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Convention on Biological Diversity

Multidisciplinary Ad Hoc Technical Expert Group on Synthetic Biology to Support the Process for Broad and Regular Horizon Scanning, Monitoring and Assessment
Second meeting
Montreal, Canada, 29 January–2 February 2024
Item 3 of the provisional agenda*
Implementation of the mandate

Considerations on synthetic biology pursuant to decision 15/31

Note by the Secretariat

I. Introduction

1. In its decision 15/31, the Conference of the Parties to the Convention on Biological Diversity established a process for broad and regular horizon scanning, monitoring and assessment of the most recent technological developments in synthetic biology and agreed to start its work for one intersessional period. The process consists of the following steps:

(a) Information gathering;

(b) Compilation, organization and synthesis of information;

(c) Assessment;

(d) Reporting on outcomes.

2. In the same decision, the Conference of the Parties also established the multidisciplinary Ad Hoc Technical Expert Group on Synthetic Biology to Support the Process for Broad and Regular Horizon Scanning, Monitoring and Assessment. To support the work of the Group, the Conference of the Parties requested the Executive Secretary to convene discussions of the Open-ended Online Forum on Synthetic Biology and invited Parties, other Governments, indigenous peoples and local communities, and relevant organizations to submit to the Executive Secretary information relevant to trends in new technological developments in synthetic biology.

3. At its first meeting, in July 2023, the multidisciplinary Expert Group agreed on a process for the first cycle of broad and regular horizon scanning, monitoring and assessment of the most recent technological developments in synthetic biology. The process for the 2023–2024 intersessional period consists of multidisciplinary expert-driven submissions by members of the Group and a literature review conducted by the Secretariat.

4. The present document has been prepared to facilitate the deliberations of the multidisciplinary Expert Group and is organized according to the elements in the terms of reference for the Group, as

*CBD/SYNBIO/AHTEG/2024/1/1.

adopted in the annex to decision 15/31. Section II contains an outline of the overall process followed to date for the broad and regular horizon scanning, monitoring and assessment of the most recent technological developments in synthetic biology; section III addresses the specific elements related to capacity-building in accordance with the terms of reference for the Group; section IV details the elements of the review of the horizon scanning process; and section V contains draft recommendations for consideration by the Subsidiary Body on Scientific, Technical and Technological Advice at its twenty-sixth meeting. The information in those sections is drawn from the submissions on synthetic biology, the discussions in the Open-ended Online Forum on Synthetic Biology and the literature review conducted by the Secretariat. Group members are also invited to review the original submissions and the online discussions for further information. Lastly, annex I contains a provisional selection list of the trends and issues in synthetic biology compiled by the Secretariat, while annex II contains a draft literature review of trends and issues in synthetic biology (2012–2023).

5. The following documents may also support the discussions:

(a) A prioritized list of trends and issues in synthetic biology;[1]

(b) A summary of discussions on capacity-building, technology transfer and knowledge-sharing needs for synthetic biology;[2]

(c) The report of the multidisciplinary Expert Group on its first meeting.[3]

6. In its discussions, the multidisciplinary Expert Group should bear in mind paragraph 4 of decision XIII/17, in which the Conference of the Parties acknowledged the outcome of the work of the Ad Hoc Technical Expert Group on Synthetic Biology on the operational definition of synthetic biology[4] and considered it useful as a starting point for the purpose of facilitating scientific and technical deliberations under the Convention and its Protocols.

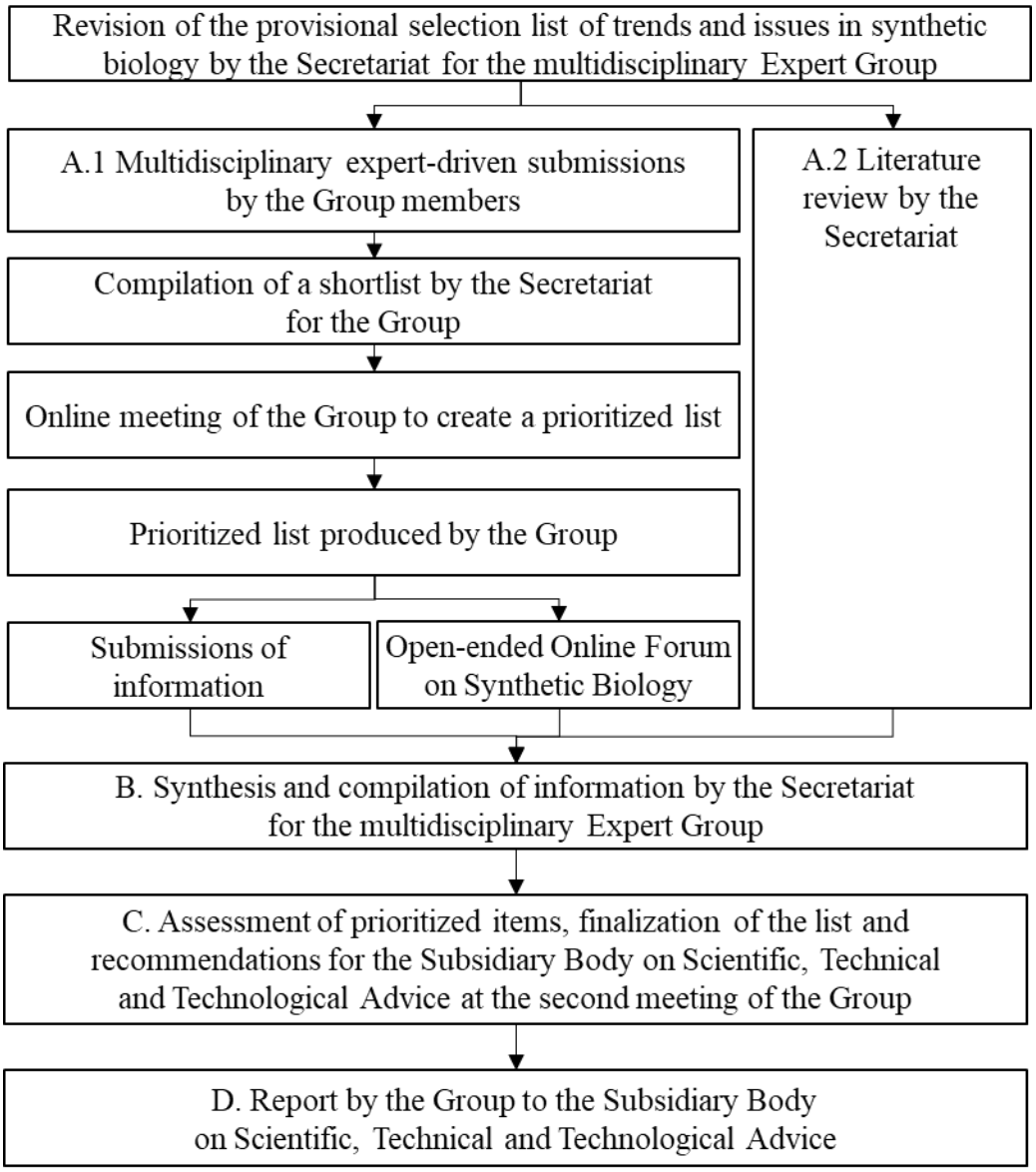
II. Process for broad and regular horizon scanning, monitoring and assessment of the most recent technological developments in synthetic biology

A. Overview of the process

7. At its first meeting, the multidisciplinary Expert Group agreed on a process for the 2023–2024 intersessional period consisting of two parallel activities, namely, multidisciplinary expert-driven submissions and a literature review (see figure I, stages A1 and A.2), that covered steps (a) (information gathering) and (b) (compilation, organization and synthesis of information) of the process outlined in the annex to decision 15/31. The work to carry out those activities was undertaken by the Secretariat with the assistance of consultants.

[1] CBD/SYNBIO/AHTEG/2024/1/INF/1.
[2] CBD/SYNBIO/AHTEG/2024/1/INF/2.
[3] CBD/SYNBIO/AHTEG/2023/1/3.
[4] "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."

Figure I
Process for the 2023–2024 intersessional period



8. The activities undertaken were based on a revised list of trends and issues in synthetic biology (the provisional selection list) produced by the Secretariat. The Secretariat drew information from several sources, including the report of the Ad Hoc Technical Expert Group on Synthetic Biology on its meeting held in June 2019,[5] the submission of information on synthetic biology, the discussions of the Open-ended Online Forum on Synthetic Biology and the publication *Technical Series No. 100: Synthetic Biology*.[6] Using those sources of information, the Secretariat compiled a list of 54 trends and issues in synthetic biology (see annex I).

9. The multidisciplinary expert-driven submissions and the literature review are detailed in sections II.A.1 and II.A.2.

[5] CBD/SYNBIO/AHTEG/2019/1/3.

[6] Available at www.cbd.int/doc/publications/cbd-ts-100-en.pdf.

1. Multidisciplinary expert-driven submissions

10. The multidisciplinary expert-driven submission process is a methodology horizon scanning based on input from experts to identify trends and issues in synthetic biology. The process was guided by the members of the multidisciplinary Expert Group, and the input received has formed the basis for the horizon scanning itself.

11. The process started with the submission of information by the members of the multidisciplinary Expert Group. Each member selected a maximum of five items from the provisional list compiled by the Secretariat or provided additional trends or issues not found on the original list. The members provided their input in a structured manner, including preliminary information on potential positive and negative impacts on the three objectives of the Convention, timelines (if possible) and other considerations, including socioeconomic, ethical and cultural considerations, that were deemed relevant by the members, as well as any supporting documentation. That stage could be considered as the "information-gathering" step.

12. A total of 96 submissions were received from 31 members of the multidisciplinary Expert Group between 31 August and 18 September 2023. Thirty-three items of the provisional selection list were the subject of contributions, 21 were not and 4 new items were proposed.[7] The information was compiled into a new list, termed the "shortlist", to support further deliberations. That stage could be considered as the "compilation, organization and synthesis of information" step.

13. An online meeting of the multidisciplinary Expert Group was convened from 10 to 12 October 2023 to exchange views and information, with a view to informing the prioritization stage, which could be considered as the "assessment" step.

14. During that meeting, the multidisciplinary Expert Group agreed not to proceed with the 21 trends and issues on the provisional list that had not received submissions and decided to use an "indicative preferencing" method for the remaining 37 items. Members were asked to provide a score between 1 and 1,000 for each item to reflect: (a) impacts on the three objectives of the Convention; (b) relevance to Parties to the Convention; and (c) urgency. To allow for comparison among the resulting scores of trends and issues in synthetic biology, z-scores[8] were calculated for all 37 items. Once the distribution of the 37 items was determined, the members agreed to take the 17 trends and issues in synthetic biology that had received positive z-scores to form the prioritized list of trends and issues in synthetic biology. Of the 17 trends and issues, the following 5 were identified for a more detailed assessment:

(a) Self-spreading vaccines for wildlife;

(b) Self-limiting insect systems;

(c) Development of engineered gene drives to control vector-borne diseases and invasive species;

(d) Integration of artificial intelligence and machine learning;

(e) Inequity in the participation of developing countries in the context of synthetic biology.

15. The remaining 12 trends and issues were identified for a less detailed assessment, namely:

(a) Engineered bacteria for nitrogen-fixation and fertilizers;

[7] Novel organisms as chassis for synthetic bioproduction (insects, fungi, plants); aquatic living modified organisms; redesign of existing synthetic promoters; and strengthening the participation of developing countries in the growth of synthetic biology.

