

A Scientometric Analysis of Global Synthetic Biology Literature

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Abstract

The current study provides a scientometric overview of the global Synthetic Biology literature from 2005 to 2019. Data for the analysis were obtained from the Web of Science Core Collection database of Clarivate Analytics. The results showed that the global Synthetic Biology literature consisted of 12,012 publications during 2005-2019. Based on the data analysis, it is observed that the publications on synthetic biology show an increasing trend during recent years. It annually increased from 202 to 1534 from the year 2005 to the year 2019, with an annual average growth rate of 16.17 per cent. The global publication output in Synthetic Biology registered an average citation per publication rate of 27.44 from 2005 to 2019. The geographical distribution of output indicates that 96 countries contributed to a total of 12,012 publications during this period. Authors from countries like the USA, U.K., and China contributed a significant share of publications. Massachusetts Institute of Technology, USA, was found to be the most productive institution with 348 publications. Fussenegger M of *Swiss Federal Institutes of Technology* (ETH), Switzerland, was the most prolific author.

Keywords: Synthetic Biology, Scientometric analysis, Relative Citation Impact, Bibexcel, VOSviewer.

1. Introduction

Synthetic Biology (S.B.) is an emerging area of research in the field of Biological sciences. The title "synthetic biology" appeared in the literature in the 1980s, first time Barbara Hobom used it to describe genetically engineered bacteria employing recombinant DNA technology (Hobom, 1980; Benner and Sismour, 2005). Synthetic biology is a broad field that impacts numerous sectors of the economy, including food and agriculture, energy and climate,

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manufacturing and chemicals, and health and medicine. There is a range of potential applications of S.B., which could monitor and respond to conditions of the human body. Synthetic biology has wide applications in developing and producing alternative routes for valuable compounds. One of the most crucial applications of S.B. research is bio-fuels (Khalil and Collins, 2010; Keshava et al., 2018). Since synthetic biology has many potential applications in various fields, funding from governmental and private sectors has significantly increased in recent years (Bueso and Tangney, 2017). In the recent past, rapid developments have been made in synthetic biology, making substantial contributions to basic life science research, human health, environmental safety, and monetary growth (Wang and Zhang, 2019).

Given the huge volume, growing significance, and diversity of synthetic biology-related research and publications, assessing the scientific literature on this topic is crucial for researchers and policymakers in this field. Evaluation of scientific literature output is essential for understanding the nature, direction, volume, and impact of the growth of disciplines. Such evaluation studies the fields and measures people's contributions, documents, institutions, and countries. These evaluation techniques are called metric studies, such as bibliometrics or scientometrics. Most of the quantitative studies reported in the literature have focused on core scientific domains (Gholampour et al. 2020; Wu et al. 2020; Roy 2019; Dehdarad et al. 2019; Singh 2018; Borthakur and Singh 2018; Santin et al. 2015; Goldman 2014) but S.B. area has received less attention.

The present study made an attempt to fill that gap. The main focus of the present study is to apply the scientometric methods to analyse the synthetic biology research output globally. Moreover, such research could better understand the distribution of the output of the lead countries, institutions and authors. In addition to that, this study will explore the research collaboration structure of the S.B. literature with the help of suitable network visualisation tools and technologies.

2. Review of literature

Oldham, Hall and Burton (2012) carried out the first quantitative study on 'synthetic biology' based on 1,255 publication records identified by applying two exclusive keywords "synthetic biology and synthetic genomics". They reported that the USA is the leading contributor, followed by the U.K. and Germany. Similarly, Hu and Rousseau (2015) analysed the synthetic biology literature published during 2000-2013 and identified significant players in synthetic biology research. They reported that the USA and China are the substantial contributors to S.B. literature. They reported exponential growth of publications in synthetic biology during this period. Later, Raimbault et al. (2016) explored the emergence of the synthetic biology domain using the data retrieved from the WOS database. They used the bibliographical details of 4,605

publications from 2000-2015 for this study. This study mainly focused on the mapping of textual and citation networks. The analysis and the results found exponential growth of publications. The USA was identified as a significant contributor, followed by European Union countries. Recently, Shapira et al. (2017) examined the emergence of the synthetic biology literature from 2000 to 2015 based on the 8064 records obtained from the WOS database. This study mainly focused on the growth of publications in leading countries and explored international authors' collaborations using simple quantitative analysis.

