Synthetic Biology Research and Innovation Profile 2018: Publications and Patents

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Abstract

A profile of synthetic biology research and innovation is presented using data on publications and patents worldwide and for the UK and selected benchmark countries. The search approach used to identify synthetic biology publications identifies a core set of synthetic biology papers, extracts and refines keywords from these core records, searches for additional papers using those keywords, and supplements with articles published in dedicated synthetic biology journals and curated synthetic biology special collections. For the period from 2000 through to mid-July 2018, 11,369 synthetic biology publication records are identified worldwide. For patents, the search approach uses the same keywords as for publications then identifies further patents using a citation-tree search algorithm. The search covered patents by priority year from 2003 to early August 2018. Following geographical matching, 8,460 synthetic biology basic patent records were identified worldwide. Using this data, analyses of publications are presented which look at the growth of synthetic biology outputs, top countries and leading organizations, international co-authoring, leading subject categories, citations, synthetic biology on the map of science, and funding sponsorship. For patents, the analysis examines growth in patenting, national variations in publications compared with patenting, leading patent assignees, and the positioning of synthetic biology on a visualized map of patents.

Overview of Methods and Sources

In this paper, we provide an overview profile of synthetic biology research and innovation using data on publications and patents worldwide and for the UK and selected benchmark countries.

The data source for publications is the Web of Science (WOS). This is a leading large-scale database of bibliometric and citation records.¹ The search approach used to identify synthetic biology publications within the WoS follows the procedures described in Shapira et al. (2017).² The approach identifies a core set of synthetic biology papers, extracts and refines keywords from these core records, searches for additional papers using those keywords, and supplements with articles published in dedicated synthetic biology journals and curated synthetic biology special collections. The search covers synthetic biology publications recorded in WoS from 2000 through to mid-July 2018.³ VantagePoint textmining software is used to clean and analyze the publication records.⁴ Records were de-duplicated using the WOS ISI Unique Article Identifier. In total, the combined and cleaned data set comprises 11,369 synthetic biology publication records.

For patents, the main data source is Derwent Innovations, which offers a recognized and curated global database of patents and patent applications.⁵ The search approach used to identify synthetic biology patents follows Kwon et al. (2016).⁶ The approach employed the same keywords as for publications (see Shapira et al., 2017) to identify an initial set of patent records. Further patents were identified using a citation-tree search algorithm. The search covered patents by priority year from 2003 to 2018 (as of Aug 3, 2018), with 9,263 Derwent Innovations patent records identified. Geographical address information for assignees was obtained by record matching with PATSTAT.⁷ This identified 8,498 matching patent records (including 8,460 records with basic patent numbers for the original invention in a patent family).

As an emerging, dynamic, multidisciplinary domain, there are multiple complexities in defining synthetic biology, as well as constraints in the available data sources. For detailed discussions of these issues, the search methods adopted, and their strengths and limitations when applied to identifying synthetic biology publications and patents, reference should be made to the Shapira et al. (2017) and Kwon et al. (2016) respectively.

The following sections present key results from our analyses of synthetic biology publication and patents.

¹ Clarivate Analytics. <u>https://clarivate.com/products/web-of-science/databases/</u>

² Shapira P, Kwon S, Youtie J. Tracking the Emergence of Synthetic Biology, *Scientometrics*, 2017, 112: 1439–1469. http://dx.doi.org/10.1007/s11192-017-2452-5.

³ The WoS databases searched comprised SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH, and A&HCI (document type: all). This search updates the original search in Shapira et al. (2017), which covered the period 2000-2015. ⁴ https://www.thevantagepoint.com/

⁵ Clarivate Analytics. <u>https://clarivate.com/products/derwent-innovation/</u>

⁶ Kwon S, Youtie J, Shapira P. 2016. Building a Patent Search Strategy for Synthetic Biology. Working Paper. Georgia

Tech Program in Science, Technology and Innovation Policy, Atlanta, GA, USA. March 10. <u>http://bit.ly/2E3Py7T</u>

⁷ European Patent Office. <u>https://www.epo.org/searching-for-patents/business/patstat.html</u>

Synthetic Biology Publications

Global Growth of Synthetic Biology Publications

Synthetic biology publications as identified in the WoS increased, on an annualized basis, from under 200 publications worldwide in the early 2000s to over 500 in 2010. We estimate that worldwide publications will reach about 1450 in 2018. The four leading countries, by authorship, in producing synthetic biology publications are the USA, the UK, China, and Germany. (Figure 1.) Authors from these four countries account for more than 70 per cent of all synthetic biology publications from 2000 through to the present (Table 1).

