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Convention on Biological Diversity

Subsidiary Body for Scientific, Technical and Technological Advice
Twenty-sixth meeting
Nairobi, 13–18 May 2024
Item 5 of the provisional agenda*
Synthetic biology

Literature review of the trends and issues in synthetic biology (2012–2023)**

Note by the Secretariat

I. Introduction

1. In decision 15/31, the Conference of the Parties established a process for broad and regular horizon scanning, monitoring and assessment of the most recent developments in synthetic biology consisting of the following steps: (a) Information gathering; (b) Compilation, organization and synthesis of information; (c) Assessment; and (d) Reporting on outcomes.

2. In the same decision, the Conference of the Parties established a multidisciplinary Ad Hoc Technical Expert Group on Synthetic Biology ("multidisciplinary Expert Group") to support this process. At the first meeting of the multidisciplinary Expert Group in July 2023, the experts agreed on a process for the 2023-2024 intersessional period consisting of both a multidisciplinary expert-driven submissions process by the experts of the Group and a literature review to be conducted by the Secretariat. The multidisciplinary Expert Group recommended that the literature review should be based on a revised list of trends and issues in synthetic biology produced by the Secretariat, using the 2019 report of the Ad Hoc Technical Expert Group on Synthetic Biology (CBD/SYNBIO/AHTEG/2019/1/3), the Open-ended Online Forum on Synthetic Biology, the submissions of information and the publication "Technical Series No. 100: Synthetic Biology". The revised list can be found in annex I to document CBD/SYNBIO/AHTEG/2024/1/2.

3. In line with the requests from the multidisciplinary Expert Group, the Secretariat commissioned a preliminary literature review on the basis of the revised list of trends and issues in synthetic biology. This literature review was conducted as part of the steps of (a) Information gathering and (b) Compilation, organization and synthesis of information of the process of broad and regular horizon scanning, monitoring and assessment pursuant to decision 15/31.

4. The literature review aims to provide a preliminary bibliometric analysis to understand identified trends and issues in synthetic biology. Thus, it seeks to provide additional quantitative analyses to describe research activity within the identified trends and issues in synthetic biology through publications and patents to support deliberations by the multidisciplinary Ad Hoc Technical

* CBD/SBSTTA/26/1.
** The present document is being issued without formal editing.

Expert Group on Synthetic Biology and the Subsidiary Body on Scientific Technical and Technological Advice at its twenty-sixth meeting, as well as complement the overall broad and regular horizon scanning, monitoring and assessment process. However, it is important to note that this literature review does not seek to describe the potential impacts of synthetic biology. Further, given the time constraints, it should be considered as a preliminary analysis rather than a definitive analysis.

II. Acknowledgements and disclaimers

5. This literature review was prepared by Ms. Madhulika Bhati, principal scientist (National Institute of Science Communication and Policy Research, New Delhi, India) and visiting professor (Department of Industrial Engineering, Dalhousie University, Halifax, Canada), as a lead author, with inputs and guidance from contributing authors from the Secretariat of the Convention on Biological Diversity. The lead author declares no conflict of interest.

6. The lead author would like to acknowledge and thank Prof. Floris Goerlandt and Prof. Ron Pelot (Department of Industrial Engineering, Dalhousie University) for their informal guidance provided on various bibliometric aspects.

7. The Secretariat would also like to thank all those Parties and observers who provided extensive review comments on the first draft of this document, which was made available for review from 16 January to 15 February 2024. Peer-review comments were provided by 10 Parties, one organization representing indigenous peoples and local communities and 10 other organizations[1]. A total of 303 comments were received during this process. The work underlying this document was kindly supported by a grant from the European Union.

8. Responses to the peer review comments, as well as a spreadsheet containing the collected and supplementary data, are available on the following website: www.cbd.int/synbio/past_activities/literature_review.shtml.

10. While acknowledging that there is no internationally agreed definition of "*synthetic biology*", for the purposes of this document, the author has used the operational definition of the Ad Hoc Technical Expert Group on Synthetic Biology, that "*synthetic biology is a further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems*", which was considered useful as a starting point for the purpose of facilitating scientific and technical deliberations under the Convention and its Protocols in decision XIII/17 (also see Technical Series No. 100). Further, the term "trends and issues" is used throughout this document pursuant to decision 15/31.

III. Methodology

11. This literature review emphasizes the quantification of trends and issues within the field of synthetic biology, which can be found on the aforementioned revised list that was produced by the Secretariat. To accomplish this quantification, a bibliometric approach was chosen based on previous analyses on nanotechnology and its application in the agricultural sector and focused on assessing temporal and geographical indicators related to the trends and issues in synthetic biology (Sujit Bhattacharya, 2012; Bhati, 2019).

[1] The original peer review comments are available on the Biosafety Clearing-House: https://bch.cbd.int/en/submissions-to-notifications?schema=submission&currentPage=1&notification=2024-003

12. The analysis was conducted in two parts. In the first part, publications related to each of the trends and issues in synthetic biology were quantified to better understand the research activity associated with each of these topics. In the second part, a brief patent analysis was performed to investigate the level of innovation associated with the field of synthetic biology more generally. Further, to align the analysis with discussions related to synthetic biology under the Convention on Biological Diversity[2], the time period 1 January 2012 to 31 December 2023 was chosen.

A. Quantitative analysis of published literature

(a) Development of search strings

13. Bibliometric analyses are based on the use of Boolean searches[3] to quantify the number of publications associated with a topic under investigation. This analysis relies on how researchers self-describe their work in the titles and abstracts of published literature (Muhuri, 2019; Utkarsh, 2021; Behl, 2022). For the analysis, an overarching bucket term was developed to restrict the results of the searches to publications that are more likely to be relevant to the field of synthetic biology (Shapira, 2017; Nerlich, 2020). Thus, to capture the range of potential descriptions of the various applications of synthetic biology, the bucket term was chosen to be: ("synthetic biology" OR "engineering biology" OR "genetic* engineer*" OR "bioengineer*" OR "synthetic genom*" OR "genetically modified" OR "genetic* modif*" OR "gene edit*" OR "genome edit*").

14. Following this, specific search strings were developed for each of the 55 trends and issues in synthetic biology. Each individual key string was developed using keywords associated with each specific trend or issue derived from terminology used in relevant publications, drawing upon resources including Technical Series No. 100, the submissions of information pursuant to paragraph 7 of the decision 15/31[4] and the Open-ended Online Forum on Synthetic Biology.[5] The search strings associated with each of the trends and issues were then further refined following the peer review process and by scanning the titles and abstracts of the top results. For certain trends and issues, more than one search string was used to capture a wider scope of the publication activity within particular trends and issues in synthetic biology. The search strings used for the analysis are presented in annex I.

(b) Data extraction and analysis

15. A search strategy was employed using the bucket term (see above) AND; followed by the key string(s) developed with respect to each identical issue and trend (annex I). These search strings were executed with the Scopus[6] database, focusing on “article title”, “abstract” and “keyword” fields and the “topic” field with the Web of Science[7] database. Exclusion criteria were implemented to consider only original articles, review papers, book chapters, conference proceeding papers, editorials, notes and short surveys papers in English. Other types of documents including letters and errata were not considered.

16. After conducting the unique Boolean searches in both Web of Science and Scopus there was a 95% confidence interval consistency between the two databases. Thus, for the quantification of publications, Scopus was ultimately chosen as the primary database due to its higher yield of scientific articles and observed redundancy of papers. Following the search, the results were exported

[2] Decision XI/11 (New and emerging issues) (also see section 8 of Technical Series No. 100)
[3] A Boolean search is a type of search that allows users to combine keywords with operators (such as AND, OR, NOT) to produce more relevant and specific results. The operator “AND” is used to narrow down a search, when used between two keywords the search engine will yield results that include both terms. The operator “OR” is used to broaden the search, when used between two keywords the search engine will yield results that include either of the terms. Lastly the operator “NOT” is to exclude specific terms from the search, when used before a keyword search engine will yield results that do not include that term.
[4] CBD/SYNBIO/AHTEG/2023/1/INF/1
[5] CBD/SYNBIO/AHTEG/2023/1/INF/2
[6] https://www.scopus.com/home.uri
[7] https://www.webofscience.com

as Microsoft Excel files for further processing. To allow for summation of the results, duplicates were removed between each subset, as well between each of the trends and issues.

(c) Temporal indicator analysis

17. Searches were conducted for the period 2012–2023 (inclusive) and the results extracted as an Excel spreadsheet. Once duplications were removed, the number of publications for each year for the period 2012–2023 were quantified using Excel. Subsequently, all 55 trends and issues were organized in descending order based on the total number of publications. Next, since there could be duplicates between the trends and issues in synthetic biology, all publications were next compiled by year and duplicates were removed to provide an overall quantification of the publications per year for the period 2012–2023. Finally, using Microsoft Excel, linear fit (R^2 value) and average growth rate calculations were then conducted.

(d) Geographic indicator analysis

18. The next analysis performed aimed to capture the publications by country. Geographical information from each publication was extracted from the corresponding author's affiliation using the available tools on the Scopus database. Once the geographic location was assigned to every publication based on the location of the corresponding author's institution, the number of publications were enumerated by country to obtain a final publication count per trend and issue for the period 2012–2023.

19. To further understand how research groups in different countries collaborate, a collaboration analysis was then conducted among the top five publishing countries amongst the 55 trends and issues in synthetic biology. Utilizing Scopus data, the analysis focused on quantifying countries based on the location of the lead author's institution and co-authors on the publications. A map was generated using Microsoft Excel to depict levels of collaboration between various countries.

B. Patent analysis

20. In the second part of the analysis and to further supplement the information obtained through publication analysis, preliminary patent analyses were performed. The analysis focused on quantifying the overall number of patents filed between 2012 and 2023, identifying relevant patent classes and understanding their geographical distribution. This involved searching for patents published in English for the period 2012–2023.

21. To conduct the analysis, PATENTSCOPE, a database maintained by the World Intellectual Property Organization (WIPO), was used to retrieve the relevant patent information due to its extensive global coverage and advanced search functionalities. Further, the International Patent Classification (IPC) classes maintained by WIPO, were also analyzed given their hierarchical system used to categorize patents and applications according to their specific subject matter from more general to more specific. The IPC system consists of several levels of classifications, including section (more general)[8], class, subclass, main groups and subgroups (more specific) (WIPO, 2023).

22. The analytical approach taken was to first run a search on PATENTSCOPE using the same Boolean bucket term[9] from the literature analysis. From the PATENTSCOPE results, information on the patents published per year for the period 2012–2023 and geographic metadata associated with the filing office and the relevant IPC patent classes were obtained.

[8] IPC sections are organized into eight categories, covering broad technological fields: (A) Human Necessities; (B) Performing Operations, Transporting; (C) Chemistry, Metallurgy; (D) Textiles, Paper; (E) Fixed Constructions; (F) Mechanical Engineering, Lighting, Heating, Weapons; (G) Physics; and (H) Electricity.

[9] ("synthetic biology" OR "engineering biology" OR "genetic* engineer*" OR "bioengineer*" OR "synthetic genom*" OR "genetically modified" OR "genetic* modif*" OR "gene edit*" OR "genome edit*")

23. Next, based on previously published literature and the results from searching the bucket term, a further investigation into the most prominent patent classification, C12N[10], was conducted (van Doren, 2013). In a similar manner, PATENTSCOPE was utilized to obtain information on the patent filings per year, geographic information and a breakdown of the most prominent classifications under C12N for the period 2012–2023. Upon further investigation for emerging patent sections and relevance to the trends and issues in synthetic biology related to bioinformatics, machine learning and automation processes, a similar analysis was conducted for the classification G16B[11] for the period 2012–2023 using PATENTSCOPE.

III. Results

A. Publication analysis related to the trends and issues in synthetic biology

24. After removing duplicate articles between all trends and issues in synthetic biology, an overall total of 60,358 publications were retrieved related to each of the trends and issues for the period 2012–2023. Of this total, 35,177 (58%) were original articles, 16,122 (27%) were review papers, 628 (1%) were short surveys, 5,041 (8%) were book chapters, 1,116 (2%) were editorials, 1,069 (2%) were notes and 1,205 (2%) were conference proceeding papers.

25. Regarding the individual trends and issues in synthetic biology, table I (below) provides an overview of the total number of publications for the period 2012-2023. The item "Medical and therapeutic synthetic biology applications" had the largest number of publications with 19,797 (32.80%), followed by "Genome-edited plants" (7,896 publications; 13.08%), "Synthetic biology-enabled production of antibiotics, natural products and medically relevant compounds" (6,745 publications; 11.17%), "Increased sophistication and expansion of genome editing tools" (4,895 publications; 8.11%) and "Synthetic biology-enabled production of petrochemical precursors and industrial chemicals" (4,371 publications; 7.24%). In contrast, "Adoption of the Kunming-Montreal Global Biodiversity Framework" (1 publication; <0.01%), "Increased scale and use in series of synthetic biology interventions" (4 publications; 0.01%), "Cyberbiosecurity" (14 publications; 0.02%), "Use of genome editors to create null or negative segregants" (14 publications; 0.02%) and "Engineered sterility of non-native plant species" (15 publications; 0.02%) had the lowest number of publications retrieved. It could also be noted that 15 trends and issues in synthetic biology had over 1000 publications, while 16 trends and issues in synthetic biology had under 100 publications.