This study noticed a rapid increase in global S.B. research output during recent years and reported that the USA was the most productive country, followed by Germany and China. The existing literature analysis reveals that so far, there were only a few partial scientometric studies have been carried out on Synthetic Biology literature. Hence, the present study is planned an in-depth analysis of the S.B. literature using various scientometric indices, which were not applied before.

3. Objectives of the study

The present study aimed to analyze the following aspects of global Synthetic Biology literature:

1. To examine the chronological growth trend of literature output and citations in Synthetic Biology;
2. To identify and analyse the productivity and impact of most productive countries, institutions, and authors;
3. To map and visualize the corporation network of most productive countries, institutions, and authors; and
4. To generate the thematic map of Synthetic Biology literature.

4. Methodology

Data for the present study were gathered from the Web of Science (WoS) Core Collection database of Clarivate Analytics. Publications records pertaining to Synthetic Biology during 2005-2019 were downloaded on August 15, 2020, from the WoS core collection using the following search string obtained from one of the earlier studies (Shapira et al., 2017):

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((TS=("syntheticbiolog*"OR"syntheticdna"OR"syntheticgenom*"OR"synthetic*nucleotide"OR"syntheticpromoter"OR"syntheticgene*cluster"))NOTTS=("photosynthe*")) OR (TS = ("synthetic mammalian gene*" AND "mammalian cell")) NOTTS = "photosynthe*" OR (TS = "synthetic gene*" NOT TS = ("synthetic gener*" OR"photosynthe*)) OR(TS =("artificial gene* network" OR ("artificialgene* circuit*"AND "biological system"))) NOT TS = "gener*" OR (TS = ("artificial cell") NOT TS =_("cell* telephone" OR "cell* phone" OR "cell* culture" OR "logic cell*" or "fuel cell*" or"battery cell*" or"load-cell*"
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or"geo-synthetic cell*" or"memory cell*"or"cellularnetwork"or"ramcell*"
"or"romcell*"or"maximumcell*"OR"electrochemicalcell*"OR "solar cell*")
OR (TS = ("synthetic cell") NOT TS = ("cell* telephone" OR "cell*phone" OR
"cell* culture" OR "logic cell*" or "fuel cell*" or "battery cell*" or "load-
cell*"or "geo-synthetic cell*" or "memory cell*" or "cellular network" or "ram
cell*" or "romcell*"or"maximumcell*" "OR"electrochemicalcell*"
"OR"solarcell*" "OR "photosynthe*")) OR(TS=("artificialnucleicacid*"
"OR"artificial*nucleotide*))OR(TS= ("biobrick"or "biobrick"or"bio-brick"))))
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Indexes=SCI-EXPANDED, SSCI,A&HCI, ESCITimespan=2005-2019.

After verification and elimination of incomplete records, a total of 12,012 publication records were selected for analysis. The researcher included all the document types and languages in the current study. The downloaded data was further processed, analysed, and visualized using Bibexcel (version 2017), Microsoft Excel (Office 2010), and VOSviewer (version 1.6.16) software and network visualization tools. The study is based on a whole count of countries, institutions, and authors, where each unique collaborating country or institution or author receives one full credit (Larsen, 2008; Elango & Rajendran, 2017). This method increases the participation of each country (Portella, 2019); and at the same time, one publication may count for more than one country. Due to this fact, this analysis's total number of publications exceeds the total number of publications under evaluation. This analysis categorises publications originating from England, Scotland, Northern Ireland, and Wales from the United Kingdom. The authors have used three relative citation indicators in the present study: Citations per Paper (CPP), Relative Citation Impact (RCI), and h-index. CPP is the total number of citations to the total number of publications. Relative Citation Impact measures both the influence and visibility of a nation's research globally. RCI can be computed as the ratio of world share of citations to world share of publications. The h-index is an author-level metric that indicates a researcher's impact and productivity based on how often their publications have been cited.

5. Results and discussions

5.1 Descriptive characteristics of Synthetic Biology literature

Table 1 provides the descriptive characteristics of global synthetic biology literature from the WoS core collection database from 2005 to 2019.