[8] Z-scores are calculated by subtracting the mean (average) from the initial score and then dividing it by the standard deviation. This ensures that scores are comparable (normalized), that is, that they can be meaningfully aggregated across participants with different means and variances in their scoring. Z-scores are commonplace in a range of areas, including in foresight and horizon scanning (in health, ecology and bioengineering) and biology (e.g. to calculate height and weight relative to the broader population distribution).

(b) Transient modification of agricultural plants, pests and pathogens using RNA interference or nanomaterials;

(c) Genome-edited plants;

(d) Microbiome engineering for non-medical purposes;

(e) Use of synthetic biology in wild organisms in the context of resilience in threatened species;

(f) Synthetic biology applications for bioremediation, biodegradation or biomining;

(g) Technical refinement of novel delivery systems and chemistries to modify organisms in the field or in nature;

(h) Ability to recreate viruses by chemical DNA synthesis;

(i) Interaction of synthetic biology organisms in the environment and potential for cumulative effects;

(j) Dual-use nature and biosecurity implications of synthetic biology;

(k) Transboundary movements and relation to detection and identification of synthetic biology organisms, parts and products;

(l) Increased field testing of synthetic biology applications, including in areas outside the national jurisdiction of the developer or funder.

16. Following the request of the multidisciplinary Expert Group at its online meeting, additional information-gathering steps were undertaken for the 17 items on the prioritized list. The five trends and issues in synthetic biology identified for a more detailed assessment formed the basis for the discussions of the Open-ended Online Forum on Synthetic Biology, held from 6 to 20 November 2023. In addition, a further submission of information step was conducted through notification No. 2023-111 for the remaining 12 trends and issues.

17. All information gathered during the process for the items on the prioritized list has been compiled and synthesized in information document CBD/SYNBIO/AHTEG/2024/1/INF/1.

2. Literature review

18. In accordance with the recommendations of the multidisciplinary Expert Group, the Secretariat conducted a complimentary literature review on the 54 topics identified in the provisional selection list, as well as of the item on “use of synthetic biology for art and design”, which had been identified after the list had been published. The review followed the consecutive steps of “information gathering” and “compilation, organization and synthesis of information”.

19. The literature review consisted of an exploration of the publication landscape over the period 2012–2023. The methodology used and the outcomes of the process are provided in annex II. As the literature review is currently undergoing a peer review, it should be noted that the results should be considered as preliminary.

20. Overall, both processes are effective at identifying complimentary trends and issues in synthetic biology. The expert-driven process allows for expert opinion to enter the horizon scanning process more easily and for high-impact trends and issues to be identified even when publications are not available. However, that process could be limited by a lack of available expertise. The literature review allows for a comprehensive review of how research and innovation are progressing and offers quantitative tools to characterize temporal trends or identify relationships. However, the lag time in the publication of articles and patents creates another kind of limitation. In addition, the search terms used for the review might not adequately capture the entire scope of each trend or issue, thereby influencing the results, and may not align with terminology commonly used under the Convention and its processes.

B. Assessment of trends and issues in synthetic biology

21. In line with the process applied by the multidisciplinary Expert Group, the assessment step will be undertaken on the basis of the information-gathering and compilation steps. In preparation for the present meeting, the Group has developed a harmonized structure for the assessment of the prioritized trends and issues to allow for a participatory approach to the "assessment" step.

22. For the five items that will be the subject of a more detailed assessment, the format of the harmonized structure is as follows:

(a) Summary/description;

(b) Contextualization, including any problems that the development in synthetic biology under review is trying to address, underlying causes and other approaches;

(c) Time frame and current level of research activity;

(d) Considerations of impacts on the objectives of the Convention;

(e) Governance considerations, including potential gaps or challenges for risk assessment, risk management and regulation, including the availability of tools for detection, identification and monitoring;

(f) Additional considerations, including considerations relevant to the programmes of work of the Convention and the Protocols, the Kunming-Montreal Global Biodiversity Framework, socioeconomics, ethics, cultural factors, human health, intellectual property, liability and redress, indigenous peoples and local communities, and public engagement.

23. The harmonized structure for assessment will be applied to all five trends and issues by the multidisciplinary Expert Group. Where it is not appropriate or possible to address the information for a particular trend or issue, especially for the topic of inequity in the participation of developing countries in the context of synthetic biology, the Group may consider noting the fact only. This is done to ensure the robustness of the process and, where necessary, to draw the conclusions necessary to inform the refinement of the overall process, as anticipated in decision 15/31.

24. For the additional 12 items that will undergo a less detailed assessment, the harmonized structure will use an amended format, as follows:

(a) Summary/description;

(b) Time frame and current level of research activity;

(c) Potential impacts on the objectives of the Convention.

C. Reporting on outcomes

25. In the annex to decision 15/31, the Conference of the Parties specified that the coordinating actors for the "reporting on outcomes" step would be the multidisciplinary Expert Group, the Subsidiary Body on Scientific, Technical and Technological Advice, the Conference of the Parties to the Convention and the Conference of the Parties serving as the meetings of the Parties to the two Protocols.

26. The report on outcomes could contain a summary of potential impacts, gaps in knowledge and state of development, among others, organized against the harmonized structure. The members may wish to consider a suitable approach for addressing the 12 additional trends and issues in synthetic biology.

27. The outcomes of the process will be complemented by an additional report outlining the capacity-building, technology transfer and knowledge-sharing needs, based on the priorities determined by Parties on issues related to synthetic biology and in the light of the outcomes of the horizon scanning process, to fulfil the mandate of the multidisciplinary Expert Group. Relevant

information can be found in section III below and in information document CBD/SYNBIO/AHTEG/2024/1/INF/2.

28. The multidisciplinary Expert Group may wish to consider the information above in the preparation for an initial report on horizon scanning, monitoring and assessment of the most recent technological developments in synthetic biology for the current intersessional period. The Group could also consider the possibility of presenting the outcomes in thematic groups when devising the format of the report.

29. Lastly, the multidisciplinary Expert Group may also need to consider elements related to the review of the horizon scanning process (see sect. IV), the communication aspects of the outcomes of the process and the feasibility of combining issues, as appropriate.

III. Identification of capacity-building, technology transfer and knowledge-sharing needs

30. In its decision 15/31, the Conference of the Parties recognized the importance of capacity-building, knowledge-sharing and technology transfer, among others, for addressing issues related to synthetic biology. In the same decision, it requested the Executive Secretary to facilitate international cooperation and promote and support capacity-building, technology transfer and knowledge-sharing regarding synthetic biology, taking into account the needs of Parties and of indigenous peoples and local communities. It also tasked the multidisciplinary Expert Group with identifying capacity-building, technology transfer and knowledge-sharing needs on the basis of priorities determined by Parties on issues related to synthetic biology and in the light of the outcomes of the horizon scanning process.

31. Capacity-building, technology transfer and knowledge-sharing are strategic priorities under the Convention. They are important contributors to creating an enabling environment for the Convention and its Protocols, with all instruments incorporating specific provisions, and they have been captured under Target 20 of the Framework, on strengthening capacity-building, technology transfer and scientific and technical cooperation for biodiversity. Furthermore, Target 17, on strengthening biosafety and distributing the benefits of biotechnology, could also be seen as related to those matters.

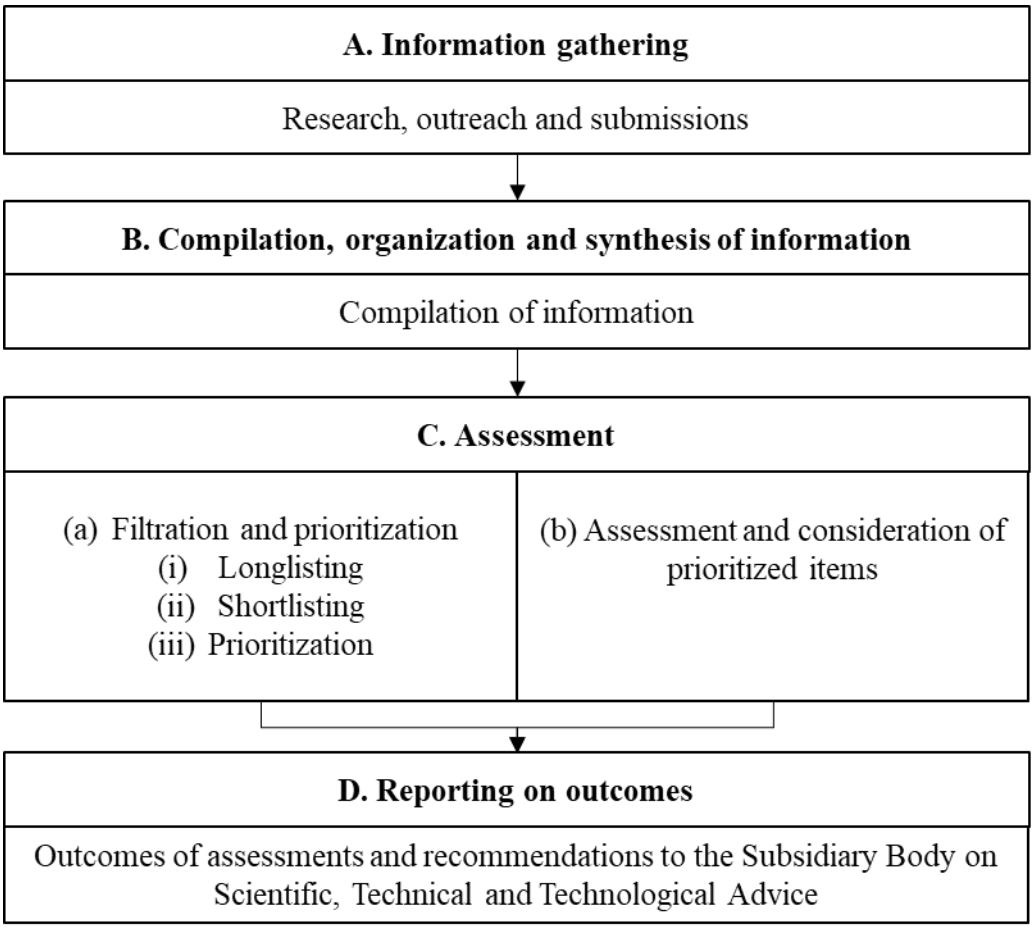
32. In this regard, it is worth noting that certain processes under the Convention and its Protocols, such as the long-term strategic framework for capacity-building and development, the Capacity-building Action Plan for the Cartagena Protocol on Biosafety and the Implementation Plan for the Cartagena Protocol, may help to address capacity-building, technology transfer and knowledge-sharing in the context of synthetic biology. Approaches in this regard should be aimed at building crucial regional and institutional capacity on the basis on a fundamental knowledge of technology, scientific risk-related knowledge and relevant socioeconomic considerations. This would then support Governments and regional authorities in assessing whether a particular application is suitable for addressing societal challenges and enable them to build up their own system of regulations and management, in line with their national priorities.

33. For the purposes of the current horizon scanning process, specific capacity-building modalities and needs have not yet been fully identified. However, the information gathered during the discussion of the Open-ended Online Forum in November 2023 and that collected by the Secretariat are presented in information document CBD/SYNBIO/AHTEG/2024/1/INF/2. In the light of the outcomes of the “assessment” step, the members of the multidisciplinary Expert Group should identify capacity-building, technology transfer and knowledge-sharing needs in relation to the identified trends and issues in synthetic biology.