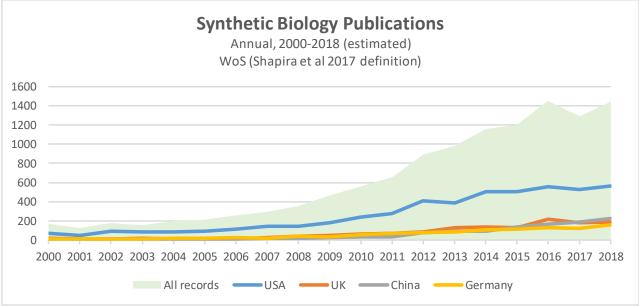


Figure 1. Synthetic Biology Publications

Source: Analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369. Annualized totals for 2018 estimated from part-year 2018 publication trends.

Table 1 shows the top 15 countries for synthetic biology publications for the 2000-2017 period, based on author countries. The USA is the leading country, producing more than two-fifths of the world's synthetic biology publications, although its share of the world total has dipped across the three periods depicted in the table. The UK, China and Germany are the next most prolific countries for synthetic biology publications over the period 2000-2017. While UK publications have grown strongly over this period, China's have recently grown at a faster rate. In 2015 and 2017, China achieved comparable output to the UK in terms of annual synthetic publications; in 2018 (papers published to date) Chinese authors published more papers (120) than UK authors (101). Overall, authors in about 90 countries have published synthetic biology publications (Figure 2).

		Publica	ntions		Percent of Total				
Country	2000-2006	2007-2012	2012-2017	2000-2017	2000-2006	2007-2012	2012-2017	2000-2017	
USA	469	1394	2786	4452	45.2	43.4	40.6	42.1	
UK	65	322	891	1188	6.3	10.0	13.0	11.2	
China	41	199	794	922	4.0	6.2	11.6	8.7	
Germany	67	282	644	930	6.5	8.8	9.4	8.8	
Japan	124	198	382	678	12.0	6.2	5.6	6.4	
France	50	156	351	539	4.8	4.9	5.1	5.1	
Canada	64	141	250	452	6.2	4.4	3.6	4.3	
Switzerland	24	130	250	386	2.3	4.0	3.6	3.6	
Spain	21	119	228	356	2.0	3.7	3.3	3.4	
Italy	39	112	189	328	3.8	3.5	2.8	3.1	
South Korea	22	74	205	288	2.1	2.3	3.0	2.7	
Netherlands	13	64	174	229	1.3	2.0	2.5	2.2	
Australia	21	43	170	218	2.0	1.3	2.5	2.1	
Denmark	13	42	178	207	1.3	1.3	2.6	2.0	
India	17	64	132	199	1.6	2.0	1.9	1.9	
Worldwide	1037	3213	6857	10582	100.0	100.0	100.0	100.0	

Table 1. Top 15 Countrie	es for Synthetic	Biology Publications
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Source: Analysis of Web of Science publication records (2000 to 2017), Shapira et al. 2017 synthetic biology search strategy, N=10,582. Totals exceed 100% as some publications are associated with authors from more than one country.

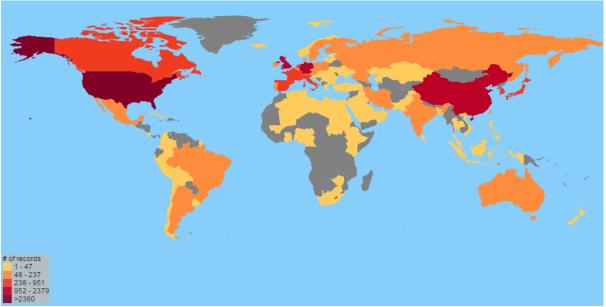


Figure 2. Synthetic Biology Publications by Country, 2000-2018*

Source: Analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369. *Part Year.

Top Organizations for Synthetic Biology Publishing

Table 2 shows the top 50 institutions (in terms of publication counts) worldwide involved in synthetic biology research publishing, by author affiliation. These top 50 institutions accounted for about one-half (49.8%) of all worldwide synthetic biology publications from 2000 through to mid-2018. Most of the top publishing institutions are universities, with representation also from other academic organizations, public research organizations, and governmental laboratories.

One half (25) of the top 50 institutions publishing in synthetic biology (by publication count) are based in the United States, led by MIT, Harvard, and the University of California, Berkeley. Nine of the top 50 institutions in this publication count list are in the UK, including Imperial College London, the University of Edinburgh, the University of Oxford, and the University of Manchester. Four institutions are in Japan, three in China, and two each in Switzerland and Denmark.