Table 1. Descriptive characteristics of Synthetic Biology literature

Sl.no	Description	Values
1	Period	2005:2019
2	Time-span	15 years
3	Number of publications	12012
4	Number of citations	329631
5	Number of document types	13
6	Number of Languages	17
7	Number of countries	96
8	Number of institutions	5402
9	Authors	33151
10	Number of sources	1922

The data set consists of 12,012 publications, and 329,631 citations come from 13 different document types and 17 languages. These publications were altogether contributed by 33,151 unique authors from 96 countries worldwide. There were 1,922 various sources for all the retrieved bibliographic data of those publications.

5.2 Chronological growth trend of publications and citations

Table 2 illustrates the year-wise distribution of publications, annual growth rate (AGR), citations, and citations per paper (CPP) of synthetic biology literature from 2005 to 2019. A total of 12,012 publications were found during this period, with an average of 800.8 publications per year. The highest number of documents (1567, 13.05%) was published in 2018, followed by 2019 with 1534 (12.77%) and 1365 (11.36%) in 2016. The lowest number of publications was in 2005 (202, 1.68%), followed by 2006 with 243 (2.02%). This analysis reveals an increasing trend of synthetic biology-related publications during recent years.

Table 2. Chronological growth trend of publications and citations

Sl.no	Year	No. of Publications	% of publication	AGR (%)	Citations	CPP
1	2005	202	1.68	--	13097	64.84
2	2006	243	2.02	20.30	13158	54.15
3	2007	257	2.14	5.76	14835	57.72
4	2008	324	2.7	26.07	17884	55.20
5	2009	407	3.39	25.62	23823	58.53
6	2010	511	4.25	25.55	26727	52.30

7	2011	585	4.87	14.48	26189	44.77
8	2012	793	6.6	35.56	31598	39.85
9	2013	838	6.98	5.67	32822	39.17
10	2014	976	8.13	16.47	30318	31.06
11	2015	1140	9.49	16.80	28037	24.59
12	2016	1365	11.36	19.74	26428	19.36
13	2017	1270	10.57	-6.96	20655	16.26
14	2018	1567	13.05	23.39	16832	10.74
15	2019	1534	12.77	-2.11	7228	4.71
Total / Avg.		12012	100	16.17	329631	27.44

It is evident from Table 2 that there were fluctuations in the growth of publications on synthetic biology during the period. The utmost AGR (35.56) is recorded in 2012, followed by AGR (25.62) in 2009, and the lowest AGR (2.11) recorded in 2019. Interestingly, nine out of fifteen years recorded AGR value more than the average rate. The AGR was found to be 16.17 per cent from 2005 to 2019. It is found that the 12,012 publications together received 329631 citations with an average of citations per publication (27.44) during the period under study. The rate of citation varied from 64.84 to 4.71. The highest rate CPP (64.84) was observed in 2005, while the lowest rate was observed in 2019 (CPP 4.71). Further, ten out of fifteen years (i.e., 2005 to 2014) recorded citation rates more than the average rate, i.e., 27.44 and the growth rate of citations per publication is not gradual over the years.

5.3 Most productive countries and their citation impact

The geographical distribution analysis of synthetic biology literature revealed that these publications had come from 96 countries scattered worldwide. Table 3 shows the publication productivity and citation impact in terms of citation per paper (CPP), relative citation impact (RCI), and h-index of most productive countries.

Countries that published 200 or more papers in the last fifteen years (2005-2019) have been considered the most productive countries. It is evident from Table 3 that eight out of the 15 most productive countries are from Europe, four countries from Asia, two countries are from North America, and one country each from Australia/ Oceania, respectively. These results indicated that researchers from European countries had contributed significantly to Synthetic Biology from 2005 to 2019. Among the most prolific countries, the USA is the leading country with the highest number of publications and citations (4859, 40.45%, 186931), followed by the U.K. (1463, 12.18%, 39114), China (1377,

11.46%, 29447) and Germany (1137, 11.37 %, 25796). It is found that India placed in 15th position with 249 publications and 2.07 per cent world share. Concerning both CPP and RCI values, variations in the ranking order of nations were noticed. In this case, the USA ranked first (38.47 CPP, 1.4 RCI), followed by Japan (28.79 CPP, 1.05) and Switzerland (28.18 CPP, 1.03 RCI). Concerning the h-index, the USA tops the list with an h-index score of 181, followed by the U.K. with (91), and Germany with (78). Three out of 15 most productive country's citation rate is higher than the world's citation rate. The remaining twelve country's citation rate is less than the world's citation rate, which indicates that the impact of research performed from these countries does not proportionate with their or world output in Synthetic Biology.

