are closely related to fermentation. Bacteria and fungi are the most used types of microorganisms in this research area (shown in green and red in this diagram), however, a large variety of bacteria and fungi strains are employed. *E. coli* is the most frequently used microorganisms for enzymic catalysis, especially in DNA sequences and protein sequences. Polysaccharides, monosaccharides, peroxycarboxylic acids, and glycerides are the major substances involved in this research topic.

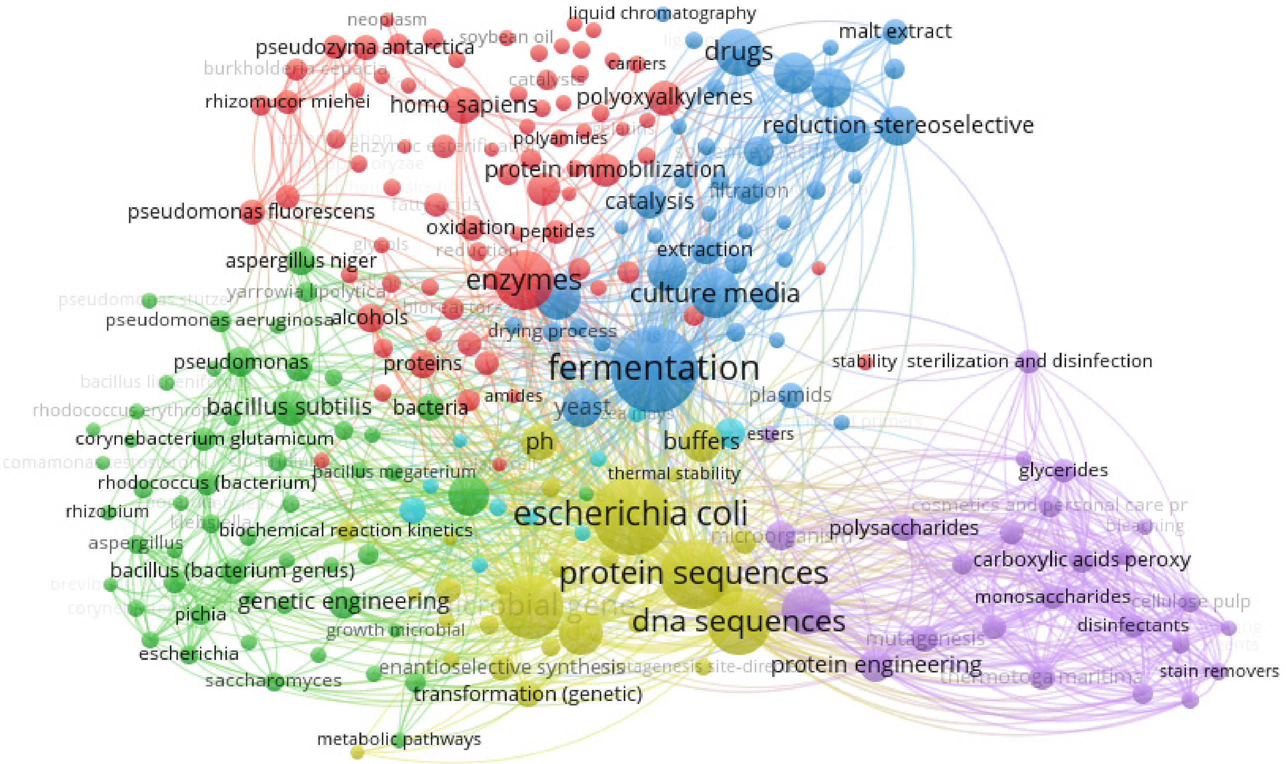


Figure 18. Network diagram of concepts in enzyme catalysis in the years 2011-2020 of patent publications

The evolvement of emerging concepts in enzyme catalysis in journals is depicted in **Figure 19**.
In 2012-2014, 1,466 enzyme catalysis-related concepts first appeared in this document set after 2000: examples include tandem reaction, enantioselective biochemical synthesis, hydrophobic materials, C-O bond formation etc. These concepts indicated applications of enzyme catalysis have been expanded to more complicated synthetic chemistry scenarios. Meanwhile, 1,522 enzyme catalysis-related concepts appeared in this document set in 2015-2017 since 2000, and 459 concepts (out of 1,466) were carried over from 2012-2014. Total synthesis, three-component reactions, one-pot reactions and syntheses, and quaternary carbon centers are examples of the added concepts, which shows that the current enzymatic catalysis research emphasizes concise synthetic methods and the efficient construction of chiral centers. Between 2018 and 2020, 1,926 new concepts were collected by CAS in enzyme catalysis together with 493 concepts that were carried over from previous time span. Pickering emulsions, a type of emulsion stabilized by solid particles, was employed in enzyme catalysis in 2018-2020. Polymer scaffolds and zeolitic imidazolate frameworks were also studied in enzyme catalysis related research. Synergistic catalysis, simultaneously active multiple substrates and allow reaction take place between activated species, started to be used in enzyme catalysis during this time frame. Carbon quantum dots, and durability of materials are among the rising concepts. [5+2] cycloaddition reactions and the tert-butoxycarbonyl group were also investigated using enzyme catalysis in this time period.

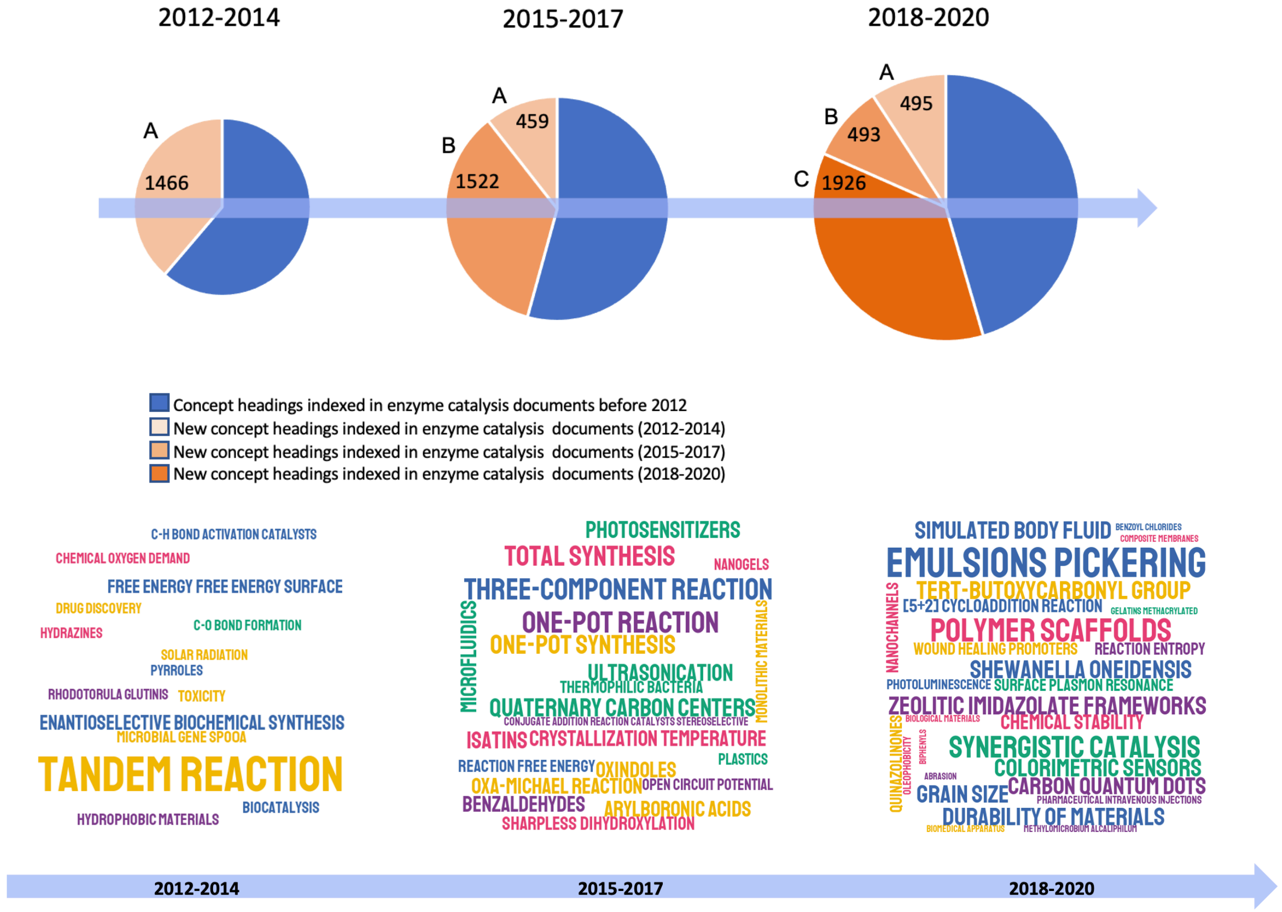


Figure 19. Rising concepts on enzyme catalysis in journals in a timeline. Top panel shows the numbers of new and carried-over concepts appearing in the enzyme catalysis documents after 2000. Bottom panel shows the most common new concepts appearing during the corresponding time frames in this document set since 2000

To further look at the trends of concept evolvement in this field, the frequencies of the most prevalent concepts related to enzymes in organic synthesis and their variation over time are shown in **Figure 20** and **21**. These concepts can be divided into two sets. The first set directly relates to the use of enzymes for organic synthesis (**Figure 20**). The concepts biotransformation and biocatalysis are general terms for the processes occurring in biologically mediated synthesis. Protein engineering, molecular docking, and optimization are necessary to implement biological systems in organic synthesis; protein engineering is needed to refine enzymes into effective tools for syntheses, molecular docking is helpful to understand the protein modifications necessary, and optimization is the process of finding conditions, reagents, and catalysts to make a given reaction most useful for a desired purpose. Concepts such as tandem reaction, enantioselective synthesis, enantioselective biochemical synthesis, and diastereoselective synthesis refer to the characteristics of reactions performed biologically, with tandem reactions referring to sequences of reactions performed at once (a common design in biological systems) while enantioselective and diastereoselective synthesis and enantioselective biochemical synthesis refer to the capabilities of the processes to generate products with defined stereochemistry. The headings biomimetics and biomass are likely to refer to potential uses for biocatalysis. Biomass conversion to useful materials, for example, could provide a method to make important chemicals renewably, while biomimetics are important molecules for drug development. The biological origin of biomass and the similarity of biomimetics to molecules found in nature make enzymic synthesis a reasonable method to approach these topics.

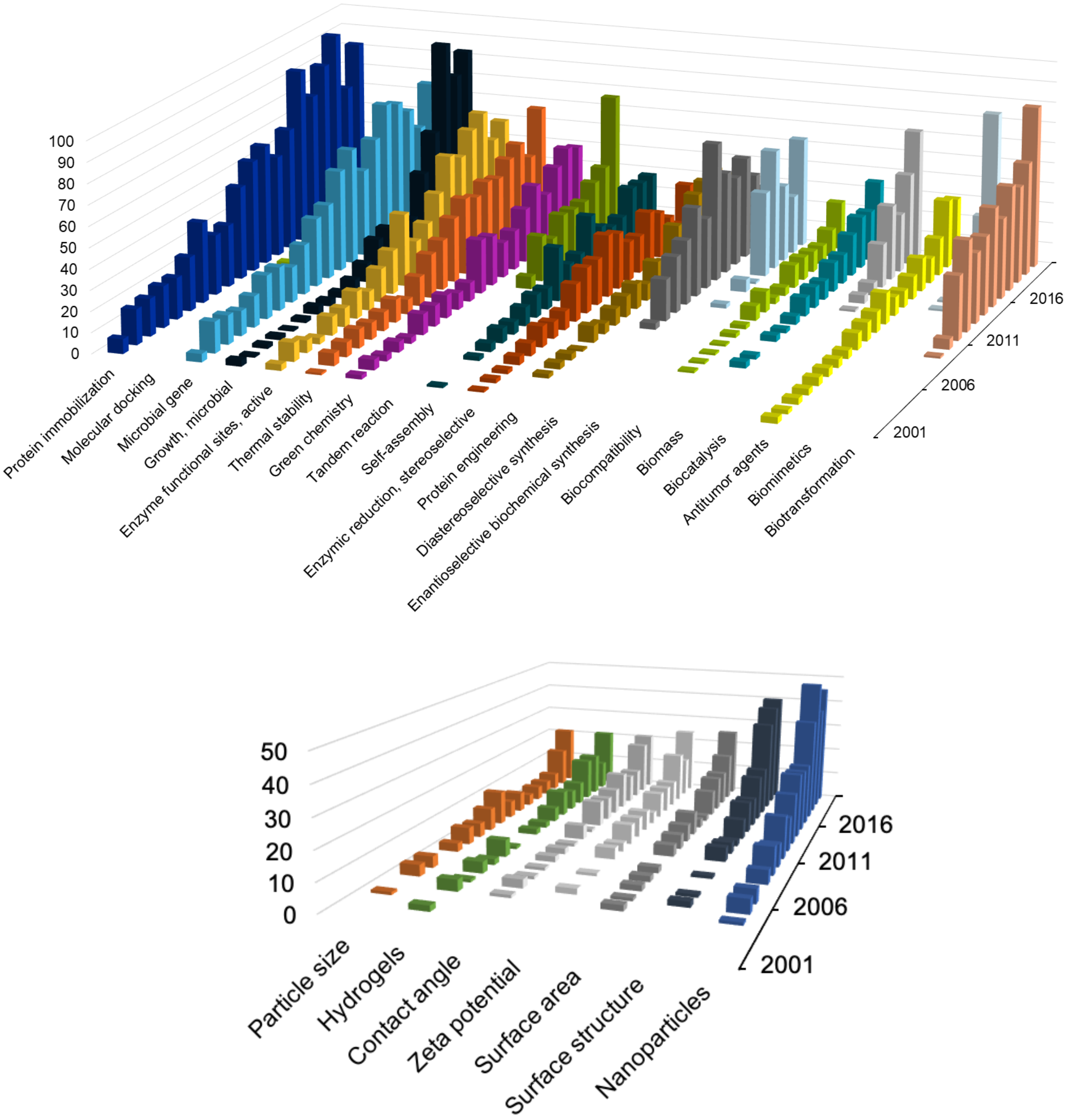


Figure 20. Rising concepts in enzyme catalysis (top) and rising concepts of supporting surface material related concepts in enzyme catalysis (bottom) in the years 2001-2020 in journal publication

A second set of concepts refer to nanotechnological methods and surface chemistry (**Figure 21**). Nanoparticles, surface structure, stability, surface area, zeta potential, contact angle, hydrogels, and particle size refer to the physical form and properties of a system. These terms do not explicitly refer to or require biological syntheses. Controlling the physical properties and sizes of particles is important to make useful and stable catalysts for reactions; particle size and surface area determine the accessibility of substrates to catalysts, while other terms determine the charge of a surface and the polarity of solvent in which it will be most effective and stable. Catalyst supports are important components in modulating catalyst activity, stability, and handling. Application of these techniques to enzyme-mediated and biological organic syntheses may indicate greater emphasis on the use of enzymes rather than whole cells (since the sizes of whole cells are larger than the length scales of nanotechnological methods). They may also indicate interest in the use of enzymes for potential industrial processes (for which the methods for studying heterogeneous catalysts are well-known).

3.5 Substance analysis of journal and patent publications on enzyme catalysis

Figure 21 shows the numbers of journal and patent publications containing substances with a particular role indicator and the number of indexed substances with that role. Role indicators are a list of terms for describing substance functions in a document. A detailed list of role indicators and their associated descriptions can be found on the CAS website.[41] These numbers in **Figure 21** provide a measure of the prevalence and use of substances in journal and patent documents. In both journal articles and patents, the number of documents decreases uniformly among the selected roles. In journals, the number of substances with reactant (RCT) and synthetic preparation (SPN) roles are significantly greater than the number of substances with other roles. Substances with biological preparation (BPN) and chemical property (PRP) roles are prevalent as well. Substances with roles for biological processes, such as biochemical process (BCP) and biological use (BSU) also occurred frequently. In patents, substances with PRP and BSU roles are most common, while substances with BPN, SPN, RCT, and catalyst (CAT) roles are also significant.

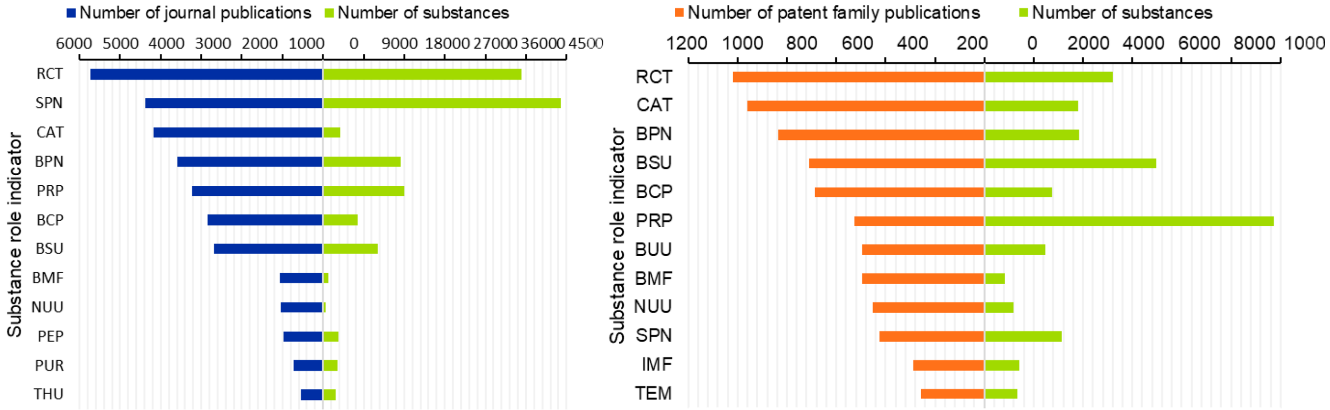


Figure 21. The distribution of substance roles in journal or patent publications 2011-2020 on enzyme catalysis. CAS role indicators42: RCT (reactant), SPN (synthetic preparation), CAT (catalyst), BPN (biological preparation), PRP (chemical property), BCP (biochemical process), BSU (biological use), BMF (biological manufacture), NUU (other use, unclassified), PEP (physical property), PUR (purification or recovery), THU (therapeutic use), IMF (industrial manufacture), TEM (technical or engineered material use)

Figure 22 shows the time dependence of substances with various roles in journal articles and patents relating to enzyme-mediated synthesis. The number of substances in journal articles increased over the period of record, though the rate of increase fell between 2011 and 2020. In patents, however, the number of indexed substances decreased dramatically, with a large decrease between 2015-2016 and 2017-2018. While substances with various roles were indexed with consistent frequencies in journal articles, in patents the number of substances with property and synthetic preparation roles fell significantly while reactants increased. The number of indexed substances in patents and the changes in role frequencies were largely influenced by the presence of a few patents with thousands of substances claimed in the years 2011-2016. This type of patent was less prevalent in the years 2017-2020.

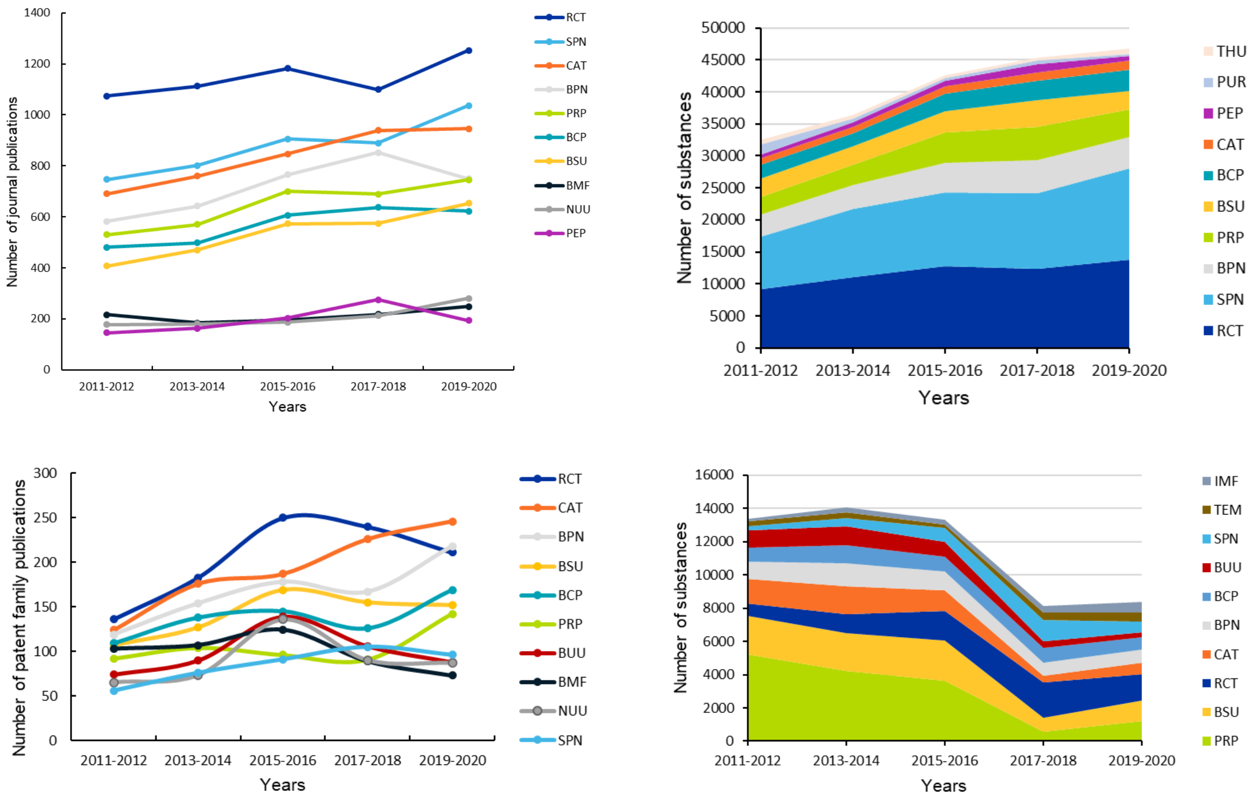
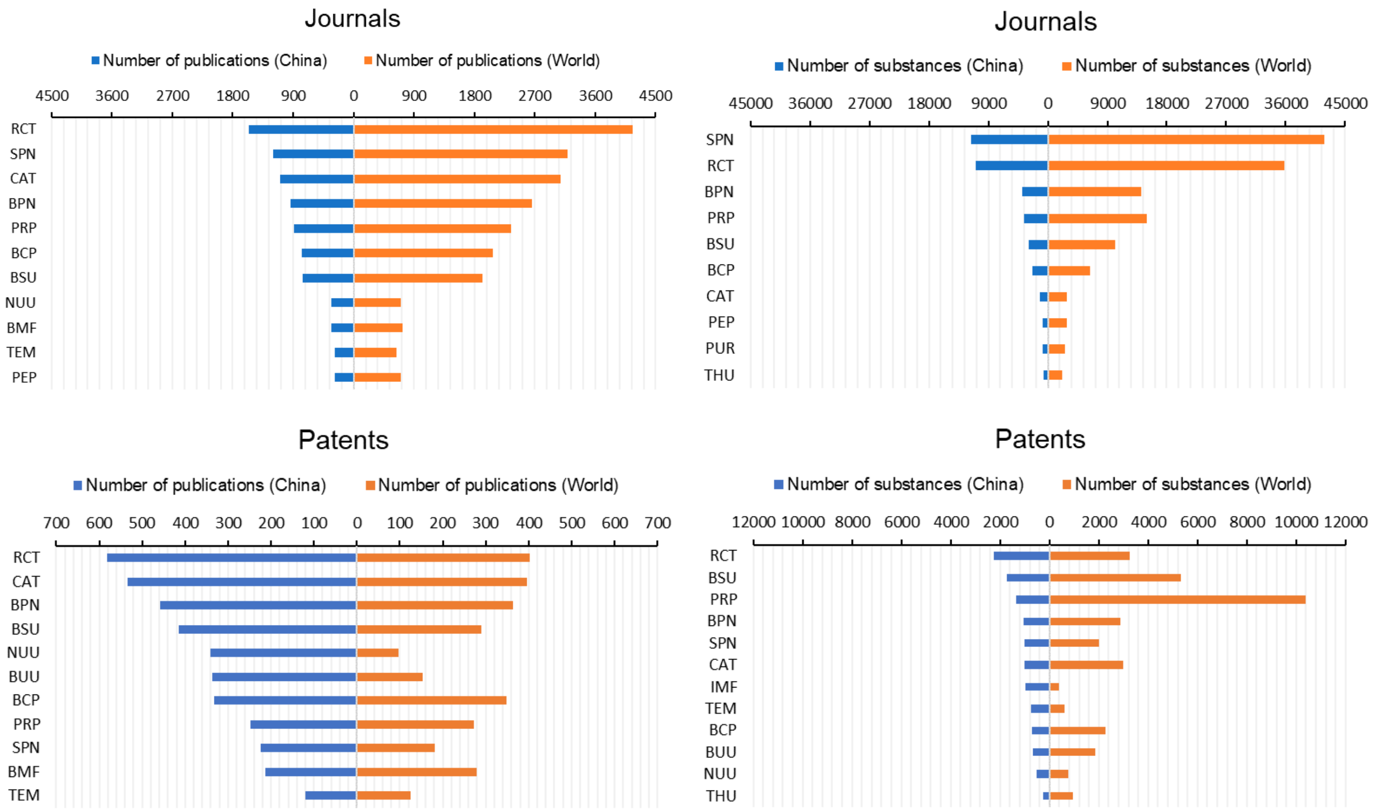


Figure 22. The trends of substance roles in journal (top) or patent (bottom) publications (2011-2020) for enzyme-mediated synthesis.

Figure 23 compares the distribution of publications containing substances with specific roles and the numbers of substances between China and the rest of the world. The numbers of journal publications and substances containing specific roles show similar patterns in both Chinese and world journal articles. In both cases, the numbers of publications containing reactant (RCT) and synthetic preparation (SPN) roles are closer to those for other roles, while the numbers of substances in journal articles with reactant (RCT) and synthetic preparation (SPN) roles are significantly greater than the numbers of substances with other roles. In patents, while the number of Chinese patents was significantly larger than the number of patents from the rest of the world, the number of substances in those patents was substantially lower than the number from the rest of the world. In addition, the distribution of documents and substances with particular roles is more uniform in Chinese patents and in journal publications elsewhere than in patents of the rest of the world. The substance distribution in patents may differ because of differing prevalences of unexemplified substances, while the differing substance counts between patents from China and from elsewhere may be due either to legal or other preferences for patent length. Enzyme-related documents are likely to require a wider variety of roles than other synthetic documents because of the need for biological roles.


Journals

Journals

Patents

Patents

Figure 23. The comparison between China and the rest of the world on the substance role distributions in journal or patent publications (2011-2020).

Figure 24 shows the dependence of documents containing and substances assigned various roles in enzyme-related journal articles. The number of articles from China increased exponentially between 2011 and 2020, while the number of substances in the articles increased roughly linearly over the same period. The roles of substances in the documents were similar over time, except for substances with the physical property (PEP) role whose prevalence decreased significantly. One possible explanation is that the prevalence of dynamic kinetic resolutions in enzyme-mediated synthesis (in which the unreacted isomers are converted to the reactive isomers and consumed) has increased, reducing the indexing of unreacted substrate with the PEP roles. On the other hand, the numbers of documents discussing enzyme-mediated synthesis in the rest of the world did not increase between 2011 and 2020, and the number of indexed substances in those documents reached a plateau in 2017-2018. Substances in journal documents in both China and elsewhere showed similar patterns, with reactants and products with synthetic preparation (SPN) roles making up the largest part of indexed substances.

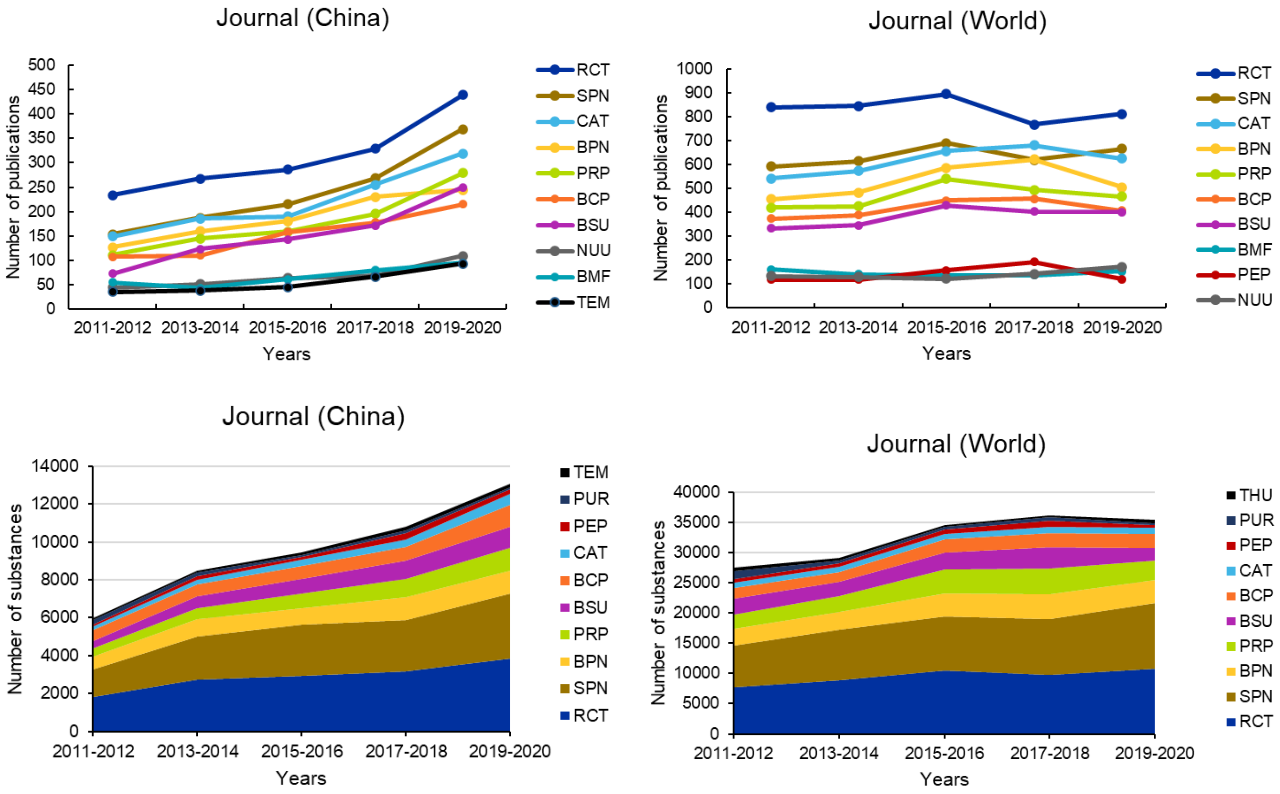


Figure 24. The comparison between China and the rest of the world on substance role trends in journal publications (2011-2020)

Figure 25 shows the number of patents containing substances and the number of substances with particular roles discussing enzymic synthesis. The contrast between both the number of patents and the number of substances between China and the rest of the world is stark. While the number of Chinese patents increased between 2011 and 2020 and reached a plateau, the number of patents elsewhere decreased massively between 2011 and 2017 and then increased slightly in 2019-2020. The number of substances in Chinese patents for enzymic synthesis increased approximately linearly between 2011 and 2020, while the corresponding substance count in patents for the rest of the world plateaued after 2015. The distribution of roles for substances in journal publications is roughly consistent regardless of the country of origin of the publication. One possible explanation for the increased interest in enzymic synthesis in China may be due to increased interest in reducing the environmental costs of industrial production and thus of chemical manufacture and development.