IV. Review of the horizon scanning process

34. The current initial horizon scanning, monitoring and assessment process has provided a basis that could be further elaborated and refined. At its first meeting, the multidisciplinary Expert Group determined an overarching process for the broad and regular horizon scanning, monitoring and assessment, as shown in figure II.

Figure II
Elements of the process for the broad and regular horizon scanning, monitoring and assessment



35. A number of additional points for consideration are detailed in the sections below, while the limitations of the literature review are outlined in annex II.

A. Resource requirement considerations

36. In order to implement the mandate given it under decision 15/31, the Secretariat has required additional human and technical resources. The Conference of the Parties specified that the coordinating actors for the "compilation, organization and synthesis of information" step would be the Secretariat, with the support of consultants, as appropriate, and work conducted to date for the horizon scanning process has involved several staff and consultants, as well as specialized software and information technology support.

37. There is therefore a need for appropriate resourcing, in terms of dedicated staff and necessary software licences, to ensure that potential future iterations may be fully supported by the Secretariat,.

B. Expert group membership considerations

38. It is important to recall that, in paragraph 18 (b) of the modus operandi of the Subsidiary Body, it is stipulated that ad hoc technical expert groups are to be composed of no more than 15 experts

nominated by Parties and a limited number of experts from relevant organizations, depending on the subject matter.[9] However, the nature of the present multidisciplinary Expert Group has required a larger number of experts, which in turn has led to a need for additional voluntary funding for eligible delegates.

39. Furthermore, the notion of "multidisciplinary" may need to be further unpacked and clearly defined. This could require an analysis of the key skills and expertise needed in the multidisciplinary Expert Group, and the applicability of participatory approaches need to be considered. For example, during the process of selecting members for the multidisciplinary Expert Group, the nomination period was re-advertised to receive more diverse nominations from Parties. In addition, there may be a need to provide for translation and stakeholder participation costs to strengthen the multidisciplinary nature of the process.

C. Time considerations

40. Any future iterations of the scanning process should factor in the time and cost of the process. The two-step process adopted by the multidisciplinary Expert Group (see figure I) has enabled the Group to address all the elements of the horizon scanning, monitoring and assessment outlined in decision 15/31, in particular in relation to data collection and synthesis, over a two-year intersessional period. However, additional time would have allowed for more in-depth analyses, as well as further expert elicitation and stakeholder consultation. Indeed, once the process for the 2023–2024 intersessional period was determined, the actual working time available to the multidisciplinary Expert Group has been of six months only.

41. Expert elicitation usually takes at least six months when there is a clearly defined goal and the process is guided by experienced facilitators. Other considerations may depend on logistical arrangements, such as whether experts hold their deliberations in person or not, the meeting location and the number of participants.

42. In terms of large-scale literature reviews, those usually take roughly 6 to 12 months or more, depending on their scope and depth. Additional analysis or quantification may also increase the time required to perform a review, in addition to the necessary peer review.

D. Definitions and scope

43. The definitions, scope and details of the process should be agreed to at the beginning of the process. This is standard practice in most horizon scanning processes. The purpose of a horizon scanning determines its scope and form. Definitions clarify what is relevant or irrelevant to the scanning and ensure that participants share the same understanding. Details ensure that participants can focus on research, deliberation and prioritization, which constitute the actual work of carrying out the process.

44. In addition, it would be helpful to further define the categories of trends and issues in synthetic biology. The members of the multidisciplinary Expert Group attempted to categorize the issues and trends during their online meeting, but concluded that there was insufficient time to conduct this work effectively and they did not pursue that endeavour.

E. Interconnections between trends and issues

45. The conceptual framework for the provisional selection list, which includes a combination of applications, products and techniques related to synthetic biology, has resulted in unintended overlaps of trends and issues. Even though the process outlined in figure I was designed to fit the

[9] "The ad hoc technical expert groups shall be composed of no more than fifteen experts nominated by Parties competent in the relevant field of expertise, with due regard to geographical representation, gender balance and to the special conditions of developing countries, in particular the least-developed and small island developing States, and countries with economies in transition, as well as a limited number of experts from relevant organizations, depending on the subject matter. The number of experts from organizations shall not exceed the number of experts nominated by Parties."

2023–2024 intersessional period, no time was allocated for further refining the definitions, scale and scope of the categories of trends and issues. Some time should therefore be dedicated to such refinement in future iterations.

F. Monitoring and evaluation elements

46. To optimize horizon scanning, it is necessary to consider the development of a mechanism for monitoring or facilitating the monitoring of issues included in the prioritized list or the provisional selection list. Similarly, the evaluation of the process could be further enhanced through the deployment of tools for maintaining the transparency, repeatability and inclusivity of the process. The monitoring element may include the use of an observatory, repositories or other knowledge management tools, such as the clearing-houses established under the Convention and its Protocols.

G. Expert solicitation

47. The use of a larger pool of experts with representation beyond the multidisciplinary Expert Group should be considered. While the Group members provide a broad range of expertise, there is no guarantee that they cover all relevant areas. Other groups, such as those formed by scientists and practitioners actively involved in research, development and innovation within their respective fields, may offer complementary expertise. A broad range of expertise would likely assist in enhancing the multidisciplinary nature of the "assessment" step (see sect. II.B). It should also be noted that using of a larger pool of experts may have time implications (see sect. IV.C) for the stakeholder mapping and expert engagement, which would need to be built in the process.

48. To widen the array of responses and encourage participation, the development of electronic tools might be required. For the current intersessional period, Microsoft Forms has been used to receive responses, in conjunction with the traditional submission by email of information funnelled through the Secretariat. However, there may be specialized software that could facilitate and increase the capacity to collect, organize and synthesize information. Should that not be the case, new information technology tools may need to be developed, which may require additional resources (see sect. IV.A).

H. Inconsistent participation of members

49. The inconsistent participation of many members of the multidisciplinary Expert Group has been an issue. Meetings, submissions and the scoring of issues were all done by a varying number of members. Horizon scanning usually requires a high level of consistency from participants. Irregular participation undermines long-term deliberations and limits the representativeness of the results.

I. Capacity development of experts

50. There may be benefit in offering participants training in foresight and the topics under discussion to improve the outcomes of the process. Ideally, future iterations should involve a minimum level of training of participants before scanning begins. In addition, participants could be offered a summary of previous horizon scanning in relevant areas.

V. Recommendations for the Subsidiary Body on Scientific, Technical and Technological Advice

51. In decision 15/31, the Conference of the Parties requested the Subsidiary Body on Scientific, Technical and Technological Advice to consider: (a) the outcomes of the horizon scanning process contained in the report of the multidisciplinary Expert Group; and (b) the report on effectiveness of that process; and to make recommendations for consideration by the Conference of the Parties at its sixteenth meeting.

52. In order to support the Subsidiary Body in meeting that request, the multidisciplinary Expert Group may wish to:

(a) Endorse the prioritized list of trends and issues in synthetic biology contained in document CBD/SYNBIO/AHTEG/2024/1/INF/1;

(b) Consider the need and develop proposals for any further intersessional work in the light of the outcomes of the process, including the assessment of the additional 12 trends and issues in synthetic biology that were selected for a less detailed assessment;

(c) Consider the implications on the periodicity of the process (e.g. the length of the process in relation to intersessional periods in the light of the experience gained to date);

(d) Consider specific modalities for capacity-building, technology transfer and knowledge-sharing in the light of the outcomes of the process, taking into account the needs of Parties and of indigenous peoples and local communities;

(e) Suggest strategies for broad international cooperation, technology transfer, knowledge-sharing and capacity-building on synthetic biology;

(f) Suggest potential resource allocations to support the broad and regular horizon scanning, monitoring and assessment of the most recent technological developments in synthetic biology.

53. In line with paragraph 7 of decision 14/19, in which the Conference of the Parties emphasized the need for a coordinated, complementary and non-duplicative approach on issues related to synthetic biology under the Convention and its Protocols, as well as among other conventions and relevant organizations and initiatives, specific recommendations may be developed for the Conference of the Parties serving as the meetings of the Parties to the Cartagena Protocol and the Nagoya Protocol on Access to genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization, in accordance with decision 15/31.

Annex I

Provisional selection list of the trends and issues in synthetic biology

Number	*Trend or issue*
1	Use of synthetic biology in wild organisms in the context of resilience in threatened species
2	Self-spreading vaccines for wildlife
3	Genome edited plants
4	Genome edited animals
5	Metabolic engineering of crops
6	Engineering photosynthesis
7	Increasing carbon capture efficiency in plants
8	Engineered sterility of non-native plant species
9	Transient modification of agricultural plants, pests and pathogens using RNA interference or nanomaterials
10	Virus-induced genome editing and genetic modifications
11	Microbiome engineering for non-medical purposes
12	Engineered bacteria for nitrogen-fixation and fertilizers
13	Synthetic biology applications for bioremediation, biodegradation or biomining
14	Development of engineered gene drives to control vector-borne and invasive species
15	Self-limiting insect systems
16	Paratransgenetic approaches for controlling vector-borne diseases
17	De-extinction of extinct animals
18	Living materials and biofilms
19	Capture and recycling of greenhouse and waste gases using synthetic biology applications
20	Synthetic biology-enabled production of petrochemical precursors and industrial chemicals
21	Synthetic biology-enabled production of cosmetics and fragrances
22	Synthetic biology-enabled production of food, food ingredients and flavours
23	Synthetic biology-enabled production of antibiotics, natural products and medically relevant compounds
24	Plant bioproduction of vaccines and anti-venoms
25	Medical and therapeutic synthetic biology applications
26	Biosensors, sensory devices and diagnostics

27	Synthetic biology-enabled production of fabrics, textile dyes and materials
28	Bio-fabricated wildlife products
29	Non-biological uses of synthetic biology
30	Cell-free systems
31	Increased sophistication of genetic circuits
32	Increased sophistication and expansion of genome editing tools
33	Mitochondrial and plastome engineering
34	Use of genome editors to create null or negative segregants
35	Genetically engineered containment systems
36	Technical refinement of novel delivery systems and chemistries to modify organisms in the field or in nature
37	Integration of artificial intelligence and machine learning
38	Automation and use of biofoundries
39	Improved next-generation sequencing and bioinformatics
40	Improvements in DNA synthesis and assembly
41	Ability to recreate viruses by chemical DNA synthesis
42	Improvements to genome and karyotype engineering
43	Development of protocells, minimal cells and artificial living machines for research purposes
44	Advances in xenobiology
45	Advances in protein engineering
46	Adoption of the Kunming-Montreal Global Biodiversity Framework
47	Inequity in the participation of developing countries in the context of synthetic biology
48	Increased field testing of synthetic biology applications, including in areas outside the national jurisdiction of the developer or funder
49	Transboundary movements and relation to detection and identification of synthetic biology organisms, parts and products
50	Increased scale and use in series of synthetic biology interventions
51	Interaction of synthetic biology organisms in the environment and potential for cumulative effects
52	Dual-use nature and biosecurity implications of synthetic biology
53	Cyberbiosecurity
54	Changes in ethical standards

Annex II*

Draft literature review of trends and issues in synthetic biology (2012-2023)

Introduction

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.

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 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.[1] The Group recommended that the literature review should be based on a revised list of trends and issues in synthetic biology produced by the Secretariat and based on 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*.

In line with the requests from the multidisciplinary Expert Group, the Secretariat commissioned a 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. It aims to assess and explore trends and issues in synthetic biology using a quantitative approach.