Table 3. Productivity and impact of most productive countries

Sl.no	Name of the country	No. of publications (% of N=12012)	No. of citations (% of N= 329631)	CPP	RCI	h-index
1	USA	4859 (40.45)	186931(56.71)	38.47	1.4	181
2	UK	1463 (12.18)	39114 (11.87)	26.74	0.97	91
3	China	1377 (11.46)	29447 (8.93)	21.38	0.78	72
4	Germany	1137 (9.47)	25796 (7.83)	22.69	0.83	78
5	Japan	648 (5.39)	18657 (5.66)	28.79	1.05	55
6	France	585 (4.87)	13636 (4.14)	23.31	0.85	57
7	Canada	492 (4.1)	12826 (3.89)	26.07	0.95	65
8	Switzerland	455 (3.79)	12821 (3.89)	28.18	1.03	59
9	Spain	420 (3.5)	10088 (3.06)	24.02	0.88	52
10	South Korea	342 (2.85)	8756 (2.66)	25.6	0.93	45
11	Italy	318 (2.65)	8126 (2.47)	25.55	0.93	40
12	Australia	297 (2.47)	7338 (2.23)	24.71	0.9	40
13	Netherlands	290 (2.41)	7051 (2.14)	24.31	0.89	47
14	Denmark	276 (2.3)	5610 (1.7)	20.33	0.74	44
15	India	249 (2.07)	4977 (1.51)	19.99	0.73	32

Research collaboration among different countries is a useful parameter to access the wideness and impact of research(Gupta et al., 2011 ; Mahala & Singh, 2021). Figure 1 shows the collaborative relationship among the most productive countries in synthetic biology research through VOSviewer. It shows, the USA, U.K., China, Germany, Japan, and France are the most productive countries, and

Table 4. Most productive institutions and their citation impact

Sl.no	Institution	Country	No. of publications (% of N=12012)	No. of citations (% of N=329631)	CPP	RCI	h-index
1	Massachusetts Institute of Technology	USA	348 (2.90)	23122 (7.01)	66.44	2.42	77
2	Chinese Academy of Sciences	China	280 (2.33)	5504 (1.67)	19.66	0.72	39
3	University of California, Berkeley	USA	265 (2.21)	15600 (4.73)	58.87	2.15	65
4	Harvard University	USA	256 (2.13)	27381 (8.31)	106.96	3.9	75
5	Swiss Federal Institutes of Technology	Switzerland	172 (1.43)	4017 (1.22)	23.35	0.85	34
6	University of Illinois	USA	171 (1.42)	7078 (2.15)	41.39	1.51	41
7	University of Edinburgh	UK	167 (1.39)	3928 (1.19)	23.52	0.86	33
8	Stanford University	USA	164 (1.37)	8841 (2.68)	53.91	1.96	49
9	University of Manchester	UK	160 (1.33)	3237 (0.98)	20.23	0.74	31
10	University of Toronto	Canada	154 (1.28)	8327 (2.53)	54.07	1.97	44

Research collaboration among different institutes increases the impact and audience of research (Mahala & Singh, 2021). Figure 2 shows the collaboration network of the most productive institutions or organizations in synthetic biology research through VOSviewer. The different patterns of color indicate the different groups of collaboration. In Figure 2, the MIT USA, Chinese Academy of Sciences, University of California Berkeley USA, Harvard University the USA, and Swiss Federal Institute of Technology are the most collaborating institutions in research globally. The MIT USA has major collaboration links reflected through the thickness of lines in Figure 2. The most productive institutions are also the most cooperating institutions in the network.