Table I
List of 55 issues and trends in synthetic biology and their corresponding publication counts for the period 2012–2023

	Identified issues and trends in synthetic biology	*Publications*	*Percentage of publications*[12]
1	Medical and therapeutic synthetic biology applications	19 797	32.80
2	Genome edited plants	7 896	13.08
3	Synthetic biology-enabled production of antibiotics, natural products and medically relevant compounds	6 745	11.17
4	Increased sophistication and expansion of genome editing tools	4 895	8.11

[10] Microorganisms or enzymes; compositions thereof; propagating, preserving, or maintaining microorganisms; mutation or genetic engineering; culture media.
[11] Bioinformatics, i.e., information and communication technology (ICT) specially adapted for genetic or protein-related data processing in computational molecular biology.
[12] The percentage of publications was calculated using the total number of publications following the removal of duplicate articles between trends and issues in synthetic biology (60,358 publications).

5	Synthetic biology-enabled production of petrochemical precursors and industrial chemicals	4 371	7.24
6	Advances in protein engineering	4 311	7.14
7	Integration of artificial intelligence and machine learning	3 950	6.54
8	Genome edited animals	2 691	4.46
9	Synthetic biology applications for bioremediation, biodegradation or biomining	2 513	4.16
10	Biosensors, sensory devices and diagnostics	2 043	3.38
11	Improved next-generation sequencing and bioinformatics	1 510	2.50
12	Metabolic engineering of crops	1 355	2.24
13	Engineering photosynthesis	1 252	2.07
14	Improvements in DNA synthesis and assembly	1 218	2.02
15	Synthetic biology-enabled production of cosmetics and fragrances	1 106	1.83
16	Increased sophistication of genetic circuits	931	1.54
17	Automation and use of biofoundries	918	1.52
18	Synthetic biology-enabled production of food, food ingredients and flavors	888	1.47
19	Microbiome engineering for non-medical purposes	668	1.11
20	Improvements to genome and karyotype engineering	641	1.06
21	Cell-free systems	630	1.04
22	Dual-use nature and biosecurity implications of synthetic biology	590	0.98
23	Development of engineered gene drives to control vector-borne and invasive species	514	0.85
24	Virus-induced genome editing and genetic modifications	484	0.80
25	Transient modification of agricultural plants, pests and pathogens using RNAi or nanomaterials	467	0.77
26	Capture and recycling of greenhouse and waste gases using synthetic biology applications	426	0.71
27	Changes in ethical standards	425	0.70
28	Advances in xenobiology	400	0.66
29	Engineered bacteria for nitrogen-fixation and fertilizers	396	0.66
30	Increasing carbon capture efficiency in plants	279	0.46
31	Development of protocells, minimal cells and artificial living machines for research purposes	250	0.41
32	Interaction of synthetic biology organisms in the environment and potential for cumulative effects	217	0.36
33	Self-limiting insect systems	209	0.35
34	Synthetic biology-enabled production of fabrics, textile dyes and materials	202	0.33
35	The use of synthetic biology for art and design	179	0.30
36	Use of synthetic biology in wild organisms in the context of resilience in threatened species	177	0.29
37	Increased field testing of synthetic biology applications, including in areas outside the national jurisdiction of the developer or funder	172	0.28
38	Living materials and biofilms	165	0.27
39	Bio-fabricated wildlife products	151	0.25

40	Technical refinement of novel delivery systems and chemistries to modify organisms in the field or in nature	62	0.10
41	Genetically engineered containment systems	58	0.10
42	De-extinction of extinct animals	52	0.09
43	Mitochondrial and plastome engineering	52	0.09
44	Paratransgenetic approaches for controlling vector-borne diseases	51	0.08
45	Non-biological uses of synthetic biology	47	0.08
46	Self-spreading vaccines for wildlife	45	0.07
47	Ability to re-create viruses by chemical DNA synthesis	24	0.04
48	Plant bioproduction of vaccines and anti-venoms	17	0.03
49	Inequity in the participation of developing countries in the context of synthetic biology	17	0.03
50	Transboundary movements and relation to detection and identification of synthetic biology organisms, parts and products	16	0.03
51	Use of genome editors to create null or negative segregants	15	0.02
52	Engineered sterility of non-native plant species	14	0.02
53	Cyberbiosecurity	14	0.02
54	Increased scale and use in series of synthetic biology interventions	4	0.01
55	Adoption of the Kunming-Montreal Global Biodiversity Framework	1	0.00

(a) Annual publication rate analysis

26. Next, to better understand how the number of publications related to the field of synthetic biology evolved annually over the period 2012–2023, the total number publications for all 55 trends and issues per year was found. As figure I demonstrates below, there has been a steady increase in the rate of publications per year within the field of synthetic biology increasing linearly from approximately 2,500 in 2012 to 7,900 in 2023 (a rough increase of 559 additional publications per year; $R^2 = 0.975$). The average growth rate per year across 2012–2023 was 11%, with the highest growth rate observed between 2015 and 2016 (19% relative to 2015).

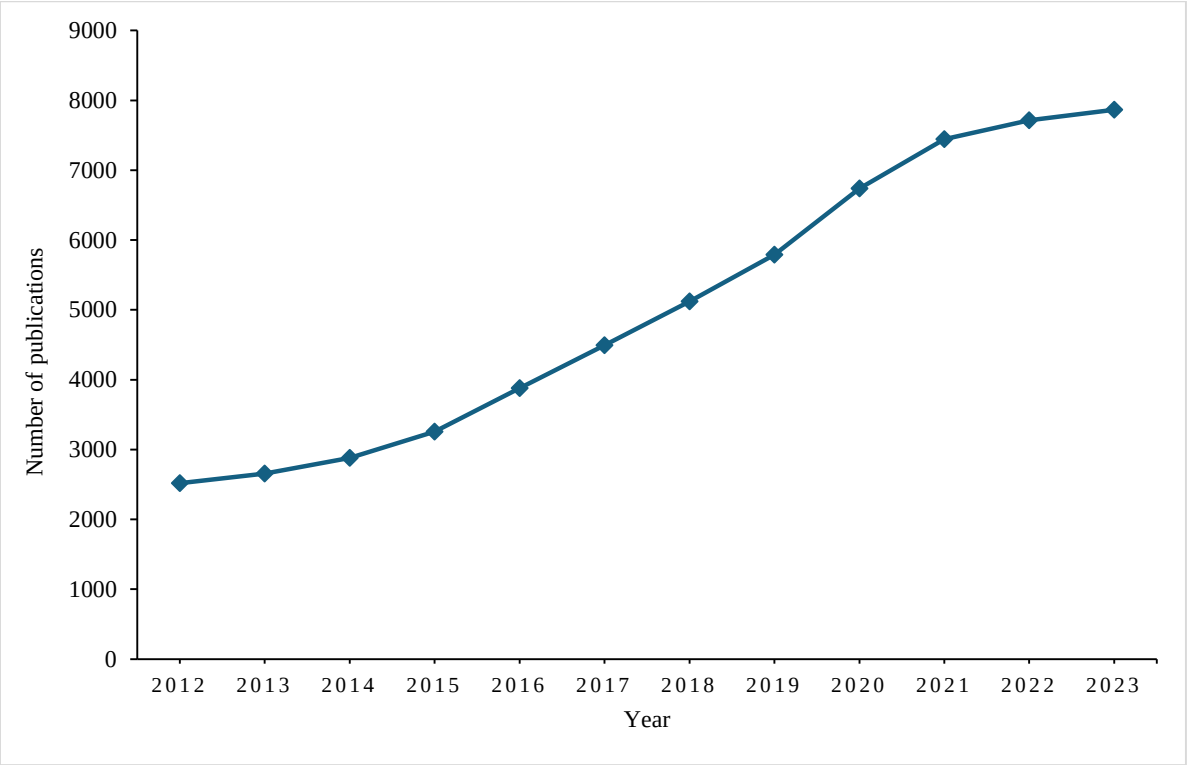

Figure I

Temporal analysis of the publication rate of the 55 55 trends and issues in synthetic biology for the period 2012–2023

The annual rate of publications in synthetic biology represents the total number of publications from all 55 trends and issues in synthetic biology after duplications were removed between trends and issues.

27. Regarding how the annual rate of publications changed over the period 2012–2023 for the individual 55 trends and issues in synthetic biology, the publication rate per item per year was quantified. The results are presented in annex II.

28. In general, the annual rate of publication for the trends and issues either grew linearly, increasing the number of publications per year, or remained relatively constant. For example, the trends related to genome editing, "Genome-edited plants", "Genome-edited animals" and "Increased sophistication and expansion of genome editing tools", demonstrated strong linear growth (between 63% and 75% over year; R^2 values between 0.94 and 0.97). Some examples of other trends with more modest growth included "Integration of artificial intelligence and machine learning" (average growth rate = 13.4%, $R^2 = 0.85$), "Improved generation sequencing and bioinformatics" (average growth rate = 18.6%, $R^2 = 0.93$) and "Microbiome engineering for non-medical purposes" (average growth rate = 21.7%, $R^2 = 0.91$). In contrast, "Synthetic biology-enable production of petrochemical precursors and industrial chemicals" (growth rate = 3.24%), "Protein engineering" (growth rate = 0.19%), "Automation and the use of biofoundries" (growth rate = 4.45%) and "Improvements in genome and karyotype engineering" (growth rate = 1.31%) remained relatively consistent in the annual number of publications made available during the period 2012–2023.

29. A geographical analysis was performed to indicate the locations that are contributing the most to the publishing landscape using the information available in the Scopus database. Table II below indicates 20 countries with the largest contribution to publications on the trends and issues in synthetic biology. Notably, the United States of America and China prominently emerge as the top two contributors in the graphical representation. The United Kingdom, India and Germany represent the next cluster of countries with the third highest publication output with similar levels of publications. Further, it can also be observed that in terms of regional grouping, six countries are

from Asia, 10 countries are from Europe, two countries are from North America, one is from Oceania and one is from South America.

Table II
Countries with the highest publication output related to the 55 trends and issues in synthetic biology for the period 2012–2023

	Country	*Number of publications*
1	United States of America	20 306
2	China	13 122
3	United Kingdom of Great Britain and Northern Ireland	4 913
4	India	4 657
5	Germany	4 433
6	Japan	3 017
7	Republic of Korea	2 256
8	Canada	2 035
9	Italy	2 033
10	Australia	1 995
11	France	1 974
12	Spain	1 719
13	Netherlands (Kingdom of)	1 461
14	Switzerland	1 228
15	Brazil	997
16	Iran (Islamic Republic of)	951
17	Denmark	874
18	Sweden	868
19	Pakistan	810
20	Russian Federation	769

30. Finally, to understand better how researchers within the countries with the highest publication output, a collaboration analysis was performed for United States of America (figure II), China (figure III), Great Britain and Northern Ireland (figure IV), India (figure V) and Germany (figure VI).

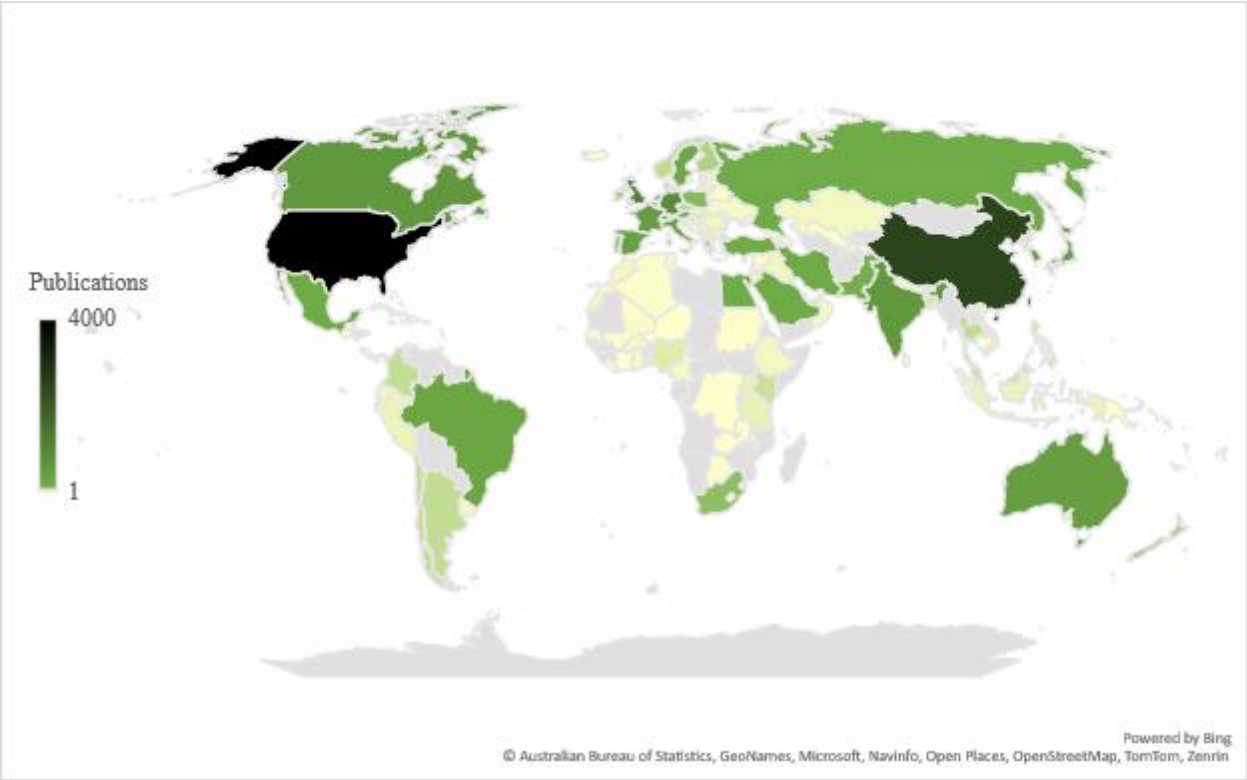

Figure II

Collaboration map for research groups based in United States of America

A global heatmap showing co-authorship patterns between lead research groups in the United States of America (black, indicating over 4000 publications) and collaborators worldwide. Yellow indicates one publication between a lead research group based in the United States of America and a collaborating research group based in another country. Green indicates 100 publications between lead research groups based in the United States of America and collaborating research groups in another country. For example, 101 publications have been published between lead research groups in the United States of America and co-authoring research groups in Mexico. Gray areas indicate that no papers were co-authored by research groups in the United States of America and research groups in that country.