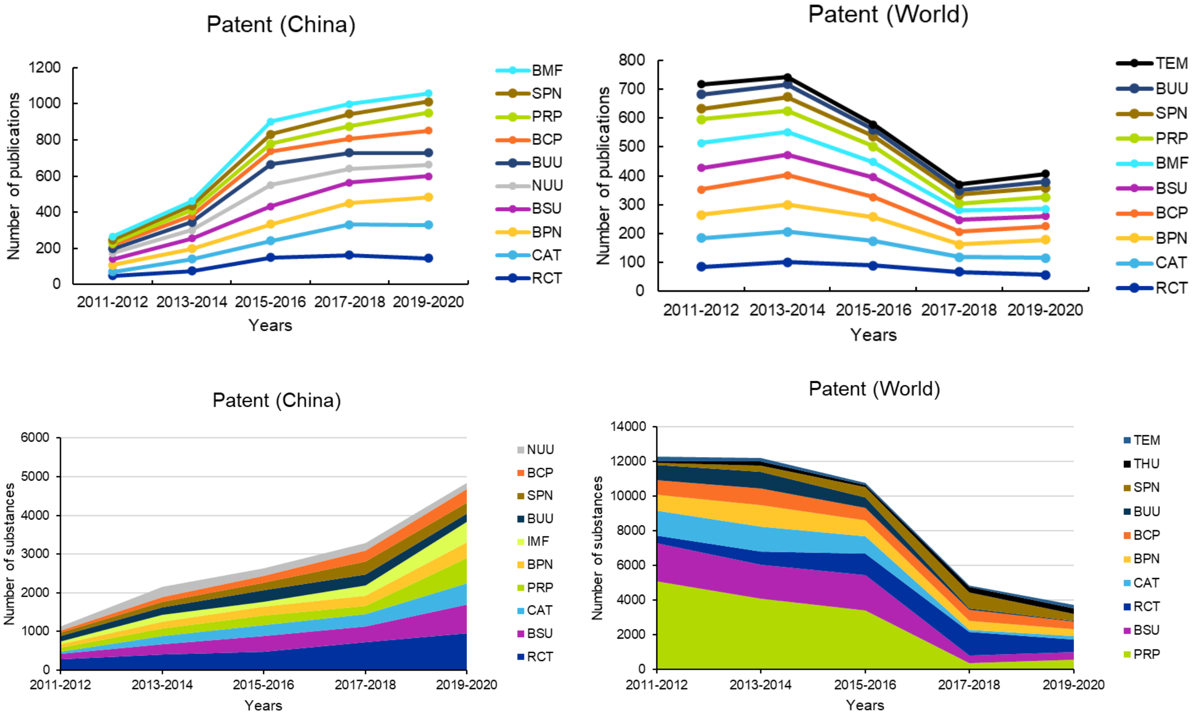


Figure 25. The comparison between China and the rest of the world on substance role trends in patent publications (2011-2020)

4. Emerging topic: Photocatalysis

Another topic of interest in organic synthesis is photochemistry, the use of light energy to drive selective chemical reactions. During the last ten years, the use of photoredox catalysts (catalysts using light to reduce and oxidize organic compounds) and flow chemistry (reactions performed by flowing solutions of reacting materials from place to place) have helped to make photochemical methods more useful in organic synthesis, both by improving their selectivities and by increasing the breadth of transformations performable using light.[42] Most of the photocatalysis reactions do not require heating, thus reactant stabilities are significantly improved. Because of these features, photocatalysis has enabled many newer types of reactions which aren't possible other ways.[43] An understanding of the time and geographical distribution of research in photochemistry is thus a useful topic and potentially enlightening for future directions in the field.

4.1 Trends of journal and patent publications in photocatalysis in the field of organic synthesis

Figure 26 shows the changes in journal and patent publications over two-year segments in the field of photocatalysis between 2011 and 2020. The rate of journal publication has accelerated over this period; new catalysts and apparatuses have been prepared and commercialized, making new reactions possible and thus increasing the breadth of journal articles possible. Patent publications discussing photocatalysis increased significantly during the period, but at a more consistent rate between years. The costs of photocatalysts (most of which rely on iridium or ruthenium) and the difficulty in scaling photochemical reactions (although improvements in flow reactors and the use of continuously stirred tank reactors may make them easier to employ on large scale) may make patentable use of photocatalysts more difficult. The development of standard photochemical reactors has occurred only recently, limiting the utility of photocatalysis in high-throughput testing and general synthesis. These developments should improve the usage of photocatalysts in the future, but their absence may have limited the previous use of photocatalysts in commercial settings and thus the increases in photocatalyst-related publications.

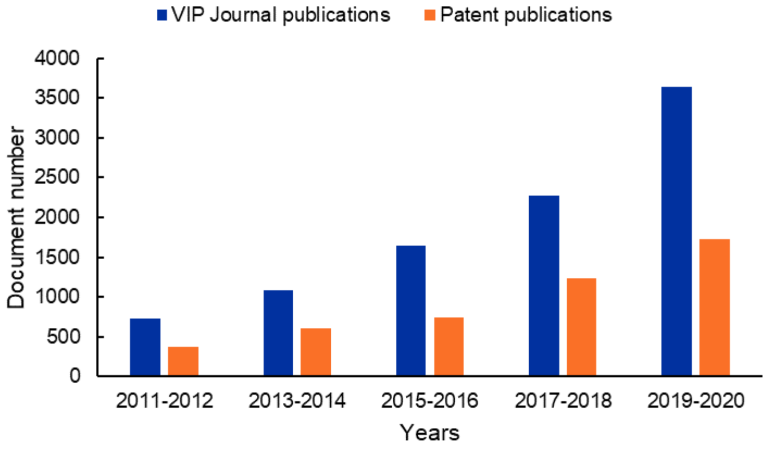


Figure 26. Trends of journal and patent publications in photo catalysis in the field of organic synthesis from the CAS Content Collection during 2011-2020.

4.2 The distribution of publications among countries/regions in photocatalysis of organic synthesis

Figure 27 shows patent and journal publications by country/region between 2011 and 2020. The largest number of patents and journals (by far) were published by authors at Chinese organizations. Journal publications are more uniformly distributed by country/region, with the United States, Japan, India, and Germany having similar levels of journal publications. Patent publications are less uniformly distributed, with only Japan, South Korea, the United States, and Germany having notable numbers of patents. The increases in journal publications are consistent with the geographic prevalence of academic research, while patent publications may correlate to potential commercial uses for photochemistry, the presence or lack of installed infrastructure for chemical methods, or increased emphasis on energy efficiency or green chemistry.

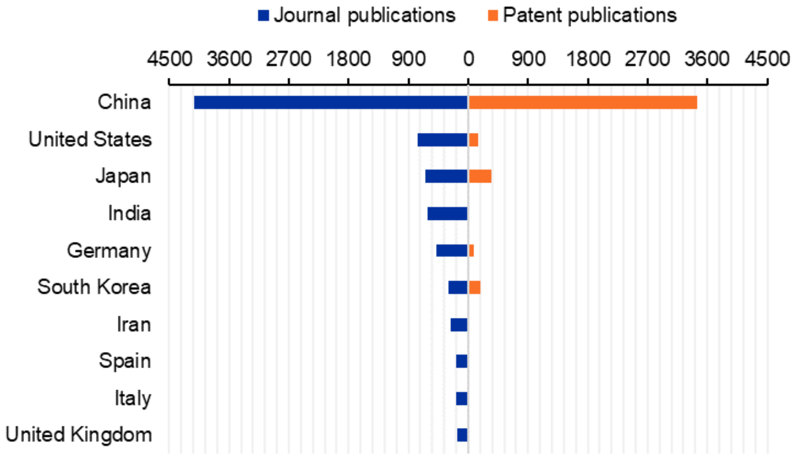


Figure 27. The distribution of journal publications among top countries/regions and their patent publications in photo catalysis of organic synthesis

Figure 28 shows the changes in journal and patent publications by country/region over time. Journal publications for all of the cited countries/regions increase over time, but the increase in photocatalyst articles from China is greater in magnitude and rate of increase than that seen for the other countries/regions shown. While increases in journal publication are consistent with overall increases in journal publication volumes, the rate of increase in Chinese journal publications in photocatalysis is higher than that for overall chemistry-related publications while that for other countries/regions is close to the changes in overall chemistry-related publication volume. While the number of Chinese patents relevant to photocatalysis also increased, it increased at a nearly linear rate between 2011 and 2020. Photocatalysis patents from other countries/regions decreased during the same period.

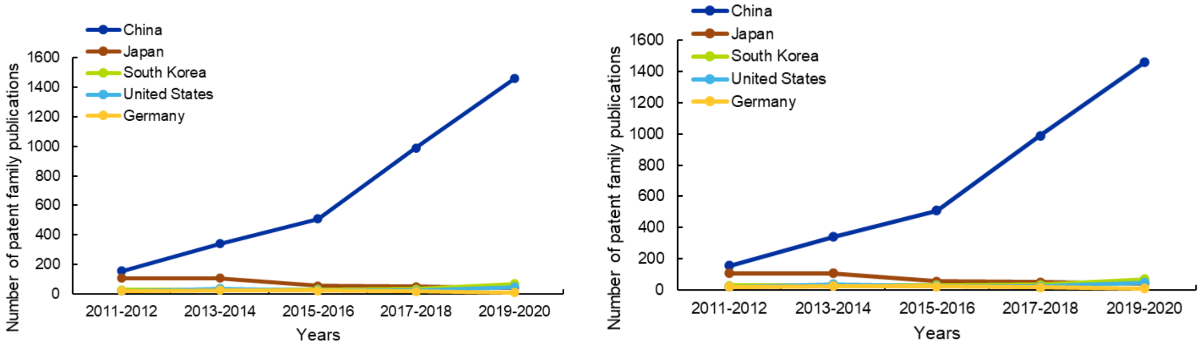
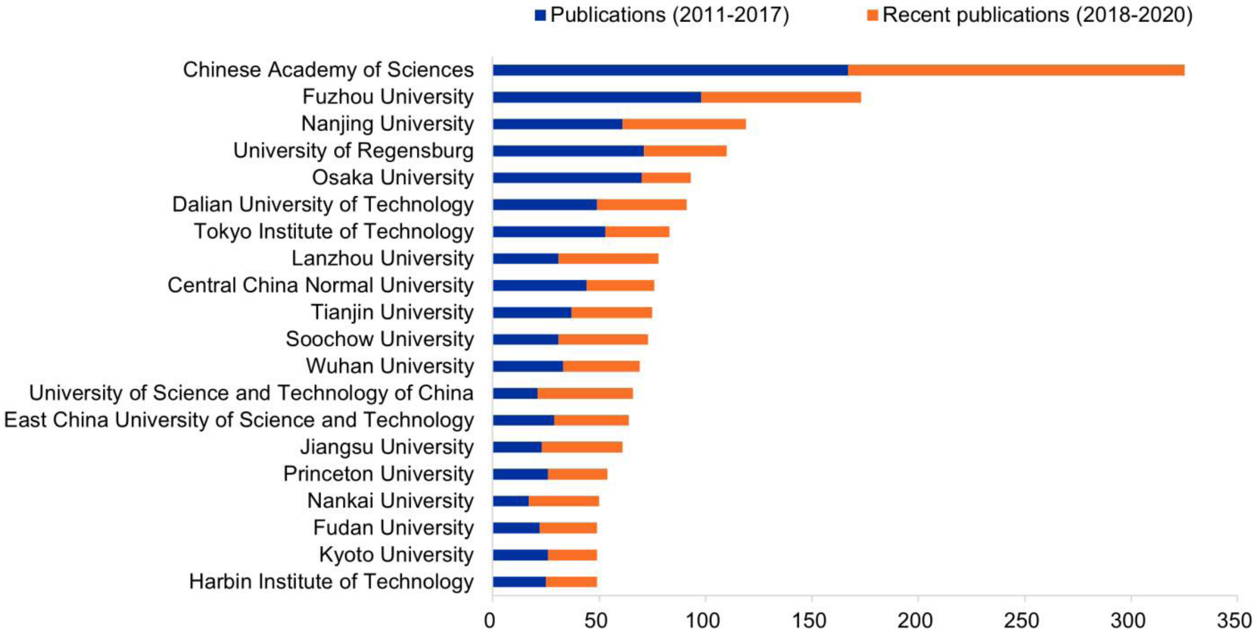


Figure 28. Journal (left) and patent (right) publication trends in photocatalysis for the top 5 countries/regions between 2011 and 2020.

4.3 Research organizations with a focus on photocatalysis in organic synthesis and their publications

The organizations with the largest number of journal articles and patents on photocatalysis are shown in **Figure 29**. Chinese institutions dominate both lists, with 15 and 19 of the largest journal and patent publishing institutions, respectively. Japan has three of the institutions in the 20 publishing the most journal articles and the only non-Chinese institution on the list of institutions publishing the largest number of patents. **Figure 29** also shows that most institutions have more publications on this topic in recent years, implying that photocatalysis is still an active topic of research for these institutions. As noted for other publication comparisons, the Chinese Academy of Science is composed of over 100 member institutions, partially explaining its gap in publication volume with other institutions.



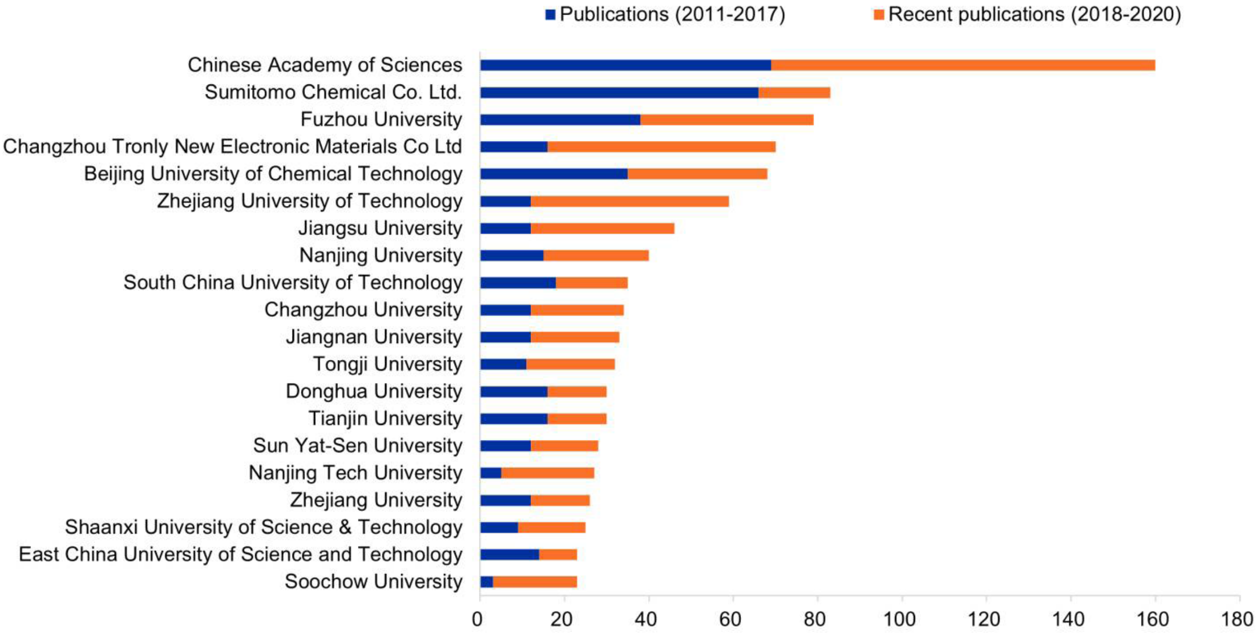


Figure 29. Research organizations with the largest numbers of journal (top) and patent (bottom) publications in photocatalysis.

4.4 Concept analysis of journal and patent publications on photocatalysis

Figure 30 shows the co-occurrence of concept entries in journal articles discussing photocatalysis. The concepts are clustered into three groups of similar sizes. The first group (green) discusses physical processes involved in photocatalysis and their physical characterization and identities. Some of the most indexed headings were nanoparticles and nanocomposites (likely used as catalysts), band gap and surface area (characterization), and photocatalytic water treatment. A second group (blue) includes photoelectrochemical processes such as the photochemical electrolysis of water, which is a likely method for the green preparation of hydrogen. A third group (red) includes photocatalysts; it also encompasses synthetic methods and uses for photocatalysis such as green chemistry, light, and photochemical redox reactions and catalysts. Reduction and oxidation reactions are prevalent in organic synthesis and often require stoichiometric reagents, making them targets for greener catalytic methods. Finally, a smaller group (yellow) includes some of the methods for photophysical characterization of photocatalysts such as UV/visible spectra, fluorescence, and fluorescence decay.

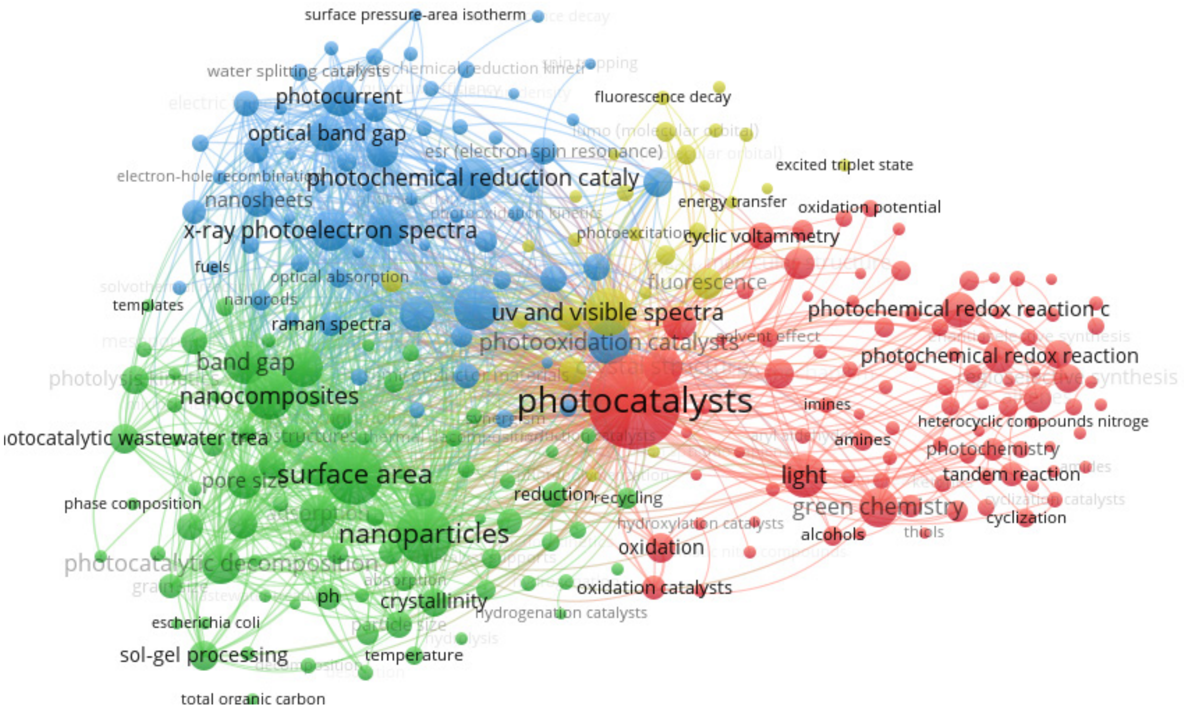


Figure 30. Network diagram of concepts in photo catalysis in the years 2011-2020 of journal publications

Figure 31 shows the network and co-occurrence of concepts in patents related to photocatalysis. One grouping (the blue and green groups) includes the core term "photocatalysts" and a variety of material- and polymer-related terms. Some of the relevant terms include photoresists, polymerization catalysts, crosslinking agents, acrylic polymers, and polysiloxanes. Many of the polymers can be polymerized using light, and the use of photocatalysis is one major method for manipulating the form and chemistry of materials. Polymers and their derived materials are articles of commerce and important for a variety of products. Finally, polymers (unlike small molecules) have properties that depend on processing and thus scale of manufacture, particularly for industries such as the manufacture of computer chips. and methods for their use may be more likely to be indexed in patents. The second large group (red) includes both synthetic methods for photocatalysts (photocatalysis, photochemical reaction catalysts) and nonpolymeric materials and uses such as compositions, photocatalytic wastewater treatment, and hydrothermal reactions.

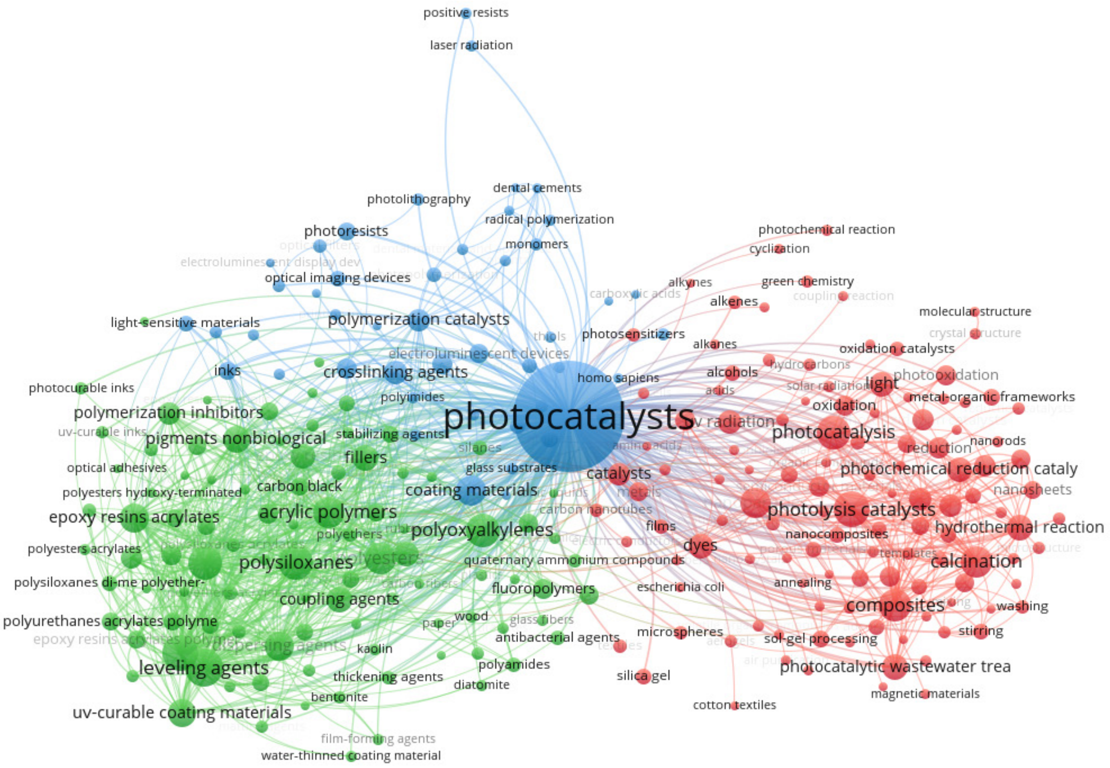


Figure 31. Network diagram of concepts in photocatalysis in the years 2011-2020 of patent publications

The development of emerging concepts in photocatalysis journal publications is depicted in **Figure 32**. There are 1,017 photocatalysis-related concepts that were first indexed in photocatalysis documents in 2012-2014 since 2000. C-C bond formation, tandem reaction, photochemical hydrogenation, and Meerwein reactions are the most indexed reaction types. Aromatic alcohols, secondary amines and sulfoxides are the top indexed substance classes. Photoluminescence, photostability, charge separation and energy-dispersive X-ray spectra are property related concepts indexed by the CAS Content Collection. In addition to half of these concepts (526 out of 1,017), 1,513 new photocatalysis relevant concepts were indexed in 2015-2017 in this document set. Photosensitizers, heterogenous catalysts, radical cyclization catalysts, and sulfonylation catalysts are the most widely used catalysts in photocatalysis. Reaction types expanded to three-component reaction, photooxidative coupling reaction, and sulfonylation. New substances involved in photocatalysis in this time span are arylboronic acids, styrenes, and fluoroborates. Core-shell materials and pollution related topics, such as photochemical corrosion, and environmental pollutants, are also explored under photocatalysis. In 2018-2020, 1,699 new concepts were indexed in photocatalysis. Hydrogen evolution reaction, and water splitting kinetics are hot and new concepts in this area, which may result from the boost of clean energy vehicle. Hydrogen is considered as an alternative energy source to replace gasoline, and its preparation from water was studied extensively. Three-component reaction catalysts, photocyclization catalysts, and dearomatization catalysts are new catalyst types investigated in this period.

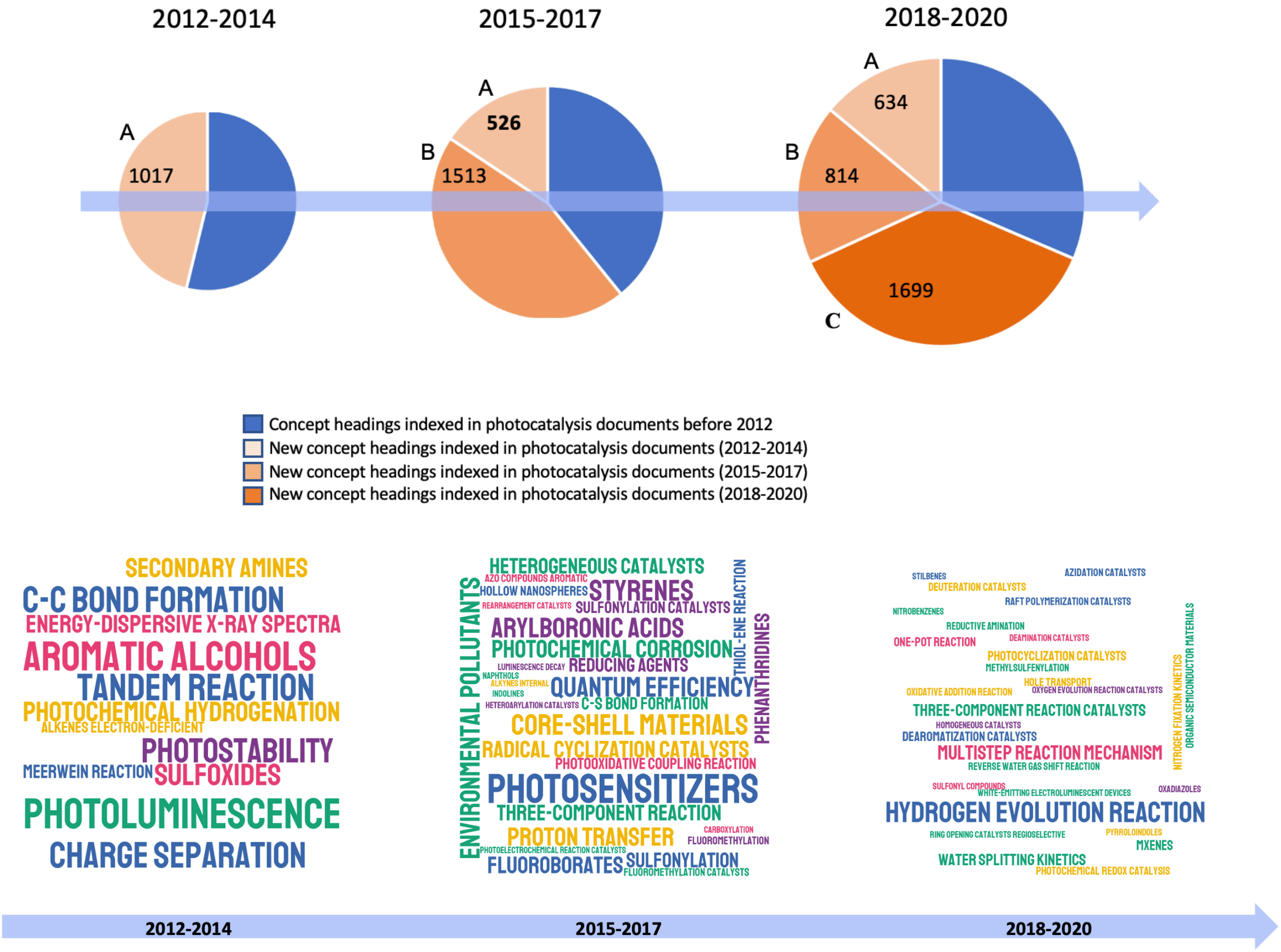


Figure 32. Rising concepts on photocatalysis journal publications in a timeline. Top panel shows the changes in numbers of new concepts related to photocatalysis added in the periods 2012-2014, 2015-2017, and 2018-2020 relative to previously added concepts. Bottom panel shows the most common new concepts appearing during the corresponding time frames in this document set since 2000.

4.5 Substance analysis of journal and patent publications on photocatalysis

Categorized by role indicators, **Figure 33** shows the volumes of photocatalysis-related publications and the numbers of substances. Role indicators are a list of terms for describing substance functions in a document. A detailed list of role indicators and their associated descriptions can be found on the CAS website.[42] In both journal and patent publications, documents containing substances with preparative roles (SPN, RCT and CAT) account for the largest volumes, followed by publications with substances assigned roles (PRP, PEP, NUU, and NAN) describing properties. Many photocatalysts are prepared, such as nanoparticles and dyes, and their properties and performance in devices are often tested as evidence of their activity under applicable conditions. Although a significant number of substances in journals have characterized properties, they are outnumbered by those with preparative roles because documents focusing on preparative methods require the preparation of many substances to investigate the utility, scope, and limitations of the methods. When counting substance numbers, substances with TEM (technical or engineered material use) roles are more prevalent in patents than in journals, likely due to commercial interest in the technical uses of materials. A subset of roles for materials and polymeric formulations has both significant numbers of documents and substances associated with it; the roles in the subset (MOA, POF, PEP) may refer to substances used in photocatalytic polymerization or polymer modification.