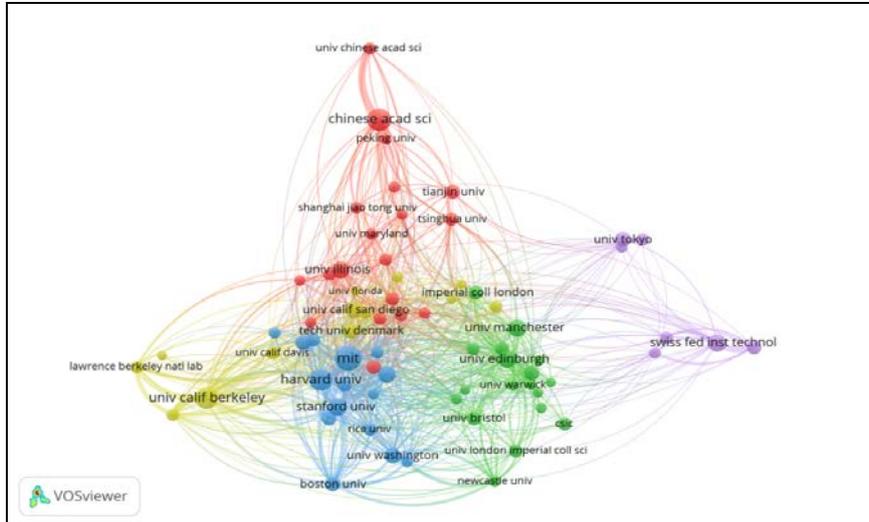


Figure 2. Collaboration network of most productive institutions

5.5 Most productive authors and their citation impact

Author analysis showed that 33,151 unique authors contributed to synthetic biology literature during the study period. The top ten most prolific authors based on the number of publications and various citation impact indices like Citations, CPP, RCI, and h-index are illustrated in Table 5.

The top author's list including seven authors from the USA, two from Switzerland, and one from China. Fussenegger M of *Swiss Federal Institutes of Technology* (ETH), Switzerland, leads the list with 118 publications, followed by Keasling JD of *the University of California, Berkeley*, USA, with 80 publications and Zhao HM of *the University of Illinois*, the USA with 62 publications. Concerning the number of citations, Keasling JD of Univ Calif Berkeley, USA ranked first with (7491) citations, followed by Collins JJ of MIT/Wyss Institute, USA (7428) citations and Voigt CA of MIT, USA (4758) citations. Concerning both CPP and RCI values Collins JJ of MIT/Wyss Institute, USA with ranked first, followed by Keasling JD of Univ Calif Berkeley, USA. While concerning by h-index, Keasling JD of Univ Calif Berkeley, USA ranked first with a highest h-index 41, followed by Fussenegger M of Swiss Fed Inst Technol (ETH), Switzerland.

Table 5. Author impact of most productive authors

Sl.no	Author	No. of Publications (% of 12012)	No. of Citations (% of N= 329631)	CPP	RCI	h-index
1	Fussenegger M (Swiss Fed Inst Technol (ETH), Switzerland)	118 (0.98)	4031 (1.22)	34.16	1.24	36
2	Keasling JD (Univ Calif Berkeley, USA)	80 (0.67)	7491 (2.27)	93.64	3.41	41
3	Zhao HM (Univ Illinois, USA)	62 (0.52)	2566 (0.78)	41.39	1.51	27
4	Weber W (Swiss Fed Inst Technol, Switzerland)	57 (0.47)	1752 (0.53)	30.74	1.12	23
5	Voigt CA (MIT, USA)	54 (0.45)	4758 (1.44)	88.11	3.21	30
6	Chen J (China Agr Univ, China)	53 (0.44)	1628 (0.49)	30.72	1.12	22
7	Lu TK (MIT, USA)	53 (0.44)	3772 (1.14)	71.17	2.59	25
8	Collins JJ (MIT/Wyss Institute, USA)	52 (0.43)	7428 (2.25)	142.85	5.21	34
9	Jewett MC (Stanford Univ, USA)	50 (0.42)	2154 (0.65)	43.08	1.57	24
10	Wang Y (Virginia Polytech Inst & State Univ, USA)	50 (0.42)	1145 (0.35)	22.9	0.83	17

It is interesting to note that these leading authors are from the most productive countries and institutions.