31. For the period 2012–2023, research groups in the United States of America collaborated with research groups in 125 other countries in all regions. During this period, they tended to collaborate internationally the most with research groups in China (2,455 publications), the United Kingdom of Great Britain and Northern Ireland (1,100 publications), Germany (844 publications), Canada (571 publications), India (542 publications), Japan (487 publications), Republic of Korea (451 publications), Australia (436 publications), France (425 publications) and Italy (389 publications).

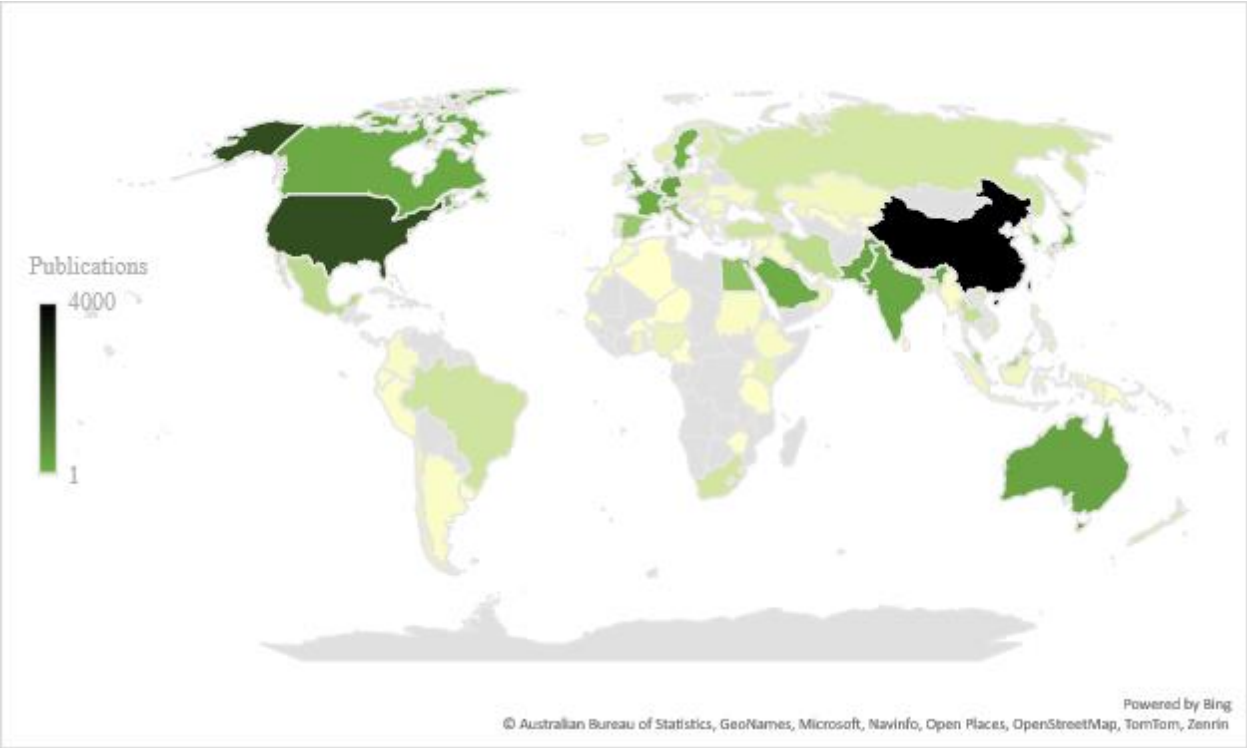

Figure III

Collaboration map for research groups based in China

A global heatmap showing co-authorship patterns between lead research groups in China (black, indicating over 4000 publications) and collaborators globally. Yellow indicates one publication between a lead research group based in China and a collaborating research group based in another country. Green indicates 100 publications between lead research groups based in China and collaborating research groups in another country. For example, 76 publications have been published between research groups in China and co-authoring research groups in Egypt. Gray areas indicate that no papers were co-authored by research groups in China and research groups in that country.

32. For the period 2012–2023, research groups in China collaborated with research groups in 100 other countries in all regions. Overall, research groups in China tended to collaborate internationally the most with research groups in United States of America (2,264 publications), the United Kingdom of Great Britain and Northern Ireland (441 publications), Australia (314 publications), Germany (292 publications), Pakistan (278 publications), India (223 publications), Japan (193 publications), Canada (190 publications), Republic of Korea (165 publications) and Denmark (131 publications).

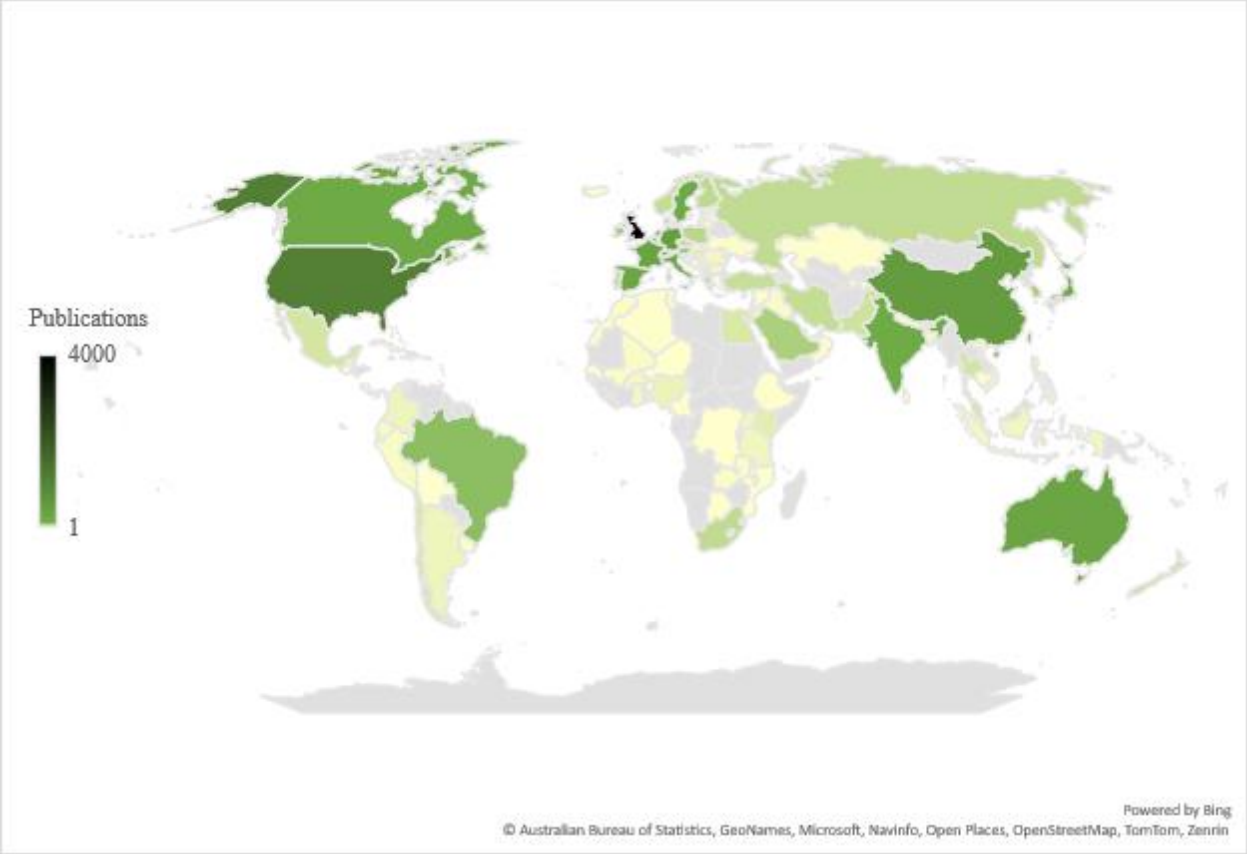

Figure IV

Collaboration map for the United Kingdom of Great Britain and Northern Ireland

A global heatmap showing co-authorship patterns between lead research groups in the United Kingdom of Great Britain and Northern Ireland (black, indicating over 4000 publications) and collaborators globally. Yellow indicates one paper between a lead research group based in the United Kingdom of Great Britain and Northern Ireland and a collaborating research group based in another country. Green indicates 100 publications between lead research groups based in the United Kingdom of Great Britain and Northern Ireland and collaborating research groups in another country. For example, 62 publications have been published between research groups in the United Kingdom of Great Britain and Northern Ireland and co-authoring research groups in Republic of Korea. Gray areas indicate that no papers were co-authored by research groups in the United Kingdom of Great Britain and Northern Ireland and research groups in that country.

33. For the period 2012–2023, research groups in the United Kingdom of Great Britain and Northern Ireland collaborated with research groups in 115 other countries in all regions. Overall, research groups in the United Kingdom of Great Britain and Northern Ireland tended to collaborate internationally the most with research groups in United States of America (1,101 publications), Germany (445 publications), China (488 publications), France (304 publications), Italy (265 publications), Australia (251 publications), Spain (242 publications), Kingdom of the Netherlands (240 publications), Canada (169 publications) and Sweden (168 publications).

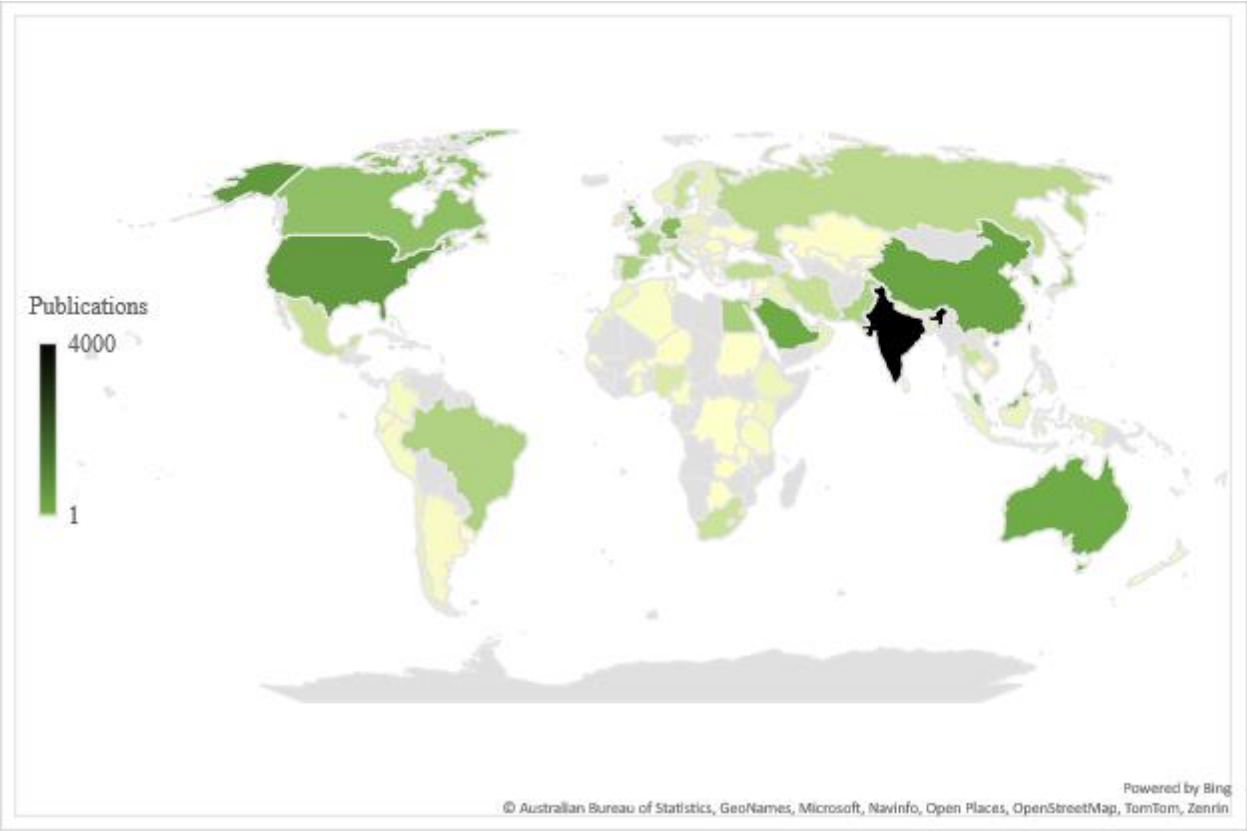

Figure V
Collaboration map for India
A global heatmap showing co-authorship patterns between lead research groups in the India (black, indicating over 4000 publications) and collaborators globally. Yellow indicates one publication between a lead research group based in the India and a collaborating research group based in another country. Green indicates 100 publications between research groups based in the India and research groups in another country. For example, 48 publications have been published between research groups in the India and co-authoring research groups in the Russian Federation. Gray areas indicate that no papers were co-authored by research groups in the India and research groups in that country.