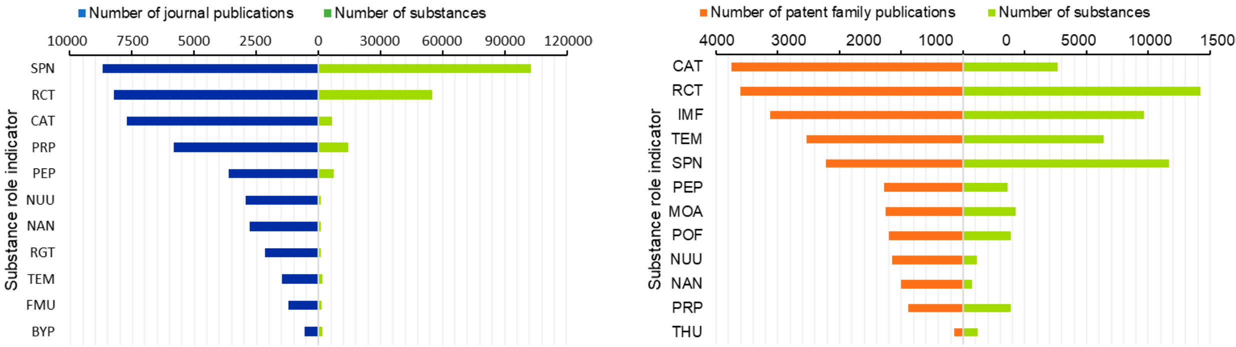


Figure 33. The distribution of substance roles in journal or patent publications 2011-2020 relating to photocatalysis. Role indicators: RCT (reactant), SPN (synthetic preparation), CAT (catalyst), PRP (chemical property), PEP (physical property), NUU (miscellaneous synthetic uses), NAN (nanoscale property or function), RGT (synthetic reagent), TEM (technical or engineered material use), FMU (synthetic formation), BYP (byproduct), IMF (industrial manufacture), MOA (modifier or additive use), POF (polymer in formulation), THU (therapeutic use)

Categorized by role indicators, **Figure 34** shows the trends of publication volumes and numbers of substances between 2011 and 2020. In journals, synthetic studies (SPN, RCT, and CAT) have the largest number, followed by documents obtaining chemical or physical properties of substances with roles in PRP, PEP, NUU, and NAN, and then documents containing substances with technical or device uses (RGT, TEM, and FMU). In patents, documents with role indicators of CAT and RCT account the most volumes and they also have the fastest growing rate. Patents claiming substances with IMF and TEM roles grew faster than that in journals, likely due to strong application and commercial interests in these roles. Most of the substances in journal documents were assigned with RCT and SPN roles. Substances are relatively more evenly distributed among role indicators in patents, there was still more substances with RCT and SPN roles than with other roles.

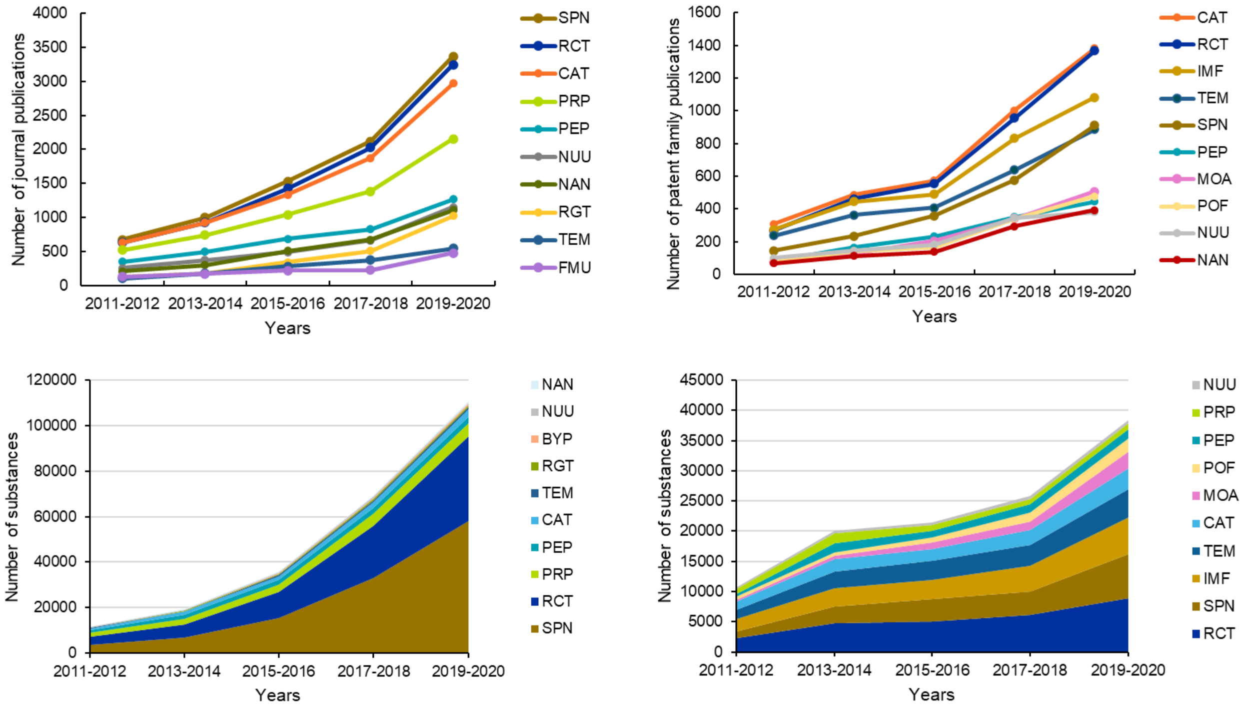


Figure 34. Trends of journal and patent documents on photocatalysis and the number of substances per role indicator in the period 2011-2020.

Figure 35 shows the comparison between China and the rest of the world in publication volumes and substance counts. The number of journal articles published in China and the number of substances in those documents are close to the corresponding numbers outside of China. However, while a significantly higher number of patents are published by patent assignees from China than elsewhere, the number of substances with assigned roles in patent documents are similar between China and the rest of the world. This indicates that patents from Chinese assignees are less likely to claim large amount of substances.

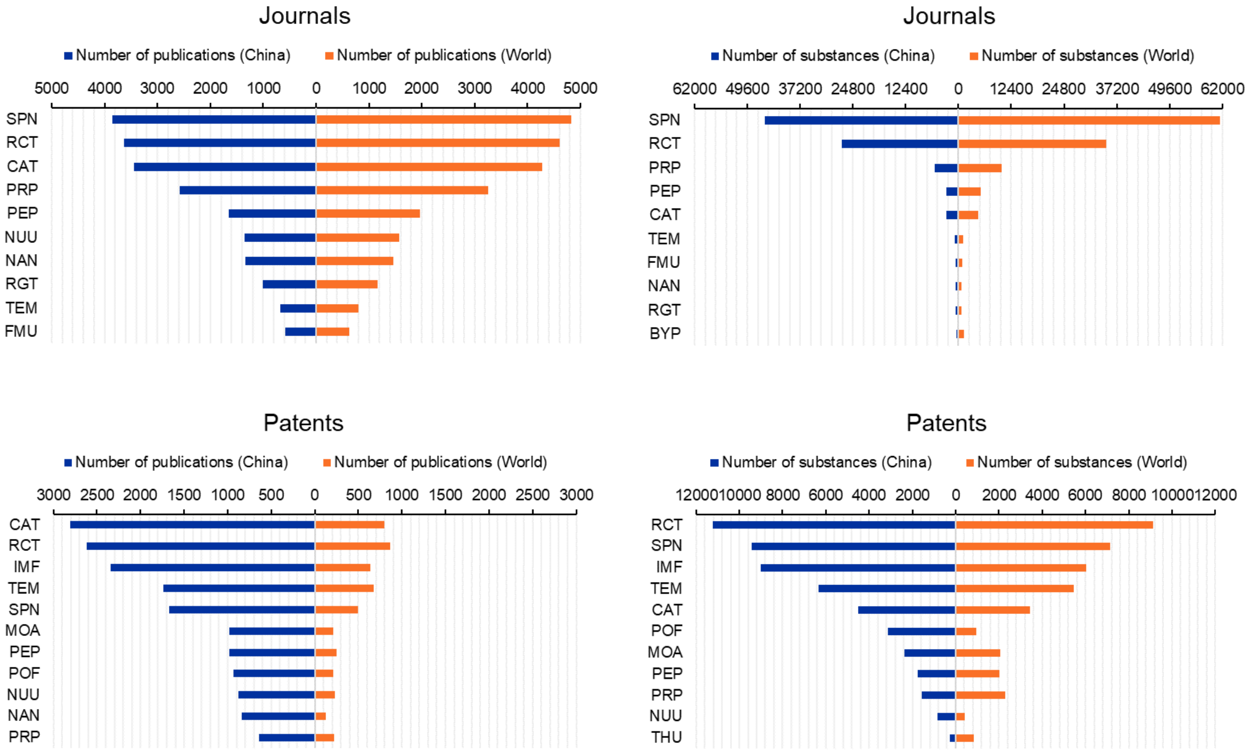


Figure 35. The comparison between China and the rest of the world on the substance role distributions in journal or patent publications (2011-2020) in photocatalysis.

Figure 36 compared the trends of journal publications and substance numbers in corresponding role indicators between China and the rest of the world. The trends of journal publications and the associated substance counts are very similar between China and the rest of the world.

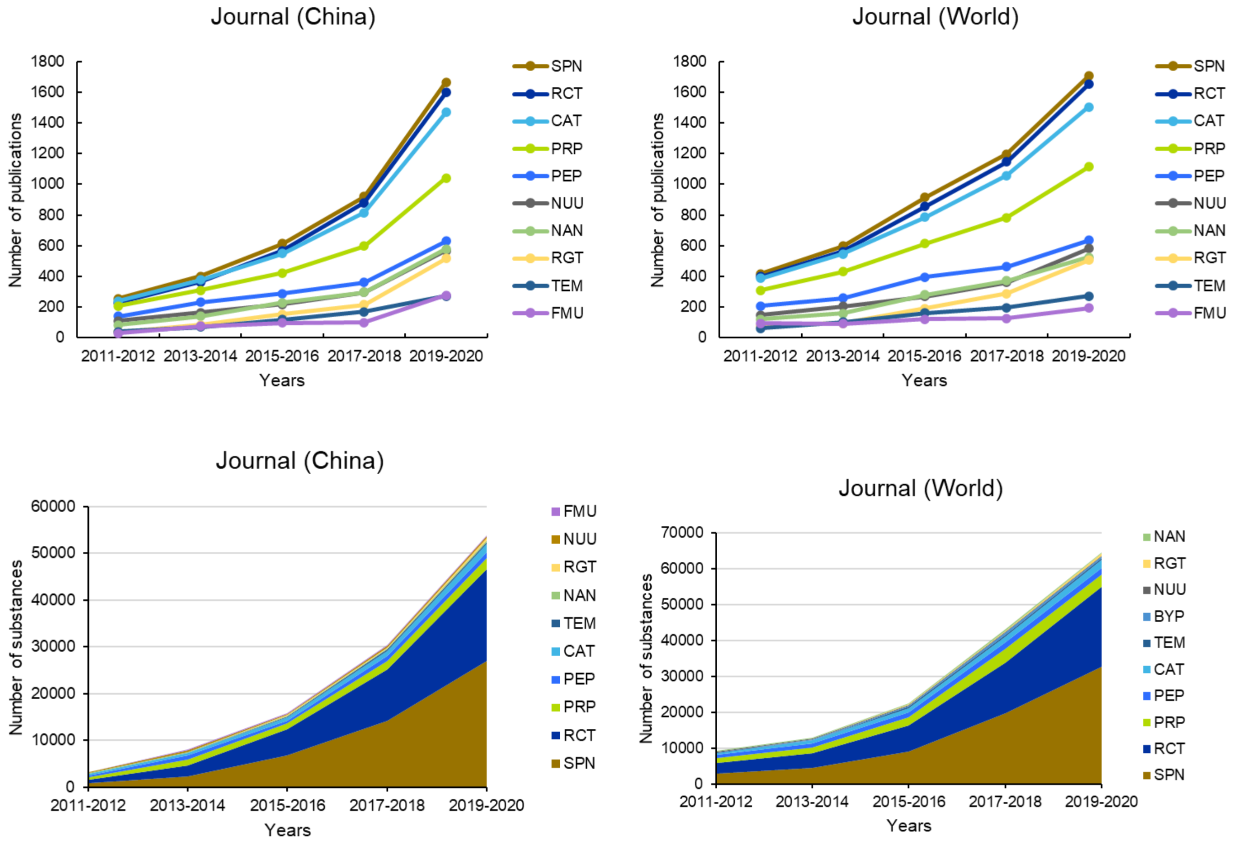


Figure 36. The comparison between China and the rest of the world on substance role trends in journal publications (2011-2020) in photocatalysis

However, when trends of patents in publication volume and the associated substance counts were compared between China and the rest of the world (**Figure 37**). Both patent publication volumes and substance numbers increased dramatically in China in the year 2011-2020, while they remained relatively flat in the rest of the world. The obvious fluctuation of substance numbers with assigned roles are mainly due to a few large patents which claimed thousands of substances. The years 2011-2012 and 2017-2018 have fewer large patents than other time periods.

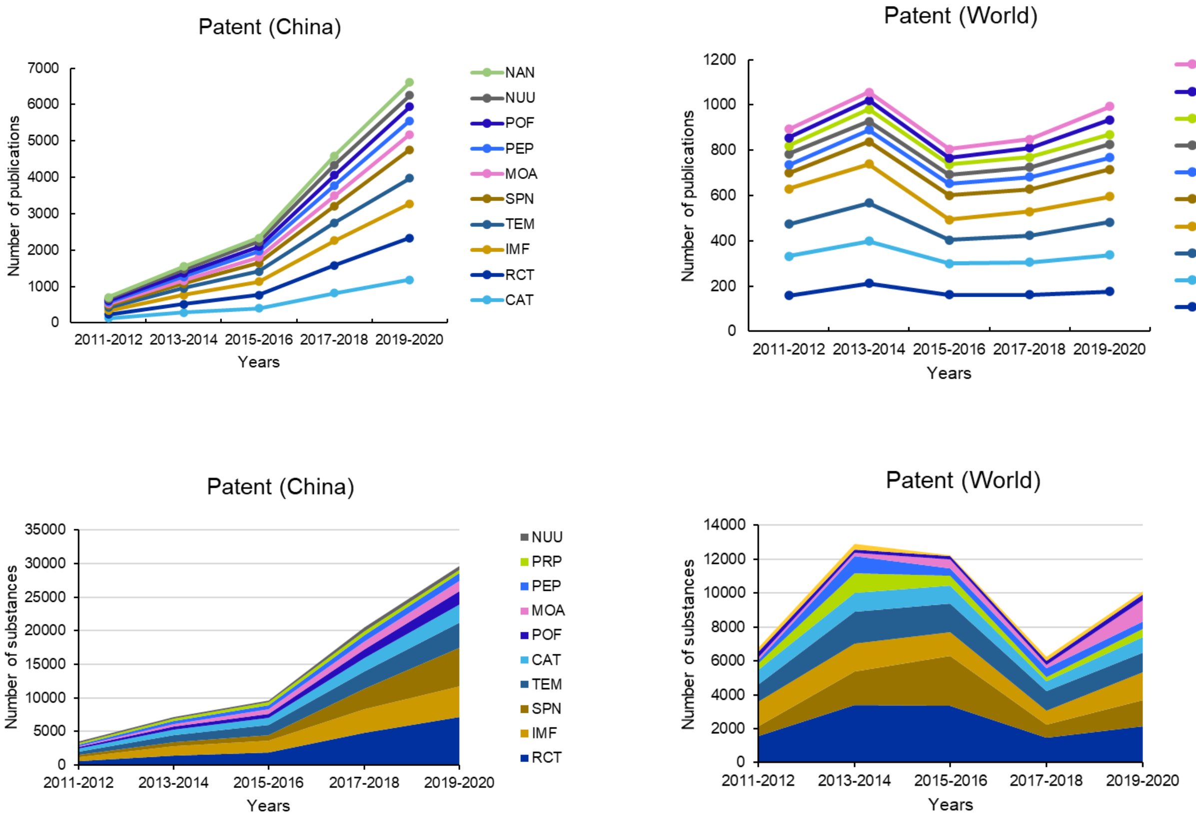


Figure 37. The comparison between China and the rest of the world on substance role trends in patent publications (2011-2020) in photocatalysis.

5. Green Chemistry

Green chemistry is a philosophy and a set of methods designed to reduce the environmental costs of chemical methods and to ensure the sustainability of the chemical enterprise. The twelve principles of green chemistry were devised by Paul Anastas and John Warner constitute a summary and aspiration for what chemical methods should be and do.[44] Reducing the complexity of processes and their costs in reagents and solvents are some of the ways in which that can be achieved. Replacing stoichiometric reagents with catalysts and replacing reductants or oxidants with electricity or light are some of the ways in which organic synthesis has tried to implement green chemistry principles. Methods to replace common solvents with less toxic, more sustainable, or cheaper ones, such as the use of surfactant-water mixtures for organic reactions or reducing the use of halogenated solvents or problematic polar aprotic amide solvents, have been developed and refined and are commonly implemented on large scales. The ability to address climate change also requires that chemical processes be made more efficient. The ability of green chemistry to address important global problems justifies interest in its research.

5.1 Trends of journal and patent publications on green chemistry in organic synthesis

Figure 38 shows the trends of journal and patent publications on green chemistry in organic synthesis. The global journal publications on green chemistry reached the peak in 2013-2014, then entered a slowly decreasing track. In general, research on the topic of green chemistry is still very active, as the total journal output on this topic is much higher than those on enzyme catalysis and photocatalysis. On the other hand, the growth in the global patent output on green chemistry has accelerated in the past ten years. Compared to the patent publication volume in 2011-2012, the number of patents published in 2019-2020 increased more than five times. The ratio between journal and patent publications decreased from 7:1 in 2011-2012 to 1.3:1 in 2019-2020, which implies more and more research finding and achievements are seeking their way to be commercialized or industrialized.

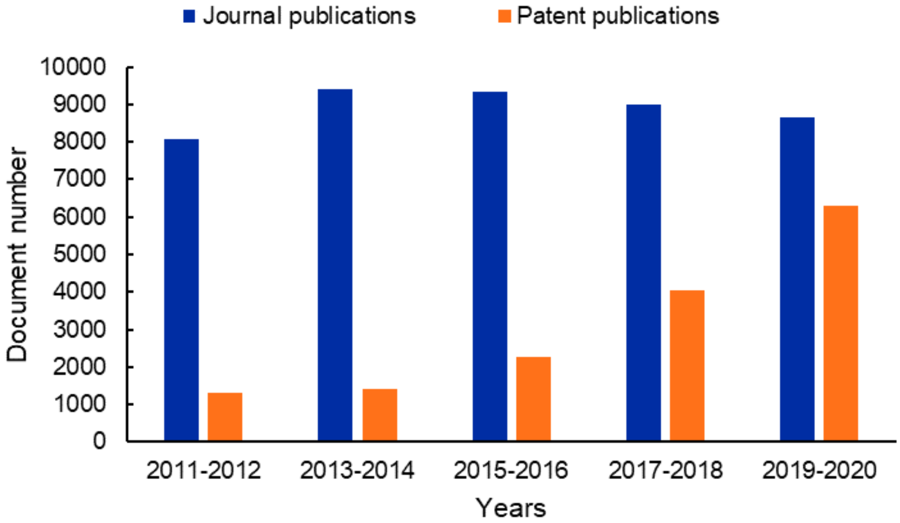


Figure 38. Trends of journal and patent publications on green chemistry in organic synthesis from the CAS Content Collection during 2011-2020.

5.2 The distribution of publications among countries/regions on green chemistry in organic synthesis

The distribution of journal and patent publications on green chemistry among different countries/regions is shown in **Figure 39**. China is the leading country in both patent and journal publications in this research field. Almost equal amount of journal papers and patents were published from China over this ten-year period. India ranked second in journal publications on green chemistry followed by Iran, United States and Japan. Unlike journal publications, patent publications on green chemistry from countries/regions other than China are relative rare. China contributed most of patent publications in green chemistry, which may relate to China's efforts on improving environment and promoting green industries.[45] South Korea, India, United States and Japan are countries/regions that contributed some patent publications in green chemistry during the past ten years. The low patent activity in these countries/regions for green chemistry in organic chemistry indicates that few of the methods have yet been translated into technologies with commercial interest. This observation is consistent with a recent study of the green chemistry patent landscape which found that few patents on green methods in organic synthesis were published.[46]

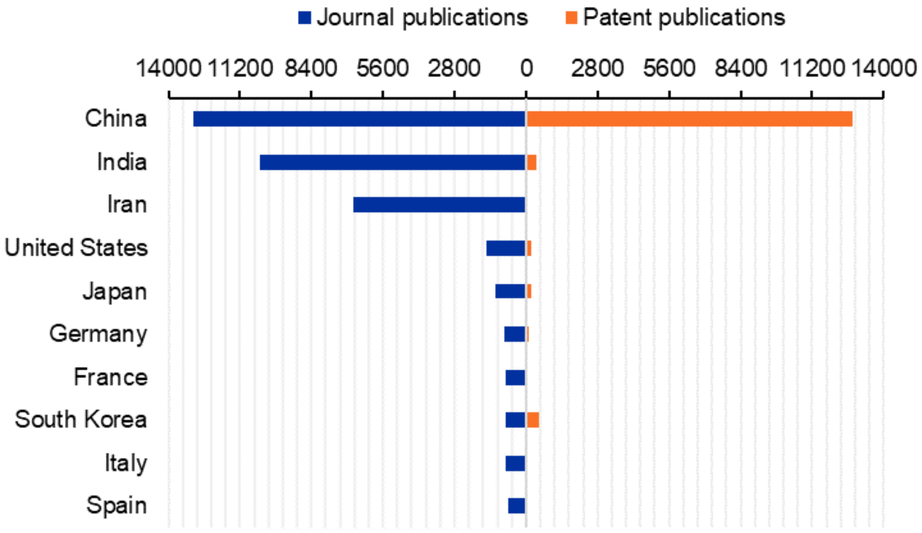


Figure 39. The distribution of journal publications among top countries/regions and their patent publications on green chemistry in organic synthesis

Top 5 countries/regions' biennial journal and patent publication data on green chemistry are displayed in **Figure 40**. For journal publications, China kept increasing trend during the past ten years, while India and Iran experienced increasing from 2011 to 2014 and decreasing from 2015 to 2020. Journal publications from United States and Japan slowly decreased from 2011 to 2020. Patent publications on green chemistry from China dramatically increased during the past ten years, however, patent publications from South Korea, India, United States and Japan stayed at a relative low volume. It can be seen from this chart that patent publications from China dominate the world's trend of patent publications on this research topic.

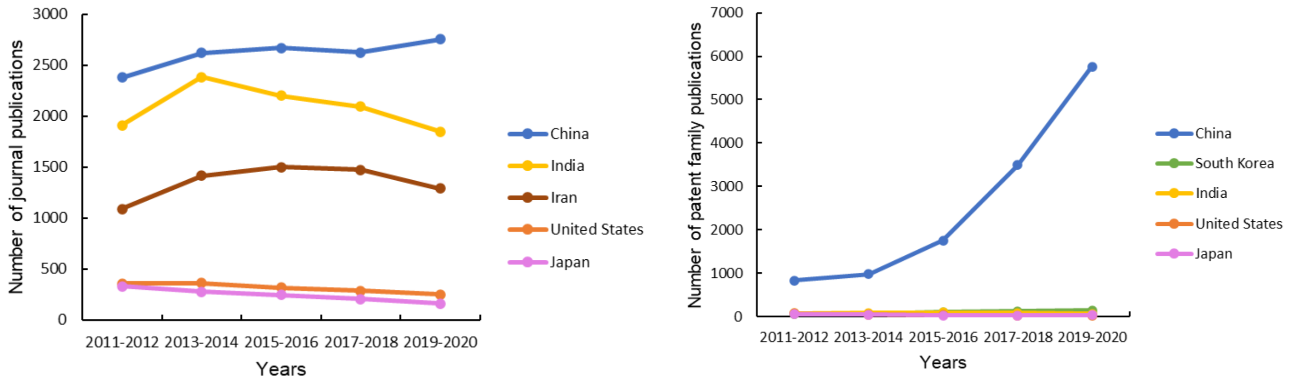


Figure 40. Journal (left) and patent (right) publication trends in green chemistry for the top 5 countries/regions between 2011 and 2020.

5.3 Research organizations with a focus on green chemistry in organic synthesis and their publications

The top 20 research institutes and organizations in journal publications on green chemistry are presented in the top panel of **Figure 41**. Among the 20 organizations, 9 organizations are from China, 6 organizations are from Iran, 4 organizations are from India, and only one organization is from Russian. Islamic Azad University is the most productive organization on green chemistry, followed by Indian Institute of Chemical Technology, and Chinese Academy of Sciences. According to this chart, only 6 (30%) organizations published more than 30% of their total journal papers during the last three years of this time period. The top 20 organizations of patent publications on green chemistry are shown in bottom panel of **Figure 41**. Research institutes/organizations from China dominate this list and Council of Scientific & Industrial Research, ranked 11th position in this list, is the only non-Chinese organization. Different from data shown in journal publications, 18 research institutes/organizations published more than 50% of their total patent output in the most recent three years (2018-2020). Research organizations from China are continually active on this research topic, and more efforts were put on green chemistry area recently.

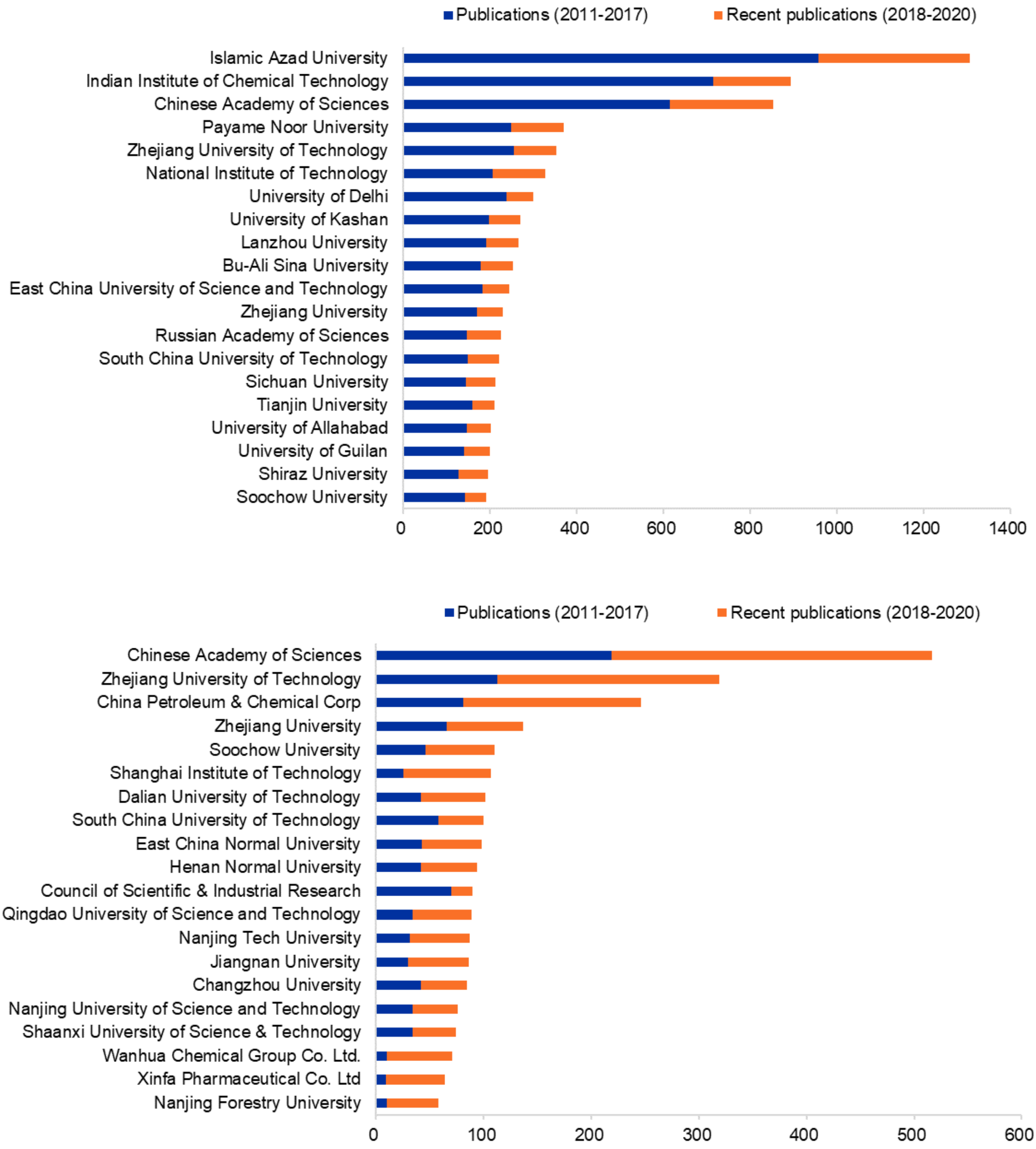


Figure 41. Top research organizations according to journal and patent publication volumes on green chemistry

5.4 Concept analysis of journal and patent publications on green chemistry

The concepts indexed in publications discussing green chemistry, their frequencies, and the co-occurrence of concepts in one document are shown in **Figure 42**. There are four major clusters of subject headings. The green cluster contains concepts referring to general synthetic reactions and their catalysts, such as chemoselectivity, regioselective and diastereoselective synthesis, tandem reaction, C-H bond activation, and nanocatalysts. As noted earlier, selectivity is a key element of green chemistry since selective reactions are those that generate fewer byproducts and thus require less work and resources to obtain pure products, while tandem reactions minimize reaction workup and purifications as well. C-H bond activations have been a major research topic in organic synthesis, as they could minimize the operations needed to make a desired product if implemented selectively. Nanocatalysts may enable selective reactions or improve the recycling of catalysts (though recycling does not occur in the diagram). A more diffuse yellow cluster encompasses a variety of palladium–catalyzed reactions such as Suzuki, Heck, and cross-coupling reactions and their products and reactants (biaryls, alkynes). Palladium-catalyzed reactions are ubiquitous in organic synthesis, and so improving their environmental costs would make synthesis significantly greener. The red cluster includes common reactants and products such as aryl aldehydes and fused heterocyclic compounds, reaction headings, and catalysts for condensations and related reactions such as three-component reactions and Biginelli reactions. Aryl aldehydes have limited ways in which they can react, and condensation reactions are more amenable to simpler catalysts or solvent-free conditions that fit under the rubric of green chemistry. Fused heterocycles are in many cases most readily prepared by cyclocondensation reactions and are a common target for green synthesis. Nearby, a purple cluster contains a smaller number of biological uses such as bacterial infection and antibacterial agents; the ease of testing antibacterial activity and ability to generate large numbers of products from a small number of reactants by condensation reactions may explain their association with green chemistry. Finally, a blue cluster incorporates components of supported or reusable catalysts (nanoparticles) and methods for the physical characterization of catalysts (surface structure, thermal stability, surface area, pore size). One method to reduce the environmental costs of reactions is to reduce the costs of catalysts and to improve their separation from other reaction components.