Methods

The objective of the literature review outlined in this document was to systematically collect and quantify relevant scientific literature pertaining to synthetic biology. In line with the publication *Technical Series No. 100: Synthetic Biology*, the literature review uses the operational definition of synthetic biology[2] of the Ad Hoc Technical Expert Group on Synthetic Biology, which was considered useful as a starting point for the purpose of facilitating scientific and technical deliberations under the Convention on Biological Diversity and its Protocols in decision XIII/17. In addition, it is recognized that there could be a divergence of views on which techniques, applications and products fall under this operational definition of synthetic biology.

This review specifically emphasizes the identification and quantification of trends and issues within the field of synthetic biology between 1 January 2012 to 31 December 2023. As mentioned above, it is based on the revised list of the trends and issues in synthetic biology by the Secretariat.

* The present annex has been issued without formal editing, as the literature review is currently undergoing a peer-review process (see https://www.cbd.int/synbio/current_activities/peer_review/). The annex is therefore not for citation purposes.

[1] See figure I of the main report.

[2] "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 system".

Limitations

This literature analysis was primarily conducted during the month of December 2023. Due to the vastness of the field and limited time, some relevant studies could have been inadvertently excluded, which could have limited the depth of the analysis. In addition, the examination of publication content was not exhaustive. Therefore, due to the similarity of some of the trends and issues in synthetic biology, there could be overlaps of applications, products and techniques of synthetic biology between the trends themselves. In addition, only publications and patents available in English were examined due to time constraints. Thus, the methodology of this present study may not completely align with a traditional literature review, but these assumptions were necessary to streamline the research process and should be considered when interpreting the results.

Protocol and Search Strategy

A protocol for the search strategy was developed in August 2023, outlining an approach that closely adhered to the 54 items from the provisional selection list in addition to an additional item "Use of synthetic biology in art and design" which was identified following the development of the "provisional selection list" (55 in total). The search was designed based on resources including the Technical Series No. 100 Synthetic Biology published by the Secretariat and literature referenced from the submissions of information pursuant to paragraph 7 of the decision 15/31 and the Open-ended Online Forum on Synthetic Biology. To identify relevant studies, a systematic search of peer-reviewed scientific literature was initially conducted using distinct Boolean search phrases and these were run on both the Web of Science and Scopus databases. For the patent analysis, the International Patent Classification code method was selected, and the search was extended to the Google Patent database to identify relevant patents.

Study Eligibility and Selection Criteria

Scientific papers were identified and analysed in December 2023. The scope was limited to studies published on or after 1 January 2012, aligning the search with the year that discussions related to the topic of synthetic biology became more prevalent under the Convention on Biological Diversity.[3] Exclusion criteria was implemented to consider only original articles, review papers, book chapters and conference proceeding papers in English. Other types of documents like erratum, editorial, note and short surveys were not considered.

Data Extraction and Analysis

The analysis strategy focused on various indicators to assess the developments in the synthetic biology field. For publications, the analyses included the identification of top trends and issues in synthetic biology representing 90 per cent of publications and the annual research growth between the top issues and trends (i.e. total number of publications, temporal publication trends, top publishing countries in top 20 issues and trends and their collaboration network). To further supplement the information obtained through publication analysis, patent trend analyses was also performed to obtain the geographical distribution of patent filings for the field of synthetic biology.

Identifying issues and trends

This scientific study aimed to investigate the research trends in the field of synthetic biology by employing a comprehensive data analysis and using electronic databases (Web of Science and

[3] Under decision XI/11 (New and emerging issues), the Conference of the Parties noted the need to consider the potential impacts of components, organisms and products resulting from synthetic biology techniques on the conservation and sustainable use of biological diversity and associated social, economic and cultural considerations.

Scopus). A search strategy was employed using the well-defined Boolean[4] search string: ("synthetic biology" OR "engineering biology" OR "genetic engineering") AND; followed by the key string(s) developed with respect to each identical issue (the complete set of Boolean strings corresponding to the 55 issues total as described in "Search Protocol and Strategy" above are presented in enclosure I). Furthermore, during initial searches, it became apparent that the terms "synthetic biology", "engineering biology", and "genetic engineering" frequently co-occurred in pertinent literature. Thus, to encompass a more comprehensive collection of literature relevant to synthetic biology, the term "genetic engineering" was incorporated into the overarching bucket term (primary search criteria). This inclusion aimed to retrieve publications that align with the operational scope of synthetic biology but might not have been explicitly labelled as "synthetic biology" or "engineering biology" by the publishing authors.

These search strings were executed with the Scopus database, focusing on "article title", "abstract" and "keyword" fields and the "topic" field with the Web of Science database. The chosen search string was developed to encompass key terms associated with the identified trends and issues in synthetic biology and based on aforementioned publications. For certain trends and issues, more than one search string was used to capture a wider scope of the publication activity within the particular field of synthetic biology. Following the search, the results were exported as Microsoft Excel files for further processing. To allow for summation of the results between subsets, duplicates were removed between each item.

After conducting the unique Boolean searches in both Web of Science and Scopus there was a 95 per cent 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. The decision to prioritize Scopus over Web of Science for further analysis was informed by the observed redundancy of papers to ensure a more detailed exploration of the existing literature pertaining to identified issues and trends.

i. Temporal trend analysis

This literature review sought to examine publication trends within the 55 identified issues and trends over the span of 1 January 2012 to 31 December 2023. Searches were conducted for each year for the period 2012 to 2023 (inclusive) and the number of publications were quantified for each year. Subsequently, the trends and issues were organized in descending order based on the total number of publications. Further refinement involved the compilation of the trends contributing to approximately 90 per cent of the total publications in the aforementioned time frame.

ii. Geographic analysis

The next analysis performed was 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 for each country to obtain a final publication count per trend for the period 2012 to 2023. Then, to understand how research groups in different countries collaborate, a collaborative network analysis was conducted using VOSviewer software for the 20 trends and issues that represented 90 per cent of the publications in the field of synthetic biology. The authors retrieved data from Scopus for all these trends, amalgamated the information and uploaded it into VOSviewer for a comprehensive collaboration network analysis among publishing countries. To construct the

[4] 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.

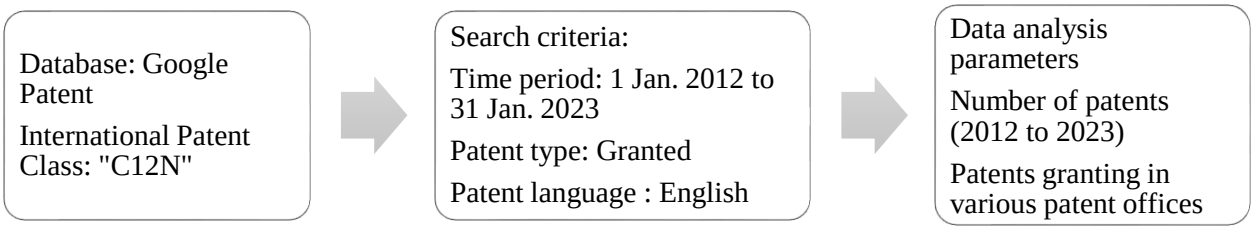
collaboration networks, a threshold was set, incorporating documents where collaborative countries had at least five documents in co-authorship and each with a minimum of five citations.[5] A total of 73 countries met these criteria.

iii. Patent trend analysis

To complement the data obtained from the quantification of publication, a preliminary patent analysis was performed. The analysis focused on quantifying the overall number of patents filed from 2012–2023 and mapping the geographical distribution of where these patents were filed. To conduct the analysis, Google Patents was used to retrieve the relevant patent information. International patent class "C12N" was chosen for this search as it aligned most closely with the operational definition of synthetic biology and previously published literature. The search was conducted for patents that were granted, published in English and for the time period 1 January 2012 to 31 January 2023. The search strategy is outlined in figure 1.

Figure I

Patent data search strategy using Google patents



Results

i. Identifying issues and trends

From the Scopus database search, a total of 32,531 scientific articles surrounding emerging issues and trends in the field of synthetic biology were identified between 2012 to 2023. A comprehensive list of 55 issues and trends along with their respective percentages of total publications are presented in table I below.

Notably, it was observed that 20 out of the 55 issues and trends comprised of 90.4 per cent of the total number of publications (29,395 unique publications). Within the top 20 trends, the distribution of original articles, review papers, book chapters and conference proceeding papers were approximately 60 per cent, 29 per cent, 9 per cent and 2 per cent, respectively. Furthermore, when examining the cumulative totals of publications for each of the trends, it can be observed that there are groups of publications, representing the top 8 (each with over 5 per cent of total publications) and 22 (over 1 per cent of total publications) in terms of total publications over the 2012–2023 period. Medical and therapeutic synthetic biology application was the top trend with 3,709 publications (11.40 per cent). The remaining 34 each have less than 1 per cent of total publications. For further quantitative analyses, the resultant dataset comprising of these 20 trends and issues in synthetic biology was employed.

[5] The threshold of five publications was informed by previously published studies and aims to demonstrate a sustained pattern of collaboration between research groups.

Table 1

List of 55 issues and trends in synthetic biology (2012–2023)

No.	*Identified issues and trends in synthetic biology*	*Number of publications*	*Percentage of publications*
1	Medical and therapeutic synthetic biology applications	3 707	11.40
2	Synthetic biology-enabled production of antibiotics, natural products and medically relevant compounds	3 261	10.02
3	Transient modification of agricultural plants, pests and pathogens using RNA interference or nanomaterials	2 553	7.85
4	Advances in protein engineering	2 492	7.66
5	Synthetic biology-enabled production of petrochemical precursors and industrial chemicals	2 393	7.36
6	Increased sophistication and expansion of genome editing tools	2 107	6.48
7	Biosensors, sensory devices and diagnostics	2 044	6.28
8	Improved next-generation sequencing and bioinformatics	1 845	5.67
9	Synthetic biology applications for bioremediation, biodegradation or biomining	1 331	4.09
10	Engineering photosynthesis	927	2.85
11	Integration of artificial intelligence and machine learning	925	2.84
12	Genome edited animals	924	2.84
13	Genome edited plants	874	2.69
14	Increased sophistication of genetic circuits	827	2.54
15	Improvements in DNA synthesis and assembly	702	2.16
16	Synthetic biology-enabled production of cosmetics and fragrances	563	1.73
17	Cell-free systems	519	1.60
18	Automation and use of biofoundries	482	1.48
19	Synthetic biology-enabled production of food, food ingredients and flavors	476	1.46
20	Microbiome engineering for non-medical purposes	443	1.36
21	Improvements to genome and karyotype engineering	374	1.15
22	Advances in xenobiology	268	0.82
23	Metabolic engineering of crops	260	0.80
24	Dual-use nature and biosecurity implications of synthetic biology	252	0.77
25	Increasing carbon capture efficiency in plants	227	0.70
26	Capture and recycling of greenhouse and waste gases using synthetic biology applications	223	0.69
27	Development of protocells, minimal cells and artificial living machines for research purposes	219	0.67
28	Engineered bacteria for nitrogen-fixation and fertilizers	203	0.62
29	Development of engineered gene drives to control vector-borne and invasive species	180	0.55
30	Virus-induced genome editing and genetic modifications	133	0.41
31	Living materials and biofilms	101	0.31