34. For the period 2012–2023, research groups in India collaborated with research groups in 106 other countries in all regions. Overall, research groups in the India tend to collaborate internationally the most with research groups in United States of America (543 publications), China (277 publications), Republic of Korea (169 publications), Australia (146 publications), the United Kingdom of Great Britain and Northern Ireland (137 publications), Saudi Arabia (133 publications), Malaysia (87 publications), Germany (81 publications), Canada (78 publications) and Israel (66 publications).

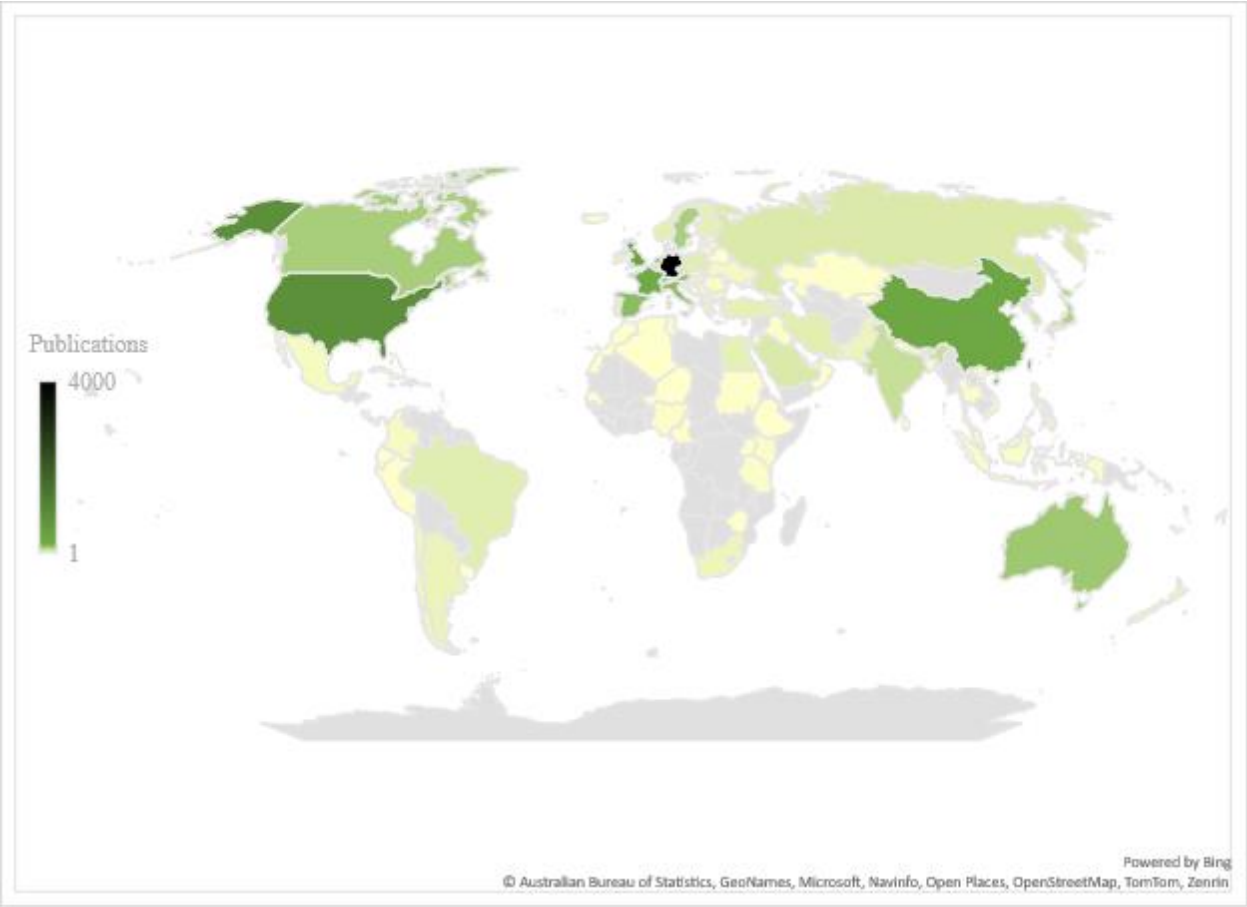

Figure VI

Collaboration map for Germany

A global heatmap showing co-authorship patterns between lead research groups in the Germany (black, indicating over 4000 publications) and collaborators globally. Yellow indicates one publication between a lead research group based in the Germany and a collaborating research group based in another country. Green indicates 100 publications between lead research groups based in the Germany and collaborating research groups in another country. For example, 118 publications have been published between research groups in the Germany and co-authoring research groups in Sweden. Gray areas indicate that no papers were co-authored by research groups in the Germany and research groups in that country.

35. For the period 2012–2023, lead research groups in Germany collaborated with research groups in 100 other countries in all regions. Overall, research groups in the Germany tended to collaborate internationally the most with research groups in United States of America (833 publications), the United Kingdom of Great Britain and Northern Ireland (441 publications), China (318 publications), Kingdom of the Netherlands (262 publications), France (242 publications), Switzerland (239 publications), Italy (169 publications), Spain (158 publications), Austria (148 publications) and Australia (135 publications).

B. Patent trend analyses

36. In the second part of the analysis and as a complement to the analysis of published literature above, a preliminary patent analysis was performed. To start, the Boolean search term used for the literature analysis was implemented for the patent searches. Thus, for the period 2012–2023, a total of 51,153 patents were retrieved. During this period the rate of patents filed per year was obtained (figure VII). It can be observed that the rate of patents filed per year steadily increased from 1,492 in 2012 to 7,343 in 2023 (roughly 625 additional patent filings per year; $R^2 = 0.96$) with an average annual growth rate of 17.7%.

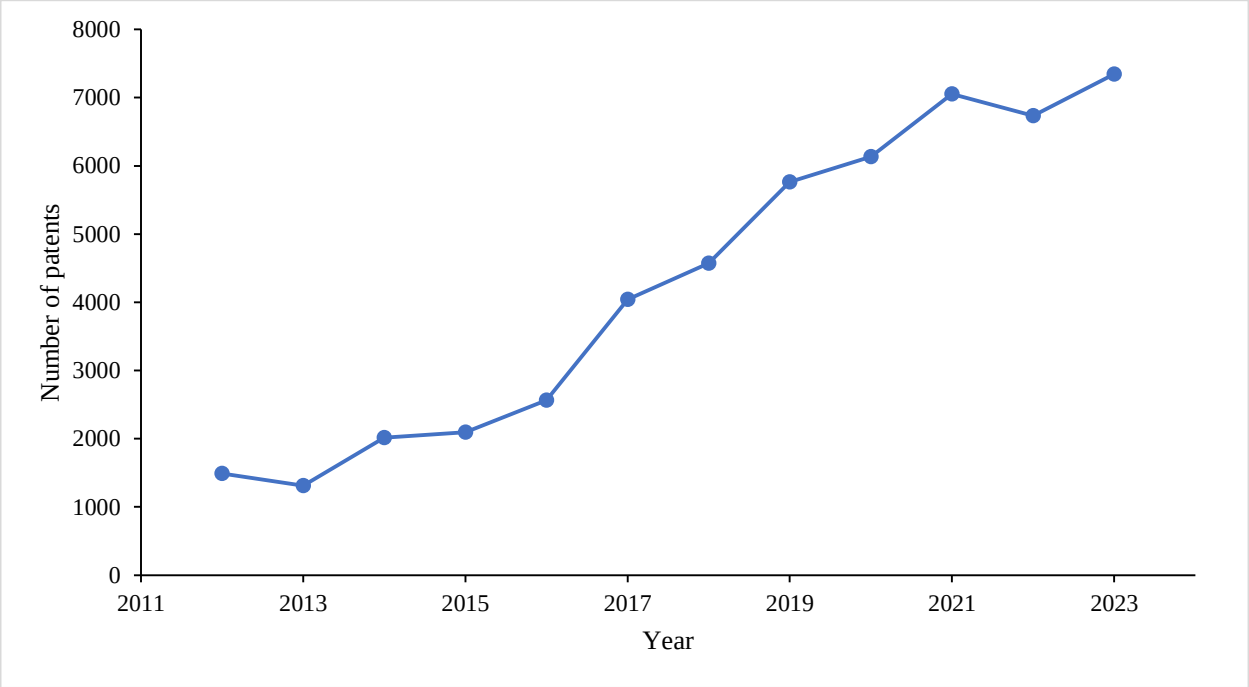

Figure VII

The annual rate of patents filed related to the Boolean bucket search term for the period 2012–2023

37. To better understand the areas of innovation driving patent filings related to the search term, the IPC classifications breakdown was retrieved using the available tools in the PATENTSCOPE database. The search results showed that IPC classifications associated with the highest number of patents filed led with C12N[13] (50,281; 31%) and followed by A61K[14](19,209; 12%), C07K[15] (18,395; 11%), C12P[16] (13,496; 8%) and A61P[17] (9,561; 6%) (figure VIII).

38. Once the information was obtained related to the breakdown of IPC class and temporal indicators, the geographical indicators were extracted from the PATENTSCOPE database. The patent office locations with the most patents filed related to the Boolean bucket search term are provided in table III below. Overall, most patents were filed in China (25,099 patents; 49.10%), followed by the

[13] Microorganisms or enzymes; compositions thereof; propagating, preserving, or maintaining microorganisms; mutation or genetic engineering; culture media.
[14] Preparations for medical, dental, or toilet purposes.
[15] Peptides
[16] Fermentation or enzyme-using processes to synthesize a desired chemical compound or composition or to separate optical isomers from a racemic mixture.
[17] Specific therapeutic activity of chemical compounds or medicinal preparations.

United States of America (6,524 patents; 12.76%), Australia (1,783 patents; 3.49%), Canada (1,722 patents; 3.47 %) and India (946 patents; 1.85%).

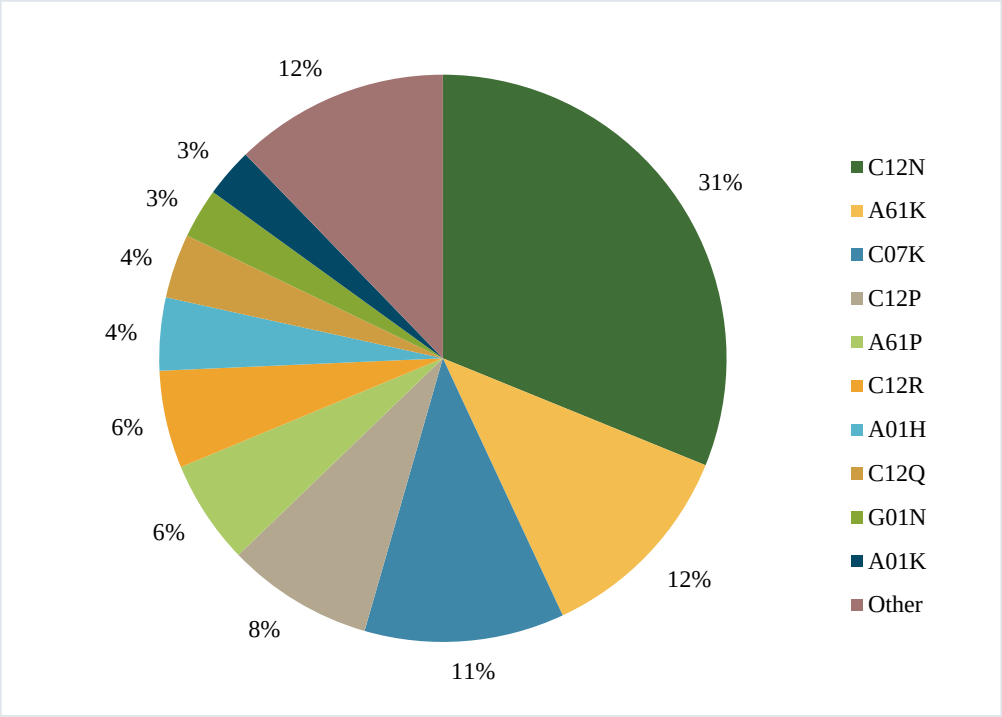

Figure VIII

Breakdown of IPC classes for patents related to the Boolean bucket term for the period 2012–2023

C12N: Microorganisms or enzymes; compositions thereof; propagating, preserving, or maintaining microorganisms; mutation or genetic engineering; culture media;
A61K: Preparations for medical, dental, or toilet purposes;
C07K: Peptides;
C12P: Fermentation or enzyme-using processes to synthesise a desired chemical compound or composition or to separate optical isomers from a racemic mixture;
A61P: Specific therapeutic activity of chemical compounds or medicinal preparations;
C12R: Indexing scheme associated with subclasses C12C-C12Q, relating to microorganisms;
A01H: New plants or processes for obtaining them; plant reproduction by tissue culture techniques;
C12Q: Measuring or testing processes involving enzymes or microorganisms; compositions or test papers therefor; processes of preparing such compositions; condition-responsive control in microbiological or enzymological processes;
G01N: Investigating or analysing materials by determining their chemical or physical properties; and
A01K: Animal husbandry; care of birds, fishes, insects; fishing; rearing or breeding animals, not otherwise provided for; new breeds of animals.