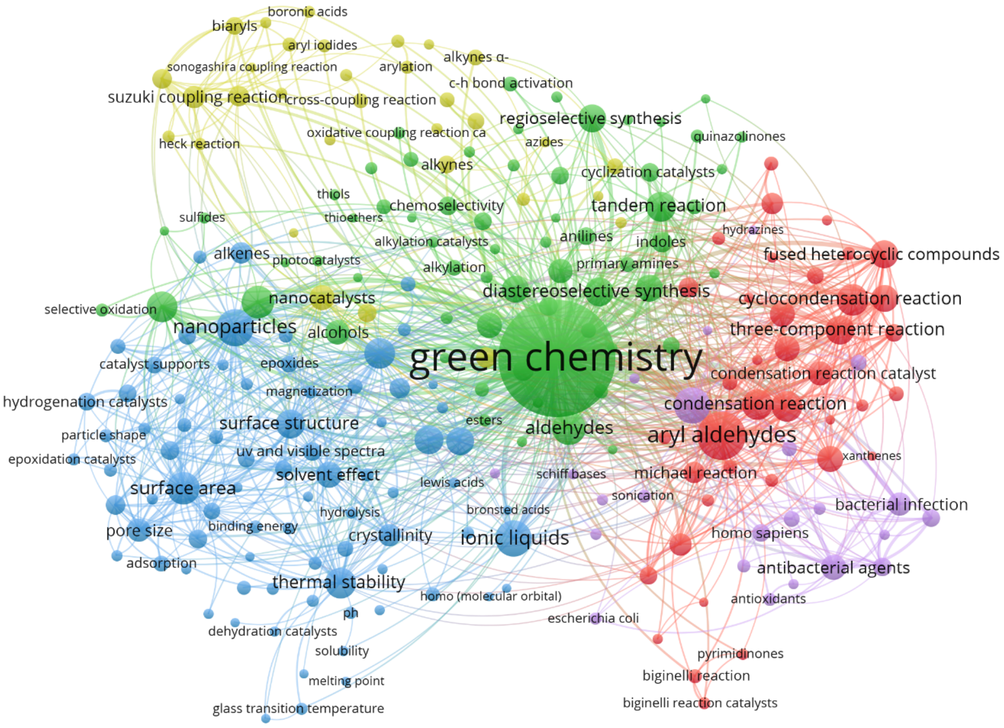


Figure 42. Network diagram of concepts from journal publications on green chemistry in the years 2011-2020.

Concepts in patent publications relevant to green chemistry and their co-occurrence are shown below in **Figure 43**. The concepts form three major clusters. The largest cluster (green and blue) contains reaction and catalyst headings such as cyclization, substitution, oxidation and oxidation catalysts, hydrogenation catalysts, chlorination, bromination, and esterification and esterification catalysts. In addition, subject headings for selected reactants and products such as alcohols and ethers, ionic liquids, and extraction were indexed.

These headings indicate that there is significant patent interest in processes in organic synthesis with reduced environmental costs (which may also translate to reduced economic costs for the patenters). A second large cluster encompasses concepts for polymers and their uses, including polymerization catalysts, polyoxyalkylenes and polyurethanes, and dispersing agents, adhesive, and fire-resistant materials. These concepts refer to materials and products close to commercial use and are consistent with the desire of customers for greener products. In addition, some American jurisdictions[47, 48, 49] have forbidden the use of some flame retardants in consumer products, making the use of other materials necessary to maintain fire resistance. A third smaller cluster (yellow) includes the concepts such as fermentation, culture media, protein sequences, microbial gene, enzymic resolution, and *Escherichia coli*. This cluster is consistent with the use of biological processes (including enzyme-catalyzed processes) to reduce the environmental burden of manufacturing. Finally, a very small and diffuse cluster (purple) contains concepts for *Homo sapiens*, insecticides, and antibacterial agents.

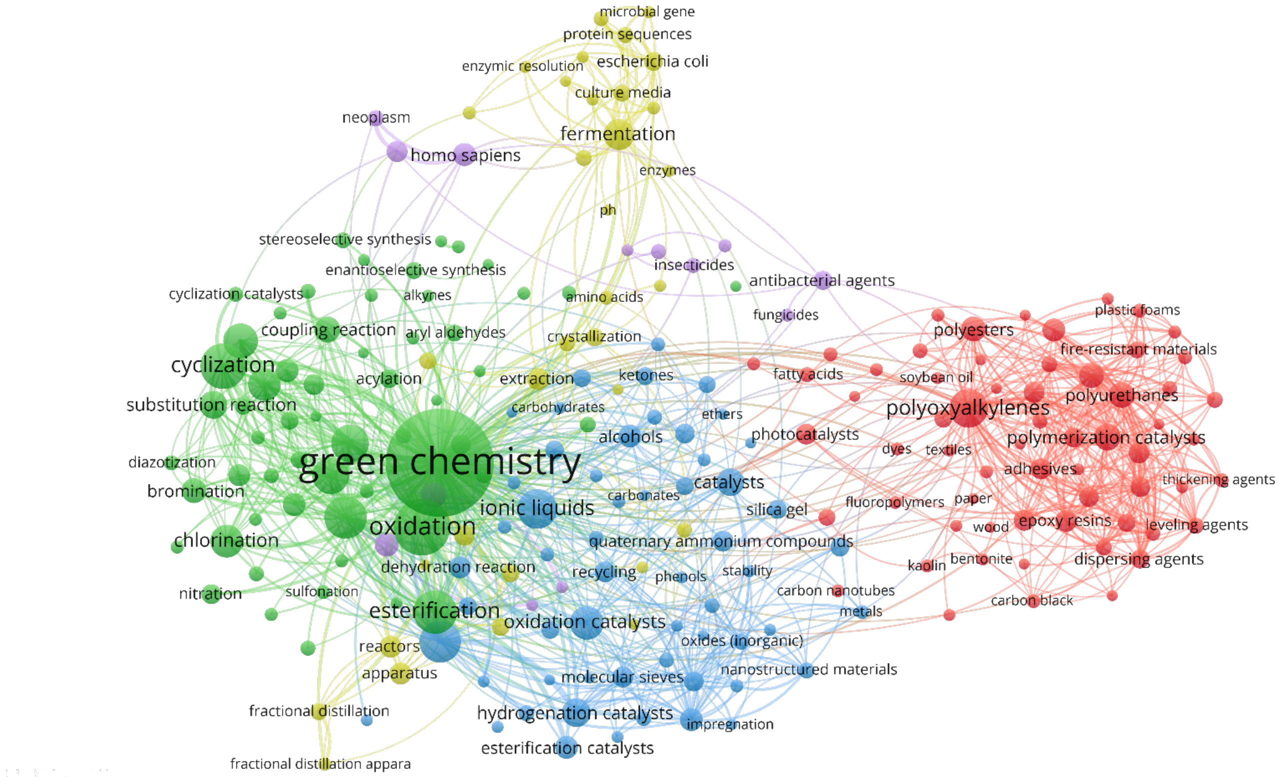


Figure 43. Network diagram of concepts in green chemistry in the years 2011-2020 of patent publications

The change of emerging concepts in green chemistry along the timeline is depicted in **Figure 44**. In 2012-2014, there were 2,482 green chemistry-related concepts that were first time indexed in green chemistry-related documents since 2000, examples including indoles, pyrimidines, pyrazoles, imidazoles, benzimidazoles and benzopyrans. These classes of substances were prepared or used in green chemistry related research at the beginning of this decade, and more than one third of them were carried to 2015-2017 period. As an addition, 2,122 green chemistry related concepts were captured by the CAS Content Collection in 2015-2017. Different reaction catalysts, such as three-component reaction catalysts, multicomponent reaction catalysts, and heterogenous catalysts became new research topics in this area. Reaction substances expanded to cyclic carbonates, benzamidines, biphenyls etc. Among them cyclic carbonates are common products of carbon dioxide fixation, which became a worldwide priority enhanced by the desire to convert this greenhouse gas into valuable chemicals. During 2018-2020 period, 1,823 new green chemistry related concepts were indexed by the CAS Content Collection. Maleimides, thiazolidinones, pyrazolopyridines, iodobenzenes and bromobenzenes are the most studied substance classes. Cycloaddition catalysts and multistep reaction mechanism are hot topics in green chemistry during this period.

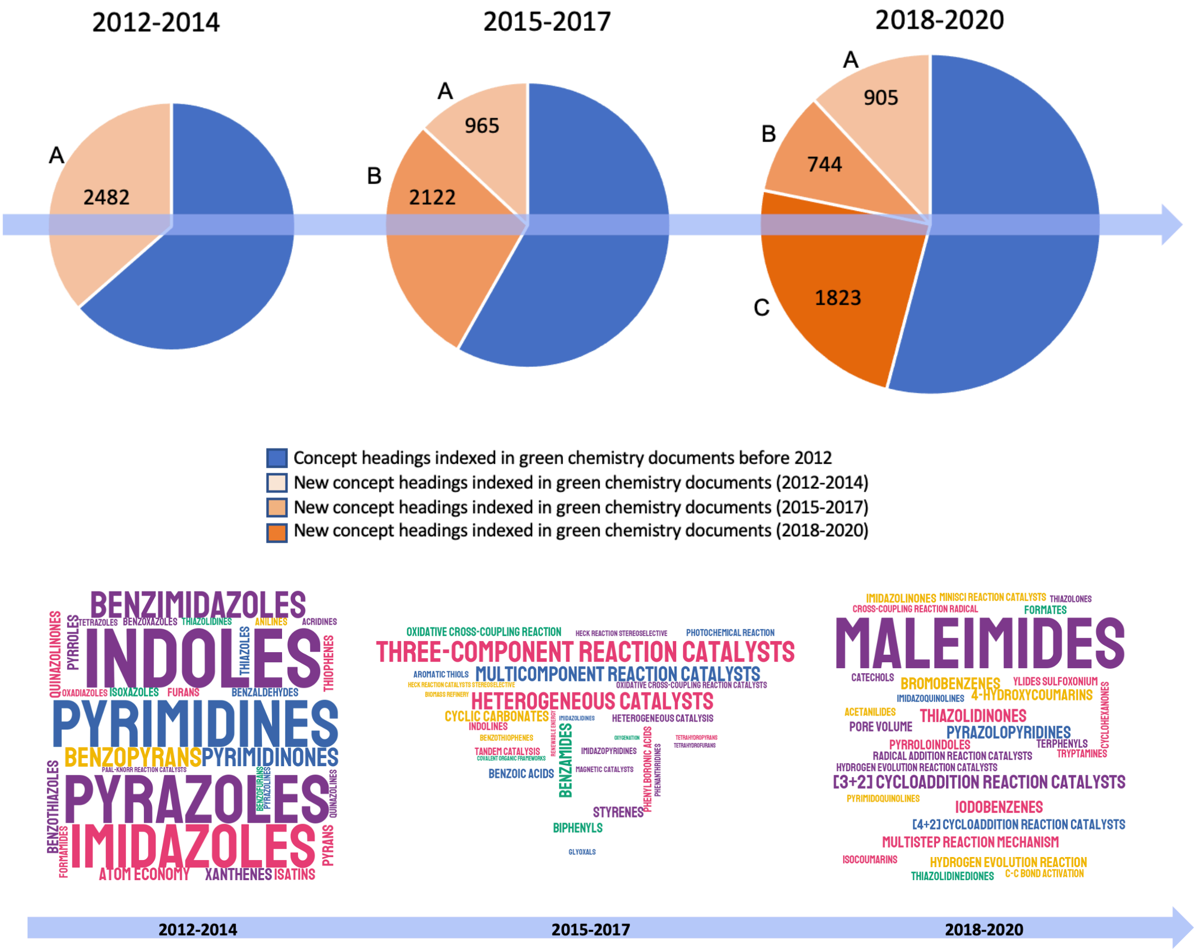


Figure 44. Rising concepts on green chemistry in a timeline. Top panel shows the changes in numbers of new concept headings related to green chemistry added in the periods 2012-2014, 2015-2017, and 2018-2020 relative to previously added concept headings. Bottom panel shows the most common new concepts appearing during the corresponding time frames in this document set since 2000.

5.5 Substance analysis of journal and patent publications on green chemistry

Figure 45 depicts the numbers of journal publications related to green chemistry that contain substances in specific roles and the numbers of substances indexed with those roles. In journal articles, substances with a variety of roles are found. The largest portion of publications contain substances with preparative roles (RCT, SPN, CAT, NUU) with a smaller number containing substances intended to be prepared on large scale (IMF) or formed as byproducts (BYP). Fewer documents contain substances indexed for nanotechnological (NAN) or pharmaceutical (PAC, THU) use or for their chemical or physical properties (PRP, PEP). The substances indexed in journal articles discussing green chemistry are almost exclusively preparative (with products indexed in much greater numbers than reactants and catalysts) with small numbers of substances with property data, pharmaceutical intent, or emphasis on industrial manufacture. The predominance of substances with preparative roles is consistent with the significant material, energy, and environmental costs of synthetic methods and the potential of green chemical methods to decrease those costs.

Patent documents relevant to green chemistry contain substances with mainly preparative roles (RCT, SPN, IMF, CAT, RGT, NUU). A smaller set of patents include substances indexed with roles for their uses as technical or engineered materials (TEM), as modifiers (MOA) or for their properties (PRP, PEP). The substances in patent related to green chemistry fall into two categories. The largest subset of substances indexed have RCT, SPN, or CAT roles; as for journals, green chemical methods are most applicable to the synthesis of chemical compounds and materials. A smaller (but significant) set of substances have prophetic (PPH) and agrochemical (AGR) roles; these may derive from agrochemical patents in which very large numbers of prophetic substances were indexed. A similar number of substances have been indexed with TEM roles.

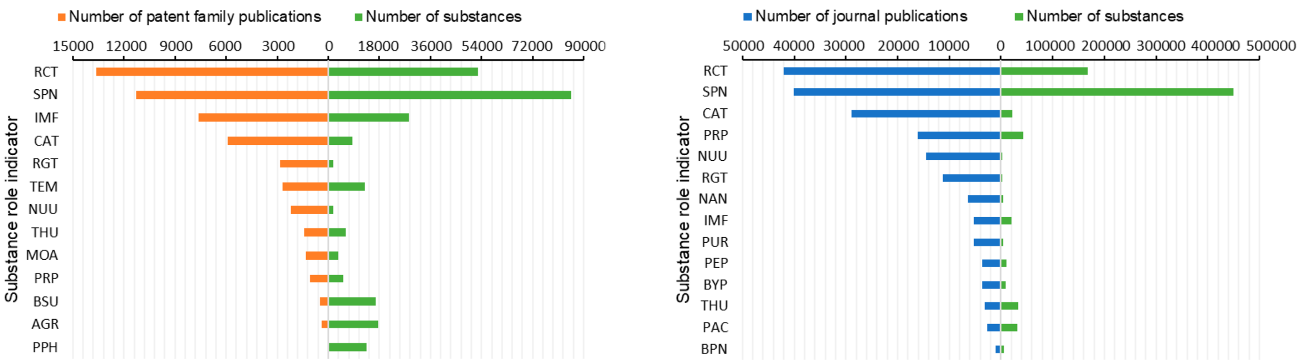


Figure 45. The distribution of substance roles in journal or patent publications 2011-2020 on green chemistry.

Figure 46 shows the number of journal and patent documents containing substances assigned specific roles and the total number of substances with those roles in journal and patent documents. The number of documents with preparative roles (RCT, SPN, CAT) increased overall between 2011 and 2020 but decreased slightly after 2012, while documents with PRP, PAC, and THU roles in green chemistry increased consistently over the same period, and substances involved in physical processes (PEP) or prepared biologically (BPN) were indexed at a low and slightly decreasing level. While the number of documents in green chemistry with various roles did not increase, the overall number of substances in journal articles did increase overall over the same period. The bulk of substances from green chemistry journal documents were used as reactants or products, consistent with the ability and emphasis of green chemistry on minimizing physical and energy costs of chemical processes and the reliance of synthesis on such processes. Both the overall numbers of patents in green chemistry and the substances increased substantially between 2011 and 2020, but the overall increase in patent documents and indexed substances is driven primarily by increases in reactants and products. Patent substances rapidly decreased between 2011-2012 and 2013-2014, driven primarily by substance- and prophetic-dense agrochemical patents, and increased rapidly afterwards (again driven by increases in the numbers of indexed reactants and products). While green chemistry may be more difficult for academic chemists to integrate into chemical discovery, the need for more efficient methods for large-scale production and environmental concerns may be driving adoption of green chemical technologies in industry.

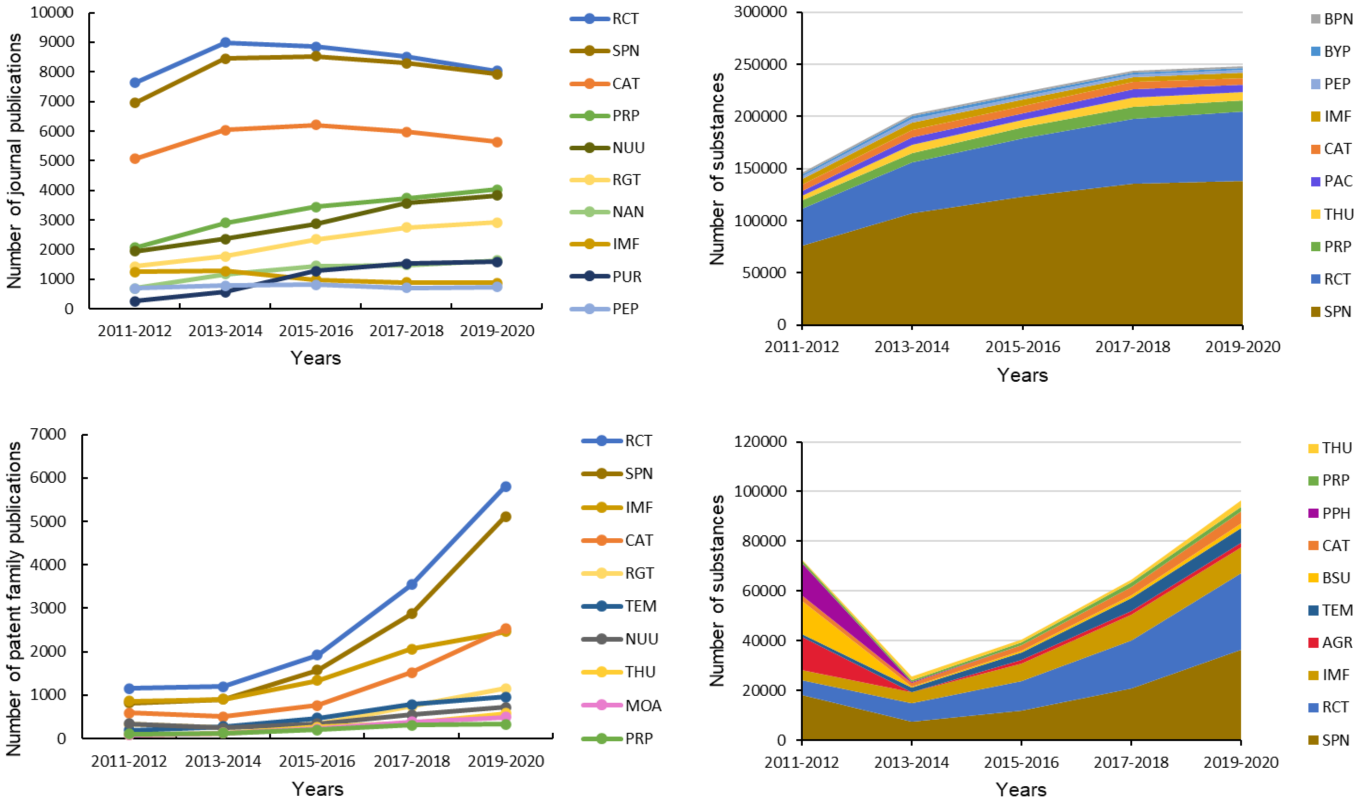


Figure 46. The trends of substance roles in journal or patent publications (2011-2020) for green chemistry.

Figure 47 shows the number of journal and patent publications in green chemistry containing substances with specific roles from China and from the rest of the world and the total numbers of substances in documents from China and from the rest of the world with those roles. In journal articles, research in the rest of the world on green chemistry is significantly higher than that from China. The diversity of roles in Chinese journal publications and in journal publications from elsewhere are similar. A larger variety of roles in both documents and substances in seen outside China than inside China; the greater apparent diversity in roles for substances and documents is likely consistent with the larger publication volumes seen. China has published many more patents containing many more substances relevant to green chemistry between 2011 and 2020 than has the rest of the world. A combination of the incentives to publish patents in China and the potential of green chemistry to address material and energy needs relevant to industrial chemistry may explain the differences between patent and journal publication in China and elsewhere. As noted with patents, the substances indexed in patents are consistent with the emphasis of green chemistry on material and energy costs and thus its relevance to synthetic methods. Patents outside China contain a significant number of agrochemical and prophetic substances; as noted above, a small number of substance-heavy patents may be responsible for their presence.

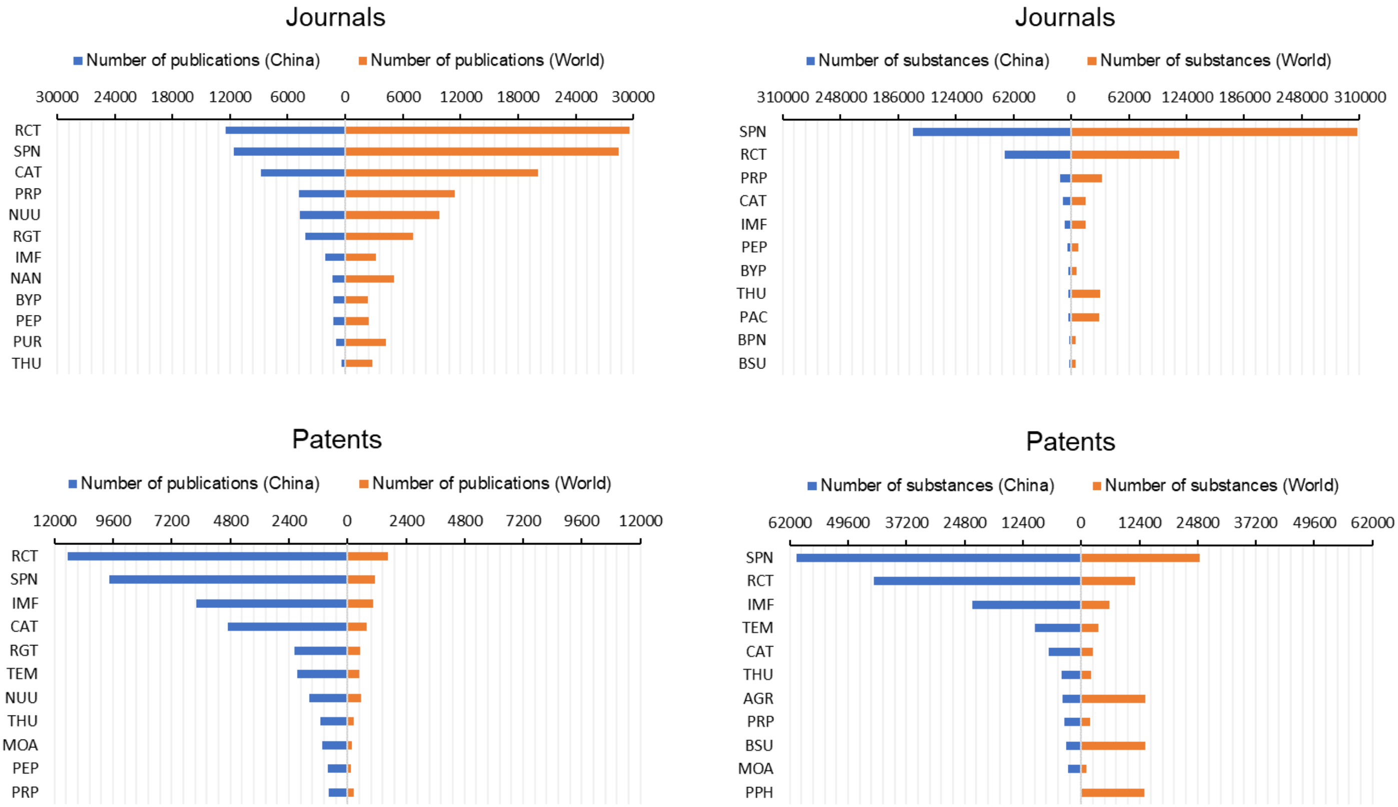


Figure 47. The comparison between China and the rest of the world on the substance role distributions in journal or patent publications (2011-2020).

Figure 48 shows the number of journal documents from China and elsewhere with specific roles in two-year periods between 2011 and 2020 and the total number of substances in the corresponding documents. The numbers of journal publications from China relevant to green chemistry increased between 2011 and 2020, but the numbers of documents with synthetic roles plateaued in 2013. Only documents with NAN, RGT, and NUU roles increased consistently between 2011 and 2020. The journal documents on green chemistry from outside China with RCT and SPN roles peaked in 2013-2014 and decreased afterwards, while journal documents containing other roles leveled off by 2020. As seen previously, green chemistry journal documents with RCT and SPN roles made up the largest portion of documents.

The relative trends of substances in green chemistry-related journal documents from China and from elsewhere were consistent with the numbers of documents but projected onto an overall increase in substance count. The numbers of substances in green chemistry journals from China increased consistently between 2011 and 2020, with most of the increase driven by increases in indexed reactants and products. The number of substances in green chemistry journal articles published outside China, on the other hand, reached a peak in 2017-2018 and decreased in 2019-2020; as with substances from China, most of the substances indexed in green chemistry journal articles outside China were reactants or products.

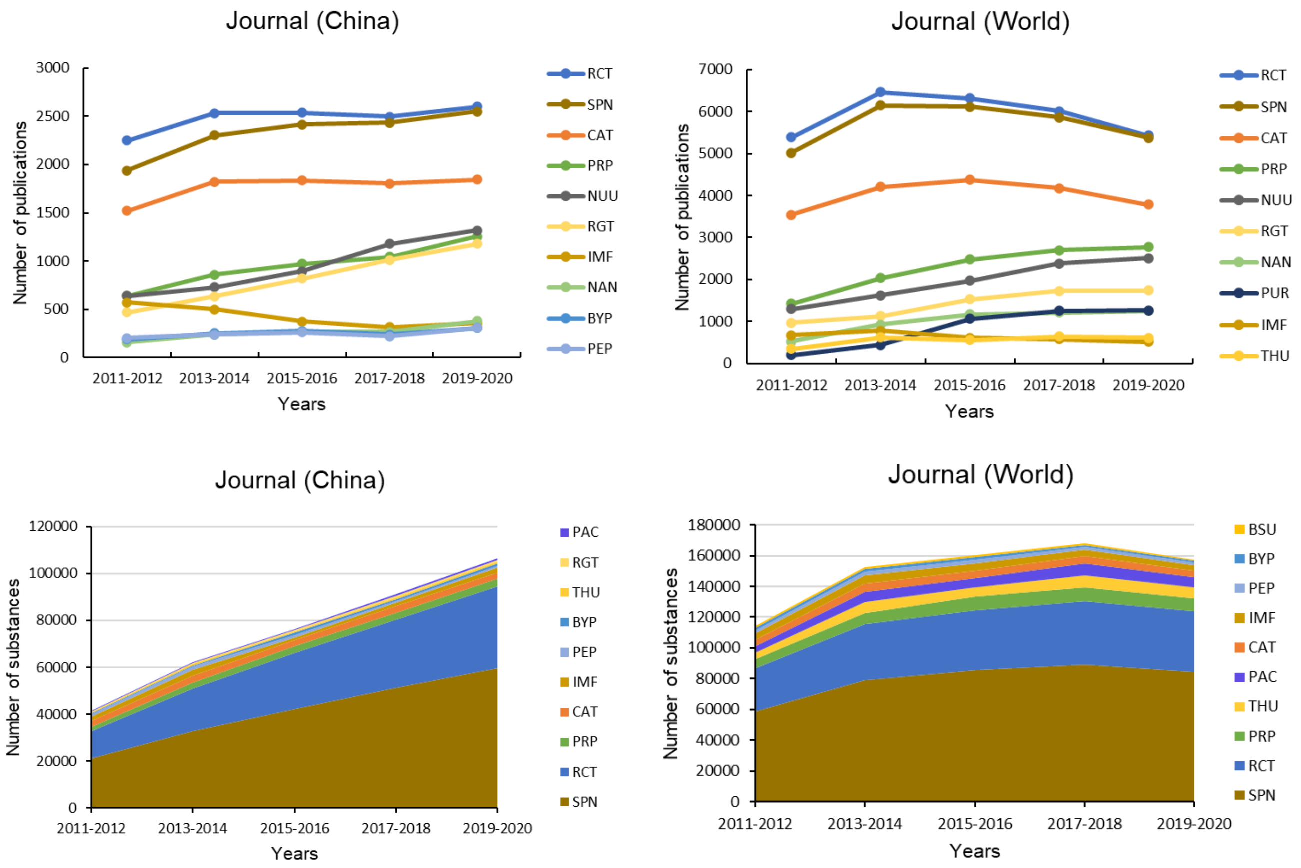


Figure 48. The comparison between China and the rest of the world on the substance role distributions in journal or patent publications (2011-2020).

Figure 49 shows the number of patent documents from China and elsewhere with specific roles in two-year periods between 2011 and 2020 and the total number of substances in the corresponding documents. Both the number of green chemistry patents and the number of substances contained in the patents increased significantly between 2011 and 2020, with the rate of growth increasing in 2015-2016. On the other hand, both the number of patents from outside China and the number of substances in the patents (excluding the large number of agrochemical and prophetic substances in patents in 2011-2012) were nearly constant between 2011 and 2020. A significant difference between journal and patent documents on green chemistry in China and elsewhere is the larger diversity of roles; while reactants and products made up most of the substances in journal articles, patents contained more substances with various roles and was less dominated by substances with preparative roles.