	Author Affiliation	Records		Author Affiliation	Records
1	MIT	330	26	Osaka Univ	91
2	Harvard Univ	278	27	Univ Calif Davis	89
3	Univ Calif Berkeley	274	28	Joint BioEnergy Inst	88
4	Swiss Fed Inst Technol	222	29	CSIC	85
5	Chinese Acad Sci	211	30	Cornell Univ	84
6	Imperial Coll London	185	31	Univ Cambridge	84
7	Univ Illinois	155	32	CNRS	83
8	Univ Toronto	152	33	Japan Sci & Technol Agcy	81
9	Stanford Univ	149	34	Univ Basel	81
10	Univ Calif San Diego	136	35	Univ Texas Austin	77
11	Univ Tokyo	134	36	Univ Wisconsin	77
12	Univ Edinburgh	129	37	Tsinghua Univ	76
13	Northwestern Univ	125	38	Univ Freiburg	76
14	CALTECH	122	39	Lawrence Berkeley Natl Lab	75
15	Univ Minnesota	120	40	Tianjin Univ	75
16	Boston Univ	119	41	Univ Calif Los Angeles	73
17	Univ Oxford	114	42	Yale Univ	73
18	Univ Washington	114	43	Univ Copenhagen	70
19	Tech Univ Denmark	109	44	UCL	69
20	Univ Manchester	107	45	Univ Warwick	68
21	Univ Calif San Francisco	98	46	Korea Adv Inst Sci & Technol	67
22	Univ Penn	97	47	Univ Maryland	66
23	Duke Univ	95	48	Arizona State Univ	65
24	Univ Bristol	93	49	Kyoto Univ	64
25	Johns Hopkins Univ	92	50	Newcastle Univ	64

Table 2. Top 50 World-Wide Affiliations for Synthetic Biology Publications (2000-2018*)

Source: Analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369. Fuzzy list clean up (using organization name without department). UK organizations shaded in blue. *Part year.

International Co-authoring in Synthetic Biology

Co-authorship is the norm in synthetic biology, as in most other areas of science. Of the 11,368 synthetic biology publications in our 2000-2018* (*part year) WoS dataset, only 10% have a single author. Over one-third (34.1%) of the publications have 2-3 authors, while more than another third (35.4%) have 4-6 authors. Another 15.6% have 7-10 authors.

Co-authorship can occur among researchers in the same institution, in the same country, and across international boundaries. There are variations in the propensity of countries for international co-authorship. For example, among the four leading producers of synthetic biology publications (by publication counts), just over one quarter of US publications are internationally co-authored, with authors from China, the UK, and Canada being the three most prevalent. For the UK, 43% of synthetic biology publications are internationally-co-authored, most noticeably with the US (about 15% of all UK synthetic biology publications), followed by Germany and France. For the UK, 21% (271, non-duplicated) of its synthetic biology publications (2000-2018 part year) are with researchers from other member states of the European Union (EU). The four largest EU co-authoring partners for the UK are Germany (6.0%), France (4.3%), Italy (3.9%) and the Netherlands (3.3%). Germany also has a high international co-authorship rate (46% of all its synthetic biology publications), with the US, the UK, and Switzerland as the leading three international co-authors for German researchers. In China, international co-authorships comprise just over one-third of its synthetic biology publications, with the US contributing to nearly one fifth of Chinese publications in the domain. The UK is the second most common international co-authorship partner for Chinese researchers. (Table 3.)

Country	Records	Internationally-		Leading Co-Authoring					
		authored ⁺			Countries ⁺⁺				
	Number	Number	Percent	1 st	2 nd	3 rd			
USA	4759	1242	26.1%	China 199 (4.2%)	UK 194 (4.1%)	Canada 140 (2.9%)			
UK	1290	559	43.3%	USA 194 (15.0%)	Germany 77 (6.0%)	France 55 (4.3%)			
China	1043	354	33.9%	USA 199 (19.1%)	UK 43 (4.1%)	Japan 29 (2.8%)			
Germany	1016	470	46.3%	USA 121 (11.9%)	UK 77 (7.6%)	Switzerland 58 (5.7%)			

 Table 3. International Co-authoring, Top Four Synthetic Biology Publishing Countries, 2000-2018*

Source: Analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369. *Part Year. *Non-duplicated. **Co-authorships are for named country.⁸ (Authors from multiple countries may contribute to some of these publications; hence totaling international co-authorships for each country with a subject country will exceed the total of subject country non-duplicated co-authorships).