Table III
Filing office for patents related to the bucket search term for the period 2012–2023

	Country	*Number of patents*	*Percentage of patents filed (%)*
1	China	25,099	49.10
2	United States of America	6,524	12.76
3	Australia	1,783	3.49
4	Canada	1,772	3.47
5	India	946	1.85
6	Japan	921	1.80
7	Brazil	762	1.49
8	Russian Federation	605	1.18
9	Mexico	584	1.14
10	New Zealand	576	1.13
11	Singapore	497	0.97
12	Republic of Korea	402	0.79
13	Denmark	363	0.71
14	Malaysia	244	0.48
15	Israel	221	0.43
16	Spain	112	0.22
17	Philippines	100	0.20
18	Indonesia	98	0.19
19	Thailand	82	0.16
20	Portugal	75	0.15

39. From the results of the patent analysis of the bucket and previous research[18] related to patent analyses of synthetic biology, the most prominent IPC class was C12N. Since, the Boolean bucket term may not have captured all developments in synthetic biology, the C12N class was also analysed for the period 2012–2023. During this period, a total of 679,807 patents were filed under this class. To understand the temporal indicators, the patent filing per year were obtained (figure IX). It can be observed that the rate of patents filed per year steadily increased from 39,359 in 2012 to 81,902 in 2023 (4,401 additional patent filings per year; $R^2 = 0.98$) with an average annual growth rate of 6.1%

40. Next, to better understand the areas of innovation driving patent filings related to the C12N class, the main group breakdown was retrieved using the available tools in the PATENTSCOPE database. The search results showed that main groups associated with the highest number of patents filed led with C12N 15/00[19] (413,679 patents; 46%) and followed by C12N 5/00[20] (168,607 patents;

[18] van Doren and others (2013)
[19] Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g., plasmids, or their isolation, preparation or purification; Use of hosts therefor.
[20] Undifferentiated human, animal or plant cells, e.g. cell lines; Tissues; Cultivation or maintenance thereof; Culture media therefor.

19%), C12N 1/00[21] (152,294 patents; 17%), C12N 9/00[22] (119,070 patents; 13%) and C12N 7/00[23] (30,968 patents; 4%) (figure X).

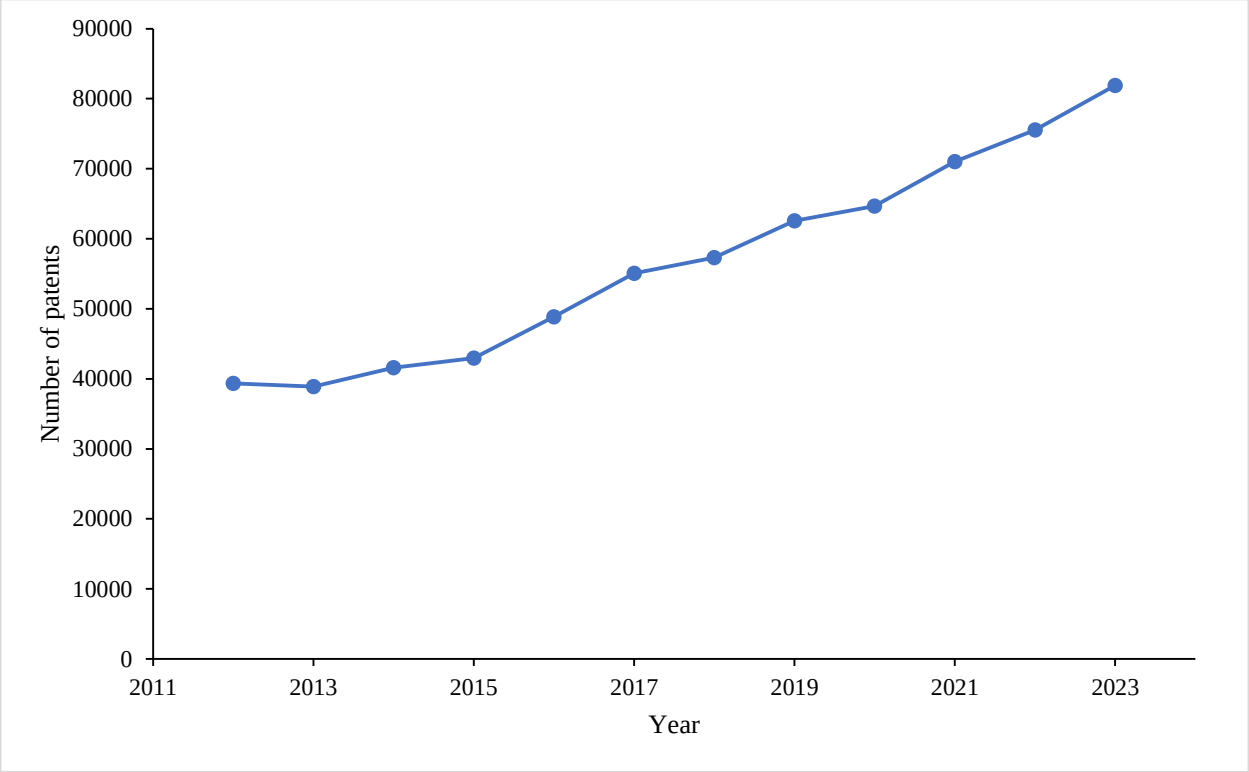

Figure IX

The annual rate of patents filed under the C12N class for the period 2012–2023

[21] Microorganisms, e.g., protozoa; Compositions thereof; Processes of propagating, maintaining or preserving microorganisms or compositions thereof; Processes of preparing or isolating a composition containing a microorganism; Culture media therefor.
[22] Enzymes, e.g., ligases; Proenzymes; Compositions thereof; Processes for preparing, activating, inhibiting, separating, or purifying enzymes.
[23] Viruses, e.g., bacteriophages; Compositions thereof; Preparation or purification thereof.

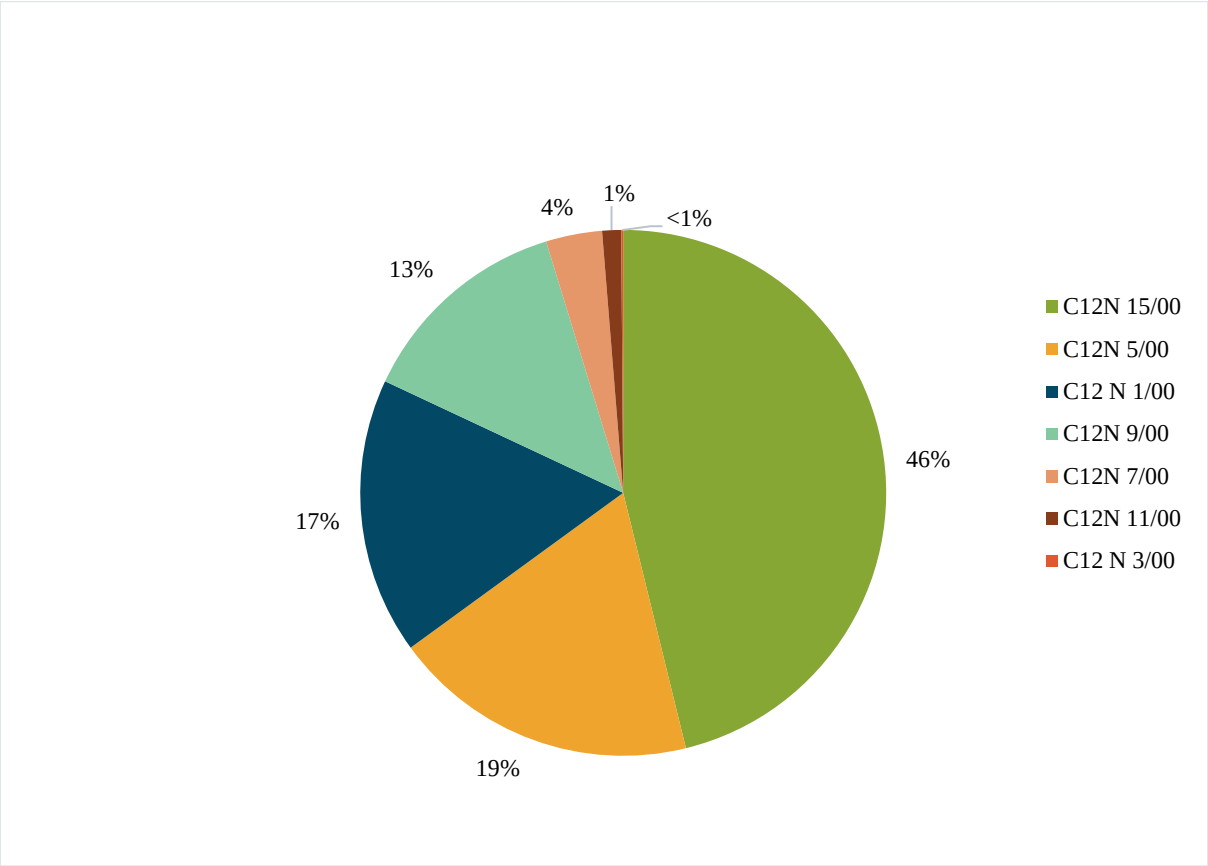

Figure X

The IPC subclass breakdown for the patents filed under the C12N class for the period 2012–2023.

C12N 15/00: Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g., plasmids, or their isolation, preparation or purification; Use of hosts therefor;
C12N 5/00: Undifferentiated human, animal or plant cells, e.g., cell lines; Tissues; Cultivation or maintenance thereof; Culture media therefor;
C12N 1/00: Microorganisms, e.g., protozoa; Compositions thereof; Processes of propagating, maintaining or preserving microorganisms or compositions thereof; Processes of preparing or isolating a composition containing a microorganism; Culture media therefor;
C12N 9/00: Enzymes, e.g. ligases; Proenzymes; Compositions thereof; Processes for preparing, activating, inhibiting, separating, or purifying enzymes;
C12N 7/00: Viruses, e.g. bacteriophages; Compositions thereof; Preparation or purification thereof;
C12N 11/00: Carrier-bound or immobilised enzymes; Carrier-bound or immobilised microbial cells; Preparation thereof; and
C12N 3/00: Spore-forming or isolating processes.

41. Once the information was obtained related to the breakdown of IPC main groups and temporal indicators, the geographical indicators for the patents filed under C12N class were extracted from the PATENTSCOPE database. The patent office locations with the most patents filed related to the C12N class are provided in table IV below. Overall, most patents were filed in China (222,276 patents; 32.70%), followed by the United States of America (97,618 patents; 14.36%), Japan (68,962 patents; 10.14%), Republic of Korea (34,839 patents; 5.12%) and Canada (24,241 patents; 3.57%).

Table IV
Filing office for patents filed under the C12N class for the period 2012–2023

	Country	*Number of patents*	*Percentage of patents (%)*
1	China	222,276	32.70
2	United States of America	97,618	14.36
3	Japan	68,962	10.14
4	Republic of Korea	34,839	5.12
5	Canada	24,241	3.57
6	Australia	21,543	3.17
7	Portugal	13,109	1.93
8	Russian Federation	10,704	1.57
9	Spain	10,050	1.48
10	New Zealand	7,246	1.07
11	India	7,086	1.04
12	Denmark	6,526	0.96
13	Singapore	4,931	0.73
14	Argentina	4,628	0.68
15	Israel	4,475	0.66
16	Poland	4,231	0.62
17	Mexico	4,032	0.59
18	Brazil	2,499	0.37
19	Indonesia	2,272	0.33
20	Philippines	2,123	0.31

42. Finally, when exploring the results and due to its direct relevance to the trends and issues related to bioinformatics, artificial intelligence and machine learning and the automation, the classification G16B[24] stood out. Thus, a patent analysis was performed on G16B for the period 2012–2023. During this period, a total of 32,476 patents were filed under G16B. To understand the temporal indicators, the patent filing per year were obtained (figure XI). It can be observed that the rate of patents filed per year steadily increased from 246 patents in 2012 to 840 in 2016. After 2016, there was a strong increase in the patents under this class, increasing from 1,234 to 7,401 in 2023. Overall, the annual rate of patents filed had a growth rate of 36% (roughly 682 additional patent filings per year; $R^2 = 0.90$).

43. To better understand the areas of innovation driving patent filings related to the G16B class, the subgroup breakdown was retrieved using the available tools in the PATENTSCOPE database. The search results showed that subgroups associated with the highest number of patents filed led with G16B 20/00[25] (13,210; 23%), G16B 40/00[26] (12,476; 22%), G16B 30/00[27] (10,517; 18%), G16B

[24] Bioinformatics, i.e., information and communication technology [ICT] specially adapted for genetic or protein-related data processing in computational molecular biology.
[25] ICT specially adapted for functional genomics or proteomics, e.g., genotype-phenotype associations
[26] ICT specially adapted for biostatistics; ICT specially adapted for bioinformatics-related machine learning or data mining, e.g., knowledge discovery or pattern finding.
[27] ICT specially adapted for sequence analysis involving nucleotides or amino acids.

50/00[28] (5,146; 9%), G16B 25/00[29] (5,027; 9%), G16B 5/00[30] (3,827; 7%) and G16B 15/00[31] (3,328; 6%) (figure XII).