No.	*Identified issues and trends in synthetic biology*	*Number of publications*	*Percentage of publications*
32	The use of synthetic biology for art and design	95	0.29
33	Engineered sterility of non-native plant species	85	0.26
34	Changes in ethical standards	69	0.21
35	Use of synthetic biology in wild organisms in the context of resilience in threatened species	52	0.16
36	Interaction of synthetic biology organisms in the environment and potential for cumulative effects	49	0.15
37	Technical refinement of novel delivery systems and chemistries to modify organisms in the field or in nature	42	0.13
38	Synthetic biology-enabled production of fabrics, textile dyes and materials	40	0.12
39	Self-limiting insect systems	40	0.12
40	Mitochondrial and plastome engineering	38	0.12
41	Non-biological uses of synthetic biology	36	0.11
42	De-extinction of extinct animals	33	0.10
43	Increased field testing of synthetic biology applications, including in areas outside the national jurisdiction of the developer or funder	25	0.08
44	Paratransgenetic approaches for controlling vector-borne diseases	24	0.07
45	Genetically engineered containment systems	19	0.06
46	Bio-fabricated wildlife products	17	0.05
47	Ability to re-create viruses by chemical DNA synthesis	13	0.04
48	Cyberbiosecurity	9	0.03
49	Plant bioproduction of vaccines and anti-venoms	5	0.02
50	Exponential growth of synthetic biology without the participation of developing countries	2	0.01
51	Transboundary movements and relation to detection and identification of synthetic biology organisms, parts and products	2	0.01
52	Increased scale and use in series of synthetic biology interventions	1	0.00
53	Use of genome editors to create null or negative segregants	0	0.00
54	Adoption of the Kunming-Montreal Global Biodiversity Framework	0	0.00
55	Self-spreading vaccines for wildlife	0	0.00
	Total	32 531	100

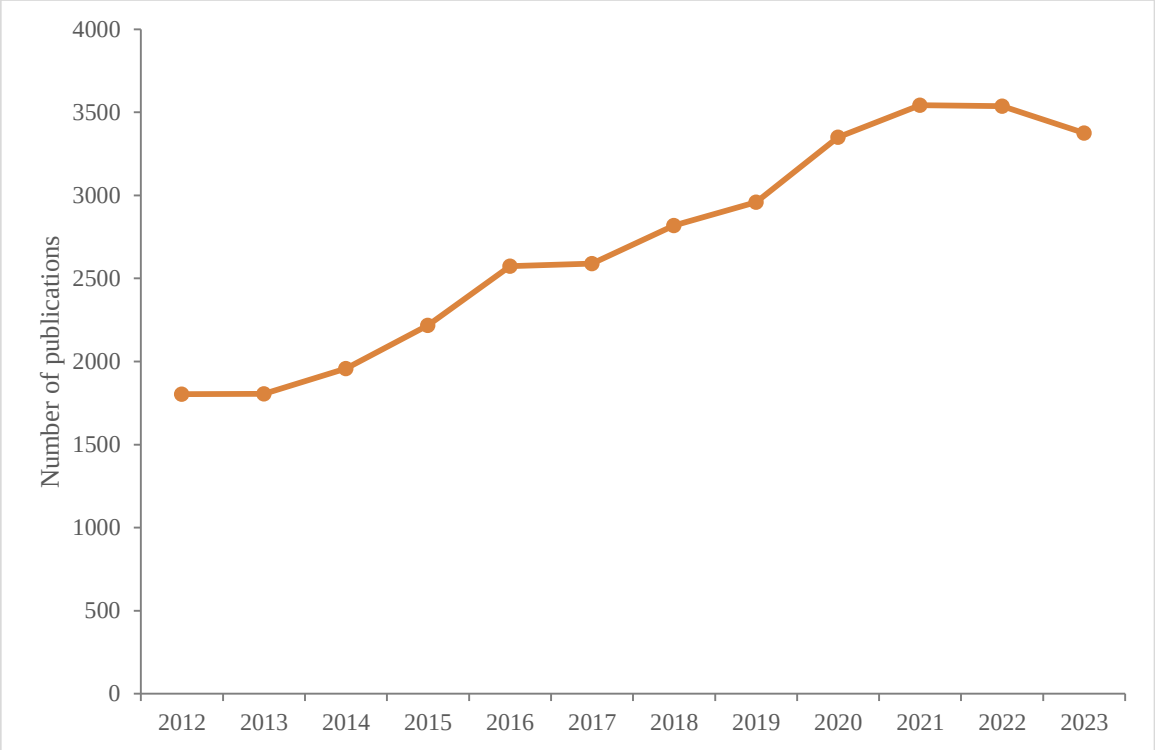
ii. Temporal trend analysis

To better understand how research output related to the field of synthetic biology evolved over the period 2012 to 2023, the number of total number publications for all 55 trends and issues per year was found. As figure II demonstrates below, there has been a steady increase in rate of publications per year within the field of synthetic biology increasing from roughly 1,800 in 2012 to 3,500 in 2021 and 2022. However, the rate appears to have slightly decreased for 2023.

Regarding how the individual 55 trends and issues in synthetic biology have evolved between 2012 and 2023, the publication rate per item per year was quantified. The results are presented in enclosure II. It can be observed that trends related to genome editing, such as "Increased sophistication and expansion of genome editing tools" and "Genome edited plants", exhibited a pronounced increase in the number of publications per year. Many other trends and issues also had increases, including "Medical and therapeutic synthetic biology applications", "Integration of artificial intelligence and machine learning", "Biosensors, sensory devices and diagnostics", "Synthetic biology applications for bioremediation, biodegradation or biomining" and "Living materials and biofilms". Other trends and issues, such as "Advances in protein engineering", "Synthetic biology-enabled production of petrochemical precursors and industrial chemicals", "Improvements in DNA synthesis and assembly" and "Automation and use of biofoundries", continued with roughly steady publication rates over the 2012–2023 period. No trend or issue in synthetic biology had a significant decline in the publication rate.

Figure II

Temporal analysis of 55 issues and trends (2012—2023)

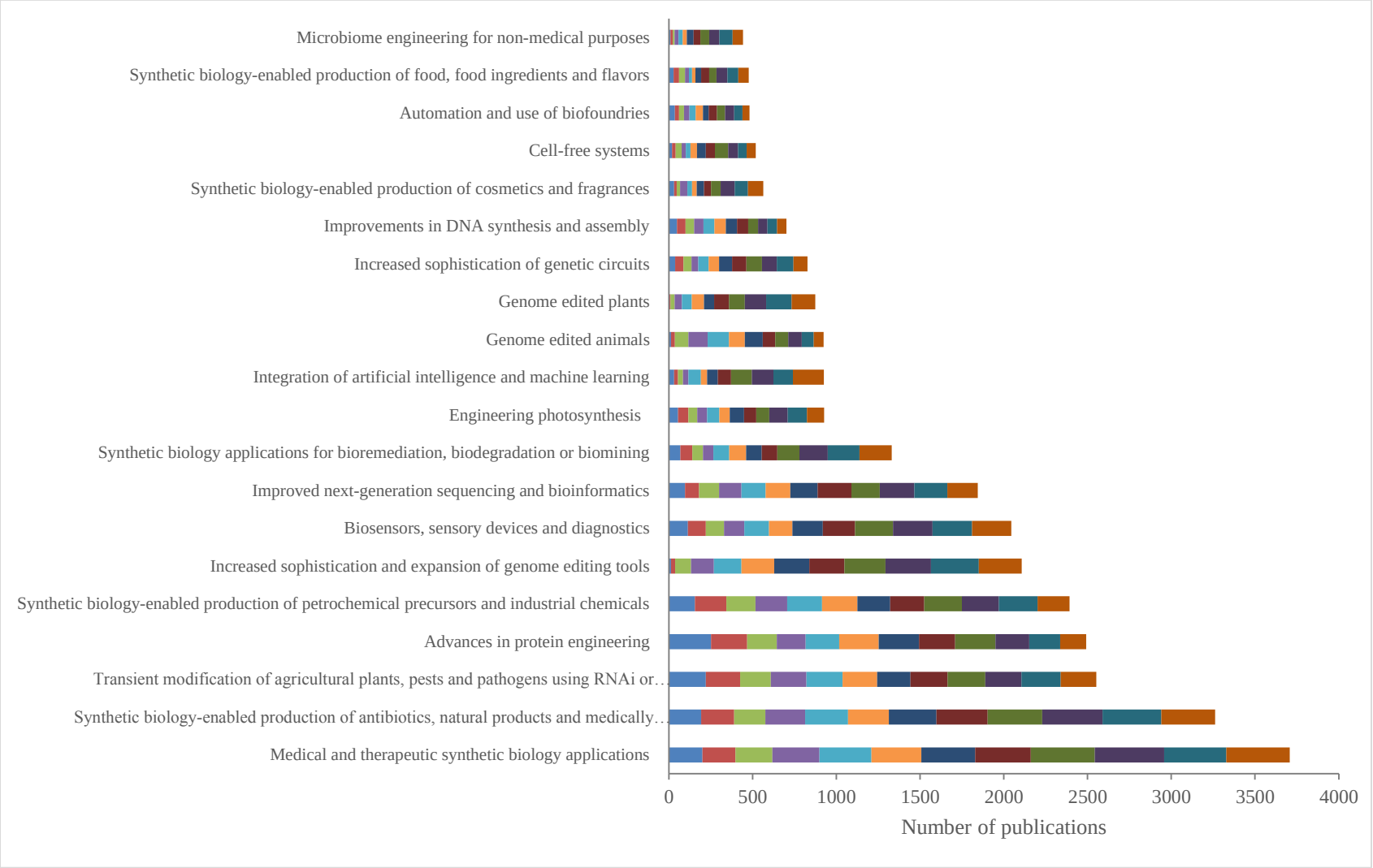


Furthermore, an examination of the annual publication of the subset of the 20 trends that represented 90 per cent of publications in the field of synthetic biology (see figure III) demonstrated that the annual publication rate generally increased for these areas with the exception of "Advances in protein engineering" which remained roughly consistent. Many publications related to the use of synthetic biology in contained settings (e.g., "Medical and therapeutic synthetic biology applications", "Synthetic biology-enabled production of antibiotics, natural products and medically relevant compounds", "Synthetic biology-enabled production of petrochemical precursors and industrial chemicals" and "Improved next-generation sequencing and bioinformatics"). "Transient modification of agricultural plants, pests and pathogens using RNAi or nanomaterials", "Synthetic biology applications for bioremediation, biodegradation or biomining", "Microbiome engineering for

non-medical purposes" and genome edited plants and animals represented the trends and issues that would most likely be associated with less confinement or introduced to the environment. In addition, it can be noted that technical refinements, such as genome editing tools, artificial intelligence, genetic circuits, DNA synthesis and sequencing, also represent a large area of research.