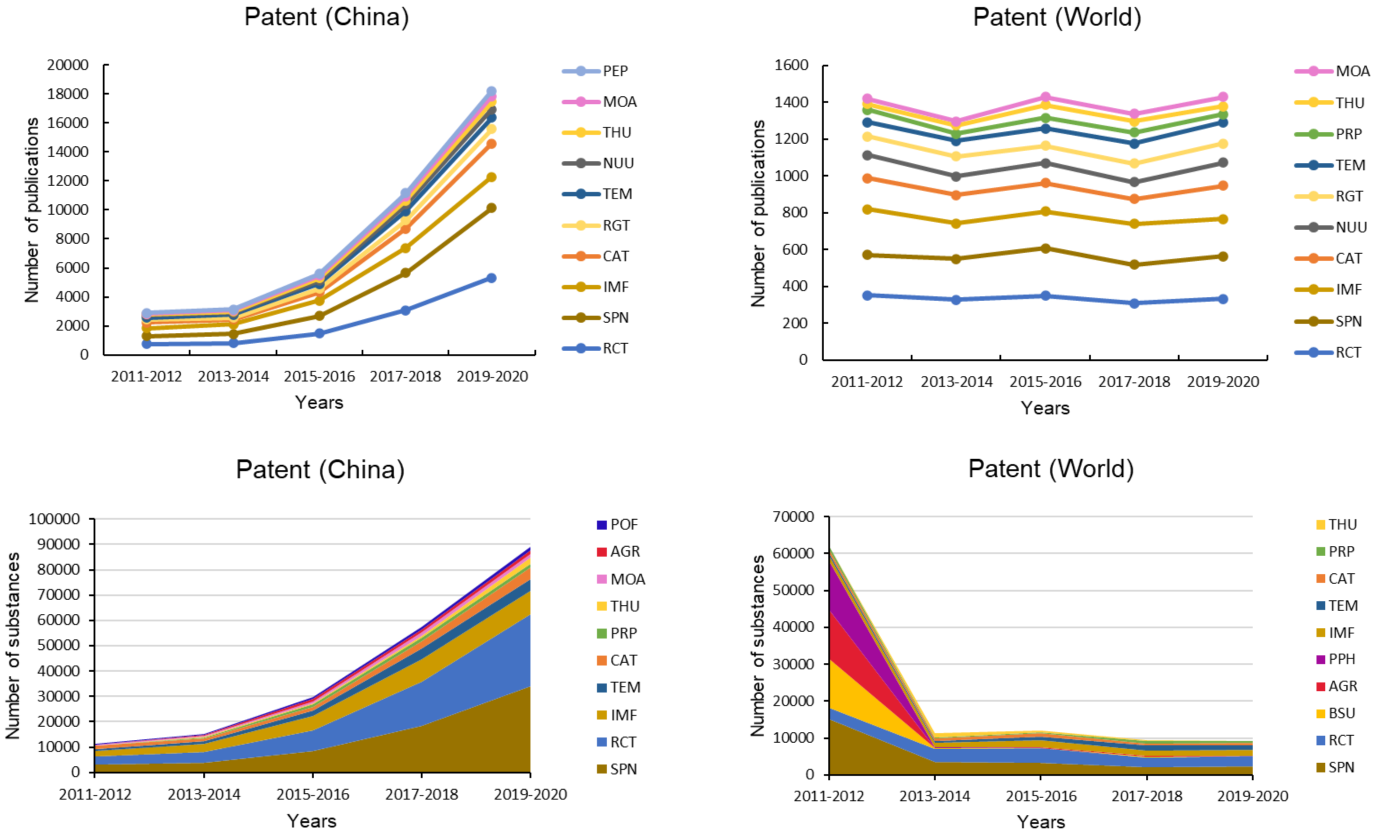


Figure 49. The comparison between China and the rest of the world on the substance role distributions in journal or patent publications (2011-2020).

6. Summary

The power to produce some of the most intriguing molecules of living nature in the laboratory was attained in the 1820's. Since then, synthetic organic chemistry has driven the exploration of molecular structure and reactivity. Although scientific discoveries and their applications have changed the world dramatically during the past two centuries, organic synthesis holds a central position in chemical research. The global research output in organic synthesis in both journal and patent publications has grown over the past decade, but the sources of that research have shifted from the United States, Europe, and Japan to China. Both journal and patent publications from Chinese authors in synthetic organic chemistry have increased in the last ten years. In addition, the overall quality of journal publications from China has improved consistently. Data presented in this report indicated that more than 60% of the top 20 most productive research institutes or organizations are from China. As the flagship Chinese research institution, the Chinese Academy of Sciences has been highly active in journal publication in organic synthesis from 2011 to 2020. In patent publications, China Petroleum & Chemical Corp. was the most productive patent assignee over the same period. Pharmaceutically related concepts and synthetically relevant terms were commonly indexed, and the relationship between molecular structure and physical and chemical properties has also been an important topic in organic synthesis documents during the last decade.

Interest in enzymic synthesis has increased significantly. Both patent and journal publication in enzymic synthesis have proliferated between 2011 and 2020, with many more journal articles than patents. China was the largest source of journal articles and patents using enzymes in synthesis. The overall numbers of journal articles and indexed substances increased more rapidly in China than elsewhere. The numbers of patents published from China and the substances indexed in them increased, while both the number of patents published elsewhere and the substances indexed in them decreased. Of the 20 largest sources of enzyme-mediated synthetic publications, nearly all were Chinese. The most common roles for substances in publications in enzyme-mediated synthesis were those for preparation and for chemical properties. A variety of concepts are common in enzyme-related synthetic publications. In journal articles, synthetic methods, catalyst optimization and structure, and protein engineering, while in patents, biological species useful for enzymic synthesis (such as *Escherichia coli*), protein and DNA sequences, their use in industrial processes such as fermentation, and cell culture are the most common subject headings. In addition, nanoparticle concepts in computation, nanoparticle stabilization, and synthesis were also prevalent, perhaps because they provide methods for stabilizing, using, and recovering enzymes in synthesis.

Photocatalysis has substantial publication interest, both in journals and in patents. The numbers of substances indexed in both journal articles and patent publications has increased consistently between 2011 and 2020. As for enzyme-mediated synthesis, the numbers of publications and substances indexed from Chinese authors are much greater than the corresponding numbers for other countries/regions. Journal articles in photocatalysis have been published from a variety of countries/regions, and journal articles and the substances in them have increased at similar rates, but the rates for Chinese articles and substances have increased more than those from other countries/regions. The numbers of patents from China and the volume of substances indexed in them have increased, but the corresponding numbers of patent publications and substances have decreased elsewhere (reaching a minimum in 2015-2017 and then increasing). The largest sources of photocatalyst-related documents are in China and Japan; most of the authors are from academic institutions but two companies (one in China and one in Japan) are among the largest publishers of patents in photocatalysis. While journal articles related to photocatalysis contain substances with roles referring to their preparation, properties, and technical uses, most of the substances were used directly in synthesis. In patents, however, both publications and substances contained a variety of roles, including synthetic, property, and technical use roles. The relative numbers of substances and articles with specific roles in photocatalysis did not vary significantly between 2011 and 2020. While both journal and patent publications photocatalytic documents contained synthetic concept headings most frequently, journal articles discussed nanotechnological uses and optoelectronic properties, while patents contained concepts relating to polymers and polymerization and technical processes and tools such as photoresists.

Green chemistry has significant publication interest as well. Green chemistry journal publications have not grown substantially, but patent publications have grown rapidly between 2011 and 2020. China, India, and Iran have published journal articles on green chemistry, while Chinese authors have published far more patents in green chemistry than authors elsewhere; in most cases, patents and journals were published by authors at academic institutions. Journal articles were mostly published before 2018, while patent publications have mainly been published after 2018. Subject headings in green chemistry journal articles are primarily synthetic, with some emphasis on catalysts and nanoparticles and their characterization, while headings in patents discuss mainly organic synthesis and polymers with some biological processes discussed. By 2020, about half of the subject headings indexed were created after 2011. The number of green chemistry documents containing substances with specific roles and the number of substances in those documents from China increased but were constant or decreased elsewhere. Both journal and patent publications contained substances with predominantly synthetic roles, but patent documents contained substances with a larger variety of roles. In general, academic interest in green chemistry does not seem to be increasing while interest in green chemistry from patent authors is increasing. While green chemistry is most relevant to organic synthesis, patents in green chemistry also discuss polymer and biological chemistry which may be of more immediate commercial interest.

7. Methods and Data

To search for publications on synthetic organic chemistry and related data, documents containing reactions with one or more organic molecules as the end products were identified and the associated information was extracted and analyzed. Organic molecules were defined as those molecules containing C-C, C-H, C-N, C-O, C-S, or halogen bonds without metals. This search resulted the big dataset named **Dataset A**. When analyzing the overall field of organic synthesis, the journal articles were limited to a selection of journals with relatively high impact to chemistry research and that have been consistent with CAS indexing coverage in the past two decades. A full list of titles of these journals can be found in the **Appendix II**.

Documents related to enzyme catalysis were searched within Dataset A based on the search terms, enzyme cataly?, Biomimetic?, Biocataly? and their presence in title, abstract or indexed fields. "?" here is a wild card that can represent any or zero character(s). A total 15,000 documents were resulted from 2000-2021, among them 9,800 were from 2011-2021. Documents related to photocatalysis were searched within dataset A based on the search term photocataly? and its presence in the title, abstract or indexed fields. A total of 14,000 documents were found in the years 2000-2021, and 13,000 were from 2011-2021. Documents related to green chemistry were searched within Dataset A with the search term: green chemistry? in the fields of title, abstract or indexed fields. A total of 85,000 documents were found from 2000-2021, and among them, about 60,000 were from 2011-2020.

When defining the affiliated countries/regions and organizations, the affiliation of the first author was taken as the affiliation of the document. When multiple organizations were affiliated with a particular journal or patent publication, only the first author or first patent assignee's affiliated organization was considered. The countries/regions of origin were assigned as the countries/regions in which the first author's or first patent assignee's affiliated organizations were located. Publications ascribed to China here only include those originating from the Mainland of China.

The concept networking graphs shown in figures 7, 8, 17, 18, 30, and 31 were generated by VOSviewer software version 1.6.18. Briefly, indexed concepts from the corresponding document sets were extracted together with cooccurrence information. The concept networking graphs were produced by calculating the top 1,000 concepts of occurrence and their cooccurrence data. Finally, parameters of label size and linkage thickness were adjusted for optimal display. The top 400 concept pairs of figures 7 and 8 are listed in appendixes.

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Appendix I. High-impact papers from the years 2011-2020

Table 1. Top 20 high-impact papers of 2011 in organic synthesis

No.	Paper Title	Journal Title/Year/Page #
1	"One-Pot" Synthesis of 5-(Hydroxymethyl)furfural from Carbohydrates using Tin-Beta Zeolite	ACS Catalysis, 2011, 1, 408-410
2	Trifluoromethylation of arenes and heteroarenes by means of photoredox catalysis	Nature, 2011, 480, 224-228
3	Rhodium(III)-Catalyzed Heterocycle Synthesis Using an Internal Oxidant: Improved Reactivity and Mechanistic Studies	Journal of the American Chemical Society, 2011, 133, 6449-6457
4	Hydrodeoxygenation of Furfural Over Supported Metal Catalysts: A Comparative Study of Cu, Pd and Ni	Catalysis Letters, 2011, 141, 784-791
5	Aqueous-phase hydrodeoxygenation of bio-derived phenols to cycloalkanes	Journal of Catalysis, 2011, 280, 8-16
6	Synthesis and Characterization of an Amino Functionalized MIL-101(Al): Separation and Catalytic Properties	Chemistry of Materials, 2011, 23, 2565-2572
7	Discovery of an α-Amino C-H Arylation Reaction Using the Strategy of Accelerated Serendipity	Science, 2011, 334, 1114-1117
8	Bifunctional transalkylation and hydrodeoxygenation of anisole over a Pt/HBeta catalyst	Journal of Catalysis, 2011, 281, 21-29
9	Selective conversion of furfural to methylfuran over silica-supported Ni-Fe bimetallic catalysts	Journal of Catalysis, 2011, 284, 90-101
10	Intermolecular Atom Transfer Radical Addition to Olefins Mediated by Oxidative Quenching of Photoredox Catalysts	Journal of the American Chemical Society, 2011, 133, 4160-4163
11	Innate C-H trifluoromethylation of heterocycles	Proceedings of the National Academy of Sciences of the United States of America, 2011, 108, 14411-14415,S14411/1-S14411/166
12	Rh(III)-Catalyzed Directed C-H Olefination Using an Oxidizing Directing Group: Mild, Efficient, and Versatile	Journal of the American Chemical Society, 2011, 133, 2350-2353
13	Design of solid acid catalysts for aqueous-phase dehydration of carbohydrates: The role of Lewis and Bronsted acid sites	Journal of Catalysis, 2011, 279, 174-182
14	Microwave-assisted synthesis of palladium nanoparticles supported on graphene: A highly active and recyclable catalyst for carbon-carbon cross-coupling reactions	Journal of Catalysis, 2011, 279, 1-11
15	Selective, Nickel-Catalyzed Hydrogenolysis of Aryl Ethers	Science, 2011, 332, 439-443
16	Highly Practical Copper(I)/TEMPO Catalyst System for Chemoselective Aerobic Oxidation of Primary Alcohols	Journal of the American Chemical Society, 2011, 133, 16901-16910
17	Collective synthesis of natural products by means of organocascade catalysis	Nature, 2011, 475, 183-188
18	Room-Temperature C-H Arylation: Merger of Pd-Catalyzed C-H Functionalization and Visible-Light Photocatalysis	Journal of the American Chemical Society, 2011, 133, 18566-18569
19	Oxidation of 5-hydroxymethylfurfural over supported Pt, Pd and Au catalysts	Catalysis Today, 2011, 160, 55-60
20	Direct Arylation as a Synthetic Tool for the Synthesis of Thiophene-Based Organic Electronic Materials	Chemistry of Materials, 2011, 23, 1594-1600

Table 2. Top 20 high-impact papers of 2012 in organic synthesis

No.	Paper Title	Journal Title/Year/Page #
1	BODIPY-Based Ratiometric Fluorescent Sensor for Highly Selective Detection of Glutathione over Cysteine and Homocysteine	Journal of the American Chemical Society, 2012, 134, 18928-18931
2	A highly selective ratiometric near-infrared fluorescent cyanine sensor for cysteine with remarkable shift and its application in bioimaging	Chemical Science, 2012, 3, 2760-2765
3	Pushing the limits of energetic materials - the synthesis and characterization of dihydroxylammonium 5,5′-bistetrazole-1,1′-diolate	Journal of Materials Chemistry, 2012, 22, 20418-20422
4	Automated design of ligands to polypharmacological profiles	Nature, 2012, 492, 215-220
5	Visible Light-Mediated Atom Transfer Radical Addition via Oxidative and Reductive Quenching of Photocatalysts	Journal of the American Chemical Society, 2012, 134, 8875-8884
6	Activation of remote meta-C-H bonds assisted by an end-on template	Nature, 2012, 486, 518-522
7	Production of 5-Hydroxymethylfurfural from Glucose Using a Combination of Lewis and Bronsted Acid Catalysts in Water in a Biphasic Reactor with an Alkylphenol Solvent	ACS Catalysis, 2012, 2, 930-934
8	Practical and innate carbon-hydrogen functionalization of heterocycles	Nature, 2012, 492, 95-99
9	o-Fluoroazobenzenes as Readily Synthesized Photoswitches Offering Nearly Quantitative Two-Way Isomerization with Visible Light	Journal of the American Chemical Society, 2012, 134, 20597-20600
10	Continuous-Flow Synthesis of the Anti-Malaria Drug Artemisinin	Angewandte Chemie, International Edition, 2012, 51, 1706-1709, S1706/1-S1706/20
11	Metal-free, visible-light-mediated direct C-H arylation of heteroarenes with aryl diazonium salts	Journal of the American Chemical Society, 2012, 134, 2958-2961
12	Merging Visible-Light Photocatalysis and Transition-Metal Catalysis in the Copper-Catalyzed Trifluoromethylation of Boronic Acids with CF3I	Journal of the American Chemical Society, 2012, 134, 9034-9037
13	Biotinylated Rh(III) Complexes in Engineered Streptavidin for Accelerated Asymmetric C-H Activation	Science, 2012, 338, 500-503
14	Discovery of 7-methyl-5-(1-{[3-(trifluoromethyl)phenyl]acetyl}-2,3-dihydro-1H-indol-5-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine (GSK2606414), a potent and selective first-in-class inhibitor of protein kinase R (PKR)-like endoplasmic reticulum kinase (PERK)	Journal of Medicinal Chemistry, 2012, 55, 7193-7207
15	Asymmetric spiroacetalization catalysed by confined Bronsted acids	Nature, 2012, 483, 315-319
16	Chitosan functionalized ionic liquid as a recyclable biopolymer-supported catalyst for cycloaddition of CO2	Green Chemistry, 2012, 14, 654-660
17	The role of gold acetylides as a selectivity trigger and the importance of gem-diaurated species in the gold-catalyzed hydroarylating-aromatization of arene-diynes	Organometallics, 2012, 31, 644-661
18	Click Synthesis, Aggregation-Induced Emission, E/Z Isomerization, Self-Organization, and Multiple Chromisms of Pure Stereoisomers of a Tetraphenylethene-Cored Luminogen	Journal of the American Chemical Society, 2012, 134, 9956-9966
19	End-group effects of piezofluorochromic aggregation-induced enhanced emission compounds containing distyrylanthracene	Journal of Materials Chemistry, 2012, 22, 18505-18513
20	Copper-Promoted Sulfenylation of sp2 C-H Bonds	Journal of the American Chemical Society, 2012, 134, 18237-18240

Table 3. Top 20 high-impact papers of 2013 in organic synthesis

No.	Paper Title	Journal Title/Year/Page #
1	Catalytic hydrotrifluoromethylation of styrenes and unactivated aliphatic alkenes via an organic photoredox system	Chemical Science, 2013, 4, 3160-3165
2	Nanoscale Fe2O3-Based Catalysts for Selective Hydrogenation of Nitroarenes to Anilines	Science, 2013, 342, 1073-1076
3	Dianhydrohexitols: new tools for organocatalysis. Application in enantioselective Friedel-Crafts alkylation of indoles with nitroalkenes	ARKIVOC, 2013 (iii), 227-244
4	Carbon-supported bimetallic Pd-Fe catalysts for vapor-phase hydrodeoxygenation of guaiacol	Journal of Catalysis, 2013, 306, 47-57
5	Olefin Cyclopropanation via Carbene Transfer Catalyzed by Engineered Cytochrome P450 Enzymes	Science, 2013, 339, 307-310
6	Sequence-Specific Peptide Synthesis by an Artificial Small-Molecule Machine	Science, 2013, 339, 189-193
7	Design and preparation of new palladium precatalysts for C-C and C-N cross-coupling reactions	Chemical Science, 2013, 4, 916-920
8	Enantio- and Diastereodivergent Dual Catalysis: α-Allylation of Branched Aldehydes	Science, 2013, 340, 1065-1068
9	Heterogenized cobalt oxide catalysts for nitroarene reduction by pyrolysis of molecularly defined complexes	Nature Chemistry, 2013, 5, 537-543
10	Direct evidence of a dinuclear copper intermediate in Cu(I)-catalyzed azide-alkyne cycloadditions	Science, 2013, 340, 457-460
11	Complex N-Heterocycle Synthesis via Iron-Catalyzed, Direct C-H Bond Amination	Science, 2013, 340, 591-595
12	Pd(II)-catalyzed alkoxylation of unactivated C(sp3)-H and C(sp2)-H bonds using a removable directing group: efficient synthesis of alkyl ethers	Chemical Science, 2013, 4, 4187-4192
13	A robustness screen for the rapid assessment of chemical reactions	Nature Chemistry, 2013, 5, 597-601
14	Potassium phthalimide-N-oxyl: a novel, efficient, and simple organocatalyst for the one-pot three-component synthesis of various 2-amino-4H-chromene derivatives in water	Tetrahedron, 2013, 69, 1074-1085
15	Metal-free oxidative tandem coupling of activated alkenes with carbonyl C(sp2)-H bonds and aryl C(sp2)-H bonds using TBHP	Chemical Science, 2013, 4, 2690-2694
16	Rh(III)-catalyzed C-H activation/[4 + 3] cycloaddition of benzamides and vinylcarbenoids: facile synthesis of azepinones	Chemical Science, 2013, 4, 3912-3916
17	Conversion of furfural into cyclopentanone over Ni-Cu bimetallic catalysts	Green Chemistry, 2013, 15, 1932-1940
18	Insights into the Interplay of Lewis and Bronsted Acid Catalysts in Glucose and Fructose Conversion to 5-(Hydroxymethyl)furfural and Levulinic Acid in Aqueous Media	Journal of the American Chemical Society, 2013, 135, 3997-4006
19	Photoredox Activation for the Direct ß-Arylation of Ketones and Aldehydes	Science, 2013, 339, 1593-1596
20	Rh(III)-Catalyzed Synthesis of Multisubstituted Isoquinoline and Pyridine N-Oxides from Oximes and Diazo Compounds	Journal of the American Chemical Society, 2013, 135, 12204-12207

Table 4. Top 20 high-impact papers of 2014 in organic synthesis

No.	Paper Title	Journal Title/Year/Page #
1	Shape-Controllable Formation of Poly-imidazolium Salts for Stable Palladium N-Heterocyclic Carbene Polymers	Scientific Reports, 2014, 4, 5478.
2	Single-electron transmetalation in organoboron cross-coupling by photoredox/nickel dual catalysis	Science, 2014, 345, 433-436
3	Formic-acid-induced depolymerization of oxidized lignin to aromatics	Nature, 2014, 515, 249-252
4	Production, properties and catalytic hydrogenation of furfural to fuel additives and value-added chemicals	Renewable & Sustainable Energy Reviews, 2014, 38, 663-676
5	Direct, Nonoxidative Conversion of Methane to Ethylene, Aromatics, and Hydrogen	Science, 2014, 344, 616-619
6	Multivalent N-Acetylgalactosamine-Conjugated siRNA Localizes in Hepatocytes and Elicits Robust RNAi-Mediated Gene Silencing	Journal of the American Chemical Society, 2014, 136, 16958-16961
7	Targeting transcription regulation in cancer with a covalent CDK7 inhibitor	Nature, 2014, 511, 616-620
8	FeOx-supported platinum single-atom and pseudo-single-atom catalysts for chemoselective hydrogenation of functionalized nitroarenes	Nature Communications, 2014, 5, 5634
9	Discovery of a Ni-Ga catalyst for carbon dioxide reduction to methanol	Nature Chemistry, 2014, 6, 320-324
10	Core-Shell Palladium Nanoparticle@Metal-Organic Frameworks as Multifunctional Catalysts for Cascade Reactions	Journal of the American Chemical Society, 2014, 136, 1738-1741
11	Reduction of aryl halides by consecutive visible light-induced electron transfer processes	Science, 2014, 346, 725-728
12	Silver nanoparticles immobilized on fibrous nano-silica as highly efficient and recyclable heterogeneous catalyst for reduction of 4-nitrophenol and 2-nitroaniline	Applied Catalysis, B: Environmental, 2014, 158-159, 129-135
13	Well-Defined Iron Catalysts for the Acceptorless Reversible Dehydrogenation-Hydrogenation of Alcohols and Ketones	ACS Catalysis, 2014, 4, 3994-4003
14	Vanillin, a promising biobased building-block for monomer synthesis	Green Chemistry, 2014, 16, 1987-1998
15	Air-stable carbonyl(pentamethylcyclopentadienyl)cobalt diiodide complex as a precursor for cationic (pentamethylcyclopentadienyl) cobalt(III) catalysis: Application for directed C-2 selective C-H amidation of indoles	Advanced Synthesis & Catalysis, 2014, 356, 1491-1495
16	Palladium-catalysed C-H activation of aliphatic amines to give strained nitrogen heterocycles	Nature, 2014, 510, 129-133
17	Ligand-controlled C(sp3)-H arylation and olefination in synthesis of unnatural chiral α-amino acids	Science, 2014, 343, 1216-1220
18	Co(III)-Catalyzed C-H Activation/Formal SN-Type Reactions: Selective and Efficient Cyanation, Halogenation, and Allylation	Journal of the American Chemical Society, 2014, 136, 17722-17725
19	Conformation-induced remote meta-C-H activation of amines	Nature, 2014, 507, 215-220
20	A Dual-Catalysis Approach to Enantioselective [2 + 2] Photocycloadditions Using Visible Light	Science, 2014, 344, 392-396

Table 5. Top 20 high-impact papers of 2015 in organic synthesis

No.	Paper Title	Journal Title/Year/Page #
1	Synthesis and antitumor activity of novel N-substituted carbazole imidazolium salt derivatives	Scientific Reports, 2015, 5, 13101
2	Parts-per-million level loading organocatalysed enantioselective silylation of alcohols	Nature Communications, 2015, 6, 7512
3	Asymmetric synthesis of syn-propargylamines and unsaturated ß-amino acids under Bronsted base catalysis	Nature Communications, 2015, 6, 8544
4	Selective hydrogenation of 1,3-butadiene on platinum-copper alloys at the single-atom limit	Nature Communications, 2015, 6, 8550
5	A C-H bond activation-based catalytic approach to tetrasubstituted chiral allenes	Nature Communications, 2015, 6, 7946
6	A general method to improve fluorophores for live-cell and single-molecule microscopy	Nature Methods, 2015, 12, 244-250
7	Phthalimide conjugation as a strategy for in vivo target protein degradation	Science, 2015, 348, 1376-1381
8	Highly efficient blue electroluminescence based on thermally activated delayed fluorescence	Nature Materials, 2015, 14, 330-336
9	Asymmetric intramolecular α-cyclopropanation of aldehydes using a donor/acceptor carbene mimetic	Nature Communications, 2015, 6, 10041
10	A Series of Simple Oligomer-like Small Molecules Based on Oligothiophenes for Solution-Processed Solar Cells with High Efficiency	Journal of the American Chemical Society, 2015, 137, 3886-3893
11	Reductive lignocellulose fractionation into soluble lignin-derived phenolic monomers and dimers and processable carbohydrate pulps	Energy & Environmental Science, 2015, 8, 1748-1763
12	A Stable Single-Site Palladium Catalyst for Hydrogenations	Angewandte Chemie, International Edition, 2015, 54, 11265-11269
13	Stable, crystalline, porous, covalent organic frameworks as a platform for chiral organocatalysts	Nature Chemistry, 2015, 7, 905-912
14	Stabilizing triplet excited states for ultralong organic phosphorescence	Nature Materials, 2015, 14, 685-690
15	Hijacking the E3 Ubiquitin Ligase Cereblon to Efficiently Target BRD4	Chemistry & Biology, 2015, 22, 755-763
16	Ni@Pd core-shell nanoparticles modified fibrous silica nanospheres as highly efficient and recoverable catalyst for reduction of 4-nitrophenol and hydrodechlorination of 4-chlorophenol	Applied Catalysis, B: Environmental, 2015, 162, 372-380
17	Site-selective arene C-H amination via photoredox catalysis	Science, 2015, 349, 1326-1330
18	In Situ-Generated Co0-Co3O4/N-Doped Carbon Nanotubes Hybrids as Efficient and Chemoselective Catalysts for Hydrogenation of Nitroarenes	ACS Catalysis, 2015, 5, 4783-4789
19	Polyoxometalate-based homochiral metal-organic frameworks for tandem asymmetric transformation of cyclic carbonates from olefins	Nature Communications, 2015, 6, 10007
20	Nickel-Catalyzed Cross-Coupling of Photoredox-Generated Radicals: Uncovering a General Manifold for Stereoconvergence in Nickel-Catalyzed Cross-Couplings	Journal of the American Chemical Society, 2015, 137, 4896-4899

Table 6. Top 20 high-impact papers of 2016 in organic synthesis

No.	Paper Title	Journal Title/Year/Page #
1	Assembled molecular face-rotating polyhedra to transfer chirality from two to three dimensions	Nature Communications, 2016, 7, 12469
2	Pd(II)-catalysed meta-C-H functionalizations of benzoic acid derivatives	Nature Communications, 2016, 7, 10443
3	Palladium-catalyzed formation of vicinal all-carbon quaternary centres via propargylation	Nature Communications, 2016, 7, 12382
4	Palladium/N-heterocyclic carbene catalysed regio and diastereoselective reaction of ketones with allyl reagents via inner-sphere mechanism	Nature Communications, 2016, 7, 11806
5	Practical carbon-carbon bond formation from olefins through nickel-catalyzed reductive olefin hydrocarbonation	Nature Communications, 2016, 7, 11129
6	Stereoselective alkoxycarbonylation of unactivated C(sp3)-H bonds with alkyl chloroformates via Pd(II)/Pd(IV) catalysis	Nature Communications, 2016, 7, 12901
7	Catalytic N-radical cascade reaction of hydrazones by oxidative deprotonation electron transfer and TEMPO mediation	Nature Communications, 2016, 7, 11188
8	Metal-organic frameworks as selectivity regulators for hydrogenation reactions	Nature, 2016, 539, 76-80
9	Enantioselective desymmetrization of cyclohexadienones via an intramolecular Rauhut-Currier reaction of allenoates	Nature Communications, 2016, 7, 13024
10	Continuous hydrogenation of ethyl levulinate to γ-valerolactone and 2-methyl tetrahydrofuran over alumina doped Cu/SiO2 catalyst: the potential of commercialization	Scientific Reports, 2016, 6, 28898
11	Radical aryl migration enables diversity-oriented synthesis of structurally diverse medium/macro- or bridged-rings	Nature Communications, 2016, 7, 13852
12	High-effective approach from amino acid esters to chiral amino alcohols over Cu/ZnO/Al2O3 catalyst and its catalytic reaction mechanism	Scientific Reports, 2016, 6, 33196
13	Donor-Acceptor Fluorophores for Visible-Light-Promoted Organic Synthesis: Photoredox/Ni Dual Catalytic C(sp3)-C(sp2) Cross-Coupling	ACS Catalysis, 2016, 6, 873-877
14	Discovery and enantiocontrol of axially chiral urazoles via organocatalytic tyrosine click reaction	Nature Communications, 2016, 7, 10677
15	A method for controlling the synthesis of stable twisted two-dimensional conjugated molecules	Nature Communications, 2016, 7, 11637
16	A general alkyl-alkyl cross-coupling enabled by redox-active esters and alkylzinc reagents	Science, 2016, 352, 801-805
17	A two-step approach to achieve secondary amide transamidation enabled by nickel catalysis	Nature Communications, 2016, 7, 11554
18	Catalytic alkylation of remote C-H bonds enabled by proton-coupled electron transfer	Nature, 2016, 539, 268-271
19	Functionalization of C(sp3)-H bonds using a transient directing group	Science, 2016, 351, 252-256
20	Spiro[pyrrolidine-3,3'-oxindole] as potent anti-breast cancer compounds: Their design, synthesis, biological evaluation and cellular target identification	Scientific Reports, 2016, 6, 32213