A global mapping, for the top 15 countries by synthetic biology publications, demonstrates the dominant role of the US in synthetic biology international co-authorship linkages (Figure 3). The US leads as a synthetic biology co-authorship partner for the other top countries. The UK, China and Germany also serve as next tier hubs in international synthetic biology co-authorships. In addition to the dominant US network, there is also a European network (including the UK, Germany, France, Switzerland, Spain and Italy) and a Chinese network (involving the UK, US, Japan, Germany, and Australia among other countries).

⁸ Authors from multiple countries may contribute to some of the publications co-authored with a named subject country. Hence totaling international co-authorships for each country with a subject country will exceed the total of subject country non-duplicated co-authorships.

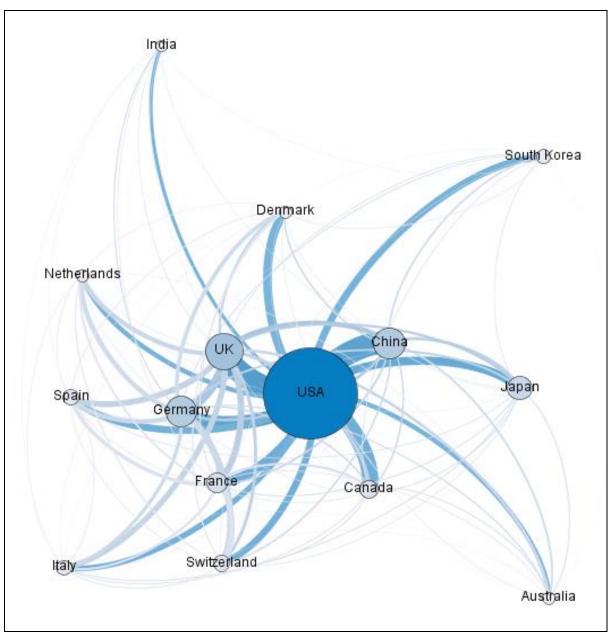


Figure 3. Synthetic Biology Co-Authorship Map, Top 15 Countries, 2000-2018*

Source: Analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369. *Part Year. Top 15 countries, co-author network; circles are proportional to number of publications for respective country, edge size is proportional to the number of publications co-authored by researchers in those two countries.

UK Co-Authoring in Synthetic Biology

Mapping co-authorship linkages of synthetic biology publications demonstrates the hub roles of the four leading locations by publication counts: Imperial College, the University of Edinburgh, the University of Oxford, and the University of Manchester. The University of Cambridge, Bristol University, the University of Warwick, and University College London also are among those with noticeable hub roles. (Figure 4.)

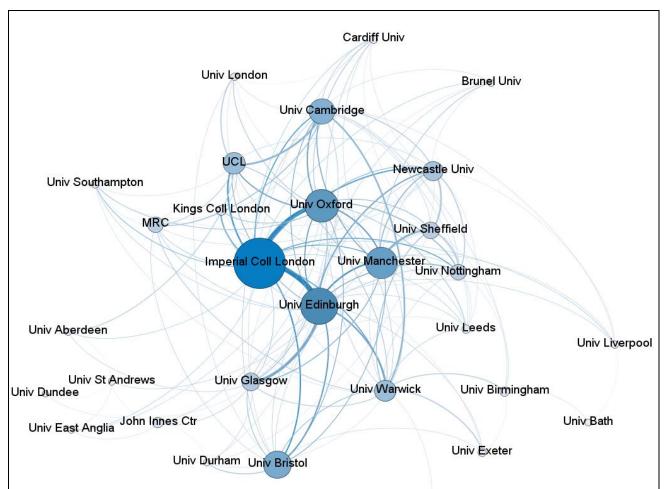


Figure 4. Synthetic Biology Publications, UK Co-Authorship Linkages

Source: Analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=1290. Top UK 30 organizations (by publication counts). Only co-authorship links among the UK organizations shown (i.e. other UK and international co-authorship links not shown). Circles are proportional to number of publications for respective organization; edge size is proportional to the number of publications co-authored by researchers in those two linked organizations.

Leading Subject Categories Addressed by Synthetic Biology

The Web of Science allocates every journal, book or other publication that it records to at least one subject category. Currently, there are more than 250 WoS subject categories.⁹ These subject categories broadly relate to disciplines, although there are also some general and interdisciplinary categories. Synthetic biology is a crosscutting domain that covers multiple disciplines of science and technology and, indeed, seeks to engage and recombine key disciplines such as biology and biotechnology, engineering, and computing. Overall, our analysis indicates that synthetic biology publications encompass 188 or about three-quarters of WoS subject categories (Table 4).