Figure III

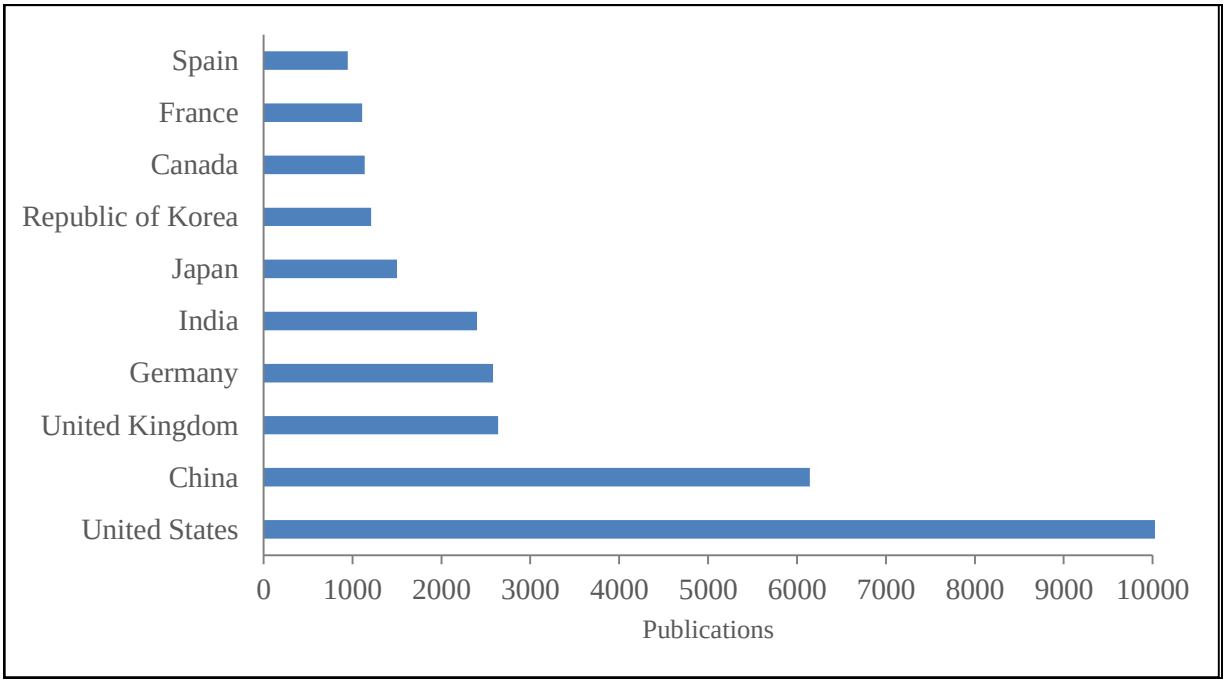
Overview of the 20 issues and trends representing 90 per cent of publications and corresponding publication patterns (2012–2023)



Next, to provide a nuanced comprehension of the current geographical distribution of research patterns, an analysis of the publishing landscape related to the 20 trends and issues that represent 90 per cent of the publications within the field of synthetic biology was conducted (see figure IV). The analysis of the global landscape of these 20 trends highlighted 10 primary contributing countries to the field of synthetic biology. Notably, the United States of America and China prominently emerge as the top contributors in the graphical representation. Next, Germany, the United Kingdom and India represent the next cluster of countries with the second highest publication output. Finally, the remaining five countries (Japan, Republic of Korea, Canada, France and Spain) constitute the rest of the top 10 countries in terms of publication output, all with roughly similar publication levels. Furthermore, it can also be observed that in terms of regional grouping, two countries are from North America, four countries are from Europe and four countries are from Asia.

Figure IV

Leading countries with the highest publication output for the 20 trends and issues in synthetic biology that represent 90 per cent of publications on the 55 trends and issues in the provisional selection list



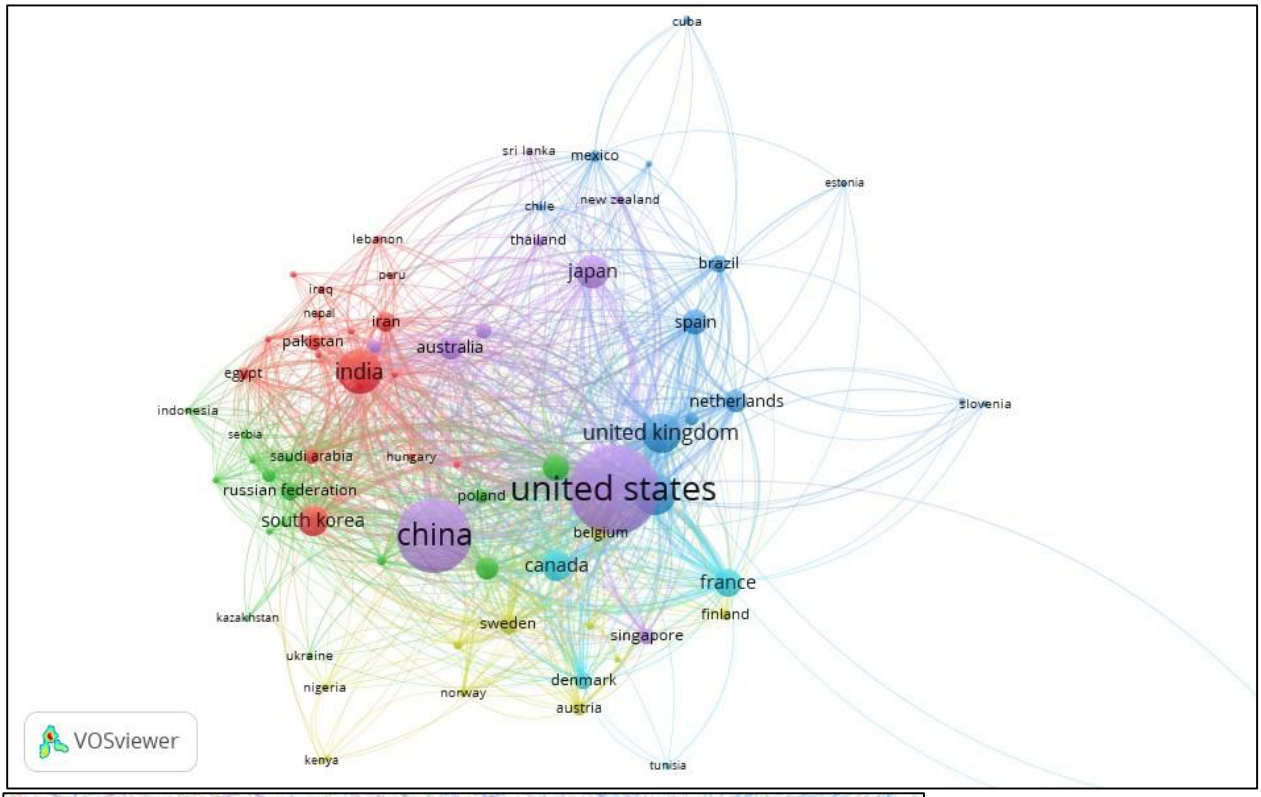
Then to unveil how research groups are engaged internationally, a collaborative network analysis was performed on the 20 trends and issues that represented 90 per cent of the publication in the field of synthetic biology to reveal large collaboration networks based on co-authorship patterns within publications. In the visual representation depicted in figure V, each circle symbolizes a country with larger circles representing countries with numerous publications and smaller circles denoting those with fewer publications. The lines connecting countries indicate the number of collaborations. The top part of figure V shows the global overview, while the bottom part shows a portion in higher resolution for the countries not clearly visible in the top part of the figure. The various colours indicate clusters of countries that exhibit authorship connections. The co-authorship patterns of the documents revealed the emergence of six collaboration networks, as further detailed in table 2.

Overall, all six of the main collaboration clusters have diverse international partnerships. However, some regionality also exists. For example, at least two European or Asian countries cluster together

when involved in international collaborations. Similarly, it also appears countries from the Latin American region have roughly also clustered together in #3, countries from West Asia in #1 and Africa into #4.

Figure V

Collaboration network analysis among publishing countries for the 20 identified trends and issues in synthetic biology



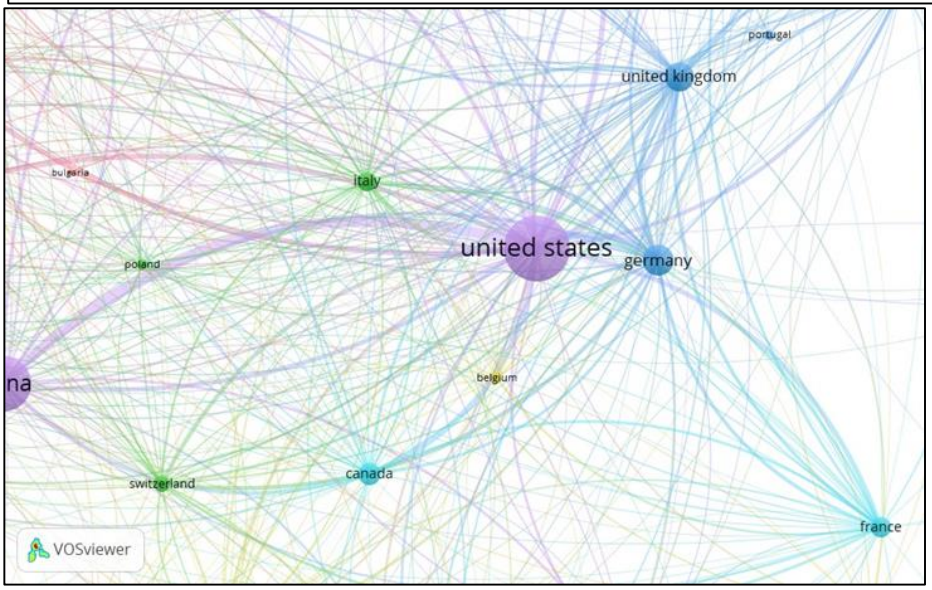


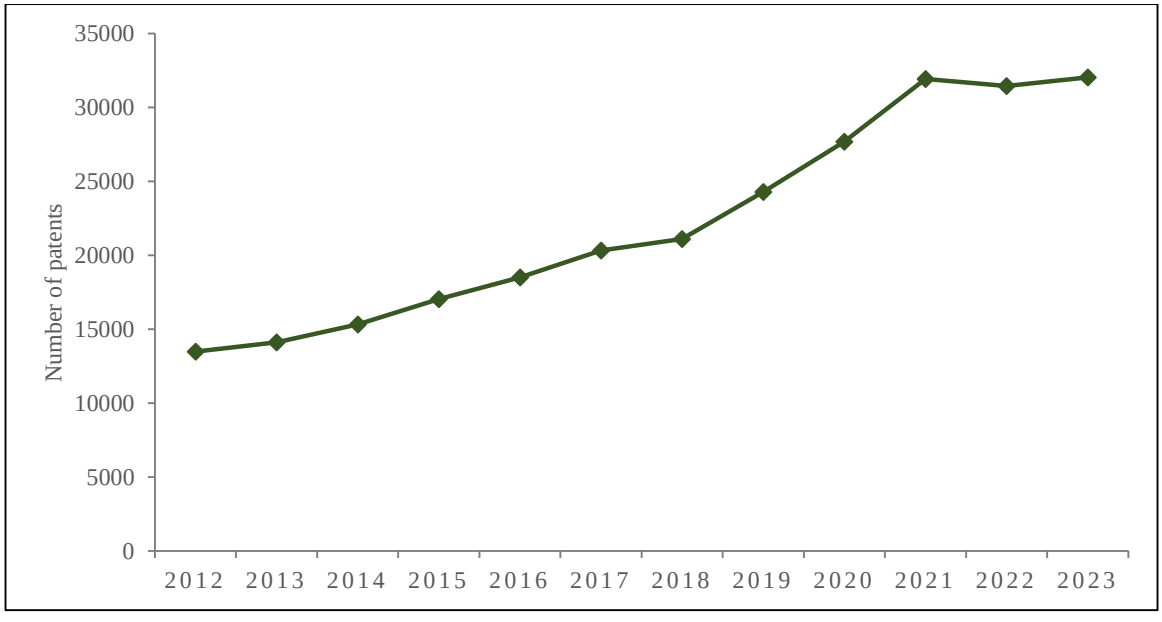
Table 2
Breakdown of collaborating countries on publications in the 20 identified trend and issues in synthetic biology

Clusters	*Participating countries*	*Number of countries*
#1	Bangladesh, Bulgaria, Egypt, Hungary India, Iran (Islamic Republic of), Iraq, Jordan, Lebanon, Nepal, Oman, Pakistan, Peru, Qatar, Romania, Saudi Arabia, Republic of Korea, United Arab Emirates	18
#2	Cyprus, Ghana, Indonesia, Ukraine, Ireland, Italy, Kazakhstan, Morocco, Philippines, Poland, Russian Federation, Serbia, Switzerland, Türkiye, Ukraine	15
#3	Argentina, Brazil, Chile, Croatia, Cuba, Ecuador, Estonia, Germany, Mexico, Netherlands (Kingdom of the), Portugal, Slovenia, Spain, United Kingdom of Great Britain and Northern Ireland	14
#4	Austria, Belgium, Czechia, Finland, Kenya, Nigeria, Norway, Slovakia, South Africa, Sweden, United Republic of Tanzania	11
#5	Australia, China, Israel, Japan, Malaysia, New Zealand, Singapore, Sri Lanka, Thailand, United States of America	10
#6	Canada, Denmark, France, Lithuania, Tunisia	5
	Total	**73**

iii. Patent Trend Analysis

Through conducting a patent trend analysis, valuable insights were provided into technological innovation within synthetic biology. An initial surge in the number of patents granted per year occurred from 2012 to 2021, followed by a horizontal progression observed from 2021 to 2023 as shown in figure VI.