Table 7. Top 20 high-impact papers of 2017 in organic synthesis

No.	Paper Title	Journal Title/Year/Page #
1	A reaction mode of carbene-catalysed aryl aldehyde activation and induced phenol OH functionalization	Nature Communications, 2017, 8, 15598
2	Controllable cyanation of carbon-hydrogen bonds by zeolite crystals over manganese oxide catalyst	Nature Communications, 2017, 8, 15240
3	Oxidative 1,2-carboamination of alkenes with alkyl nitriles and amines toward γ-amino alkyl nitriles	Nature Communications, 2017, 8, 14720
4	Biomimetically inspired asymmetric total synthesis of (+)-19-dehydroxyl arisandilactone A	Nature Communications, 2017, 8, 14233
5	A bioinspired and biocompatible ortho-sulfiliminyl phenol synthesis	Nature Communications, 2017, 8, 15912
6	Synthesis and biological evaluation of novel ursolic acid analogues as potential α-glucosidase inhibitors	Scientific Reports, 2017, 7, 45578
7	Synthesis, Fungicidal Activity, and Structure Activity Relationship of ß-Acylaminocycloalkylsulfonamides against Botrytis cinerea	Scientific Reports, 2017, 7, 42096
8	Photo-induced oxidant-free oxidative C-H/N-H cross-coupling between arenes and azoles	Nature Communications, 2017, 8, 14226
9	Catalytic asymmetric radical aminoperfluoroalkylation and aminodifluoromethylation of alkenes to versatile enantioenriched-fluoroalkyl amines	Nature Communications, 2017, 8, 14841
10	Synergy of Lewis and Bronsted acids on catalytic hydrothermal decomposition of carbohydrates and corncob acid hydrolysis residues to 5-hydroxymethylfurfural	Scientific Reports, 2017, 7, 40908
11	Palladium-catalysed synthesis of triaryl(heteroaryl)methanes	Nature Communications, 2017, 8, 14641
12	Regioselectivity and Mechanism of Synthesizing N-Substituted 2-Pyridones and 2-Substituted Pyridines via Metal-Free C-O and C-N Bond-Cleaving of Oxazoline[3,2-a]pyridiniums	Scientific Reports, 2017, 7, 41287
13	Photo-driven redox-neutral decarboxylative carbon-hydrogen trifluoromethylation of (hetero)arenes with trifluoroacetic acid	Nature Communications, 2017, 8, 14353
14	Nickel-catalyzed retro-hydroamidocarbonylation of aliphatic amides to olefins	Nature Communications, 2017, 8, 14993
15	Selective production of arenes via direct lignin upgrading over a niobium-based catalyst	Nature Communications, 2017, 8, 16104
16	Synthesis and biological activity of myricetin derivatives containing 1,3,4-thiadiazole scaffold	Chemistry Central Journal, 2017, 11, 106
17	Predictive compound accumulation rules yield a broad-spectrum antibiotic	Nature, 2017, 545, 299-304
18	A unique Pd-catalysed Heck arylation as a remote trigger for cyclopropane selective ring-opening	Nature Communications, 2017, 8, 14200
19	Synthesis and protective effect of new ligustrazine-vanillic acid derivatives against CoCl2-induced neurotoxicity in differentiated PC12 cells	Chemistry Central Journal, 2017, 11, 20
20	Formation of diverse polycyclic spirooxindoles via three-component reaction of isoquinolinium salts, isatins and malononitrile	Scientific Reports, 2017, 7, 41024

Table 8. Top 20 high-impact papers of 2018 in organic synthesis

No.	Paper Title	Journal Title/Year/Page #
1	Ultrasound-promoted Bronsted acid ionic liquid-catalyzed hydrothiocyanation of activated alkynes under minimal solvent conditions	Green Chemistry, 2018, 20, 3683-3688
2	Synthesis and evaluation of a new type of small molecule epigenetic modulator containing imidazo[1,2-b][1,2,4]triazole motif	Frontiers in Chemistry, 2018, 6, 642pp.
3	Incorporation of Imidazolium-Based Poly(ionic liquid)s into a Metal-Organic Framework for CO2 Capture and Conversion	ACS Catalysis, 2018, 8, 3194-3201
4	Predicting reaction performance in C-N cross-coupling using machine learning	Science, 2018, 360, 186-190
5	Metal-free deoxygenative sulfonylation of quinoline N-oxides with sodium sulfinates via a dual radical coupling process	Organic Chemistry Frontiers, 2018, 5, 2604-2609
6	Benzoxazole-Linked Ultrastable Covalent Organic Frameworks for Photocatalysis	Journal of the American Chemical Society, 2018, 140, 4623-4631
7	Nitrogen vacancy engineered graphitic C3N4-based polymers for photocatalytic oxidation of aromatic alcohols to aldehydes	Applied Catalysis, B: Environmental, 2018, 221, 626-634
8	Design and synthesis of novel 3-(thiophen-2-yl)-1,5-dihydro-2H-pyrrol-2-one derivatives bearing a hydrazone moiety as potential fungicides	Chemistry Central Journal, 2018, 12, 83
9	Photoinduced Remote Functionalisations by Iminyl Radical Promoted C-C and C-H Bond Cleavage Cascades	Angewandte Chemie, International Edition, 2018, 57, 744-748
10	Controlling an organic synthesis robot with machine learning to search for new reactivity	Nature, 2018, 559, 377-381
11	Decarboxylative C(sp3)-N cross-coupling via synergetic photoredox and copper catalysis	Nature Catalysis, 2018, 1, 120-126
12	Efficient Syntheses of Diverse, Medicinally Relevant Targets Planned by Computer and Executed in the Laboratory	Chem, 2018, 4, 522-532
13	Rhodium(III)-catalyzed annulative coupling between arenes and sulfoxonium ylides via C-H activation	Organic Chemistry Frontiers, 2018, 5, 998-1002
14	Direct arylation of strong aliphatic C-H bonds	Nature, 2018, 560, 70-75
15	Catalytic enantioselective Minisci-type addition to heteroarenes	Science, 2018, 360, 419-422
16	Cooperative Multifunctional Organocatalysts for Ambient Conversion of Carbon Dioxide into Cyclic Carbonates	ACS Catalysis, 2018, 8, 9945-9957
	Selective Electrochemical Production of Formate from Carbon Dioxide with Bismuth-Based Catalysts in an Aqueous Electrolyte	ACS Catalysis, 2018, 8, 931-937
	Solvent-enabled control of reactivity for liquid-phase reactions of biomass-derived compounds	Nature Catalysis, 2018, 1, 199-207
19	Iron-Catalyzed Methylation Using the Borrowing Hydrogen Approach	ACS Catalysis, 2018, 8, 6440-6445
20	Cobalt(II)-Catalyzed Electrooxidative C-H Amination of Arenes with Alkylamines	Journal of the American Chemical Society, 2018, 140, 4195-4199
	Decarboxylative sp3 C-N coupling via dual copper and photoredox catalysis	Nature, 2018, 559, 83-88
	Magnetically retrievable nanocomposite adorned with Pd nanocatalysts: efficient reduction of nitroaromatics in aqueous media	Green Chemistry, 2018, 20, 3809-3817
	Metal-Free Visible-Light-Induced C-H/C-H Cross-Dehydrogenative-Coupling of Quinoxalin-2(H)-ones with Simple Ethers	ACS Sustainable Chemistry & Engineering, 2018, 6, 17252-17257

Table 9. Top 20 high-impact papers of 2019 in organic synthesis

No.	Paper Title	Journal Title/Year/Page #
1	Copper-catalyzed enantioselective Sonogashira-type oxidative cross-coupling of unactivated C(sp3)-H bonds with alkynes	Nature Communications, 2019, 10, 5689
2	Palladium-catalyzed Suzuki-Miyaura coupling of thioureas or thioamides	Nature Communications, 2019, 10, 5709
3	Synthesis of higher carboxylic acids from ethers, CO2 and H2	Nature Communications, 2019, 10, 5395
4	Stereodivergent assembly of tetrahydro-γ-carbolines via synergistic catalytic asymmetric cascade reaction	Nature Communications, 2019, 10, 5553
5	Synthesis and biological evaluation of 4ß-N-acetylamino substituted podophyllotoxin derivatives as novel anticancer agents	Frontiers in Chemistry, 2019, 7, 253
6	Atomically dispersed Fe3+ sites catalyze efficient CO2 electroreduction to CO	Science, 2019, 364, 1091-1094
7	Heterogeneous synergistic catalysis for promoting Aza-Michael-Henry tandem reaction for the synthesis of chiral 3-nitro-1,2-dihydroquinoline	Catalysts, 2019, 9, 713
8	Selective synthesis of spirobiindanes, alkenyl chlorides, and monofluoroalkenes from unactivated gem-difluoroalkanes controlled by aluminum-based Lewis acids	Scientific Reports, 2019, 9, 19113
9	Synergy between ionic liquids and CuCl2 in gas-liquid phase reactions of acetylene hydrochlorination	Catalysts, 2019, 9, 504
10	A near-infrared ratiometric fluorescent probe for highly selective recognition and bioimaging of cysteine	Frontiers in Chemistry, 2019, 7, 32
11	Highly selective oxidation of 5-Hydroxymethylfurfural to 5-Hydroxymethyl- 2-Furancarboxylic acid by a robust whole-cell biocatalyst	Catalysts, 2019, 9, 526
12	Visible-light-induced deoxygenative C2-sulfonylation of quinoline N-oxides with sulfinic acids	Green Chemistry, 2019, 21, 3858-3863
13	Photocatalytic decarboxylative alkylations mediated by triphenylphosphine and sodium iodide	Science, 2019, 363, 1429-1434
14	Pd-Co nanoparticles supported on calcined Mg-Fe hydrotalcites for the Suzuki-Miyaura reaction in water with high turnover numbers	Catalysts, 2019, 9, 1061
15	Heterogeneous bimetallic Cu-Ni nanoparticle-supported catalysts in the selective oxidation of benzyl alcohol to benzaldehyde	Catalysts, 2019, 9, 538
16	Design, synthesis and herbicidal activity evaluation of novel aryl-naphthyl methanone derivatives	Frontiers in Chemistry, 2019, 7, 2
17	Photoredox catalysis using infrared light via triplet fusion upconversion	Nature, 2019, 565, 343-346
18	The steric effect in green benzylation of arenes with benzyl alcohol catalyzed by hierarchical H-beta zeolite	Catalysts, 2019, 9, 869
19	Metal-free C3-alkoxycarbonylation of quinoxalin-2(1H)-ones with carbazates as ecofriendly ester sources	Science China: Chemistry, 2019, 62, 460-464
20	Aluminium-biochar composites as sustainable heterogeneous catalysts for glucose isomerisation in a biorefinery	Green Chemistry, 2019, 21, 1267-1281
	Catalyst-free visible-light-initiated oxidative coupling of aryldiazo sulfones with thiols leading to unsymmetrical sulfoxides in air	Green Chemistry, 2019, 21, 1609-1613

Table 10. Top 20 high-impact papers of 2020 in organic synthesis

No.	Paper Title	Journal Title/Year/Page #
1	α-Ketoamides as Broad-Spectrum Inhibitors of Coronavirus and Enterovirus Replication: Structure-Based Design, Synthesis, and Activity Assessment	Journal of Medicinal Chemistry, 2020, 63, 4562-4578
2	Additive-free Baeyer-Villiger oxidation of cyclic ketone catalyzed by carboxylic-functionalized poly(ionic liquids) and polyoxometalate ionic self-assemblies	Catalysts, 2020, 10, 127
3	Titania supported synergistic palladium single atoms and nanoparticles for room temperature ketone and aldehydes hydrogenation	Nature Communications, 2020, 11, 48
4	Ligand-promoted cobalt-catalyzed radical hydroamination of alkenes	Nature Communications, 2020, 11, 783
5	Coordination structure dominated performance of single-atomic Pt catalyst for anti-Markovnikov hydroboration of alkenes	Science China Materials, 2020, 63, 972-981
6	Radical-mediated C-C cleavage of unstrained cycloketones and DFT study for unusual regioselectivity	Nature Communications, 2020, 11, 672
7	Visible-light-initiated regioselective sulfonylation/cyclization of 1,6-enynes under photocatalyst- and additive-free conditions	Green Chemistry, 2020, 22, 1388-1392
8	Atroposelective Synthesis of 3,3'-Bisindoles Bearing Axial and Central Chirality: Using Isatin-Derived Imines as Electrophiles	Chinese Journal of Chemistry, 2020, 38, 583-589
9	Axially Chiral Aryl-Alkene-Indole Framework: A Nascent Member of the Atropisomeric Family and Its Catalytic Asymmetric Construction	Chinese Journal of Chemistry, 2020, 38, 543-552
10	Bromide-Promoted Visible-Light-Induced Reductive Minisci Reaction with Aldehydes	ACS Catalysis, 2020, 10, 154-159
11	The clean preparation of multisubstituted pyrroles under metal- and solvent-free conditions	Green Chemistry, 2020, 22, 118-122
12	Photochemical oxidation of benzylic primary and secondary alcohols utilizing air as the oxidant	Green Chemistry, 2020, 22, 471-477
13	Acyl Migration versus Epoxidation in Gold Catalysis: Facile, Switchable, and Atom-Economic Synthesis of Acylindoles and Quinoline Derivatives	Angewandte Chemie, International Edition, 2020, 59, 471-478
14	Endo-selective construction of spiro-[butyrolactone-pyrrolidine] via Ag(I)/CAAA-amidphos-catalyzed 1,3-dipolar cycloaddition between azomethine ylides and α-methylene-γ-butyrolactone	Catalysts, 2020, 10, 28
15	Highly Active ZnO-ZrO2 Aerogels Integrated with H-ZSM-5 for Aromatics Synthesis from Carbon Dioxide	ACS Catalysis, 2020, 10, 302-310
16	Metal-free photoredox-catalysed formal C-H/C-H coupling of arenes enabled by interrupted Pummerer activation	Nature Catalysis, 2020, 3, 163-169
17	Palladium-decorated o-phenylenediamine-functionalized Fe3O4/SiO2 magnetic nanoparticles: A promising solid-state catalytic system used for Suzuki-Miyaura coupling reactions	Journal of Physics and Chemistry of Solids, 2020, 136, 109200
18	Potent Reductants via Electron-Primed Photoredox Catalysis: Unlocking Aryl Chlorides for Radical Coupling	Journal of the American Chemical Society, 2020, 142, 2093-2099
19	Reductive Electrophotocatalysis: Merging Electricity and Light To Achieve Extreme Reduction Potentials	Journal of the American Chemical Society, 2020, 142, 2087-2092
20	Visible-light-induced decarboxylative acylation of quinoxalin-2(1H)-ones with α-oxo carboxylic acids under metal, strong oxidant and external photocatalyst-free conditions	Green Chemistry, 2020, 22, 1720-1725

Appendix II. Selected journal titles

Accounts of Chemical Research

Accounts of Materials Research

ACS Agricultural Science & Technology

ACS Applied Bio Materials

ACS Applied Electronic Materials

ACS Applied Energy Materials

ACS Applied Materials & Interfaces

ACS Applied Nano Materials

ACS Applied Polymer Materials

ACS Bio & Med Chem Au

ACS Biomaterials Science & Engineering

ACS Catalysis

ACS Central Science

ACS Chemical Biology

ACS Chemical Health & Safety

ACS Chemical Neuroscience

ACS Earth and Space Chemistry

ACS Energy Letters

ACS Engineering Au

ACS Environmental Au

ACS ES&T Engineering

ACS ES&T Water

ACS Food Science & Technology

ACS Infectious Diseases

ACS Macro Letters

ACS Materials Au

ACS Materials Letters

ACS Measurement Science Au

ACS Medicinal Chemistry Letters

ACS Nano

ACS Nanoscience Au

ACS Omega

ACS Organic & Inorganic Au

ACS Pharmacology & Translational Science

ACS Photonics

ACS Physical Chemistry Au

ACS Polymers Au

ACS Sensors

ACS Sustainable Chemistry & Engineering

ACS Synthetic Biology

Acta Materialia

Advanced Functional Materials

Advanced Materials (Weinheim, Germany)

Advanced Synthesis & Catalysis

AIChE Journal

Analyst (Cambridge, United Kingdom)

Analytica Chimica Acta

Analytical and Bioanalytical Chemistry

Analytical Biochemistry

Analytical Chemistry (Washington, DC, United States)

Analytical Letters

Angewandte Chemie, International Edition

Applied Catalysis, A: General

Applied Catalysis, B: Environmental

Applied Organometallic Chemistry

Applied Physics Letters

Applied Surface Science

Archiv der Pharmazie (Weinheim, Germany)

Archives of Pharmacal Research

Australian Journal of Chemistry

Biochemical Pharmacology (Amsterdam, Netherlands)

Biochemistry

Biochimica et Biophysica Acta, Biomembranes

Biochimica et Biophysica Acta, General Subjects

Biochimica et Biophysica Acta, Molecular Basis of Disease

Biochimica et Biophysica Acta, Proteins and Proteomics

Bioconjugate Chemistry

Biomacromolecules

Biomaterials

Bioorganic & Medicinal Chemistry

Bioorganic & Medicinal Chemistry Letters

Bioorganic Chemistry

Biophysical Journal

Biopolymers

Bulletin of the Chemical Society of Japan

Canadian Journal of Chemistry

Carbohydrate Polymers

Carbohydrate Research

Carbon

Catalysis Communications

Catalysis Letters

Catalysis Science & Technology

Catalysis Today

Cell (Cambridge, MA, United States)

ChemCatChem

Chemical Biology & Drug Design

Chemical Communications (Cambridge, United Kingdom)

Chemical Engineering & Technology

Chemical Engineering Communications

Chemical Engineering Journal (Amsterdam, Netherlands)

Chemical Engineering Science

Chemical Engineering Science: X

Chemical Geology

Chemical Physics

Chemical Physics Letters

Chemical Research in Toxicology

Chemical Reviews (Washington, DC, United States)

Chemistry - A European Journal

Chemistry - An Asian Journal

Chemistry & Biodiversity

Chemistry and Technology of Fuels and Oils

Chemistry of Heterocyclic Compounds (New York, NY, United States)

Chemistry of Materials

Chemistry of Natural Compounds

ChemMedChem

ChemPhysChem

ChemRxiv

ChemSusChem

Chinese Chemical Letters

Chromatographia

Colloid and Polymer Science

Comptes Rendus Chimie

Corrosion Science

Crystal Growth & Design

Current Biology

Dalton Transactions

Diamond and Related Materials

Dyes and Pigments

Electroanalysis

Electrochimica Acta

Electrophoresis

EMBO Journal

Energy & Fuels

Environmental Science & Technology

Environmental Science & Technology Letters

Environmental Toxicology and Chemistry

Environmental Toxicology and Pharmacology

European Journal of Inorganic Chemistry

European Journal of Medicinal Chemistry

European Journal of Organic Chemistry

European Polymer Journal

FEBS Journal

FEBS Letters

Food Chemistry

Food Chemistry: X

Free Radical Biology & Medicine

Fuel

Gene

Geochimica et Cosmochimica Acta

Green Chemistry

Helvetica Chimica Acta

Heteroatom Chemistry

Human Molecular Genetics

Industrial & Engineering Chemistry Research

Inorganic Chemistry

Inorganic Chemistry Communications

Inorganica Chimica Acta

International Journal of Antimicrobial Agents

International Journal of Chemical Kinetics

International Journal of Hydrogen Energy

International Journal of Pharmaceutics (Amsterdam, Netherlands)

International Journal of Pharmaceutics: X

JACS Au

JBIC, Journal of Biological Inorganic Chemistry

Journal of Agricultural and Food Chemistry

Journal of Alloys and Compounds

Journal of Analytical Atomic Spectrometry

Journal of Analytical Chemistry

Journal of Antibiotics

Journal of Antimicrobial Chemotherapy

Journal of Applied Physics (Melville, NY, United States)

Journal of Applied Polymer Science

Journal of Biological Chemistry

Journal of Biomedical Materials Research, Part A

Journal of Biomedical Materials Research, Part B: Applied Biomaterials

Journal of Carbohydrate Chemistry

Journal of Catalysis

Journal of Chemical & Engineering Data

Journal of Chemical Information and Modeling

Journal of Chemical Physics
Journal of Chemical Theory and Computation
Journal of Chromatography A
Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences
Journal of Colloid and Interface Science
Journal of Computational Chemistry
Journal of Coordination Chemistry
Journal of Crystal Growth
Journal of Electroanalytical Chemistry
Journal of Enzyme Inhibition and Medicinal Chemistry
Journal of Fluorine Chemistry
Journal of Hazardous Materials
Journal of Heterocyclic Chemistry
Journal of Inorganic Biochemistry
Journal of Labelled Compounds and Radiopharmaceuticals
Journal of Magnetism and Magnetic Materials
Journal of Mass Spectrometry
Journal of Materials Chemistry A: Materials for Energy and Sustainability
Journal of Materials Chemistry B: Materials for Biology and Medicine
Journal of Materials Chemistry C: Materials for Optical and Electronic Devices
Journal of Materials Science
Journal of Medicinal Chemistry
Journal of Membrane Science
Journal of Molecular Biology
Journal of Molecular Structure
Journal of Natural Products
Journal of Neurochemistry
Journal of Non-Crystalline Solids
Journal of Non-Crystalline Solids: X
Journal of Organic Chemistry
Journal of Organometallic Chemistry
Journal of Peptide Science
Journal of Pharmaceutical and Biomedical Analysis
Journal of Pharmaceutical Sciences (Philadelphia, PA, United States)
Journal of Physical Chemistry A
Journal of Physical Chemistry B
Journal of Physical Chemistry C
Journal of Physical Chemistry Letters
Journal of Physical Organic Chemistry
Journal of Physics B: Atomic, Molecular and Optical Physics
Journal of Physics: Condensed Matter
Journal of Plant Physiology
Journal of Polymer Science (Hoboken, NJ, United States)
Journal of Power Sources
Journal of Proteome Research
Journal of Radioanalytical and Nuclear Chemistry
Journal of Separation Science
Journal of Solid State Chemistry
Journal of the American Ceramic Society
Journal of the American Chemical Society
Journal of the American Society for Mass Spectrometry
Journal of the Electrochemical Society
Langmuir
Letters in Organic Chemistry
Lipids
Macromolecular Chemistry and Physics
Macromolecular Rapid Communications
Macromolecular Research
Macromolecules (Washington, DC, United States)
Magnetic Resonance in Chemistry
Materials Chemistry and Physics
Materials Letters
Materials Letters: X
Materials Science & Engineering, A: Structural Materials: Properties, Microstructure and Processing
Materials Science & Engineering, B: Advanced Functional Solid-State Materials
Medicinal Chemistry Research
Mendeleev Communications
Microporous and Mesoporous Materials
Molecular Catalysis
Molecular Immunology
Molecular Pharmaceutics
Monatshefte fuer Chemie
Nano Letters
Natural Product Research
Nature (London, United Kingdom)
Nature Chemical Biology
Nature Chemistry
Nature Materials
Nature Nanotechnology
New Journal of Chemistry
Nucleic Acids Research

Nucleosides, Nucleotides & Nucleic Acids

Oncogene

Organic & Biomolecular Chemistry

Organic Letters

Organic Preparations and Procedures International

Organic Process Research & Development

Organometallics

Peptide Science (Hoboken, NJ, United States)

Pharmaceutical Chemistry Journal

Pharmaceutical Research

Phosphorus, Sulfur and Silicon and the Related Elements

Physical Chemistry Chemical Physics

Phytochemistry (Elsevier)

Polycyclic Aromatic Compounds

Polyhedron

Polymer

Polymer Bulletin (Heidelberg, Germany)

Polymer Degradation and Stability

Polymer Engineering & Science

Polymer International

Polymer Journal (Tokyo, Japan)

Polymers for Advanced Technologies

Proceedings of the National Academy of Sciences of the United States of America

Proteins: Structure, Function, and Bioinformatics

Rapid Communications in Mass Spectrometry

Reactive & Functional Polymers

Research on Chemical Intermediates

Review of Scientific Instruments

Russian Chemical Bulletin

Russian Journal of Applied Chemistry

Russian Journal of General Chemistry

Russian Journal of Organic Chemistry

Science (Washington, DC, United States)

Science of the Total Environment

Separation and Purification Technology

Small

Soil Biology & Biochemistry

Spectrochimica Acta, Part A: Molecular and Biomolecular Spectroscopy

Spectrochimica Acta, Part B: Atomic Spectroscopy

Steroids

Structural Chemistry

Surface Science

Synlett

Synthesis

Synthetic Communications

Synthetic Metals

Talanta

Tetrahedron

Tetrahedron Letters

Thin Solid Films

Topics in Catalysis

Toxicological Sciences

Toxicology

Toxicology In Vitro

Toxicology Letters

Virology

Nature Catalysis

Nature Communications

Science Advances

Matter

Joule

Chemical Science

CCS Chemistry

Science China Chemistry

Science China Materials

Advanced Science

Materials Horizons

Chem

Organic Chemistry Frontiers

Inorganic Chemistry Frontiers

Polymer Chemistry

Appendix III. Journal 4.0.0. cluster list

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
263	crystal structure	-0.1281	-0.0739	Blue	414	79016	15257
600	molecular structure	-0.1632	-0.2044	Blue	414	72031	13561
156	biomedical	-0.1806	0.8846	Yellow	407	61076	13176
968	uv and visible spectra	0.5912	-0.0727	Blue	410	55479	7741
296	diastereoselective synthesis	-0.9243	-0.1491	Red	359	29221	7683
99	antitumor agents	-0.2621	0.8481	Yellow	392	38257	7243
936	thermal stability	0.7179	0.0221	Green	411	40948	6365
399	fluorescence	0.4341	0.3015	Blue	411	38147	5994
354	enantioselective synthesis	-0.8746	-0.2167	Red	356	19956	5724
913	surface area	0.3063	-0.6736	Green	403	36076	5631
835	regioselective synthesis	-0.9724	-0.2932	Red	349	22089	5491
439	green chemistry	-0.5481	-0.1606	Red	399	25491	5461
619	nanoparticles	0.3785	-0.3073	Green	406	28895	5372
926	tandem reaction	-0.9466	-0.2376	Red	371	22631	4864
629	neoplasm	-0.4294	0.8501	Yellow	370	24311	4422
901	structure-activity relationship	-0.4355	1.037	Yellow	351	15529	4373
465	homo (molecular orbital)	0.8016	-0.1302	Blue	398	36165	4289
553	lumo (molecular orbital)	0.7439	-0.102	Blue	397	35841	4233
270	cyclization	-0.8576	-0.1215	Red	399	18579	4232
819	reaction mechanism	-0.1459	-0.5217	Red	397	22839	4108
595	molecular docking	-0.5623	0.72	Yellow	352	22183	4061
478	hydrogen bond	0.2061	0.2883	Blue	411	26680	4050
288	density functional theory	0.1968	-0.308	Blue	409	20927	3806
915	surface structure	0.4251	-0.3898	Green	398	24875	3670
774	pore size	0.3849	-0.6164	Green	380	22284	3447
22	adsorption	0.5378	-0.56	Green	373	21268	3409
674	oxidation	-0.1469	-0.3998	Red	411	15998	3333
514	ir spectra	0.6028	-0.4796	Green	387	22328	3109
35	alkenes	-0.4892	-0.5477	Red	366	12354	2981
853	self-assembly	0.5497	0.3559	Green	393	17038	2966
775	pore size distribution	0.5353	-0.6663	Green	376	20793	2965
988	x-ray photoelectron spectra	0.6535	-0.7771	Green	339	19153	2825
332	electric current-potential relationship	1.0432	-0.3951	Blue	341	19947	2794
269	cyclic voltammetry	0.6398	-0.6188	Blue	387	20423	2756
957	transition state structure	-0.396	-0.4226	Red	380	16542	2755
406	fluorescent indicators	0.4737	0.9884	Yellow	335	12777	2713
75	antibacterial agents	-0.4052	0.5997	Yellow	395	16072	2621

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
420	fused heterocyclic compounds	-1.005	0.1422	Red	327	12788	2535
700	ph	0.4246	0.4478	Yellow	372	12779	2418
431	glass transition temperature	1.0962	0.2559	Green	319	14063	2359
479	hydrogenation	0.0614	-0.7149	Green	376	11260	2313
264	crystallinity	0.4695	-0.3011	Green	374	15903	2307
675	oxidation catalysts	-0.0635	-0.7727	Green	356	10917	2275
877	solvent effect	0.1976	0.0074	Blue	409	13284	2243
691	particle size	0.3915	0.0821	Green	383	13928	2162
480	hydrogenation catalysts	0.132	-0.8376	Green	326	10406	2145
173	c-h bond activation	-0.8703	-0.5427	Red	332	10101	2141
504	indoles	-1.0032	-0.1074	Red	337	9584	2135
466	homo (molecular orbital), lumo gap	0.4896	0.1138	Blue	382	18415	2131
53	amines	-0.6458	-0.098	Red	378	9696	2127
639	nmr (nuclear magnetic resonance)	0.5352	-0.2632	Blue	393	15132	2105
208	chemoselectivity	-0.8249	-0.3994	Red	347	9083	2072
401	fluorescence imaging	0.4348	1.0492	Yellow	296	11212	2061
28	aldehydes	-0.6615	-0.2978	Red	373	9223	2049
886	stability	0.3752	0.2385	Green	401	12571	2046
587	microstructure	0.6773	-0.4501	Green	361	13572	2037
711	pharmacokinetics	-0.2736	0.9775	Yellow	319	10312	2031
412	free energy	0.0201	-0.4389	Blue	404	12698	2026
726	photoluminescence	0.9452	-0.3425	Blue	359	14137	2014
146	binding energy	0.2904	-0.2192	Green	401	12670	1996
692	particle size distribution	0.481	-0.1757	Green	379	13171	1985
39	alkynes	-0.7838	-0.2011	Red	365	9286	1939
874	solubility	0.3829	0.4924	Green	396	10800	1923
824	recycling	-0.2433	-0.4574	Red	374	13116	1916
654	one-pot synthesis	-0.796	0.0345	Red	380	9700	1873
271	cyclization catalysts	-1.0473	-0.3552	Red	311	9005	1837
919	suzuki coupling reaction	-0.3613	-0.5214	Red	391	9319	1767
828	reduction	-0.0958	-0.2328	Red	405	9721	1763
278	cytotoxicity	-0.0055	0.7695	Yellow	376	10532	1745
348	electron transfer	0.5027	-0.438	Blue	387	11909	1739
593	molecular association	-0.1464	0.8273	Yellow	350	8291	1710
513	ionic liquids	0.1745	-0.0427	Green	391	7323	1703
865	simulation and modeling	0.3179	-0.1087	Green	361	6719	1703
574	metal-organic frameworks	0.291	-0.5272	Green	374	9046	1702
523	ketones	-0.6451	-0.4333	Red	359	7380	1699
404	fluorescence spectroscopy	0.5787	0.9588	Yellow	258	8905	1696
11	activation energy	0.299	-0.443	Green	365	10032	1674