Figure 3 shows the collaboration network of top authors in synthetic biology research. It was evident from Figure 3 that the Chinese authors maintain good connectivity in research activities. Liu, Y obtained the highest link strength (146), followed by Li, J and Chen, J with link strength 131 each, and Liu, L with link strength 97. This network shows strong collaboration among the following authors: Du, G – Chen, J (link strength =35), Weber, W – Fussenegger, M (link strength= 21), Liu, J – Li, J (link strength = 20), Du, g –Li, J (link strength = 15) and Du, g – Liu, L (link strength = 13).

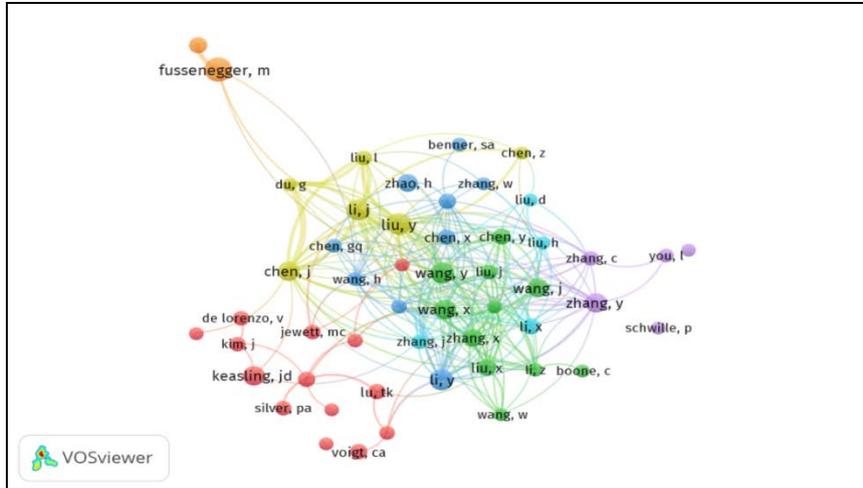


Figure 3. Collaboration network of most productive authors

5.6 Thematic map

Figure 4 illustrates the thematic representation of essential themes in synthetic biology which is based on the theory of density and centrality measures. This map was generated using the Biblioshny web interface of the Bibliometrix 3.1.0 R package. It could be seen that the map is divided into four parts, namely basic theme (lower right part), emerging or declining theme (lower left part), motor theme (upper right part), and niche theme (upper left part). The researcher constructed this thematic map (Figure 4) based on a full-time span from 2005 to 2019. The researcher selected the top 400 author keywords for creating this thematic map.

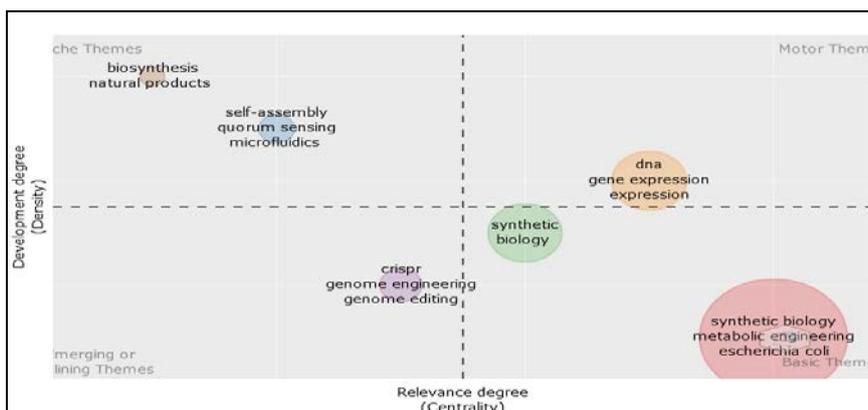


Figure 4. Thematic map

Table 6 illustrates the clusters shown in Figure 4, the first cluster represented by Synthetic biology.