Figure VI
Patent trend analysis (2012–2023)



Finally, to complement the annual rate of patent grants, an overview of the patent distribution from different regions 2012–2023 is presented in table 3. The collective data underscores the diverse and widespread efforts in intellectual property across nations, each making distinct contributions to the field of synthetic biology. However, it can be observed that the United Sates, China, Republic of Korea, Japan and the Europe Union represent the majority of patent filings for the field of synthetic biology. Outside these countries, Canada, the Russian Federation and Australia are also included in the distribution.

Table 3
Patent distribution among various patent offices (2012–2023)

	Country or region	*Number of patents*	*Contribution (percentage)*
	United States	42 177	37.715
	China	21 016	18.793
	Republic of Korea	11 128	9.951
	Japan	10 540	9.425
	Europe[a]	9 633	8.614
	Australia	6 798	6.079
	Spain	4 057	3.629
	Russian Federation	2 756	2.464
	Canada	2 700	2.414
	Denmark	621	0.555
	Netherlands	120	0.107
	Germany	106	0.095
	Luxembourg	68	0.061
	Belgium	59	0.053
	Finland	33	0.030
	France	11	0.009
	Austria	7	0.006
	Total	111 830	100.000

[a] European Patent Office.

Discussion and conclusion

This literature review aimed to analyse the trends and issues in synthetic biology through systematically gathering and quantifying scientific literature from 2012 to 2023. Overall, it can be the rate of publications and patents filed for the field of synthetic biology has increased linearly until the year 2021, demonstrated an increasing interest in both research and innovation within the field of synthetic biology since 2012. However, the rate of publications and patents have both plateaued between the years 2021 and 2023, which could hypothetically be a result of the COVID-19 public health crisis.

More specifically, the search yielded a list of 20 trends and issues in the field that collectively constituted 90 per cent of the total publications between 2012 to 2023 from a unique dataset of 32,531 publications. For the majority of these 20 trends and issues, there was a growing publication rate. Possible factors contributing to this growth could include technical refinements and advances (e.g., genome editing, artificial intelligence, laboratory tools), increased awareness of potential applications and a growing recognition of the significance of this trend in various fields. However, it might be important to recognize that many of the most prevailing trends are related to microbial

systems and many are for contained use (e.g., laboratories or closed industrial facilities)[15]. Similar findings were also described in Technical Series No. 100.

Furthermore, an examination of the annual publication rate issues and trends across all identified themes revealed considerable variations. For another subset of 24 trends and issues in synthetic biology, these exhibited a relatively low number of publication output, each accumulating less than 100 publications over the entire period between 2012 to 2023. This observation raises important questions regarding the underlying factors influencing the scientific focus directed towards these specific themes. Possible interpretations suggest that these issues and trends might have received comparatively limited attention from the research community, indicating areas with restricted exploration or recognition. Alternatively, these issues and trends could represent emerging research domains that have only recently gained attention within the scientific community. This prompts a need for further investigation to discern the nature of the observed disparity in publication output, as illustrated by the temporal growth of the issues and trends in enclosure II.

The global analysis of these 20 trends and issues demonstrates the global distribution of contributions in the field of synthetic biology. The United States and China, emerge as primary contributors, with India, Germany and the United Kingdom also playing significant roles in shaping the landscape as a cluster representing the next largest output of publications within the field. Finally, Japan, Republic of Korea, France, Canada and Spain as a grouping with the third most publications over the period 2012–2023. Similarly, emerging trends can be identified through analysis of patent fillings, with significant contributions from the United States, China, the Republic of Korea, Japan and Europe. This may indicate that both research and innovation are concentrated in the Global North and potentially that the majority of activity occurs in developed nations. Despite this, there could be opportunities for collaboration. Through the collaboration network analysis, all clusters demonstrated varied and diverse patterns of cooperation between both developed and developing nations in advancing synthetic biology research. Further investigation may be required to illuminate mechanisms for supporting and fostering international collaboration.

Despite the valuable insights that this literature review offers on the trends and issues in synthetic biology, it is important to acknowledge the present limitations. The constraints imposed by time and the chosen methodology is essential for understanding the scope and boundaries of this literature analysis. For example, if a publication did not include the term “synthetic biology”, “engineering biology” or “genetic engineering” in its title or abstract, it may have been excluded. Furthermore, additional work could have been conducted to further refine the search strings to capture the limited number of additional papers that could have been missing. 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.

More specifically, 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”, as 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 databases (i.e., Scopus, Web of Science).. However, for other trends, 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

[15] Containment, industrial processes, or laboratory settings refer to controlled and regulated environments. In these places, a combination of physical design parameters and operational practices prevent exposure of personnel, the immediate work environment, and the wider community to the synthetic biology-based applications. The use of said applications and products in industrial or laboratory premises fall under this classification (also see Technical Series No. 100).

supplementary information. Thus, future iterations of literature reviews may wish to consider other metric analyses to inform on trends such as these.

Overall, this study provides a valuable reference framework for future research projects. It is essential to recognize this exercise as an important initial reference point. The steady growth in publications signifies the increasing importance in the field, while collaboration networks emphasize the potential for global cooperation. Research and innovation told through publications and patents continue to show a dominance of the Global North in the field of synthetic biology. Further research should address the identified limitations, ensuring a more exhaustive exploration of emerging trends. Continuous horizon scanning and 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.

Acknowledgements

The technical work underlying this document was kindly supported by a grant from the European Union.

Enclosure I

Boolean search strings for 55 identified issues and trends

No.	*Identified issues and trends in synthetic biology*	*New search terms*
1	Use of synthetic biology in wild organisms in the context of resilience in threatened species	Subset 1: (“conservation” OR “resilience”) AND (“endangered” OR “threatened”) Subset 2: (“conservation” OR “resilience”) AND (“climate change”)
2	Self-spreading vaccines for wildlife	Subset 1: “wildlife” AND (“vaccine delivery” OR “vaccine dissemination”) Subset 2: “wildlife” AND (“vaccine” AND “spreading”)
3	Genome edited plants	(“genome edit*”) AND (“plant*” OR “crop*” OR “tree*” OR “flower*”)
4	Genome edited animals	(“genome edit*”) AND (“animal*” OR “livestock”)
5	Metabolic engineering of crops	Subset 1: (“metabolic engineering”) AND (“crop*”) Subset 2: “C4 Engineering” OR “C4 photosynthesis” OR “C4 Plant” OR “C-4 plant” OR “SCC4” OR “PEPC GENE”
6	Engineering photosynthesis	(“photosynthesis” OR “photorespirat*”) AND “engineering”)
7	Increasing carbon capture efficiency in plants	Subset 1: (“carbon capture”) OR (“Carbon sequestration”) OR (“Carbon storage”) OR (“CO2 fixation” AND “plant*”) Subset 2: “rubisco” AND “engineering”
8	Engineered sterility of non-native plant species	(“genetic biocontrol”) OR (“sterility”) AND (“plant*” OR “tree”)
9	Transient modification of agricultural plants, pests and pathogens using RNAi or nanomaterials	Subset 1: (“agricultural plant*” OR “crop*” OR “pest*” OR “insect*” OR “disease vector*” OR “pathogen*” OR “microorganism*”) AND (“RNAi” OR “RNA interference” OR “nanomaterial*”) Subset 2: “dsRNA” OR “silencing” OR “biopesticide” OR “crop protection”
10	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*”
11	Microbiome engineering for non-medical purposes	(“microbiome” OR “consorti*”) AND NOT (“medic*” OR “therap*” OR “human” OR “biomedic*”)
12	Engineered bacteria for nitrogen-fixation and fertilizers	(“nitrogen fixation” OR “fertilizer”) AND (“bacteria*” OR “strain*”)

No.	*Identified issues and trends in synthetic biology*	*New search terms*
13	Synthetic biology applications for bioremediation, biodegradation or biomining	"bioremediation" OR "biodegradation" OR "biomining"
14	Development of engineered gene drives to control vector-borne and invasive species	Subset 1: ("gene drive*") AND ("mosquito*" OR "rodent*" OR "vector*") Subset 2: ("gene drive*") AND ("vector borne" OR "invasive species") Subset 3: ("gene drive*" AND "CRISPR" OR "homing endonuclease*")
15	Self-limiting insect systems	Subset 1: ("self-limiting" OR "self-limiting") AND ("Insect") Subset 2: ("Insect*" AND "dominant lethal") Subset 3: ("RIDL" OR "Sterile Insect Technique") OR ("release of insects with dominant lethality")
16	Paratransgenetic approaches for controlling vector-borne diseases	"paratransgene*" OR "transmission blocking"
17	De-extinction of extinct animals	Subset 1: ("de-extinction") OR ("resurrection biology") Subset 2: ("de-extinction") AND ("animal cloning")
18	Living materials and biofilms	"Living material*"
19	Capture and recycling of greenhouse and waste gases using synthetic biology applications	("greenhouse gas*") OR ("waste gas*")
20	Synthetic biology-enabled production of petrochemical precursors and industrial chemicals	"petrochemical precursor*" OR "industrial chemical*" OR "biofuel*" OR "bioenergy"
21	Synthetic biology-enabled production of cosmetics and fragrances	"cosmetic*" OR "fragrance*"
22	Synthetic biology-enabled production of food, food ingredients and flavours	Subset 1: "synthetic food" OR "ingredient*" OR "flavour*" OR "food science" Subset 2: "cultured meat" OR "cell-cultured meat" OR "cellular agriculture" OR "bio-manufacturing cultured meat" OR "artificial food"
23	Synthetic biology-enabled production of antibiotics, natural products and medically relevant compounds	Subset 1: "antibiotic*" Subset 2: "natural product*" OR "cannabidiol" OR "CBD"
24	Plant bioproduction of vaccines and anti-venoms	Subset 1: "vaccine*" AND ("plant production" OR "plant bioproduction")