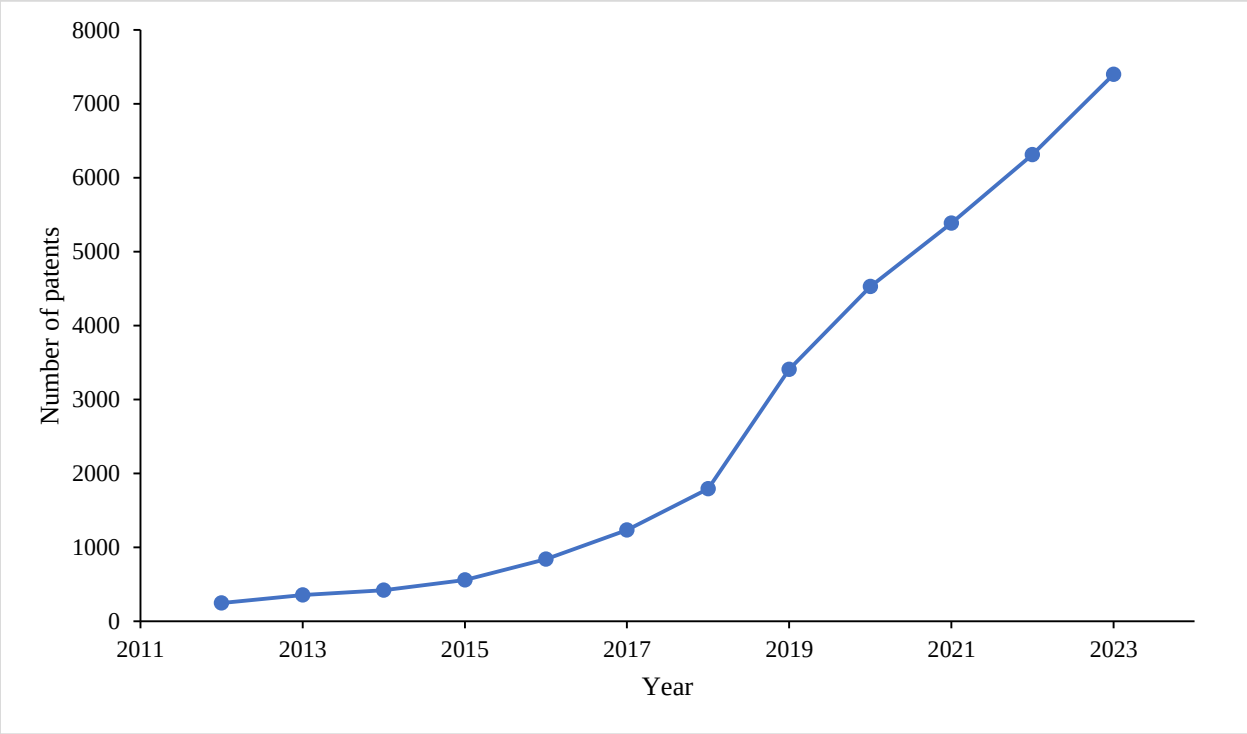

Figure XI

The annual rate of patents filed under the G16B class for the period 2012–2023

[28] ICT programming tools or database systems specially adapted for bioinformatics.
[29] ICT specially adapted for hybridisation; ICT specially adapted for gene or protein expression.
[30] ICT specially adapted for modelling or simulations in systems biology, e.g., gene-regulatory networks, protein interaction networks or metabolic networks.
[31] ICT specially adapted for analysing two-dimensional or three-dimensional molecular structures, e.g., structural or functional relations or structure alignment.

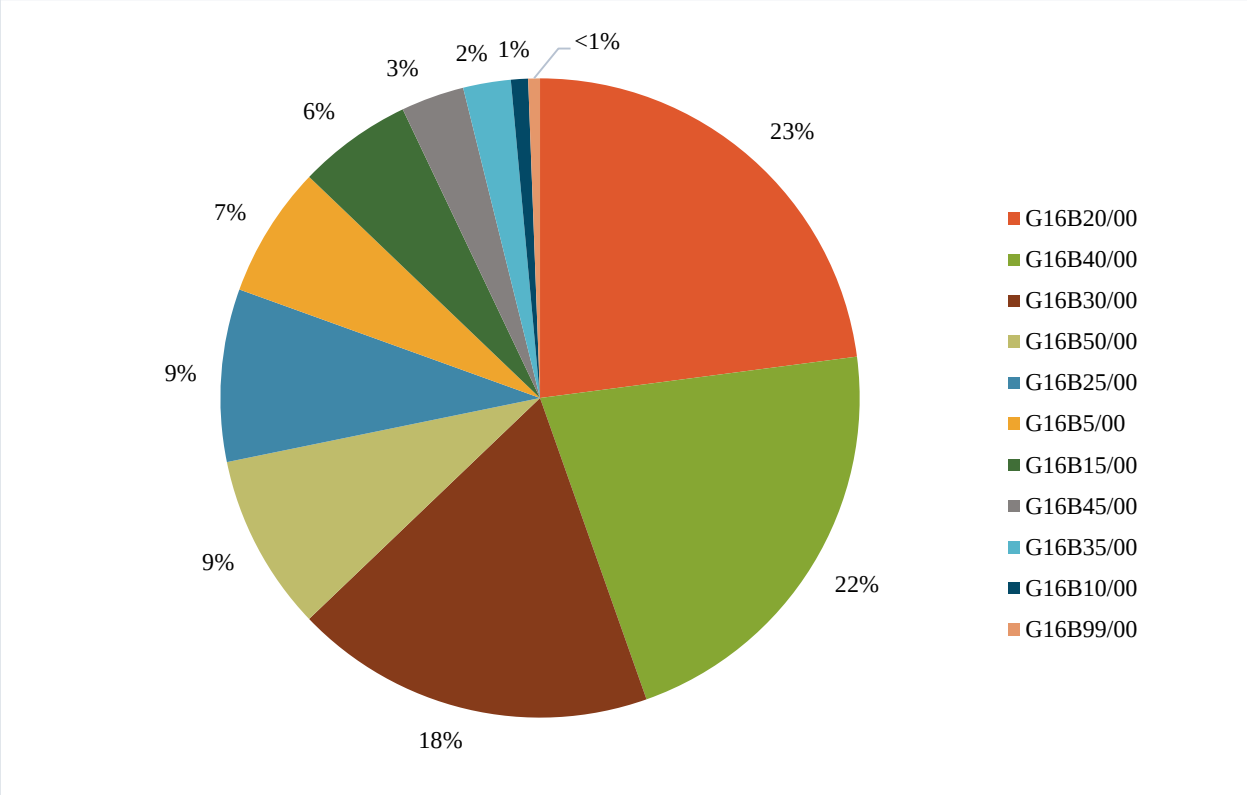

Figure XII

The IPC subclass breakdown for the patents filed under the G16B class for the period 2012–2023

G16B 20/00: ICT specially adapted for functional genomics or proteomics, e.g., genotype-phenotype associations;
G16B 40/00: ICT specially adapted for biostatistics; ICT specially adapted for bioinformatics-related machine learning or data mining, e.g., knowledge discovery or pattern finding;
G16B 30/00: ICT specially adapted for sequence analysis involving nucleotides or amino acids;
G16B 50/00: ICT programming tools or database systems specially adapted for bioinformatics;
G16B 25/00: ICT specially adapted for hybridisation; ICT specially adapted for gene or protein expression;
G16B 5/00: ICT specially adapted for modelling or simulations in systems biology, e.g., gene-regulatory networks, protein interaction networks or metabolic networks;
G16B 15/00: ICT specially adapted for analysing two-dimensional or three-dimensional molecular structures, e.g., structural or functional relations or structure alignment;
G16B 45/00: ICT specially adapted for bioinformatics-related data visualisation, e.g., displaying of maps or networks;
G16B 35/00: ICT specially adapted for in silico combinatorial libraries of nucleic acids, proteins or peptides;
G16B 10/00: ICT specially adapted for evolutionary bioinformatics, e.g., phylogenetic tree construction or analysis; and
G16B 99/00: Subject matter not provided for in other groups of this subclass.

44. Once the information was obtained related to the breakdown of IPC subgroups and temporal indicators, the geographical indicators for the patents filed under G16B class were extracted from the PATENTSCOPE database. The patent office locations with the most patents filed related to the C12N class are provided in table V below. Overall, most patents were filed in China (12,381 patents; 38.12%), followed by the United States of America (6,790 patents; 20.91%), Republic of Korea (2,292 patents; 7.06%), Canada (1,413 patents; 4.35%) and Japan (943 patents; 2.90%).

Table V
Filing office for patents filed under the G16B class for the period 2012–2023

	Country	*Number of patents*	*Percentage of patents (%)*
1	China	12,381	38.12
2	United States of America	6,790	20.91
3	Republic of Korea	2,292	7.06
4	Canada	1,413	4.35
5	Japan	943	2.90
6	Australia	734	2.26
7	Israel	422	1.30
8	United Kingdom of Great Britain and Northern Ireland	189	0.58
9	New Zealand	142	0.44
10	Spain	124	0.38
11	Singapore	113	0.35
12	Mexico	88	0.27
13	Russian Federation	76	0.23
14	Denmark	73	0.22
15	Germany	66	0.20
16	Brazil	60	0.18
17	France	57	0.18
18	Poland	38	0.12
19	Lithuania	35	0.11
20	India	30	0.09

IV. Limitations

45. This literature review was conducted throughout the month of December 2023 and updated following the peer review during the period March-April 2024. It aims to provide an overview of the field of synthetic biology and provide complementary quantitative information to support the broad and regular horizon scanning, monitoring and assessment process. The literature review offers valuable insights on the trends and issues in synthetic biology. The constraints imposed by time and methodology is essential for understanding the scope and boundaries of this literature analysis. Researchers and policymakers should be mindful of these limitations when extrapolating implications for future research and policy decisions, as the dynamic nature of synthetic biology implies that ongoing developments may alter the landscape beyond what is captured in this study.

46. Given the quantity of retrieved publications and the limited time to complete the review, adaptations were necessary to streamline the process and address the objectives within the allotted timeframe. As such, certain elements associated with both systematic and bibliometric literature reviews were not performed. For example, despite the removal of duplicate publications during the analyses, other more thorough data cleaning (e.g., screening of abstracts and titles, examination of publication content, determination of article quality) could not be conducted. In addition, other bibliometric analyses and data visualizations were also limited (e.g., bibliographic mapping tools, citation analytics, funding analysis) (EFSA, 2010; Shapira and others, 2017; Xiao and Watson, 2017; Li others, 2019). Moreover, given the time, this literature review did not seek to analyze or detail the potential impacts of synthetic biology on the objective of the Convention on Biological Diversity.

Other approaches, such as systematic reviews, would be better placed to provide insights on these (Pullin and Stewart, 2006; EFSA and others, 2019; Thonemann and others, 2020).

47. It should also be noted that the aim of this literature review was to provide complementary quantitative information to the horizon scanning process as a whole. Thus, despite efforts made to encompass a wide range of publications, it is acknowledged that some relevant studies may have inadvertently been omitted, potentially limiting the depth of the anal ysis, since the search strategy is based on searches for exact words or phrases in titles and abstracts. For example, if a publication did not include a term within the bucket term ("synthetic biology" OR "engineering biology" OR "genetic* engineer*" OR "bioengineer*" OR "synthetic genom*" OR "genetically modified" OR "genetic* modif*" OR "gene edit*" OR "genome edit*") in its title, abstract or keywords, it may have been excluded. While efforts were made following the peer review to address this concern, further refinement may still be required on the search strings.

48. The use of the term “trends and issues” is not well defined. There is a lack of clarity and potential overlap between trends in technical developments and their associated issues. For example, it can be noted that there was a level of similarity between certain trends and issues, which resulted in some publications being related to more than one topic, as observed by the removal of duplications. Further, the level of specificity between the various trends and issues was not always consistent, resulting in some trends and issues being product-based and others that were broader applications of synthetic biology techniques. Therefore, an overall clearer distinction between technical trends and the issues that may be associated with them might need further consideration.

49. In addition, the methodology for the literature review, based on Boolean searches within the Scopus database, meant that the pool of potential publications is restricted to those that are incorporated into the database. Other important sources of information would be important to integrate, such as certain reports published by organizations, regulatory documents, policy briefs, market analysis reports and the other types of knowledge systems, including those held by indigenous peoples and local communities (Tennant, 2020). Furthermore, only publications and patents available in English were reviewed. This language limitation may have led to the exclusion of insights from non-English sources, which could impact the comprehensiveness of the findings.

50. Certain trends and issues in synthetic biology, such as “Transboundary movements and relation to detection and identification of synthetic biology organisms, parts and products” and “Increased field testing of synthetic biology applications, including in areas outside the national jurisdiction of the developer or funder”, might be more difficult to assess through published literature. It could be a result that that researchers generally do not publish on these topics or relevant information is published in other fora, such as regulatory documents, which are not included in scientific databases (i.e., Scopus, Web of Science). For other issues, such as “Inequity in the participation of developing countries in the context of synthetic biology”, other complementary analyses, such as geographic analysis or collaboration network analysis, can offer clues and provide supplementary information. Thus, future iterations of literature reviews may wish to consider other metric analyses to inform on such trends.

51. Finally, regarding the patent analysis, a further challenge related to the fact that the current patent classification system does not provide a ready means to distinguish synthetic biology from other areas of biotechnology within the patent system (Rutz, 2009). While efforts were made to incorporate this wider range of potential inventions in the patent analysis, it is also acknowledged that all 55 identified trends and issues were not thoroughly examined. The absence of fully developed search strings for each of these trends and issues might have limited the depth of analysis for some areas within synthetic biology. These additional points underscore the need for readers to approach the findings with a lens that recognizes the potential limitations stemming from the initial conceptualization of the trends and issues, methodology employed and the scope of the analysis.