Table 6. Themes and keywords in thematic map

Cluster representation	Theme	Keywords in clusters
Synthetic biology	Basic theme	Synthetic biology, metabolic engineering, escherichia coli, engineering, systems biology, saccharomyces cerevisiae, protein engineering, yeast, biotechnology, directed evolution, protein, metabolic, biocatalysis, biosensor, evolution, biofuels
Synthetic	Basic theme	Synthetic, biology
CRISPR	Emerging / declining theme	Crispr, genome engineering, genome editing, genetic engineering
Self-assembly	Niche theme	Self-assembly, quorum sensing, microfluidics
Biosynthesis	Niche theme	Biosynthesis, natural products
DNA	Motor theme	DNA, gene expression, expression, synthetic gene, gene, RNA, promoter, gene regulation

The main topics under this cluster are *metabolic engineering, escherichia coli, engineering, systems biology, saccharomyces cerevisiae, protein engineering, yeast, biotechnology, directed evolution, protein, metabolic, bio-catalysis, biosensor, evolution, and bio-fuels*. According to the thematic map, these themes come under the primary themes with high density and low centrality. There was much work on these themes, but it is not easy to find a future direction because most of these topics are covered. The next cluster represented by the term "*synthetic*" is also listed under the basic theme, which is a general concept related to synthetic biology. The research theme cluster represented by *Crispr* is an emerging theme in synthetic biology literature. This theme has high centrality and high density. This theme covers prominent research areas like genome engineering, genome editing, and *genetic engineering*. The research theme cluster represented by *self-assembly* and *biosynthesis* is in the niche theme position in the thematic map. Both themes are highly developed and isolated. The centrality is high, but the density is low. Researchers could observe various potential areas like *quorum sensing, micro-fluidics, and natural products* under this theme. The next theme is the motor theme—this research theme cluster is represented by the term *DNA*. The main keywords under this cluster are *gene expression, expression, synthetic gene, gene, RNA, promoter, and gene regulation*. These terms are highly contributory themes in synthetic biology literature.

6. Conclusion

This study provides an up-to-date assessment of the body of synthetic biology literature published from 2005 to 2019. The results showed rapid growth and the global spread of publications in synthetic biology during recent years. The annual increase of publications from 202 to 1,534 from the year 2005 to the year 2019, with an annual average growth rate of 16.17 per cent. The global publication output in synthetic biology registered an average citation per publication rate of 27.44 from 2005 to 2019. Authors from 96 countries were made contributions to synthetic biology during this period. The leading contenders are the USA, U.K., China, Canada, France, etc. It was found that the lowest populated and high-income countries are more productive than the most populated and low-income countries. India placed 15th position in global publication output in synthetic biology literature during 2005-2019, with 249 publications and 2.07 per cent world share. The USA alone contributed 56.71 shares in global citation output among the top 15 leading countries, followed by U.K. and China. Only 3 out of 15 leading countries have achieved high values of RCI. Similarly, top institutions also originated from the most productive countries. The *Massachusetts Institute of Technology, USA*, was the most productive institution with 348 publications in S.B. during this period. Fussenegger, M of *Swiss Federal Institutes of Technology (ETH), Switzerland*, was the most influential author with 118 publications. During the analysis period, strong collaborations were found between the most productive countries and institutions in synthetic biology research activities. Hence, it is very much needed for countries with low productivity and low impact to give more attention to developing more collaborative research with the leading countries in synthetic biology research activities. It is expected that the findings will help future researchers in synthetic biology to focus their research efforts on various areas and fill up the gaps based on the stated scenario. There are several implications to this study. First, this study provides an up-to-date assessment of the body of SB literature published from 2005 to 2019. Secondly, this study was based on the data indexed in one of the world-renowned databases, i.e., WOS. The result helps us better understand SB from a researcher's perspective. It enhances our understanding of SB as a significant discipline with more comprehensive applications in all spheres of human life today. Another important implication is that this study investigates recent trends in the multidisciplinary research field of SB. Therefore, the findings will help researchers interested in SB to focus their efforts on high impact and relevance to advance knowledge in the area. Finally, this research allows administrators and policymakers, especially those directly connected to the science and technology (S&T) field, can benefit and develop their current awareness regarding the recent SB topics identified and brought to light by this study. In addition, this study's results will positively affect one who engages in biological sciences research and developmental activities. This research also paves the way for further research regarding a more in-depth analysis of subfields of the SB discipline. Finally, the

investigation will be helpful to academicians and practitioners interested in the SB discipline.

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