	<u> </u>	USA	UK	China	Germany	Worldwide
1	Biochemistry & Molecular Biology	22.2%	19.1%	14.3%	21.8%	20.7%
2	Biotechnology & Applied Microbiology	17.2%	13.6%	32.1%	21.4%	20.2%
3	Biochemical Research Methods	17.8%	16.0%	12.9%	14.5%	15.5%
4	Multidisciplinary Sciences	12.8%	14.7%	11.4%	10.9%	11.2%
5	Chemistry, Multidisciplinary	8.1%	8.5%	8.0%	8.9%	7.8%
6	Cell Biology	5.8%	4.0%	3.2%	5.6%	4.8%
7	Microbiology	4.0%	5.5%	5.2%	5.4%	4.8%
8	Biophysics	3.9%	3.3%	4.1%	5.0%	4.4%
9	Genetics & Heredity	4.2%	2.6%	2.5%	2.8%	3.7%
10	Mathematical & Computational Biology	3.0%	4.7%	3.0%	3.9%	3.6%
11	Plant Sciences	2.3%	3.2%	3.9%	4.5%	2.8%
12	Nanoscience & Nanotechnology	2.3%	2.6%	4.0%	2.1%	2.6%
13	Medicine, Research & Experimental	2.7%	1.9%	1.6%	1.6%	2.6%
14	Chemistry, Physical	2.2%	2.8%	2.4%	3.2%	2.3%
15	Engineering, Electrical & Electronic	2.2%	3.0%	1.3%	0.4%	2.3%
16	Biology	2.0%	2.9%	2.3%	2.2%	2.3%
17	Materials Science, Multidisciplinary	2.2%	2.3%	2.5%	2.8%	2.1%
18	Chemistry, Analytical	1.6%	1.6%	3.5%	1.1%	2.0%
19	Chemistry, Medicinal	1.8%	1.2%	1.2%	2.3%	1.9%
20	Pharmacology & Pharmacy	1.3%	1.2%	0.9%	1.9%	1.8%
21	Engineering, Chemical	1.4%	0.5%	2.4%	0.8%	1.6%
22	Immunology	1.6%	0.9%	0.9%	2.1%	1.6%
23	Computer Science, Interdisciplinary Applications	1.0%	2.0%	1.3%	1.1%	1.5%
23 24	Computer Science, Theory & Methods	0.9%	2.4%	1.0%	1.7%	1.5%
24	Chemistry, Organic	1.2%	1.2%	1.0%	2.0%	1.5%
26	Engineering, Biomedical	1.6%	1.6%	1.0%	0.6%	1.5%
	Computer Science, Artificial					
27	Intelligence	0.7%	2.2%	1.1%	1.3%	1.3%
28	Physics, Applied	0.9%	1.2%	1.1%	1.5%	1.2%
29	Automation & Control Systems	1.1%	1.8%	0.8%	0.5%	1.0%
30	Materials Science, Biomaterials	0.9%	0.5%	1.3%	0.9%	0.9%

Table 4. Leading Synthetic Biology Subject Categories

Source: Analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369. Shows top 30 (by worldwide publication count) of 188 WoS Subject categories that include synthetic biology publications. A publication can be assigned more than one subject category, so totals of subject categories exceed 100%. *Part Year.

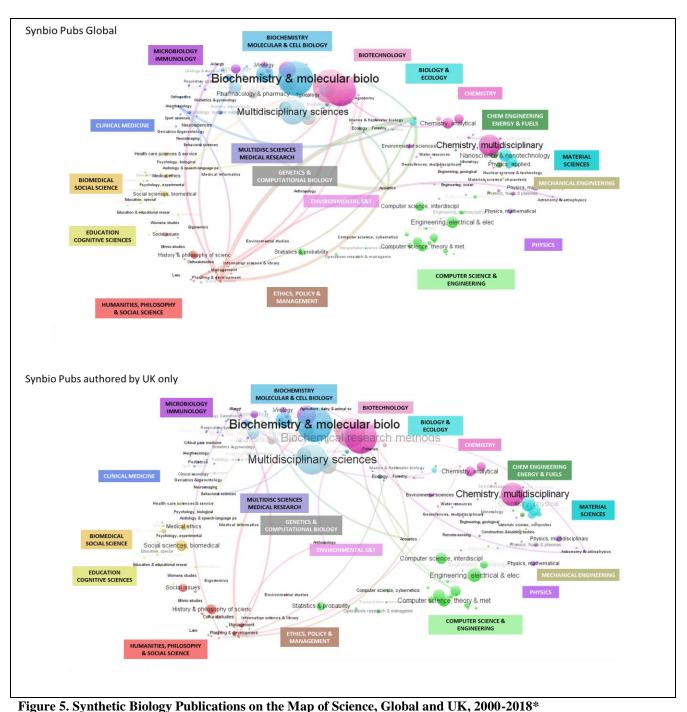
⁹ <u>https://images.webofknowledge.com/images/help/WOS/hp_subject_category_terms_tasca.html</u>