V. Discussion and conclusions

52. This literature review aimed to analyse the trends and issues in synthetic biology through gathering and quantifying scientific literature from 2012 to 2023. Overall, it can be seen that the rate of both publications and patents filed for the field of synthetic biology has increased linearly during the period 2012–2023, indicating an increasing interest in both research and development within the field of synthetic biology. In particular, the trends and issues related to genome editing tools and applications, had strong growth during this period. The growth associated with these trends and issues could have been catalyzed by the development of a method for genome editing (resulting in the Nobel Prize of Chemistry in 2020), and its subsequent application in eukaryotic cells and other systems (Chen and others, 2019; Gostimskaya, 2022). However, it appears likely that genome editing is being taken up rapidly and applied within the field of synthetic biology.

53. Regarding other trends and issues in synthetic biology, the trends related to synthetic biology-enable production, such as antibiotics, natural compounds, cosmetics, fragrances, food, food ingredients and flavours, also experienced moderate increases in their publication rate. Further, it can be noted that for the synthetic biology-enabled production of biofuels, petrochemical precursors and industrial chemicals, the publication rate remained consistently elevated. Taken together, this could indicate a greater interest in using synthetic biology applications or systems to produce high-value compounds. Moreover, the trends and issues "Synthetic biology applications for bioremediation, biodegradation or biomining", "Biosensors, sensory devices and diagnostics", "Metabolic engineering of crops", "Microbiome engineering for non-medical purposes" and "Development of engineered gene drives to control vector-borne and invasive species" and "Living martials and biofilms" might be considered emerging trends and issues in synthetic biology due to their positive growth in their rate of publication.

54. From the preliminary patent analysis of both the Boolean bucket search term, C12N is the IPC classification most relevant to the overall bucket search term, which is similar to previously published patent analyses related to synthetic biology (van Doren and others, 2013). When further exploring the C12N class, innovation related to mutation and genetic engineering (e.g., C12N 15/00) have spurred a large portion of the patent filings (van Doren and others, 2013). Since biotechnological and synthetic biological innovations are not distinguished under the current patent system (Rutz, 2009), it is understandable that many more general subgroups, such as mutation and genetic engineering, cell lines (e.g., C12N 5/00) and microorganisms (e.g., C12N 1/00) would appear as top subgroups during the analysis of the C12N classification. Without further analysis, it may be difficult to distinguish if the developments in patent filings correlate to the trends and issues explored during the publication analysis. However, it can be still noted that that in the case of the bucket term analysis, a significant number of patents were filed under the classification A61K, used for medical, dental or toilet purposes, which may relate to the large research interest related to medical and therapeutic synthetic biology applications, having the largest number of publications during the period 2012–2023. Along similar lines there also appeared to be classifications (e.g., C07K and C12P, C12N 9/00 and C12N 11/00), which might relate to advances in protein engineering, which was one of the top trends and issues identified during the publication analysis.

55. Further, during the patent analysis, the IPC class, G16B, related to innovations in bioinformatics and information technology specially adapted for genetic or protein-related data processing in molecular biology, was identified as an emerging trend. From the annual patent filing rate, it can be seen that there is strong growth. Analyses published several years ago also picked up on increasing growth in the area (Chatterjee, 2017; Mago and others, 2017). Interestingly, this strong growth was mirrored in the publication analysis. For example, artificial intelligence and machine learning, which was the seventh largest set of publications, represented in subgroup G16B 40/00, had 22% of the patents filed under the class G16B. Another example also includes improvements in bioinformatics and sequencing, which was eleventh in the total number of publications, could be represented by G16B 30/00, having 18% of patents under G16B during the period 2012–2023.

Overall, these results suggest that artificial intelligence, machine learning and bioinformatics in synthetic biology are emerging areas of both research and innovation.

56. The literature analysis indicated that research groups in the United States of America were the largest contributors to the publications related to the 55 trends and issues in synthetic biology with research groups in China contributing the second largest amount. With regards to patents, the largest amount were filed in China, while the second largest amount were filed in the United States of America. Previous studies exploring both the literature and patent landscapes indicated that the United States led with the largest number of both publications and patents, followed by European nations (Oldham and others, 2012; van Doren and others, 2013). Since over 10 years have passed since these publications were made available and the period of investigation focused on 2012–2023, the preliminary analysis suggests that shifts in the global research and innovation landscape have occurred, including the increase in participation globally of research groups in more diverse countries. Further, it can also be noted that there are also variations between the countries that publish literature more and those where patents are filed. For example, the Russian Federation, Israel, Brazil, Singapore and New Zealand appear in the lists of countries related to patent filings in higher positions than for their contributions to the total amount of publications. This might indicate the need to look at both the literature and the patents published to capture a greater depth of developments within the field of synthetic biology globally.

57. Finally, in the analysis of these 55 trends and issues, the five countries that contributed the most publications during the period 2012–2023 were the United States, China, the United Kingdom of Great Britain and Northern Ireland, India and Germany. From the collaboration analysis exploring the co-authorship patterns between lead research groups in these countries and collaborators in other countries, there is a significant level of collaboration between research groups in top contributing countries, as well with those in European countries. However, it is important to highlight that all five analyses indicated collaboration between research groups in at least 100 other countries in all regions. Thus, there is an indication that potential avenues exist for collaboration within the synthetic biology research. Further investigation would be required to identify those mechanisms, which could support and foster international collaboration. These might also be important for supporting scientific and technical cooperation, including North-South, South-South and triangular cooperation efforts.

58. Overall, this study provides a preliminary overview of the field of synthetic biology and may be considered as an important initial reference point. The steady growth in publications and patents signifies the increasing importance in the field for both research and development. Despite the prominence of developed nations, evidence of shifts is occurring and international collaboration exists. Further refinement of the research should address the identified limitations, ensuring a more exhaustive exploration of emerging trends. Broad and regular horizon scanning, monitoring and assessment, as well as collaboration, will enhance the understanding of the dynamic landscape of synthetic biology and contribute to more informed decision-making within the Convention on Biological Diversity.

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Annex I

Boolean search strings for 55 identified issues and trends

	Identified trends and issues in synthetic biology	*New search terms*
1	Medical and therapeutic synthetic biology applications	Subset 1: ("biomedic*" OR "medic*" OR "therap*") AND "application*" AND NOT ("crop*" OR "agricultur*" OR "plant*" OR "livestock" OR "wildlife") Subset 2: ("human") AND ("germline" OR "embryo") AND ("edit*") AND NOT ("crop*" OR "agricultur*" OR "plant*" OR "livestock" OR "wildlife") Subset 3: ("CAR T- cell*") OR ("gene* therap*") OR ("engineer* therap*") OR ("engineer* probiotic*") AND NOT ("crop*" OR "agricultur*" OR "plant*" OR "livestock" OR "wildlife")
2	Genome edited plants	Subset 1: (("genome edit*" OR "gene edit*") AND ("plant*" OR "crop*" OR "grass*" OR "tree*" OR "flower*" OR "fruit*" OR "vegetable*" OR "ornamental*")) Subset 2: (("CRISPR*" OR "TALEN" OR "ZFN") AND ("plant*" OR "crop*" OR "grass*" OR "tree*" OR "flower*" OR "fruit*" OR "vegetable*" OR "ornamental*" Subset 3: (("Site-directed nucleas*" OR "SDN*") AND ("plant*" OR "crop*" OR "grass*" OR "tree*" OR "flower*" OR "fruit*" OR "vegetable*" OR "ornamental*"))
3	Synthetic biology-enabled production of antibiotics, natural products and medically relevant compounds	"biologics" OR "natural product*" OR "cannabidiol" OR "cannabinoid" OR "antibiotic*"
4	Increased sophistication and expansion of genome editing tools	Subset 1: "genome edit*" AND "tool*" AND ("novel" OR "sophisticat*") Subset 2: "genome edit*" AND "multiplex*" AND ("novel" OR "new" OR "increas*") Subset 3: (("Cas" OR "CRISPR*") AND ("novel" OR "sophisticat*"))
5	Synthetic biology-enabled production of petrochemical precursors and industrial chemicals	"petrochemical*" OR "petrochemical precursor*" OR "industrial chemical*" OR "biofuel*" OR "bioenergy"

6	Advances in protein engineering	("protein engineering" OR "synthetic protein*" OR "enzyme optimization" OR "engineered protein*" OR "engineered enzyme*" OR "enzyme engineering" OR "synthetic enzyme*")
7	Integration of artificial intelligence and machine learning	"artificial intelligence" OR "AI" OR "machine learning" OR "ML" OR "big data"
8	Genome edited animals	Subset 1: (("genome edit*" OR "gene edit*") AND ("animal*" OR "livestock" OR "fish*" OR "poultry")) AND NOT ("medic*" OR "human" OR "therap*" OR "model" OR "disorder" OR "clinic*" OR "cancer") Subset 2: (("CRISPR*" OR "TALEN" OR "ZFN") AND ("animal*" OR "livestock" OR "fish*" OR "poultry")) AND NOT ("medic*" OR "human" OR "therap*" OR "model" OR "disorder" OR "clinic*" OR "cancer") Subset 3: (("genome edit*" OR "gene edit*") AND ("husbandry" OR "aquaculture"))
9	Synthetic biology applications for bioremediation, biodegradation or biomining	"bioremediation" OR "biodegradation" OR "biomining"
10	Biosensors, sensory devices and diagnostics	("biosensor*" OR "sensory device*" OR "engineered diagnostic*" OR "biodiagnostic*")
11	Improved next-generation sequencing and bioinformatics	("improv*" OR "future" OR "increase* efficiency") AND ("next generation sequenc*" OR "next-generation sequenc*" OR "bioinformatics" OR "bioinformatic* analys*" OR "bioinformatic* algorithm*")
12	Metabolic engineering of crops	Subset 1: ("metabolic* engineering*") AND ("crop*") Subset 2: "bioforti*" Subset 3: ("multigene*" OR "transgene*") AND ("metabolic* OR "biosynthesi*") AND "crop*" Subset 4: "novel" AND ("pathway* OR biosynthe*") AND "crop*"
13	Engineering photosynthesis	Subset 1: ("photosynthesis" OR "photorespirat*") AND "engineering" Subset 2: "C4 engineering" OR "C4 photosynthesis" OR "C4 plant*" OR "C-4 plant*" OR "PEPC"

14	Improvements in DNA synthesis and assembly	"DNA synthesis" OR "DNA assembly" OR "goldengate" OR "Gibson assembly" OR "ligase cycling reaction" OR "modular cloning" OR "MoClo" OR "modular overlap-directed assembly with linkers" OR "GoldenBraid"
15	Synthetic biology-enabled production of cosmetics and fragrances	"cosmetic*" OR "fragrance*" OR "perfume*"
16	Increased sophistication of genetic circuits	"genetic circuit*" OR "DNA circuit*" OR "RNA circuit*" OR "protein circuit*"
17	Automation and use of biofoundries	"automation" OR "biofoundr*"
18	Synthetic biology-enabled production of food, food ingredients and flavors	Subset 1: "synthetic food*" OR "food ingredient*" OR "flavour*" OR "flavor*" OR "food science" OR "artificial food*" Subset 2: "cultured meat*" OR "cell-cultured meat*" OR "cell* agricultur*" OR "bio-manufacturing cultured meat*"
19	Microbiome engineering for non-medical purposes	("microbiome" OR "consorti*") AND NOT ("medic*" OR "therap*" OR "human" OR "biomedic*" OR "mouse" OR "mice" OR "rat*")
20	Improvements to genome and karyotype engineering	("genome level engineering" OR "karyotype engineering" OR "chromosome engineering" OR "chromosomal engineering" OR "artificial chromosome*" OR "engineered chromosome*")
21	Cell-free systems	Subset 1: "cell-free system*" OR "cell free system*" OR "cell-free expression" OR "cell free expression" OR "cell-free synthesis" OR "cell free synthesis" Subset 2: "TX-TL system*"
22	Dual-use nature and biosecurity implications of synthetic biology	Subset 1: ("biosecurity" OR "dual use*" OR "dual-use*" OR "bioweapon*" OR "military" OR "bioterrorism") Subset 2: (("weapon*" OR "terror*" OR "biosecurity" OR "dual use" OR "military") AND ("gain of function" OR "GOF"))
23	Development of engineered gene drives to control vector-borne and invasive species	Subset 1: ("gene drive*") AND ("mosquito*" OR "rodent*" OR "mouse" OR "mice" OR "rat*" OR "vector*") Subset 2: ("gene drive*") AND ("vector borne" OR "invasive species" OR "non native" OR "non-native") Subset 3: ("gene drive*" OR "mutagenic chain reaction") AND ("CRISPR*"OR "homing endonuclease*")