No.	*Identified issues and trends in synthetic biology*	*New search terms*
		Subset 2: (“plant production” OR “plant bioproduction”) AND (“antivenoms” OR “recombinant polyclonal antibodies” OR “venom”)
25	Medical and therapeutic synthetic biology applications	Subset 1: “gene therapy” Subset 2: “CAR T-cell*” Subset 3: “medical application” OR “therapeutic application” OR “probiotic*”
26	Biosensors, sensory devices and diagnostics	“biosensor” OR “sensory devices” OR “diagnostics”
27	Synthetic biology-enabled production of fabrics, textile dyes and materials	“fabric” OR “textile dye”
28	Bio-fabricated wildlife products	Subset 1: “bio-fabricated” OR “biologically fabricated” OR “wildlife products” Subset 2: “ivory” OR “horn”
29	Non-biological uses of synthetic biology	“bio comput*” OR “DNA storage”
30	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*”
31	Increased sophistication of genetic circuits	“genetic circuit*” OR “DNA circuit*” OR “RNA circuit*” OR “protein circuit*”
32	Mitochondrial and plastome engineering	“Mitochondrial engineering” OR “plastid engineering” OR “plastome engineering” OR “chloroplast engineering”
33	Use of genome editors to create null or negative segregants	(“genome edit*” OR “CRISPR”) AND (“null segregant” OR “negative segregant”)
34	Genetically engineered containment systems	“containment system*” OR “biocontainment system*” OR “killswitch*”
35	Technical refinement of novel delivery systems and chemistries to modify organisms in the field or in nature	“pollen-mediated” OR “nano material*” OR “nano tubule*” OR “Novel Delivery System*”
36	Integration of artificial intelligence and machine learning	“artificial intelligence” OR “machine learning” OR “big data”
37	Automation and use of biofoundries	“automation" OR "biofoundr*”
38	Improved next-generation sequencing and bioinformatics	“next generation sequencing” OR “next-generation sequencing” OR “bioinformatics”
39	Improvements in DNA synthesis and assembly	“DNA synthesis” OR “DNA assembly” OR “goldengate”
40	Ability to recreate viruses by chemical DNA synthesis	(“virus*”) AND (“recreat*” OR “construction”) AND (“chemical DNA synthesis” OR “DNAb fragment*” OR “oligonucleotide*”)

No.	*Identified issues and trends in synthetic biology*	*New search terms*
41	Improvements to genome and karyotype engineering	“genome-level engineering” OR “karyotype engineering” OR “chromosome engineering” OR “artificial chromosome”
42	Development of protocells, minimal cells and artificial living machines for research purposes	“protocell*” OR “minimal cell*” OR “artificial living machine*”
43	Advances in xenobiology	Subset 1: (“alien” OR “noncanonical” OR “non-canonical”) AND (“amino acid” OR “nucleotide”) Subset 2: “xenobiology” Subset 3: (“expand* gene* cod*”)
44	Advances in protein engineering	“protein engineering” OR “synthetic protein*” OR “enzyme optimization” OR “Engineered protein*”
45	Adoption of the Kunming-Montreal Global Biodiversity Framework	“Global Biodiversity Framework” OR “GBF” OR “KMGBF”
46	Inequity in the participation of developing countries in the context of synthetic biology	(“developing countr*”) AND (“participation” OR “capacity-building” OR “inequity”)
47	Increased field testing of synthetic biology applications, including in areas outside the national jurisdiction of the developer or funder	“field testing”
48	Transboundary movements and relation to detection and identification of synthetic biology organisms, parts and products	“transboundary” AND “movement*”
49	Increased scale and use in series of synthetic biology interventions	“intervention*” AND “scale” AND “series”
50	Interaction of synthetic biology organisms in the environment and potential for cumulative effects	Subset 1: “cumulative effects” OR “sequential use” OR "organism interaction environment" Subset 2: "unintended consequences" OR "ecosystem interaction" OR "ecological balance" OR
51	Dual-use nature and biosecurity implications of synthetic biology	“biosecurity” OR “dual use” OR “dual-use” OR “bioweapon*” OR “military”
52	Cyberbiosecurity	“cyberbiosecurity”
53	Changes in ethical standards	(“ethic*” OR “ethical standard*” OR “norm erosion” OR "bioethics*") NOT “medical”
54	The use of synthetic biology for art and design	“biomimicry” OR “biodesign” OR “bio art” OR “bio-art”
55	Increased sophistication and expansion of genome editing tools	Subset 1: (“Genome edit*” AND “tool*”) Subset 2: (“Genome edit*” AND “multiplex”) Subset 3: (“Cas” OR “CRISPR”) AND “novel”

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Enclosure II

Temporal analysis of 55 issues and trends in synthetic biology (2012–2023)

No.	*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	201	197	220	281	310	299	321	332	382	414	371	379	3 707
2	Synthetic biology-enabled production of antibiotics, natural products and medically relevant compounds	193	197	186	238	256	244	284	305	326	360	351	321	3 261
3	Transient modification of agricultural plants, pests and pathogens using RNAi or nanomaterials	221	205	183	213	215	206	200	221	226	215	235	213	2 553
4	Advances in protein engineering	252	216	177	171	201	236	241	215	241	202	185	155	2 492
5	Synthetic biology-enabled production of petrochemical precursors and industrial chemicals	156	187	174	190	207	212	196	203	225	220	232	191	2 393
6	Increased sophistication and expansion of genome editing tools	13	24	95	136	166	195	209	210	245	272	286	256	2 107
7	Biosensors, sensory devices and diagnostics	113	107	110	120	148	140	181	193	226	236	237	233	2 044
8	Improved next-generation sequencing and bioinformatics	96	84	119	134	145	147	163	202	169	206	197	183	1 845
9	Synthetic biology applications for bioremediation, biodegradation or biomining	69	71	63	62	95	101	93	93	133	169	189	193	1 331
10	Engineering photosynthesis	55	62	53	58	73	62	86	72	79	110	114	103	927
11	Integration of artificial intelligence and machine learning	31	23	30	32	75	38	63	79	125	128	116	185	925
12	Genome edited animals	12	24	80	115	128	95	106	75	78	80	72	59	924
13	Genome edited plants	4	6	24	43	59	73	62	87	96	126	153	141	874
14	Increased sophistication of genetic circuits	37	50	48	41	61	63	77	86	93	89	98	84	827
15	Improvements in DNA synthesis and assembly	48	52	51	56	65	68	67	66	60	56	57	56	702
16	Synthetic biology-enabled production of cosmetics and fragrances	31	15	21	43	28	29	42	43	57	84	79	91	563
17	Cell-free systems	18	23	35	25	28	39	53	54	79	59	51	55	519
18	Automation and use of biofoundries	36	24	30	33	37	43	35	50	47	55	49	43	482
19	Synthetic biology-enabled production of food, food ingredients and flavors	28	33	36	22	19	21	33	48	44	65	66	61	476
20	Microbiome engineering for non-medical purposes	9	14	11	23	25	25	41	40	53	60	79	63	443
21	Improvements to genome and karyotype engineering	40	31	35	42	34	38	16	24	41	25	23	25	374
22	Advances in xenobiology	12	8	19	12	16	25	33	24	29	29	35	26	268

No.	*Identified issues and trends in synthetic biology*	*2012*	*2013*	*2014*	*2015*	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*2022*	*2023*	*2012–2023*
23	Metabolic engineering of crops	19	17	13	15	26	19	31	12	33	30	23	22	260
24	Dual-use nature and biosecurity implications of synthetic biology	17	21	15	15	8	21	21	29	25	32	21	27	252
25	Increasing carbon capture efficiency in plants	9	12	5	7	28	20	20	14	28	26	31	27	227
26	Capture and recycling of greenhouse and waste gases using synthetic biology applications	16	15	10	10	16	12	15	10	14	32	36	37	223
27	Development of protocells, minimal cells and artificial living machines for research purposes	8	22	20	15	15	14	19	32	22	19	16	17	219
28	Engineered bacteria for nitrogen-fixation and fertilizers	8	11	23	15	13	14	18	19	20	22	23	17	203
29	Development of engineered gene drives to control vector-borne and invasive species	4	4	5	7	8	12	22	30	29	26	19	14	180
30	Virus-induced genome editing and genetic modifications	11	11	8	13	14	7	11	16	12	9	9	12	133
31	Living materials and biofilms	–	1	–	2	–	2	5	12	13	21	26	19	101
32	Use of synthetic biology for art and design	3	3	5	4	7	4	4	14	18	15	12	6	95
33	Engineered sterility of non-native plant species	10	7	8	2	13	6	7	5	8	9	3	7	85
34	Changes in ethical standards	3	6	11	9	5	6	3	4	10	3	3	6	69
35	Use of synthetic biology in wild organisms in the context of resilience in threatened species	2	1	–	–	2	8	1	4	10	9	8	7	52
36	Interaction of synthetic biology organisms in the environment and potential for cumulative effects	1	–	6	1	3	6	6	3	11	3	5	4	49
37	Technical refinement of novel delivery systems and chemistries to modify organisms in the field or in nature	2	4	5	1	–	4	4	5	8	5	1	3	42
38	Synthetic biology-enabled production of fabrics, textile dyes and materials	1	2	4	–	4	4	4	6	3	3	3	6	40
39	Self-limiting insect systems	3	4	5	3	1	4	4	–	6	3	6	1	40
40	Mitochondrial and plastome engineering	–	1	2	1	2	3	3	4	3	5	2	12	38
41	Non-biological uses of synthetic biology	1	–	2	2	3	1	6	5	3	3	3	7	36
42	De-extinction of extinct animals	–	–	2	1	1	18	2	–	5	1	2	1	33
43	Increased field testing of synthetic biology applications, including in areas outside the national jurisdiction of the developer or funder	5	1	1	–	3	2	3	2	3	1	1	3	25
44	Paratransgenetic approaches for controlling vector-borne diseases	1	2	3	2	4	1	4	2	1	1	3	–	24
45	Genetically engineered containment systems	2	1	1	–	2	1	2	3	4	1	1	1	19
46	Bio-fabricated wildlife products	1	2	4	2	3	1	–	1	1	1	1	–	17

No.	*Identified issues and trends in synthetic biology*	*2012*	*2013*	*2014*	*2015*	*2016*	*2017*	*2018*	*2019*	*2020*	*2021*	*2022*	*2023*	*2012–2023*
47	Ability to re-create viruses by chemical DNA synthesis	1	4	–	1	1	–	2	1	1	–	2	–	13
48	Cyberbiosecurity	–	–	–	–	–	–	–	3	1	2	1	2	9
49	Plant bioproduction of vaccines and anti-venoms	–	–	–	–	–	–	–	1	2	1	1	–	5
50	Exponential growth of synthetic biology without the participation of developing countries	–	–	–	–	1	–	–	–	1	–	–	–	2
51	Transboundary movements and relation to detection and identification of synthetic biology organisms, parts and products	–	–	–	–	–	–	–	1	1	–	–	–	2
52	Increased scale and use in series of synthetic biology interventions	–	–	–	–	–	–	–	–	–	–	–	1	1
53	Use of genome editors to create null or negative segregants	–	–	–	–	–	–	–	–	–	–	–	–	–
54	Adoption of the Kunming-Montreal Global Biodiversity Framework	–	–	–	–	–	–	–	–	–	–	–	–	–
55	Self-spreading vaccines for wildlife	–	–	–	–	–	–	–	–	–	–	–	–	–
	Total	**1 803**	**1 805**	**1 958**	**2 218**	**2 574**	**2 589**	**2 819**	**2 960**	**3 350**	**3 543**	**3 537**	**3 375**	**32 531**

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Enclosure III

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