Worldwide, the top three WoS subject categories for synthetic biology publications are Biochemistry and Molecular Biology, Biotechnology & Applied Microbiology, and Biochemical Research Methods. For the first and third categories, UK synthetic biology publication outputs as a percentage of the total are similar to those observed worldwide, although the UK is a bit lower than worldwide level for Biotechnology & Applied Microbiology. Compared with the worldwide levels, China's synthetic biology publication outputs are proportionately higher for Biotechnology & Applied Microbiology but lower in the other two top classifications. Both the US and the UK have above worldwide average levels of synthetic biology publications in the multidisciplinary subject classification. This includes prestigious multidisciplinary journals with exceptionally high impact factors such as *Nature* and *Science*, as well as recognized multidisciplinary journals such as *PloS* One, Proceedings of the National Academy of Sciences (USA), Science Reports (Nature), and Nature *Communications*. Among the next set of subject categories, and again compared with worldwide levels, the UK has a greater relative proportion of its synthetic biology publication outputs in Microbiology, Mathematical & Computational Biology, Plant Sciences, Engineering, Electrical & Electronic, Biology, and Chemistry, Physical, Computer Science, Theory & Methods, Computer Science, Artificial Intelligence, Computer Science, Interdisciplinary Applications, and Automation & Control Systems. The later set is of interest, indicating a relatively higher proportion of UK synthetic biology research activity related to information, data and automation technologies. (Table 4.)

To visualize the subject distributions and interdisciplinary linkages between subjects, we overlay our synthetic biology publication dataset onto a base map of science. ¹⁰ Our dataset covers synthetic biology publications in the WoS from 2000 through to mid-July 2018. While the visualization for all publications worldwide shows a spread of synthetic biology publications across disciplines, there are larger macro clusters in "Biochemistry, Molecular and Cell Biology," "Biotechnology" (including plant sciences), and "Chemistry" (including biochemical research methods and chemistry, multidisciplinary). UK synthetic biology publications on the map of science are broadly comparable, with relatively more prominent clustering in multidisciplinary sciences and relatively greater linkages with computer science and engineering. (Figure 5.)

¹⁰ The base map represents the foundational organization of science, drawing on co-citation patterns for subject categories of WoS journals. See Porter, A. L., & Rafols, I. (2009). Is science becoming more interdisciplinary? Measuring and mapping six research fields over time. *Scientometrics, 81,* 719–745, doi: <u>10.1007/s11192-008-2197-2</u>; and Rafols, I., Porter, A. L., & Leydesdorff, L. (2010). Science overlay maps: A new tool for research policy and library management. *Journal of the Association for Information Science and Technology, 61*(9), 1871–1897, doi: <u>10.1002/asi.21368</u>. As noted in Shapira et al, 2017, "the map visualizes the distance and intensity of co-citations between corresponding subject categories. Each node represents individual WoS subject categories, with colors used to depict subject categories within the same macro-discipline group. The subject categories that are assigned to synthetic biology articles in our publication dataset are matched to the 18 macro-disciplines and displayed on the base map" and "the node size is proportional to the number of articles in that subject category." For the method to construct the 18 macro disciplines, see Carley, S., Porter, A. L., Rafols, I., & Leydesdorff, L. (2017). Visualization of disciplinary profiles: Enhanced science overlay maps. *Journal of Data and Information Science*, *2*(3), 68–111, https://content.sciendo.com/view/journals/jdis/2/3/article-p68.xml. The VOSviewer clustering method and algorithm is used, see: van Eck, N. J., & Waltman, L. (2010). Software survey: VOSviewer, a computer program for bibliometric

mapping. Scientometrics, 84(2), 523-538. doi: 10.1007/s11192-009-0146-3.



Source: Analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369. *Part Year. Map of science method from Carley et al. (2016), using VOSviewer (Van Eck and Waltman 2016), with customization of 2015 WoS 18-category macro-discipline labels for synthetic biology. Shows top 30 (by worldwide publication count) of 188 WoS Subject categories that include synthetic biology publications. A publication can be assigned more than one subject category, so totals of subject categories exceed 100%.