24	Virus-induced genome editing and genetic modifications	Subset 1: ("virus induced" OR "virus-induced") AND ("genome edit*" OR "gene* modification*" OR "CRISPR*" OR "silencing") Subset 2: "horizontal environmental genetic alteration agent*"
25	Transient modification of agricultural plants, pests and pathogens using RNAi or nanomaterials	Subset 1: "agricultur*" AND ("plant*" OR "crop*" OR "pest*" OR "insect*" OR "disease*" OR "pathogen*" OR "fung*") AND ("RNAi" OR "RNA interference" OR "nanomaterial*" OR "transient* modifi*" OR "dsRNA" OR "silencing") AND NOT ("human" OR "therap*" OR "medic*") Subset 2: ("agricultur*" OR "biopesticid*" OR "crop protect*") AND ("RNAi" OR "RNA interference" OR "nanomaterial*" OR "transient* modifi*" OR "dsRNA" OR "silencing") AND NOT ("human" OR "therap*" OR "medic*")
26	Capture and recycling of greenhouse and waste gases using synthetic biology applications	("greenhouse gas*" OR "waste gas*" OR "industrial gas*")
27	Changes in ethical standards	("ethic*" OR "bioethic*") AND ("cost of inaction" OR "norm erosion" OR "change*" OR "welfare" OR "nature" OR "biodiversity" OR "conservation" OR "sustainab*" OR "wildlife") AND NOT ("medic*" OR "neuro*" OR "therap*" OR "embryo*" OR "sport*" OR "clinic*" OR "cancer")
28	Advances in xenobiology	Subset 1: ("alien" OR "noncanonical" OR "non-canonical") AND ("amino acid*" OR "nucleotide*") Subset 2: "xenobiology" Subset 3: ("expand* gene* cod*")
29	Engineered bacteria for nitrogen-fixation and fertilizers	("nitrogen fixation" OR "fertilizer*") AND ("bacteria*" OR "strain*")
30	Increasing carbon capture efficiency in plants	Subset 1: (("carbon capture") OR ("carbon sequestration") OR ("carbon storage") OR ("CO2 fixation")) AND ("plant*") Subset 2: ("rubisco" OR "Ribulose-1,5-bisphosphate carboxylase/oxygenase" OR "RUBPCase" OR "RuBPCO") AND ("engineering")
31	Development of protocells, minimal cells and artificial living machines for research purposes	"protocell*" OR "minimal cell*" OR "artificial living machine*"

32	Interaction of synthetic biology organisms in the environment and potential for cumulative effects	Subset 1: "cumulative effect*" OR "sequential use*" OR "environment* interact*" AND NOT ("human" OR "cancer*" OR "medic*" OR "clinic*" OR "therap*") Subset 2: "unintended consequence*" OR "ecosystem interact*" OR "ecological balance" AND NOT ("human" OR "cancer*" OR "medic*" OR "clinic*" OR "therap*")
33	Self-limiting insect systems	Subset 1: ("self limiting" OR "self-limiting" OR "non-gene drive*" OR "non gene drive*") AND ("insect*" OR "fly" OR "flies" OR "mosquito*" OR "moth*" OR "worm*" OR "tick*" OR "looper*" OR "screwworm*" OR "armyworm*") Subset 2: ("insect*" OR "fly" OR "flies" OR "mosquito*" OR "moth*" OR "worm*" OR "tick*" OR "looper*" OR "screwworm*" OR "armyworm*") AND ("dominant lethal*" OR "transgenic steril*") Subset 3: ("RIDL" OR "Sterile Insect Technique" OR "release of insects carrying a dominant lethal")
34	Synthetic biology-enabled production of fabrics, textile dyes and materials	("fabric" OR "fabrics" OR "textile dye*" OR "leather" OR "silk") AND ("production" OR "bio production" OR "bioproduction" OR "bio-production")
35	The use of synthetic biology for art and design	("biomimicry" OR "biodesign" OR "bio art" OR "bio-art" OR "transgenic art")
36	Use of synthetic biology in wild organisms in the context of resilience in threatened species	("conservation" OR "resilience") AND ("endangered" OR "threatened" OR "climate change" OR "genetic rescue") AND NOT ("agricultur*" OR "crop*")
37	Increased field testing of synthetic biology applications, including in areas outside the national jurisdiction of the developer or funder	Subset 1: ("field test*" OR "field trial*" OR "field release*" OR "deliberate release*") AND ("synthetic" OR "gene drive" OR "gen* edit*" OR "transient" OR "RNAi" OR "vaccine*") AND NOT ("medic*" OR "therap*" OR "neuro*" OR "disorder" OR "psych*") Subset 2: ("outside" OR "beyond") AND ("jurisdiction" OR "countr*" OR "geograph*") AND ("fund*" OR "develop*") AND ("field test*" OR "field trial*" OR "field release*" OR "deliberate release*")
38	Living materials and biofilms	("Living material*") OR ("engineer* biofilm*")

39	Bio-fabricated wildlife products	Subset 1: ("bio-fabricate*" OR "biologically fabricate*" OR "biofabricate*") AND "wildlife product*" Subset 2: "ivory" OR "horn*"
40	Technical refinement of novel delivery systems and chemistries to modify organisms in the field or in nature	("pollen" OR "nano material*" OR "nanomaterial*" OR "nano tubule*" OR "nanotubule*") AND ("nature" OR "field" OR "crop*") AND ("carrier*" OR "delivery") AND NOT ("human" OR "medic*" OR "therap*" OR "pharmac*")
41	Genetically engineered containment systems	"containment system*" OR "biocontainment system*" OR "killswitch*" OR "kill switch*"
42	De-extinction of extinct animals	("de-extinct*" OR "resurrection biology" OR "species resurrection" OR "resurrect* species")
43	Mitochondrial and plastome engineering	"mitochondrial engineering" OR "plastid engineering" OR "plastome engineering" OR "chloroplast engineering"
44	Paratransgenetic approaches for controlling vector-borne diseases	("paratransgene*") AND ("transmission blocking" OR "vector*" OR "disease*")
45	Non-biological uses of synthetic biology	"bio comput*" OR "biocompt*" OR "DNA storage"
46	Self-spreading vaccines for wildlife	Subset 1: ("wildlife" OR "zoono*") AND ("vaccine dissemination") Subset 2: (("wildlife" OR "zoono*" OR "animal*") AND ("vaccin*" OR "virus*") AND ("self-spreading" OR "self-disseminating" OR "transmissible"))
47	Ability to re-create viruses by chemical DNA synthesis	("virus*") AND ("re-creat*" OR " re creat*" OR "construction" OR "de novo assembly") AND ("chemical DNA synthesis" OR "DNA fragment*" OR "oligonucleotide*")
48	Plant bioproduction of vaccines and anti-venoms	Subset 1: "vaccine*" AND ("plant production" OR "plant bioproduction") Subset 2: ("plant production" OR "plant bioproduction") AND ("anti venom*" OR "recombinant polyclonal antibod*" OR "venom*")
49	Inequity in the participation of developing countries in the context of synthetic biology	("developing countr*") AND ("participation" OR "capacity building" OR "inequit*")
50	Transboundary movements and relation to detection and identification of synthetic biology organisms, parts and products	("transboundary") AND ("movement*" OR "detect*" OR "identif*")

51	Use of genome editors to create null or negative segregants	("genome edit*" OR "CRISPR*") AND ("null segregant*" OR "negative segregant*")
52	Engineered sterility of non-native plant species	("steril*") AND ("plant*" OR "crop*" OR "grass*" OR "tree*" OR "flower*") AND ("non-native" OR "invasive")
53	Cyberbiosecurity	"cyberbiosecurity"
54	Increased scale and use in series of synthetic biology interventions	"intervention*" AND "scale" AND "series"
55	Adoption of the Kunming-Montreal Global Biodiversity Framework	"Global Biodiversity Framework" OR "GBF" OR "KMGBF"

Annex II

Temporal analysis of 55 issues and trends in synthetic biology

	Identified issues and trends in synthetic biology	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2012-2023
1	Medical and therapeutic synthetic biology applications	659	762	790	986	1 235	1 464	1 674	1 974	2 266	2 649	2 555	2 783	19 797
2	Genome edited plants	12	31	80	144	276	407	560	801	1 079	1 316	1 577	1 613	7 896
3	Synthetic biology-enabled production of antibiotics, natural products and medically relevant compounds	382	352	354	461	468	483	573	664	692	737	800	779	6 745
4	Increased sophistication and expansion of genome editing tools	7	17	75	122	233	353	481	530	727	780	816	754	4 895
5	Synthetic biology-enabled production of petrochemical precursors and industrial chemicals	276	325	327	350	378	364	365	357	413	416	420	380	4 371
6	Advances in protein engineering	332	331	329	310	331	391	401	382	430	418	334	322	4 311
7	Integration of artificial intelligence and machine learning	187	198	180	182	245	220	246	355	429	473	568	667	3 950
8	Genome edited animals	5	27	76	89	158	234	267	311	349	358	420	397	2 691
9	Synthetic biology applications for bioremediation, biodegradation or biomining	139	135	140	126	161	168	172	171	249	305	379	368	2 513
10	Biosensors, sensory devices and diagnostics	125	108	112	136	166	145	171	163	206	213	255	243	2 043
11	Improved next-generation sequencing and bioinformatics	40	52	54	63	94	95	122	177	149	202	243	219	1 510
12	Metabolic engineering of crops	77	83	72	98	101	113	119	89	144	154	159	146	1 355
13	Engineering photosynthesis	72	78	76	82	105	91	108	113	109	141	137	140	1 252
14	Improvements in DNA synthesis and assembly	68	75	79	89	94	106	111	124	113	115	122	122	1 218
15	Synthetic biology-enabled production of cosmetics and fragrances	49	36	53	80	73	81	89	82	121	148	138	156	1 106
16	Increased sophistication of genetic circuits	41	57	50	45	68	75	84	103	103	100	107	98	931
17	Automation and use of biofoundries	68	43	67	64	77	78	74	90	88	102	83	84	918
18	Synthetic biology-enabled production of food, food ingredients and flavors	52	58	57	45	49	42	73	74	103	91	110	134	888
19	Microbiome engineering for non-medical purposes	18	12	26	32	36	37	58	63	76	93	122	95	668
20	Improvements to genome and karyotype engineering	62	50	62	64	54	60	46	43	57	36	59	48	641
21	Cell-free systems	26	27	43	31	36	50	63	63	88	70	66	67	630
22	Dual-use nature and biosecurity implications of synthetic biology	51	41	41	36	23	49	52	56	54	69	56	62	590

23	Development of engineered gene drives to control vector-borne and invasive species	13	8	21	19	25	44	56	60	67	73	76	52	514
24	Virus-induced genome editing and genetic modifications	24	30	30	39	36	32	45	58	44	48	52	46	484
25	Transient modification of agricultural plants, pests and pathogens using RNAi or nanomaterials	25	17	18	26	23	29	28	45	55	65	70	66	467
26	Capture and recycling of greenhouse and waste gases using synthetic biology applications	25	27	24	20	24	24	27	22	36	58	73	66	426
27	Changes in ethical standards	19	36	19	31	23	42	41	32	47	52	37	46	425
28	Advances in xenobiology	15	8	23	19	21	33	42	40	52	52	51	44	400
29	Engineered bacteria for nitrogen-fixation and fertilizers	15	24	35	27	26	24	37	32	35	46	54	41	396
30	Increasing carbon capture efficiency in plants	14	15	12	12	37	24	30	19	38	26	30	22	279
31	Development of protocells, minimal cells and artificial living machines for research purposes	8	22	21	16	14	18	22	35	25	20	23	26	250
32	Interaction of synthetic biology organisms in the environment and potential for cumulative effects	17	16	19	17	19	20	20	12	26	18	15	18	217
33	Self-limiting insect systems	10	18	17	15	16	18	16	10	24	22	23	20	209
34	Synthetic biology-enabled production of fabrics, textile dyes and materials	13	15	14	11	13	22	21	17	16	19	19	22	202
35	The use of synthetic biology for art and design	4	6	6	10	15	10	12	21	29	28	25	13	179
36	Use of synthetic biology in wild organisms in the context of resilience in threatened species	3	9	9	7	14	22	9	15	21	25	19	24	177
37	Increased field testing of synthetic biology applications, including in areas outside the national jurisdiction of the developer or funder	9	6	8	7	9	9	14	21	18	30	19	22	172
38	Living materials and biofilms	3	1	3	4	2	6	11	19	18	34	34	30	165
39	Bio-fabricated wildlife products	13	12	14	10	15	11	8	18	11	17	10	12	151
40	Technical refinement of novel delivery systems and chemistries to modify organisms in the field or in nature	2	2	3	1	3	5	3	10	10	11	2	10	62
41	Genetically engineered containment systems	4	1	2	1	8	3	3	10	9	5	5	7	58
42	De-extinction of extinct animals	0	0	3	2	3	22	4	1	5	5	5	2	52
43	Mitochondrial and plastome engineering	1	1	5	2	2	3	4	6	4	6	6	12	52
44	Paratransgenetic approaches for controlling vector-borne diseases	4	3	2	3	5	4	4	3	3	4	11	5	51

45	Non-biological uses of synthetic biology	2	0	2	2	3	2	6	6	6	4	6	8	47
46	Self-spreading vaccines for wildlife	6	1	1	1	3	4	2	5	5	5	7	5	45
47	Ability to re-create viruses by chemical DNA synthesis	2	3	0	1	1	0	3	4	4	1	4	1	24
48	Plant bioproduction of vaccines and anti-venoms	0	4	2	1	0	0	0	2	3	2	1	2	17
49	Inequity in the participation of developing countries in the context of synthetic biology	3	0	4	0	1	4	2	1	2	0	0	0	17
50	Transboundary movements and relation to detection and identification of synthetic biology organisms, parts and products	0	2	2	0	1	0	0	1	5	0	4	1	16
51	Use of genome editors to create null or negative segregants	0	0	0	0	1	2	2	1	3	3	2	1	15
52	Engineered sterility of non-native plant species	1	0	0	0	0	0	2	2	3	4	0	2	14
53	Cyberbiosecurity	0	0	0	0	0	0	2	4	1	3	1	3	14
54	Increased scale and use in series of synthetic biology interventions	0	0	0	1	0	0	0	0	0	0	1	2	4
55	Adoption of the Kunming-Montreal Global Biodiversity Framework	0	0	0	0	0	0	0	0	0	0	1	0	1
	Total (duplicates removed)	**2 519**	**2 658**	**2 879**	**3 257**	**3 878**	**4 495**	**5 122**	**5 791**	**6 739**	**7 443**	**7 713**	**7 864**	**60 358**