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
987	x-ray diffraction	0.6361	-0.7111	Green	358	12094	1670
103	apoptosis	-0.2868	1.0634	Yellow	321	9665	1669
135	bacterial infection	-0.6365	0.5991	Yellow	342	11301	1662
616	nanocomposites	0.7472	-0.1792	Green	358	10200	1661
946	three-component reaction	-0.9857	-0.0005	Red	327	8420	1660
561	mammalian cell	0.494	1.1821	Yellow	199	8297	1655
337	electrochemical reduction	0.7343	-0.8235	Green	299	9592	1639
114	aryl aldehydes	-0.812	0.1013	Red	358	7960	1634
912	supramolecular structure	0.5058	0.2868	Blue	377	10307	1613
462	heterocyclization	-1.0614	-0.0064	Red	313	7646	1589
238	conformation	0.0124	0.2102	Blue	381	9836	1574
721	photocatalysts	0.0963	-0.4824	Red	375	7234	1564
27	alcohols	-0.4658	-0.4794	Red	365	7130	1562
241	contact angle	1.0256	0.0887	Green	311	9200	1554
371	escherichia coli	-0.0546	0.6136	Yellow	352	7364	1492
63	anilines	-0.8173	-0.0877	Red	349	7231	1486
37	alkylation	-0.5048	-0.2007	Red	385	6558	1460
251	coupling reaction	-0.5885	-0.2114	Red	380	6492	1440
50	amides	-0.7681	-0.0847	Red	342	6121	1432
817	raman spectra	0.7107	-0.6838	Green	343	10461	1432
884	spiro compounds	-0.9999	0.0469	Red	331	6635	1407
959	triazoles	-0.7016	0.3662	Red	356	7826	1379
763	polyoxyalkylenes	0.4479	0.3957	Green	395	7401	1376
997	zeta potential	0.592	0.5161	Green	326	9313	1352
148	biocompatibility	0.4807	0.7991	Yellow	278	7691	1311
777	porosity	0.6256	-0.3376	Green	362	9124	1303
338	electrochemical reduction catalysts	0.8221	-0.8423	Green	207	7609	1289
256	cross-coupling reaction	-0.7183	-0.5576	Red	332	5544	1284
898	storage modulus	1.1122	0.4303	Green	271	8683	1276
732	pi-pi interaction, stacking	0.5295	0.1909	Blue	385	9759	1271
141	benzaldehydes	-0.8736	0.2072	Red	332	7012	1270
218	click chemistry	-0.2258	0.4023	Yellow	392	7188	1268
931	tensile strength	1.2127	0.2765	Green	234	8684	1262
570	mesoporous materials	0.3973	-0.4902	Green	351	7948	1249
235	condensation reaction	-0.4876	0.1589	Red	394	6261	1248
320	drug design	-0.4802	0.7856	Yellow	306	8027	1227
806	pyridines	-0.8778	0.0116	Red	341	5543	1213
902	structure-activity relationship, antitumor	-0.8483	0.7173	Yellow	273	7856	1213
991	young's modulus	1.1433	0.3629	Green	251	8219	1206

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
934	thermal decomposition	0.517	-0.4867	Green	366	6601	1190
562	mammary gland neoplasm	-0.0893	1.0523	Yellow	301	6338	1160
782	potential energy surface	-0.2094	-0.5206	Red	357	7380	1157
120	arylation	-0.7921	-0.5381	Red	326	5284	1149
597	molecular modeling	-0.2279	0.6192	Yellow	378	5608	1149
402	fluorescence microscopy	0.5652	1.1479	Yellow	208	6844	1142
289	density functional theory, b3lyp	0.3512	-0.0669	Blue	388	8009	1140
419	fungicides	-0.6867	0.5826	Yellow	324	7262	1138
899	stress-strain relationship	1.1576	0.3093	Green	242	7819	1135
94	antioxidants	-0.3872	0.6866	Yellow	346	6506	1131
459	heterocyclic compounds, nitrogen	-0.9084	-0.0461	Red	322	5588	1105
811	quinolines	-0.8724	0.0542	Red	318	5195	1102
755	polymer morphology	0.9653	0.2443	Green	294	6832	1096
155	biomass	0.1372	-0.3323	Green	309	3915	1086
360	enzyme inhibitors	-0.6176	0.8039	Yellow	262	5608	1081
657	optical band gap	0.94	-0.42	Blue	306	8750	1070
373	esr (electron spin resonance)	0.25	-0.5978	Blue	355	7323	1057
487	hydrophobicity	0.6965	0.3258	Green	360	6373	1050
137	band gap	0.8857	-0.4461	Blue	329	7990	1048
273	cycloaddition reaction	-0.3839	-0.0825	Red	372	5041	1045
333	electric impedance	0.9589	-0.5817	Green	265	7098	1045
358	enzyme functional sites, active	-0.3177	0.6172	Yellow	280	4787	1030
715	phenols	-0.5291	-0.2611	Red	353	4201	1028
258	crosslinking	0.932	0.4287	Green	300	5628	1024
818	reaction kinetics	0.0352	-0.3444	Green	379	5099	1021
608	multicomponent reaction	-0.9241	0.0884	Red	315	5359	1019
274	cycloaddition reaction catalysts	-0.5094	-0.0354	Red	343	5328	1015
539	light	-0.1344	0.0642	Red	384	4648	1013
411	formation constant	0.2031	0.4066	Blue	351	6364	1012
708	pharmaceutical nanoparticles	0.3378	0.8121	Yellow	241	6119	1007
615	nanocatalysts	-0.0309	-0.64	Green	322	6394	1004
567	melting point	0.9429	0.1788	Green	325	6744	992
783	powder x-ray diffraction	0.3575	-0.7336	Green	330	7474	992
189	carboxylic acids	-0.5543	-0.1081	Red	374	4334	984
621	nanosheets	0.7346	-0.4932	Green	327	5671	984
54	amino acids	-0.3744	0.2213	Red	384	4797	983
677	oxidation potential	0.5685	-0.4099	Blue	360	8675	977
781	potential barrier	-0.2228	-0.5963	Red	367	6665	975
403	fluorescence quenching	0.3246	0.3021	Blue	363	6104	966
355	encapsulation	0.4558	0.5227	Green	354	6478	962

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
907	substituent effects	0.0821	-0.2246	Blue	376	6181	958
484	hydrolysis	-0.0383	0.0435	Red	407	4552	957
829	reduction catalysts	0.1125	-0.6241	Green	325	5136	949
351	elongation at break	1.2268	0.3324	Green	220	7024	947
694	peptides	-0.1433	0.4412	Yellow	351	4584	940
121	arylation catalysts	-0.8743	-0.6075	Red	285	4496	937
920	suzuki coupling reaction catalysts	-0.5068	-0.7215	Red	322	5020	932
154	biological uptake	0.2254	0.8661	Yellow	274	5991	929
117	aryl halides	-0.6271	-0.6777	Red	289	4438	928
805	pyrazoles	-0.9197	0.2938	Red	302	4594	927
640	nmr (nuclear magnetic resonance), carbon-13	0.5753	-0.2239	Blue	350	7717	926
581	michael reaction	-0.5948	0.1183	Red	371	4833	924
596	molecular dynamics simulation	0.0598	0.5075	Yellow	371	4461	918
325	drug toxicity	-0.5693	0.9521	Yellow	272	5006	913
41	alkynes, α-	-0.8216	-0.172	Red	310	4362	912
756	polymer morphology, surface	1.045	0.1666	Green	257	5479	908
598	molecular recognition	0.0076	0.5269	Yellow	320	4329	905
976	viscosity	0.9031	0.3332	Green	313	5120	883
293	desorption	0.4798	-0.6252	Green	318	6268	878
416	frontier molecular orbital	0.2824	-0.2766	Blue	350	5731	875
888	staphylococcus aureus	-0.12	0.7228	Yellow	339	5610	874
413	free energy of activation	-0.3063	-0.4176	Red	323	5761	870
502	inclusion compounds	0.3293	0.4261	Blue	326	5323	868
268	current density	1.0448	-0.4877	Blue	258	5288	864
588	microwave irradiation	-0.5943	0.2023	Red	380	4540	863
820	reactive oxygen species	0.1122	0.8371	Yellow	305	5104	863
904	structure-activity relationship, enzyme-inhibiting	-0.6564	0.7352	Yellow	225	4823	861
257	cross-coupling reaction catalysts	-0.7518	-0.636	Red	278	3859	860
747	polyesters	0.8215	0.4819	Green	298	4117	859
69	anti-inflammatory agents	-0.5296	0.8746	Yellow	291	4047	858
839	ring opening	-0.4589	-0.109	Red	371	3722	855
110	aromatic hydrocarbons	-0.5132	-0.6001	Red	319	3555	852
196	catalysts	0.1931	-0.5224	Green	340	3986	852
174	c-h bond activation catalysts	-0.9789	-0.5531	Red	273	4597	850
107	aromatic amines	-0.6438	-0.2308	Red	334	4172	849
376	esters	-0.7662	-0.32	Red	301	3534	847
641	nmr (nuclear magnetic resonance), chemical shift	0.2788	0.1016	Blue	341	6556	844
144	biaryls	-0.7056	-0.6762	Red	299	4271	843
825	redox potential	0.1989	-0.4135	Blue	369	5389	837

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602	molecular structure-property relationship	0.7578	0.1301	Blue	357	4556	834
303	diffusion	0.6184	-0.1232	Green	342	5103	832
119	aryl ketones	-0.8627	-0.3416	Red	306	3539	825
195	catalyst supports	0.2075	-0.785	Green	308	5324	822
312	dissolution	0.4193	0.7069	Yellow	268	5165	822
252	coupling reaction catalysts	-0.7172	-0.4307	Red	309	4081	821
331	electric conductivity	1.0254	-0.1398	Green	288	4972	821
283	dehydrogenation	-0.2209	-0.7174	Red	317	4017	820
519	isomerization	-0.2535	-0.3765	Red	352	3558	819
23	aggregation	0.6035	0.2483	Blue	357	5808	818
917	surface treatment	0.8174	0.0308	Green	319	4393	806
624	nanostructures	0.6648	-0.1804	Green	346	4658	805
921	swelling, physical	0.9864	0.3768	Green	267	4740	805
51	amination	-0.7611	-0.369	Red	344	3831	802
400	fluorescence decay	0.833	-0.0321	Blue	302	6705	798
638	nitriles	-0.8405	-0.2645	Red	302	3406	797
822	rearrangement	-0.7044	-0.1978	Red	288	3268	792
369	epoxides	-0.3429	-0.3291	Red	316	3748	789
928	temperature	0.3806	0.0099	Green	342	4066	789
275	cyclocondensation reaction	-0.8169	0.17	Red	328	4105	787
830	reduction potential	0.4284	-0.5436	Blue	333	6871	785
971	uv-visible absorption	0.6473	-0.2634	Blue	365	5513	785
613	mycosis	-0.7983	0.6024	Yellow	263	5742	784
530	knoevenagel reaction	-0.339	0.0556	Red	371	5006	779
620	nanoscale particle size	0.0986	-0.1584	Green	367	6208	779
496	imines	-0.6074	-0.2855	Red	341	3872	776
720	photocatalysis	-0.0495	-0.4268	Red	337	3280	776
211	chirality	-0.0693	0.1248	Blue	373	4362	775
667	organocatalysts	-0.7688	-0.2658	Red	310	3263	766
314	dna	0.0483	0.6669	Yellow	335	3517	762
407	fluorescent substances	0.6308	0.1636	Blue	350	5070	758
216	circular dichroism	0.2193	0.2229	Blue	362	4846	755
670	oscillator strength	0.7757	-0.3169	Blue	269	7621	752
551	luminescence	0.547	-0.153	Blue	346	4272	749
233	complexation	0.2335	0.4725	Blue	373	4182	748
678	oxidative coupling reaction	-0.5185	-0.436	Red	327	3024	745
172	c-c bond formation	-0.6914	-0.4732	Red	307	3580	742
680	oxidative stress, biological	-0.3701	0.8056	Yellow	294	4231	738
591	molar absorptivity	0.442	-0.1278	Blue	333	6707	736
324	drug targets	-0.4592	0.9868	Yellow	220	4089	732

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
265	crystallization	0.6794	-0.0281	Green	337	4185	718
96	antiproliferative agents	-0.5152	1.1097	Yellow	239	3878	717
118	aryl iodides	-0.916	-0.5118	Red	267	3157	713
335	electrochemical oxidation	0.4375	-0.6933	Green	329	4286	713
549	loss modulus	1.0457	0.467	Green	244	5007	713
664	organic electroluminescent devices	1.1845	-0.374	Blue	202	6032	713
655	open circuit potential	1.1065	-0.3345	Blue	216	4372	711
336	electrochemical redox reaction	0.0166	-0.584	Blue	301	3539	705
240	conformers	0.0854	0.0863	Blue	331	5012	703
808	pyrroles	-0.9605	-0.0907	Red	285	3271	703
506	inflammation	-0.4985	0.91	Yellow	273	3593	699
793	protective groups	-0.4446	0.2448	Red	307	2877	697
418	functional groups	-0.4163	-0.1538	Red	359	3417	695
129	azide-alkyne 1,3-dipolar cycloaddition reaction	-0.1476	0.3777	Yellow	359	3786	692
182	carbon nanotubes	0.6896	-0.3885	Green	324	3702	690
282	dehydration reaction	-0.0888	-0.6385	Green	321	3221	688
346	electron density	0.3615	-0.3676	Blue	367	5000	677
798	proteins	0.1266	0.5603	Yellow	306	2278	675
893	steric effects	-0.2765	-0.0603	Red	376	3880	672
938	thermogravimetric analysis	0.7008	-0.5955	Green	328	5215	670
306	dipole moment	0.5061	0.0312	Blue	327	6089	668
227	colorimetry	0.624	0.6968	Blue	223	2939	656
881	sonogashira coupling reaction	-0.3902	-0.2668	Red	365	3632	655
476	hydrodynamic radius	0.6346	0.5705	Green	295	4309	653
922	synergism	0.1994	-0.1065	Green	393	3829	653
175	calcination	0.4758	-0.7355	Green	257	3938	652
486	hydrophilicity	0.7795	0.3181	Green	304	4193	651
557	magnetic nanoparticles	-0.0366	-0.1113	Green	328	3590	651
477	hydrogels	0.7549	0.4106	Green	286	3344	648
974	vibrational frequency	0.3913	-0.232	Blue	300	5444	647
914	surface roughness	1.0937	-0.0364	Green	264	4431	645
458	heterocyclic compounds	-0.62	-0.1558	Red	300	2665	643
584	microbial gene	-0.0629	0.441	Yellow	162	1204	642
983	wettability	0.9917	0.1282	Green	247	3790	642
42	allenes	-1.0105	-0.3994	Red	223	2693	639
49	amidation	-0.5338	0.0082	Red	366	2795	639
232	complex modulus, tan δ	1.2404	0.3941	Green	194	4540	638
322	drug metabolism	-0.3862	1.0747	Yellow	189	2913	638
374	esterification	-0.0942	-0.018	Red	363	2815	638

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542	lipophilicity	-0.4478	0.7458	Yellow	302	3981	637
100	antiviral agents	-0.4979	0.6673	Yellow	257	2255	633
165	bond length	0.2958	-0.3483	Blue	356	4831	633
130	azides	-0.6528	0.1981	Red	312	3456	630
116	aryl bromides	-0.7855	-0.6064	Red	289	2923	628
3	absorption	0.7012	0.1049	Green	347	3738	627
38	alkylation catalysts	-0.5825	-0.5302	Red	276	3036	626
463	heterocyclization catalysts	-1.1161	-0.1161	Red	243	3581	622
815	radicals	-0.1545	-0.2787	Red	344	3006	615
788	prodrugs	0.0189	0.9266	Yellow	235	3139	614
969	uv radiation	0.5488	0.4495	Blue	309	3252	614
272	cyclization, stereoselective	-1.1202	-0.2854	Red	209	2376	612
409	fluoropolymers	0.9928	-0.172	Green	267	3312	597
903	structure-activity relationship, bactericidal	-0.7038	0.651	Yellow	258	4214	597
604	molecular weight distribution	0.8587	0.3141	Green	250	2726	595
21	adsorbents	0.7921	-0.2454	Green	244	3298	594
690	particle shape	0.439	0.0453	Green	323	4479	594
807	pyrimidines	-0.8753	0.3316	Red	282	2870	588
48	alzheimer disease	-0.3603	0.9388	Yellow	212	2153	585
521	isotope effect, deuterium	-0.4712	-0.6327	Red	292	3318	581
814	radical scavengers	-0.4621	0.6023	Yellow	321	3952	577
414	friedel-crafts reaction	-0.4338	-0.2131	Red	350	2701	575
778	porous materials	0.754	-0.4048	Green	300	3654	573
648	nucleophilic substitution reaction	-0.5196	0.0874	Red	337	2434	571
4	absorption spectra	0.4302	-0.0572	Blue	326	3333	570
279	decarboxylation	-0.5164	-0.301	Red	312	2416	570
8	acidity	0.1317	-0.5725	Green	328	3522	569
876	solvatochromism	0.7549	-0.0312	Blue	285	4567	565
52	amination catalysts	-0.8559	-0.4711	Red	261	2681	564
105	aralkyl alcohols	-0.6681	-0.5287	Red	273	2561	564
452	heck reaction	-0.5902	-0.4513	Red	332	2815	562
495	imidazoles	-0.7673	0.1383	Red	306	2584	561
300	diels-alder reaction	-0.1698	-0.0186	Red	359	2387	559
731	pi-pi interaction	0.4201	0.1783	Blue	357	4211	559
935	thermal polymer degradation	1.1084	0.1907	Green	222	3169	559
873	solid phase synthesis, solid-phase peptide synthesis	-0.2898	0.4482	Yellow	274	3120	556
857	sensors	0.6269	0.3657	Blue	292	2353	555
16	addition reaction	-0.7112	-0.3153	Red	283	2267	554
556	macrocyclic compounds	-0.1221	0.1856	Blue	330	3013	553

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15	acylation	-0.5809	0.0397	Red	336	2421	550
340	electroluminescence	1.2302	-0.4129	Blue	174	4945	549
249	coumarins	-0.6208	0.2708	Red	318	2753	547
910	sulfonamides	-0.7343	0.0775	Red	295	2367	545
392	films	0.9366	-0.0873	Blue	274	3128	543
436	glycosides	-0.4226	0.3083	Red	223	1528	542
494	imaging agents	0.2061	0.999	Yellow	231	2889	542
242	controlled-release drug delivery systems	0.4122	0.7902	Yellow	209	3691	541
284	dehydrogenation catalysts	-0.2131	-0.7915	Red	245	2641	540
115	aryl alkenes	-0.9133	-0.4206	Red	263	2219	538
537	lewis acids	-0.3604	-0.4675	Red	309	2497	536
344	electrolysis	0.5694	-0.8076	Green	257	3167	535
786	primary amines	-0.7276	-0.0601	Red	305	2601	533
367	epoxidation	-0.0662	-0.3363	Red	318	2475	532
723	photodynamic therapy	0.2683	0.9441	Yellow	197	2928	531
944	thiols	-0.437	-0.0314	Red	333	2148	531
511	intramolecular hydrogen bond	0.1834	0.1388	Blue	324	3814	529
799	protonation	0.1001	0.0174	Blue	357	3246	529
892	stereoselective synthesis	-0.6883	-0.1214	Red	260	1752	529
665	organic solar cells	1.1415	-0.2711	Blue	149	2620	528
321	drug discovery	-0.5264	0.814	Yellow	234	2787	524
923	synthesis gas	0.2992	-0.7619	Green	165	1699	521
617	nanocrystals	0.7017	-0.2606	Green	298	2791	520
927	targeted drug delivery systems	0.3092	0.9098	Yellow	173	3225	520
510	insertion reaction	-0.784	-0.4487	Red	269	2204	519
800	pseudomonas aeruginosa	-0.183	0.7268	Yellow	303	3349	517
847	schiff bases	-0.0463	0.3027	Blue	357	3239	516
2	absolute configuration	-0.3176	0.231	Yellow	238	1734	514
40	alkynes, aryl	-0.9281	-0.3255	Red	274	2383	507
112	aromatization	-0.4695	-0.3567	Red	296	2354	504
290	deoxidation	-0.1146	-0.5861	Green	272	1938	503
727	photolysis	0.2248	0.0736	Blue	325	2446	501
879	solvent polarity effect	0.561	-0.0172	Blue	326	4210	501
582	michael reaction, stereoselective	-1.0978	-0.1851	Red	220	2081	500
142	benzimidazoles	-0.7841	0.2388	Red	293	2473	498
234	composites	0.7612	-0.5405	Green	261	2844	498
438	grain size	0.4442	-0.7914	Green	258	3217	498
213	chromophores	0.6137	0.055	Blue	291	2902	489
564	mass spectra	0.5077	-0.3556	Blue	335	3773	488

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
850	secondary amines	-0.7328	-0.1457	Red	307	2381	488
194	catalysis	0.0223	-0.2761	Green	328	2613	487
280	decomposition	0.3448	-0.1847	Green	330	2472	487
220	coating materials	0.8247	0.1964	Green	252	2546	486
961	tuberculostatics	-0.7519	0.8017	Yellow	234	2917	482
298	dielectric constant	1.0548	0.0004	Green	272	3056	481
474	hydrazones	-0.7202	0.2205	Red	306	2122	476
661	optimization	0.0812	-0.0661	Green	285	1445	471
34	alkanes	-0.2974	-0.6771	Red	276	2192	468
568	membranes, nonbiological	0.8965	0.0937	Green	240	2396	466
679	oxidative cyclization	-0.7035	0.0134	Red	286	1907	466
860	silanes	-0.6024	-0.6066	Red	242	1676	465
57	amphiphiles	0.4907	0.587	Green	289	2601	464
580	micelles	0.5696	0.3979	Green	312	2419	461
745	polydispersity	0.6	0.6368	Green	274	3176	461
65	annealing	0.9823	-0.2712	Green	245	2999	460
90	antimicrobial agents	-0.039	0.6788	Yellow	291	2425	460
1	1,3-dipolar cycloaddition reaction	-0.6059	0.3226	Red	309	2604	459
326	drugs	-0.4207	0.5186	Yellow	312	3289	459
518	isocyanides	-0.9918	-0.1573	Red	252	2076	458
533	lattice parameters	0.6228	-0.5574	Blue	284	3638	458
717	phosphines	-0.6353	-0.5718	Red	241	1961	458
388	fermentation	0.0046	0.3262	Yellow	175	843	453
891	stereochemistry	-0.2212	0.2397	Yellow	292	1806	453
951	total energy	-0.0655	-0.5029	Blue	283	2282	451
698	permeability	0.7064	0.4743	Green	273	2781	450
111	aromatic nitro compounds	-0.2182	-0.331	Red	299	2370	447
618	nanofibers	0.7232	0.197	Green	295	2807	447
653	oligosaccharides	-0.3272	0.3434	Red	213	1052	447
204	chalcones	-0.7544	0.3319	Red	302	2388	446
347	electron donors	0.9044	-0.2333	Blue	252	2729	444
627	natural products	-0.4965	0.3388	Yellow	243	1958	444
826	redox reaction	0.1566	-0.151	Blue	349	2578	444
305	dimerization	-0.1369	-0.1412	Red	338	2163	442
106	aromatic amides	-0.8158	-0.0143	Red	257	1906	440
646	nucleophiles	-0.7289	-0.2462	Red	271	1846	440
718	phosphonates	-0.6507	-0.0237	Red	269	1401	440
180	carbon black	0.8801	-0.6144	Green	216	2467	437
558	magnetization	0.1029	-0.4198	Green	296	3319	437
524	ketones, unsaturated	-1.0306	-0.2493	Red	239	1781	434

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
323	drug screening	-0.314	0.8976	Yellow	232	2348	433
361	enzyme kinetics	-0.2054	0.5621	Yellow	233	1456	424
612	mycobacterium tuberculosis	-0.7011	0.8038	Yellow	225	2439	424
225	color	0.9383	-0.0221	Blue	266	3240	423
482	hydrogenation, stereoselective	-0.5884	-0.3628	Red	237	1558	422
328	dyes	0.5037	-0.0561	Blue	308	2330	421
960	tuberculosis	-0.7584	0.7644	Yellow	227	2640	417
780	positron emission tomography	-0.0906	0.9268	Yellow	159	1020	415
424	gelation	0.8072	0.4102	Green	284	2618	413
995	zeolite zsm-5	0.1813	-0.7419	Green	182	1852	413
816	raft polymerization	0.7654	0.4755	Green	226	1621	412
840	ring-closing metathesis	-0.4444	0.0952	Red	252	1368	412
187	carbonylation	-0.5347	-0.4915	Red	267	1570	410
656	optical absorption	0.8901	-0.2903	Blue	267	2763	409
676	oxidation kinetics	0.0583	-0.8152	Green	243	2482	409
317	drug bioavailability	-0.1833	1.0181	Yellow	195	2190	408
370	epoxy resins	1.2105	0.1923	Green	185	2126	405
186	carbonyl compounds (organic)	-0.5325	-0.3884	Red	282	1853	403
503	inclusion reaction	0.2928	0.3655	Blue	266	3008	402
163	bond angle	0.2653	-0.1649	Blue	321	3432	401
164	bond cleavage	-0.289	-0.1451	Red	313	1850	401
380	ethers	-0.6497	-0.3594	Red	285	1795	401
281	dehydration catalysts	-0.001	-0.7557	Green	216	1879	400

Appendix IV. Patent 4.0.0. cluster list

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
155	biomedical	0.7722	0.0301	Yellow	456	128363	14224
98	antitumor agents	0.8779	0.1557	Yellow	423	112178	10808
760	polyoxyalkylenes	-0.7708	-0.12	Red	494	55014	10802
755	polymerization catalysts	-0.9385	-0.1316	Red	340	35380	8250
625	neoplasm	0.9456	0.1402	Yellow	409	95435	8119
257	crosslinking agents	-0.9234	-0.2801	Red	411	43325	7983
744	polyesters	-0.841	-0.2398	Red	410	36625	7515
762	polysiloxanes	-0.9421	-0.2031	Red	368	40095	6318
368	epoxy resins	-0.909	-0.3197	Red	337	30807	5751
660	organic electroluminescent devices	-0.3461	-0.3898	Red	236	8244	5639
386	fermentation	-0.0205	0.4117	Blue	421	21104	5561
765	polyurethanes	-0.9734	-0.1738	Red	378	30339	4983
248	coupling agents	-1.0774	-0.1744	Red	344	30834	4883
195	catalysts	-0.6699	0.2039	Red	422	20404	4752
698	pharmaceutical carriers	0.8945	-0.0306	Yellow	419	57973	4647
219	coating materials	-0.7943	-0.1735	Red	394	23190	4594
93	antioxidants	-0.7746	-0.2126	Red	481	26773	4366
389	fillers	-1.0467	-0.2074	Red	328	31804	4279
307	dispersing agents	-0.9693	-0.2849	Red	366	29520	4087
670	oxidation	-0.2748	0.111	Red	464	10906	4061
84	antifoaming agents	-1.0324	-0.3428	Red	333	29009	3829
19	adhesives	-0.8968	-0.26	Red	335	19143	3579
10	acrylic polymers	-0.8476	-0.3159	Red	413	21080	3549
824	reduction	-0.2327	0.1006	Red	454	12584	3499
739	polyamides	-0.8973	-0.1512	Red	410	20291	3380
477	hydrogenation	-0.3233	0.1812	Red	423	9708	3295
700	pharmaceutical excipients	0.9423	-0.0606	Yellow	363	42885	3262
558	mammary gland neoplasm	1.0378	0.2989	Green	358	56521	3240
179	carbon black	-0.9821	0.0155	Red	328	18995	3236
793	protein sequences	0.3308	0.3692	Blue	371	21231	3232
174	calcination	-0.5702	0.3376	Red	317	15000	3068
394	fireproofing agents	-1.0993	-0.1336	Red	301	19866	3065
74	antibacterial agents	0.1371	-0.0635	Blue	470	21146	3043
68	anti-inflammatory agents	1.0978	-0.0821	Yellow	367	48743	3034
664	organosilicon compounds	-1.0512	-0.1473	Red	321	18193	2939
482	hydrolysis	-0.1828	0.0603	Red	480	9581	2912
369	escherichia coli	0.1598	0.3391	Blue	451	15987	2875
730	pigments, nonbiological	-0.9526	-0.3359	Red	322	19991	2844

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
735	plastic films	-0.8003	-0.3124	Red	322	11654	2816
407	fluoropolymers	-0.8218	-0.0555	Red	361	14778	2798
533	leveling agents	-1.0739	-0.3863	Red	260	22702	2783
372	esterification	-0.2305	-0.0399	Red	461	7395	2743
504	inflammation	1.1757	-0.0617	Yellow	336	44173	2623
341	electroluminescent substances	-0.3461	-0.45	Red	145	4757	2586
550	lung neoplasm	1.0826	0.3545	Green	324	46253	2579
268	cyclization	-0.0904	-0.0586	Red	402	4687	2576
914	surfactants	-0.6216	-0.0816	Red	467	14669	2568
615	nanoparticles	-0.5331	0.0379	Red	465	12078	2494
514	isocyanates	-1.0439	-0.2583	Red	310	15684	2480
233	condensation reaction	-0.1209	-0.0606	Red	441	6188	2414
228	combination chemotherapy	1.0556	0.016	Yellow	298	35843	2406
313	dna sequences	0.2815	0.438	Blue	341	14167	2379
580	microbial gene	0.1381	0.4762	Blue	299	10931	2282
788	prostate gland neoplasm	1.1458	0.3046	Green	322	45787	2264
883	stabilizing agents	-0.891	-0.079	Red	421	14437	2213
350	emulsifying agents	-0.8273	-0.1189	Red	413	13082	2198
741	polycarbonates	-0.8741	-0.2205	Red	363	13490	2187
478	hydrogenation catalysts	-0.4443	0.2743	Red	353	7059	2176
393	fire-resistant materials	-1.0908	-0.0933	Red	271	11915	2161
103	apparatus	-0.376	0.1436	Red	417	3754	2149
194	catalyst supports	-0.5383	0.3238	Red	318	11721	2106
404	fluorescent indicators	0.0217	-0.1672	Red	373	3998	2092
571	metals	-0.6944	0.0361	Red	441	15488	2085
737	plasticizers	-0.9975	-0.0835	Red	350	14810	2078
857	silica gel	-0.6382	0.2461	Red	409	9374	2031
681	pancreatic neoplasm	1.2614	0.3258	Green	313	44584	2010
544	liver neoplasm	1.1386	0.3753	Green	319	36287	1995
669	ovary neoplasm	1.1772	0.4273	Green	314	42731	1987
52	amines	-0.5485	-0.1002	Red	480	11697	1944
747	polyethers, hydroxy-containing	-1.1777	-0.1697	Red	245	12604	1939
736	plastic foams	-1.1386	-0.0843	Red	268	12643	1921
339	electroluminescent devices	-0.4431	-0.3986	Red	298	5523	1906
726	photopolymerization catalysts	-0.8437	-0.4396	Red	248	8597	1898
380	extraction	-0.2243	0.2962	Red	396	4760	1889
47	alzheimer disease	1.1403	-0.3314	Yellow	317	35448	1870
265	culture media	-0.0054	0.4495	Blue	345	8304	1846
751	polymer blends	-1.0823	-0.0288	Red	279	9220	1839