Citations to Synthetic Biology Publications

Using citations to scientific publications as measures of research quality and impact is an imperfect but nonetheless commonly used indicator.¹¹ Bearing in mind the limitations of using citation measures, we do observe significant differences among the top synthetic biology publishing countries in mean citations to papers attributed to one or more authors affiliated with institutions in those countries. Two North American countries – Canada and the US – both average more than 30 citations per publication in synthetic biology (noting that the US produces 10 times more publications than Canada). Switzerland averages almost 24 citations per publication, with Germany, the UK, and Netherlands each averaging around 20 citations per publication. Although third-ranked by publication count, China has the lowest mean citation rate among the top 15 synthetic biology countries. (Figure 6.)

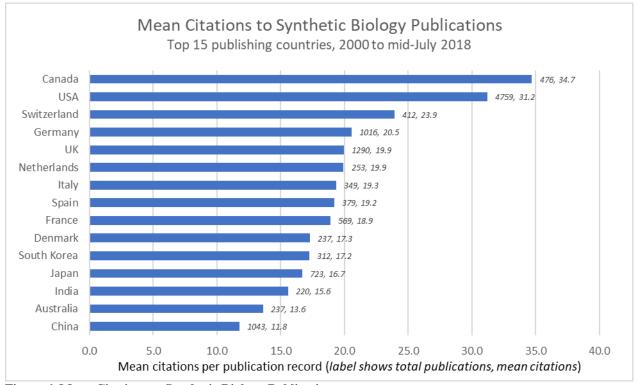


Figure 6. Mean Citations to Synthetic Biology Publications

Source: Analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369.

Funding Sponsorship

The top 15 funding organizations, by publication counts, in synthetic biology account for about 42% of all records in the synthetic biology publications data set.¹² Among these top 15 funding organizations, six are in North America (with five in the US), five are in Europe (including two in the UK), and four are located in Asia (with two in China and Japan respectively). (Figure 7.) A publication may acknowledge funding from more than one sponsor, with some papers sponsored by funders in different countries. The highest mean citations per publication are garnered by publications that acknowledge funding from the US Office of Naval Research, followed by the US

¹¹ On problems associated with using citation analyses, see, for example, MacRoberts, M. H. and MacRoberts, B. R. (1989), Problems of citation analysis: A critical review. *Journal of the American Society for Information Science*, 40: 342-349. doi:10.1002/(SICI)1097-4571(198909)40:5<342::AID-ASI7>3.0.CO;2-U.

¹² 67% of synthetic biology publication records report funding acknowledgments information.

	Funding Agency	Rec	ords	Citations	Mean	Cites
1	US National Institutes of Health (NIH)		1550	61103		<u>39.</u> 4
2	US National Science Foundation (NSF)		1120	31979		28.6
3	China National Natural Science Foundation (NNSFC)		575	6379		11.1
4	European Union		443	11396		25.7
5	UK Biotechnology and Biological Sciences Research Council		369	8375		22.7
6	UK Engineering and Physical Sciences Research Council		314	6321		20.1
7	US Department of Energy (DOE)		282	8522		30.2
8	European Research Council (ERC)		250	4715		18.9
9	Germany Deutsche Forschungsgemeinschaft		235	4905		20.9
10	US Defense Advanced Research Projects Agency		235	8563		36.4
11	China National Basic Research (973) Program		228	3005		13.2
12	US Office of Naval Research		169	7490		44.3
13	Japan Society for the Promotion of Science		158	2095		13.3
14	Canada Natural Sciences and Engineering Research Council (NSERC)		147	2974		20.2
15	Japan Ministry of Education, Culture, Sports, Science and Technology		144	2370		16.5

National Institutes of Health (NIH), the US Defense Advanced Research Projects Agency, the US Department of Energy (DOE), and the US National Science Foundation (NSF).

Figure 7. Citations to Publications sponsored by Top 15 Synthetic Biology Funding Agencies, 2000-2018* Source: Analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369 (of which 67% report funding acknowledgement information). VantagePoint used for list cleaning of funding agency organizational names.

Synthetic Biology Patents

A granted patent provides exclusive rights to an invention and allows the patent owner to prevent others from using the patented invention for a period (typically twenty years). The broad policy objectives of patenting are to incentivize research and development of useful and novel applications by allowing patent owners time to recoup costs and generate revenues and to encourage disclosure to facilitate technological progress. An application for a patent does not mean that the relevant patent examining authority will grant the patent. Additionally, the grant of a patent does not necessarily mean that there will be use, commercialization, or licensing of the invention. In short, patenting is not the same as innovation, as there are multiple other steps and factors involved in the commercialization of new technology. However, from a technological landscape scanning perspective, patent applications do provide useful signals. Patenting activity can indicate interest in the exploitation of a new technology, particularly from a corporate perspective (as corporation are the leading filers of patents in most countries), and can suggest fields of invention that are viewed as promising. Patents can serve as signals for venture financing and can generate markets for inventions, although they can also be deployed in strategic ways to extract economic returns.