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
99	antiviral agents	0.9077	0.072	Yellow	366	23221	1820
677	oxides (inorganic)	-0.6392	0.1668	Red	360	11460	1816
750	polyimides	-0.744	-0.3265	Red	307	8514	1814
820	recycling	-0.4047	0.2915	Red	325	6047	1813
893	stomach neoplasm	1.251	0.4442	Green	301	38164	1797
532	leukemia	1.2287	0.2152	Green	299	35306	1789
263	crystallization	-0.2128	0.2677	Red	450	7343	1782
718	photocatalysts	-0.6288	-0.1484	Red	341	7330	1775
223	colon neoplasm	1.1957	0.3389	Green	318	34574	1768
232	composites	-0.6063	0.1847	Red	346	8589	1766
325	drying process	-0.4355	0.3486	Red	391	8968	1765
800	purification	-0.2299	0.2443	Red	396	4766	1765
324	drugs	0.3235	0.1133	Blue	464	13892	1753
82	antidiabetic agents	1.193	-0.1301	Yellow	320	32284	1740
562	melanoma	1.2063	0.2694	Green	307	38881	1736
48	amidation	0.0085	-0.0603	Red	387	5132	1730
34	alkenes	-0.5169	0.2113	Red	374	7242	1697
181	carbon nanotubes	-0.8486	0.0841	Red	354	10883	1697
460	heterocyclization	-0.02	-0.1183	Red	301	4321	1690
936	thickening agents	-0.9988	-0.2651	Red	319	14212	1685
381	extrusion of polymeric materials	-1.0395	0.0032	Red	291	8245	1684
127	autoimmune disease	1.2745	0.0071	Yellow	295	32351	1662
26	alcohols	-0.3418	0.0898	Red	477	9126	1650
770	polyurethanes, polyoxyalkylene-	-1.1644	-0.2119	Red	233	9726	1624
711	phenolic resins	-0.8808	-0.1175	Red	302	9590	1617
806	quaternary ammonium compounds	-0.5204	0.0125	Red	446	8730	1602
759	polyolefins	-0.9002	-0.0298	Red	295	7930	1595
701	pharmaceutical formulations	0.7247	-0.0441	Yellow	371	16291	1585
794	proteins	0.2292	0.2	Blue	452	13728	1581
510	ionic liquids	-0.4876	0.0345	Red	362	4738	1551
745	polyesters, hydroxy-terminated	-1.099	-0.2592	Red	246	8813	1521
656	optical imaging devices	-0.5668	-0.4453	Red	241	4509	1510
427	glass fibers	-1.0027	-0.0235	Red	297	10048	1500
76	antibodies and immunoglobulins	0.5852	0.1728	Blue	393	17976	1487
990	zeolites, synthetic	-0.6496	0.2886	Red	334	8000	1478
65	anti-alzheimer agents	1.3392	-0.3645	Yellow	274	30158	1466
161	blowing agents	-1.157	-0.0438	Red	252	11247	1460
306	disease, animal	1.1043	-0.1411	Yellow	310	26440	1458
211	chlorination	-0.1085	0.006	Red	353	3318	1457
671	oxidation catalysts	-0.4146	0.1894	Red	269	4030	1436

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
978	wetting agents	-0.9739	-0.3797	Red	351	12214	1422
817	reactors	-0.4164	0.242	Red	283	3641	1421
854	separation	-0.3317	0.2747	Red	390	5045	1419
708	pharmacokinetics	0.934	-0.2268	Yellow	312	17487	1418
588	molded plastics	-1.0092	-0.1844	Red	241	5623	1399
658	oral drug delivery systems	0.8223	-0.166	Yellow	327	17648	1397
227	coloring materials	-0.7945	-0.3884	Red	364	10776	1383
448	heat-resistant materials	-0.8498	-0.2774	Red	279	5641	1368
417	fungicides	0.21	-0.0427	Blue	448	11687	1365
551	lymphoma	1.3177	0.2971	Green	283	31955	1363
768	polyurethanes, polyester-	-1.1243	-0.2376	Red	243	7601	1363
685	parkinson disease	1.2958	-0.4013	Yellow	295	27977	1358
929	textiles	-0.7836	-0.0751	Red	334	6983	1352
904	substitution reaction	-0.0318	-0.0869	Red	354	3701	1323
497	immunomodulators	1.1709	0.0038	Yellow	297	26487	1315
963	uterine cervical neoplasm	1.2373	0.397	Green	302	29269	1315
180	carbon fibers	-0.9609	0.0525	Red	295	8499	1310
292	diabetes mellitus	1.1137	-0.224	Yellow	320	22836	1303
629	neurodegenerative disease	1.1013	-0.2828	Yellow	290	24118	1294
134	bacterial infection	0.6431	0.0527	Blue	314	12158	1294
595	molecular sieves	-0.6297	0.3088	Red	306	5948	1290
590	molecular cloning	0.4525	0.3798	Blue	301	11187	1287
763	polysiloxanes, polyether-	-1.1175	-0.3462	Red	234	9806	1286
405	fluorescent substances	-0.1995	-0.2572	Red	423	4820	1280
249	coupling reaction	-0.055	-0.0687	Red	406	3610	1278
311	distillation	-0.2898	0.2742	Red	308	3815	1271
546	lubricants	-0.931	-0.009	Red	370	9474	1270
316	drug delivery systems	0.5844	-0.0876	Yellow	401	12995	1263
392	filtration	-0.2953	0.3329	Red	388	6157	1234
524	kidney neoplasm	1.3626	0.339	Green	291	31542	1225
437	green chemistry	-0.2263	0.0309	Red	318	2234	1224
606	multiple sclerosis	1.4496	-0.262	Yellow	276	30731	1221
834	rheumatoid arthritis	1.4412	0.0172	Yellow	280	29245	1219
757	polymers	-0.3387	-0.0918	Red	483	8588	1219
746	polyethers	-0.8677	-0.1789	Red	364	8731	1212
690	peptides	0.2498	0.0825	Blue	449	9627	1205
190	cardiovascular agents	1.3166	-0.2509	Yellow	276	26479	1196
144	binders	-0.7471	0.0214	Red	386	6720	1182
756	polymerization inhibitors	-0.8291	-0.3501	Red	292	5882	1182

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
983	yeast	-0.0187	0.3766	Blue	380	5940	1180
139	bentonite	-0.9457	0.1197	Red	333	9189	1175
158	bladder neoplasm	1.3535	0.4192	Green	282	30259	1174
902	styrene-butadiene rubber	-1.0335	0.0752	Red	241	5517	1168
53	amino acids	0.0151	0.1668	Blue	473	7151	1167
605	multiple myeloma	1.4068	0.2067	Green	285	28689	1164
970	viral infection	1.0134	0.051	Yellow	296	19089	1163
519	kaolin	-0.841	0.1874	Red	334	8409	1161
499	impregnation	-0.5604	0.3979	Red	322	6936	1160
638	non-small-cell lung carcinoma	1.0893	0.2665	Green	296	23318	1158
295	diatomite	-0.7663	0.2262	Red	373	7521	1157
55	aminoplasts	-0.985	-0.224	Red	282	6899	1146
154	biomass	-0.3284	0.3237	Red	327	4891	1130
225	colorectal neoplasm	1.0988	0.4148	Green	291	23753	1130
699	pharmaceutical diluents	0.9421	-0.1047	Yellow	315	16144	1128
258	crosslinking catalysts	-0.8795	-0.3735	Red	247	7096	1126
707	pharmaceutical tablets	0.6769	-0.1676	Yellow	348	11489	1120
473	hydrocarbons	-0.5263	0.2912	Red	355	5807	1118
191	cardiovascular disease	1.1557	-0.1797	Yellow	301	21643	1117
919	synthesis gas	-0.4679	0.4095	Red	244	3951	1117
326	dyes	-0.4887	-0.2404	Red	426	6083	1105
21	adsorption	-0.3844	0.2623	Red	336	4115	1100
734	plasmid vectors	0.184	0.4517	Blue	283	6484	1094
59	analgesics	1.0128	-0.3643	Yellow	310	17035	1093
36	alkylation	-0.1635	0.0375	Red	400	3267	1089
94	antiparkinsonian agents	1.4002	-0.4523	Yellow	262	24066	1080
749	polyhydric alcohols	-0.6709	-0.1835	Red	406	7111	1080
840	saccharomyces cerevisiae	0.0614	0.4355	Blue	275	5243	1064
775	porous materials	-0.6332	0.1977	Red	339	5027	1059
261	crystal structure	0.226	-0.1047	Red	379	5050	1058
475	hydrogels	-0.5448	-0.1347	Red	387	4384	1057
713	phosphates	-0.6611	-0.0195	Red	428	6533	1050
989	zeolite zsm-5	-0.5784	0.3643	Red	226	4728	1049
167	brain neoplasm	1.3876	0.2687	Green	275	26747	1048
787	prophylaxis	0.8599	0.0235	Yellow	303	14971	1028
567	metabolic disorders	1.2538	-0.1634	Yellow	272	20661	1019
426	glass	-0.6736	-0.1334	Red	385	5602	1018
383	fatty acids	-0.2892	0.0253	Red	460	6322	1008
360	enzymes	0.066	0.2364	Blue	442	6878	1006
391	filters	-0.4781	0.2442	Red	297	2321	997

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Oc-currences>
447	heat treatment	-0.4527	0.2356	Red	339	4537	996
582	microspheres	-0.7726	0.065	Red	335	5376	993
443	head and neck neoplasm	1.3061	0.3918	Green	279	26511	990
680	pain	1.0307	-0.3261	Yellow	293	14772	986
882	stability	-0.0373	0.1754	Red	448	6609	985
370	esophagus neoplasm	1.4202	0.3967	Green	273	25468	983
823	reducing agents	-0.5824	-0.0324	Red	399	4656	981
542	lithium-ion secondary batteries	-0.6986	0.1169	Red	259	3273	979
797	psoriasis	1.5046	0.0307	Yellow	259	25300	974
697	pharmaceutical capsules	0.661	-0.1212	Yellow	348	10075	965
766	polyurethanes, acrylates	-0.9142	-0.4452	Red	226	5175	965
678	oxidizing agents	-0.5602	0.0164	Red	395	4178	961
892	stirring	-0.3677	0.2892	Red	341	5235	961
769	polyurethanes, polyether-	-1.2009	-0.126	Red	215	5905	957
896	stroke	1.2843	-0.329	Yellow	290	20466	952
245	cosmetics and personal care products	-0.1367	0.0785	Red	448	4820	951
122	asthma	1.4764	-0.1	Yellow	263	24320	950
976	waxes	-0.9266	-0.0695	Red	333	6519	943
856	silanes	-0.8209	0.0175	Red	330	5033	941
168	bromination	-0.0789	-0.1153	Red	294	2301	935
449	heating	-0.4135	0.27	Red	387	4690	935
95	antiproliferative agents	1.1175	0.0867	Yellow	291	16399	932
531	leather	-0.7679	-0.0393	Red	223	2119	923
845	sealing compositions	-0.9461	-0.2425	Red	242	6364	922
556	mammalia	0.9136	-0.1621	Yellow	306	13279	912
784	prodrugs	0.87	-0.1087	Yellow	305	10923	901
702	pharmaceutical injections	0.6571	-0.0337	Yellow	333	8781	898
767	polyurethanes, acrylic	-0.9972	-0.436	Red	213	4760	894
97	antirheumatic agents	1.5983	-0.0934	Yellow	245	23216	885
540	liquid crystal displays	-0.5657	-0.393	Red	203	2371	885
619	nanostructured materials	-0.5634	0.1569	Red	347	5306	882
202	chain transfer agents	-0.7278	-0.1849	Red	253	3056	873
575	mica-group minerals	-1.0427	-0.0459	Red	257	6989	871
123	atherosclerosis	1.4243	-0.186	Yellow	266	21626	869
935	thermoplastics	-0.9853	-0.1421	Red	256	4792	868
646	obesity	1.2116	-0.2068	Yellow	275	16927	865
487	hydrothermal reaction	-0.5453	0.2478	Red	274	4180	864
727	photoresists	-0.6199	-0.3716	Red	196	1706	862
863	skin neoplasm	1.4741	0.2963	Green	270	23023	861

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
503	infection	0.9487	0.0225	Yellow	316	15513	860
256	crosslinking	-0.5958	-0.1195	Red	395	4807	852
83	antifibrotic agents	1.4057	-0.0351	Yellow	248	19755	850
876	solvents	-0.329	-0.0396	Red	461	4782	849
431	glioblastoma	1.3033	0.1427	Green	274	21808	839
20	adsorbents	-0.4736	0.1816	Red	327	3038	838
374	esters	-0.3947	-0.0452	Red	443	5385	838
682	paper	-0.7009	-0.0878	Red	330	4223	836
390	films	-0.57	-0.1639	Red	320	2912	832
695	pesticides	-0.0422	0.0783	Blue	319	2237	830
188	carboxylic acids	-0.3329	0.0144	Red	466	4652	825
328	electric apparatus	-0.6422	-0.3198	Red	285	3735	822
507	insecticides	0.0159	0.0804	Blue	337	2070	820
455	herbicides	-0.0176	0.0946	Blue	253	1834	819
785	proliferative disorders	1.1487	0.125	Yellow	270	13672	815
944	thyroid gland neoplasm	1.4295	0.3439	Green	264	22260	815
696	ph	-0.1389	0.2917	Red	418	4371	813
9	acids	-0.3913	0.1076	Red	418	4351	812
975	water-thinned coating materials	-1.0953	-0.312	Red	203	4644	810
505	inflammatory bowel disease	1.4801	-0.1815	Yellow	261	21448	807
178	carbohydrates	-0.1166	0.2493	Red	420	5034	806
289	depression	1.0747	-0.4265	Yellow	260	13385	804
596	molecular structure	0.1765	-0.1275	Red	343	3658	801
3	absorption	-0.418	0.3132	Red	273	1543	796
601	monoclonal antibodies	0.6125	0.237	Blue	318	8740	795
201	ceramics	-0.7254	0.0809	Red	336	4515	793
566	mesoporous materials	-0.5639	0.3008	Red	292	4077	792
57	amyotrophic lateral sclerosis	1.4351	-0.3959	Yellow	244	18921	787
192	castor oil	-0.8438	-0.0077	Red	346	4848	786
570	metal-organic frameworks	-0.4749	0.1229	Red	322	2788	786
81	antidepressants	1.0693	-0.4737	Yellow	264	13319	785
109	aromatic hydrocarbons	-0.4992	0.179	Red	363	4163	781
432	glioma	1.2878	0.1985	Green	264	18409	776
72	antiasthmatics	1.5856	-0.2042	Yellow	235	20913	773
49	amides	-0.0897	-0.169	Red	462	5736	770
377	etherification	-0.1646	-0.0105	Red	345	1977	766
662	organic solvents	-0.4372	-0.0814	Red	412	3767	754
253	crohn disease	1.5118	-0.1456	Yellow	255	21232	753
50	amination	-0.1263	-0.0272	Red	379	2297	752
564	membranes, nonbiological	-0.5553	0.0885	Red	341	3124	750

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
27	aldehydes	-0.344	0.0419	Red	403	3458	746
200	centrifugation	-0.2488	0.34	Red	325	4078	746
520	ketones	-0.3741	-0.012	Red	430	4252	746
980	wood	-0.703	-0.0007	Red	325	4614	743
858	silicone rubber	-0.9683	-0.0504	Red	248	4215	742
743	polyester fibers	-0.9229	0.0366	Red	242	2980	739
884	staphylococcus aureus	0.2182	0.1034	Blue	409	5143	737
13	acute myeloid leukemia	1.3458	0.2104	Green	257	16780	737
91	antiobesity agents	1.2671	-0.2328	Yellow	269	14781	734
468	huntington disease	1.3791	-0.4034	Yellow	252	17279	734
624	natural rubber	-1.0808	0.0757	Red	234	3252	733
15	addition reaction	-0.1722	-0.0636	Red	302	1605	732
281	dehydrogenation	-0.4408	0.3879	Red	242	2898	730
783	printed circuit boards	-0.7703	-0.3603	Red	242	3857	729
337	electrodes	-0.5458	-0.0253	Red	316	2867	726
969	vegetable oils	-0.5976	0.1092	Red	360	3631	725
928	tertiary amines	-0.6691	-0.2311	Red	328	4226	724
930	thermal decomposition	-0.4749	0.2886	Red	286	2573	720
80	anticorrosive coating materials	-1.0429	-0.1067	Red	220	4070	711
879	soybean oil	-0.6647	0.0857	Red	344	3436	711
132	bacillus subtilis	0.1385	0.3788	Blue	299	4073	709
33	alkanes	-0.5021	0.2668	Red	371	4161	706
332	electric insulators	-0.7672	-0.2533	Red	272	3519	700
779	powder x-ray diffraction	0.4274	-0.069	Yellow	319	5211	700
506	inks	-0.7047	-0.3103	Red	273	3663	699
454	hepatocellular carcinoma	1.2287	0.1382	Green	261	16319	698
731	pipes and tubes	-0.7037	0.1588	Red	298	2889	693
644	nucleophilic substitution reaction	0.0058	-0.1104	Red	304	2038	692
754	polymerization	-0.4929	-0.0228	Red	382	2885	691
280	dehydration reaction	-0.277	0.1355	Red	298	1851	689
216	clays	-0.7846	0.1743	Red	313	5035	687
89	antimicrobial agents	0.1307	0.0194	Blue	438	5359	678
342	electrolysis	-0.454	0.2027	Red	250	1883	676
214	chronic obstructive pulmonary disease	1.5315	-0.1	Yellow	244	16874	674
428	glass substrates	-0.6695	-0.349	Red	248	2999	673
67	anti-infective agents	1.0229	-0.0488	Yellow	291	13043	672
626	nervous system agents	1.1774	-0.3665	Yellow	233	13801	671
452	hematopoietic neoplasm	1.2735	0.2562	Green	242	15305	671
945	tires	-1.1031	0.0992	Red	201	2392	671

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
661	organic solar cells	-0.3986	-0.432	Red	90	1456	669
351	emulsions	-0.8069	-0.019	Red	328	3948	666
703	pharmaceutical intravenous injections	0.8273	-0.0482	Yellow	301	10241	665
851	semiconductor devices	-0.6047	-0.3397	Red	258	2287	665
73	antiatherosclerotics	1.5641	-0.2676	Yellow	230	18384	661
75	antibiotics	0.4587	0.072	Blue	389	7183	657
184	carbonization	-0.5585	0.2728	Red	266	2730	656
655	optical filters	-0.6337	-0.4484	Red	141	2062	655
866	solar cells	-0.5328	-0.2836	Red	246	1791	655
387	fibrosis	1.5225	-0.0274	Yellow	221	15814	654
548	luminescent substances	-0.3043	-0.2924	Red	338	2043	651
915	suzuki coupling reaction	-0.1484	-0.2075	Red	314	2082	650
960	ulcerative colitis	1.5769	-0.1502	Yellow	241	17628	649
397	fluorescence	-0.0841	-0.206	Red	323	2064	648
959	type 2 diabetes	1.2871	-0.143	Yellow	272	13233	648
639	nonionic surfactants	-0.6542	-0.0689	Red	348	3525	647
425	genetic vectors	0.3241	0.4174	Blue	252	4030	646
282	dehydrogenation catalysts	-0.5148	0.4315	Red	180	2629	644
909	surface area	-0.4893	0.3364	Red	274	3726	644
835	ring opening	-0.1779	-0.0309	Red	316	1787	643
627	nervous system disease	1.2297	-0.3686	Yellow	249	11749	641
683	paraffin oils	-0.8136	0.1116	Red	349	3749	640
841	salts	-0.4269	0.0888	Red	433	3963	638
952	transition metals	-0.511	0.2344	Red	317	4169	638
273	cyclocondensation reaction	-0.0708	-0.0904	Red	226	1245	636
421	gelatins	-0.3861	-0.1471	Red	398	3363	635
445	heat exchangers	-0.4922	0.3117	Red	241	1966	635
631	neuroprotective agents	1.2002	-0.3208	Yellow	255	13172	633
786	promoter (genetic element)	0.2181	0.4798	Blue	241	3880	632
14	acylation	-0.0382	-0.0259	Red	348	1900	630
852	semiconductor materials	-0.5109	-0.2184	Red	312	2254	630
423	gels	-0.7554	0.1033	Red	320	4357	629
220	coating process	-0.6271	-0.0068	Red	329	3607	627
780	precipitation	-0.3233	0.3611	Red	322	2970	617
523	kidney disease	1.3986	-0.2307	Yellow	247	14894	616
748	polyethers, polyimide-	-0.7725	-0.292	Red	257	2703	615
972	washing	-0.3796	0.3656	Red	301	3898	615
490	hypertension	1.1872	-0.2629	Yellow	268	12065	613
844	schizophrenia	1.13	-0.5271	Yellow	244	11119	612
496	immune disease	1.2143	0.0168	Yellow	243	11057	611

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
712	phenols	-0.4354	-0.0485	Red	405	3150	603
246	cotton textiles	-0.7336	-0.0639	Red	250	2156	602
692	peptones	-0.0701	0.4326	Blue	234	3012	600
761	polysaccharides	-0.1715	0.1364	Red	415	3747	599
87	antihypertensives	1.239	-0.277	Yellow	254	11747	598
819	recrystallization	-0.0419	0.1334	Red	327	1789	597
373	esterification catalysts	-0.4514	0.001	Red	278	1874	595
529	laminated plastics	-0.9187	-0.3712	Red	197	2907	595
738	plastics	-0.7094	-0.0335	Red	329	3968	595
921	systemic lupus erythematosus	1.5798	-0.0293	Yellow	224	16514	594
859	silsesquioxanes	-0.7582	-0.1631	Red	260	2354	594
842	sarcoma	1.4703	0.2423	Green	255	16459	594
974	wastewater treatment	-0.3978	0.1714	Red	290	1864	594
241	cooling	-0.4041	0.3656	Red	326	2882	590
314	doping	-0.5566	0.1909	Red	263	3007	588
96	antipsychotics	1.2176	-0.5464	Yellow	237	10903	588
137	bases	-0.3627	0.0743	Red	396	2986	587
541	liquid crystals	-0.4853	-0.3277	Red	219	1198	587
71	antiarthritics	1.3924	-0.095	Yellow	237	15779	582
424	genetic engineering	0.1768	0.4921	Blue	224	3030	580
853	sensors	-0.5249	-0.1565	Red	363	3337	580
781	pressure	-0.4014	0.3351	Red	243	2034	579
984	yeast extract	-0.0612	0.4587	Blue	211	2678	571
574	methylation	-0.051	0.0041	Red	288	1675	566
799	pulmonary fibrosis	1.4716	-0.0444	Yellow	230	13667	566
457	heterocyclic compounds, nitrogen	-0.1518	-0.2692	Red	330	1644	565
243	corrosion inhibitors	-0.7329	-0.1283	Red	276	2846	559
855	signal transduction	1.0185	0.1025	Yellow	259	10609	559
358	enzyme inhibitors	0.8364	-0.2085	Yellow	313	7482	557
870	solubility	0.3525	-0.0543	Yellow	408	4396	553
966	uv-curable coating materials	-0.9499	-0.4614	Red	176	2630	553
365	epoxidation	-0.3201	0.0601	Red	262	1722	551
832	respiratory system agents	1.4931	-0.2861	Yellow	211	13330	549
986	zea mays	-0.0515	0.2908	Blue	340	2466	547
106	aromatic amines	-0.5386	-0.2523	Red	330	2795	544
924	temperature	-0.3748	0.3328	Red	343	4204	543
406	fluorination	-0.2222	0.0047	Red	242	992	542
534	lewis acids	-0.3948	-0.0863	Red	290	1712	541
66	anti-hiv agents	1.0393	-0.1644	Yellow	258	9315	541

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
913	surface treatment	-0.5996	0.0365	Red	330	2581	540
183	carbonates	-0.5094	0.0763	Red	368	3250	539
867	solid neoplasm	1.1343	0.2198	Green	250	11757	537
687	particle size	-0.2672	0.2174	Red	405	3354	536
498	immunosuppressants	1.3377	0.0149	Yellow	268	13980	536
809	radical polymerization catalysts	-0.7188	-0.2369	Red	245	2028	536
611	nanocatalysts	-0.5612	0.2219	Red	220	3073	534
950	transformation (genetic)	0.2379	0.4221	Blue	255	3251	534
63	animal gene	0.65	0.2872	Blue	284	6108	532
612	nanocomposites	-0.6383	0.0598	Red	289	2338	530
259	crystal morphology	0.4797	-0.0573	Yellow	265	2834	530
260	crystal polymorphs	0.415	-0.0334	Yellow	303	3949	530
610	myocardial infarction	1.3609	-0.281	Yellow	254	12437	529
946	topical drug delivery systems	0.7335	-0.1111	Yellow	294	6517	527
379	evaporation	-0.3052	0.3007	Red	338	2715	526
222	cognitive disorders	1.1507	-0.4822	Yellow	235	10168	524
133	bacteria	0.0956	0.2952	Blue	377	3884	523
338	electroluminescence	-0.2862	-0.4324	Red	59	1522	521
948	transesterification	-0.3888	0.058	Red	281	1301	521
218	coal	-0.5161	0.3703	Red	223	1612	520
628	neuroblastoma	1.3828	0.1575	Green	254	14152	519
641	nucleic acids	0.3621	0.155	Blue	360	5457	516
932	thermal stability	-0.1351	0.1836	Red	342	2076	515
705	pharmaceutical nanoparticles	0.2507	0.0217	Blue	346	3793	513
825	reduction catalysts	-0.4366	0.1476	Red	258	1977	512
244	corynebacterium glutamicum	0.0959	0.4926	Blue	161	2481	511
516	isomerization	-0.3515	0.2057	Red	245	1436	509
537	ligroine	-0.3288	0.1316	Red	366	2047	508
493	imidazoles	-0.434	-0.2919	Red	404	3311	507
740	polyamines	-0.623	-0.1965	Red	318	2869	507
156	biotransformation	0.0203	0.4234	Blue	177	1926	504
61	anhydrides	-0.5821	-0.2322	Red	331	3735	503
419	gasoline	-0.6349	0.3414	Red	248	2611	503
112	arthritis	1.2978	-0.0809	Yellow	256	12385	501
198	central nervous system agents	1.3516	-0.46	Yellow	205	10049	499
581	microorganism	-0.0272	0.3168	Blue	338	2811	498
142	beta zeolites	-0.6038	0.3838	Red	187	2546	494
361	enzymic hydrolysis	-0.1265	0.3422	Red	273	2139	490
886	steam	-0.4895	0.394	Red	207	2019	488
565	mental and behavioral disorders	1.2495	-0.488	Yellow	218	8853	487

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
221	cognition enhancers	1.1945	-0.5053	Yellow	225	9777	484
805	quantum dots	-0.4422	-0.1913	Red	285	2065	484
940	thiols	-0.4574	-0.1169	Red	373	2588	483
433	glycols	-0.4245	-0.1068	Red	386	2892	482
23	agrochemical fungicides	0.0052	0.0639	Blue	176	907	482
367	epoxides	-0.5019	-0.0892	Red	304	2202	481
251	cracking (reaction)	-0.5495	0.3702	Red	198	1836	480
796	pseudomonas aeruginosa	0.3096	0.1841	Blue	368	3969	479
492	imaging agents	0.2856	-0.1258	Blue	331	2980	474
46	aluminoxanes, me	-0.8941	0.088	Red	171	1397	473
213	chronic myeloid leukemia	1.4599	0.1719	Green	233	12375	472
733	plantae	0.0044	0.136	Blue	351	1923	471
378	ethers	-0.4064	-0.0115	Red	387	3174	470
79	anticonvulsants	1.1236	-0.421	Yellow	233	9278	470
667	osteoarthritis	1.5204	-0.219	Yellow	242	13295	469
151	biogas	-0.2981	0.3827	Red	211	1474	466
85	antigens	0.4655	0.1626	Blue	325	4289	466
958	type 1 diabetes	1.4334	-0.1289	Yellow	231	13099	466
926	templates	-0.6044	0.2822	Red	262	2852	466
408	food	0.094	0.1678	Blue	373	2959	465
586	mixing	-0.4584	0.3241	Red	324	2917	461
283	dementia	1.2303	-0.4318	Yellow	242	10146	461
293	diamines	-0.4911	-0.1691	Red	381	2298	460
340	electroluminescent display devices	-0.5314	-0.4189	Red	169	1501	459
709	phase transfer catalysts	-0.3136	-0.1079	Red	256	1125	454
384	fatty acids, esters	-0.5411	-0.0632	Red	356	2933	452
352	enantioselective synthesis	-0.1075	-0.094	Red	201	728	451
170	buffers	-0.1363	0.1213	Red	403	3019	446
343	electrolytes	-0.5711	0.0634	Red	316	1627	446
420	gastrointestinal agents	1.489	-0.3327	Yellow	210	13113	446
148	biodegradable materials	-0.6333	-0.1116	Red	277	1987	445
347	electronic packaging materials	-0.7612	-0.4223	Red	183	2148	445
684	parenteral drug delivery systems	0.8105	-0.1086	Yellow	267	6584	445
732	plant gene	0.1465	0.4287	Blue	140	2116	444
907	sulfonation	-0.2591	0.0617	Red	246	1188	444
204	chelating agents	-0.1953	-0.1534	Red	408	2943	443
965	uv radiation	-0.2982	-0.0717	Red	424	2055	441
659	organic acids	-0.296	0.1626	Red	395	2688	439
364	epilepsy	1.1683	-0.4279	Yellow	239	9181	438

ID	Label	x	y	Cluster	Weight<Links>	Weight<Total link strength>	Weight<Occurrences>
444	heart failure	1.4042	-0.3186	Yellow	213	8777	438
382	eye disease	1.3258	-0.1961	Yellow	246	10136	435
617	nanosheets	-0.6329	0.1369	Red	257	1963	434
633	nitration	-0.0911	-0.0095	Red	219	916	433
630	neuropathic pain	1.3012	-0.4605	Yellow	219	7909	427
299	diesel fuel	-0.6155	0.3501	Red	225	2069	423
874	solvent extraction	-0.1879	0.3037	Red	308	1921	421
312	dna	0.2237	0.1392	Blue	359	3160	421
277	decarboxylation	-0.12	0.0366	Red	215	1022	420
654	optical films	-0.678	-0.4452	Red	165	1422	418
323	drug toxicity	0.7501	-0.1666	Yellow	273	4828	418
954	transplant rejection	1.5688	0.0268	Yellow	212	12445	418
7	acid hydrolysis	-0.1638	0.1806	Red	310	1468	416
308	dispersion of materials	-0.5307	0.1506	Red	307	2776	415
802	pyridines	0.1166	-0.1461	Red	363	2260	414
278	decomposition	-0.3803	0.2127	Red	263	1211	412
399	fluorescence imaging	0.0659	-0.1753	Red	229	1384	412
58	anaerobic fermentation	-0.2113	0.3988	Red	180	1541	408
572	metastasis	1.0889	0.1671	Green	235	7713	408
538	lipids	0.1652	0.1	Blue	389	3770	406
609	mycosis	0.7318	0.0627	Blue	274	5876	405
849	self-assembly	-0.2598	-0.0031	Red	331	1698	404
43	allergy inhibitors	1.3436	-0.0459	Yellow	246	10268	403
290	dermatological agents	1.3542	-0.1405	Yellow	237	10413	403
665	oryza sativa	0.0064	0.2678	Blue	298	1799	402
254	cross-coupling reaction	-0.0561	-0.161	Red	183	898	400

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