It is in the nature of emerging technologies that relevant patents are not always easily defined, especially as standard patent classifications typically lag in being updated and also because patent applicants may use new terminology or deliberately not use specific terminologies. We have developed a method for discerning synthetic biology patents based on identifying a core set of relevant patents and keywords, then extending from this corpus to other relevant patents using a citation-tree algorithm (see section on methods and sources for added details and references). For the priority year period 2003 to August 3, 2018, from 9,263 Derwent Innovations synthetic biology patent records we matched 8,460 PATSTAT basic patent application records (for the original invention in a patent family) to obtain assignee geographical information. There are over 10,600 original patent assignees named in these records, comprised of about 3,600 original assignees standardized by name in PATSTAT. Nearly 16% of the patent records indicate more than one assignee. Some 36% of the assignees are associated with multiple patents, while some assignees are part of larger multinational corporations. The majority of patents are associated with multiple inventors (for patents where inventor names are recorded, just 5% are single inventor patents). In total, our synthetic biology patent records name about 23,000 inventors, of whom 23% are inventors who have filed more than one patent.

As in many patent landscapes searches, we acknowledge that the boundaries of the domain, in this case synthetic biology, are hard to delineate. We have pursued a broad definition of the domain (noting that few patents actually use the exact terminology "synthetic biology"). We recognize that there are inevitably trade-offs in precision and recall. At an aggregated level, however, the search approach is useful for indicating broad patenting trends.

We primarily analyze patent applications. Unless otherwise indicated, the use of the term "patent" in the text denotes a patent application. In addition to the caveats noted above (e.g. patent applications may signal interests in innovation but they are not in themselves innovations), patent applications are usually not disclosed until at least 18 months from being filed, and there are procedures that applicants can use to further extend disclosure. This means that patent application records for the most recent years are not complete.

Growth in Synthetic Biology Patenting

Our analysis indicates upward worldwide growth in synthetic biology patent applications. Synthetic biology publications also have an upward worldwide growth (Figure 8). From 2007 through to 2011, there was a noticeable increase in synthetic biology patent applications. Since 2011, the growth rate of patenting tracks that of publishing, suggesting broadly comparable growth levels of global activity in knowledge exploration and invention exploitation in the synthetic biology domain. (We again note that the apparent drop-off in published patent applications from 2015-2016 to the present should not be taken as a real decline, as it reflects the gap between patent filing and publication. This gap is typically 18 months but can be longer in some circumstances.)

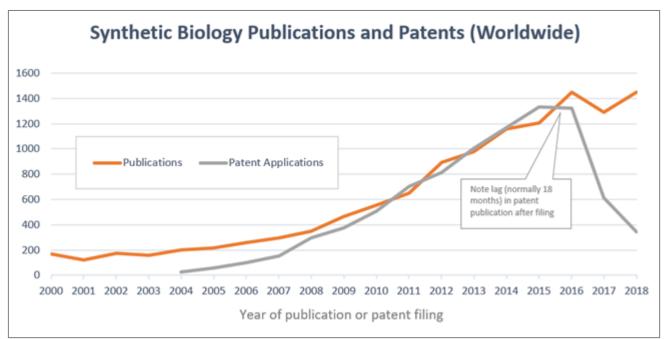
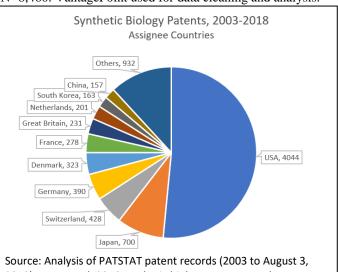


Figure 8. Synthetic Biology Publications and Patents

Source: Publications – analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369. Patents – analysis of PATSTAT patent records (2003 to August 3, 2018), Kwon et al. 2016 synthetic biology patent search strategy, N=8,460. VantagePoint used for data cleaning and analysis.

The United States accounts for more than one-half of all synthetic biology patent applications, by location of the original patent assignee. (Figure 9). Assignees based in Japan account for about 9% of worldwide patents, followed by those located in Switzerland (5.5%, Germany (5%) and other European countries. Great Britain accounts for about 3% of worldwide patents. Our data does not as yet show a high level of Chinese synthetic biology patenting (there may be time lags in capturing applications from China's State Intellectual Property Office).



2018), Kwon et al. 2016 synthetic biology patent search strategy, N=8,460 [7,847 with identified assignee country locations]

Figure 9. Synthetic Biology Patents, By Country

National Patenting Variations

While at an aggregated global scale, the growth of synthetic biology publications has been mirrored by comparable growth in synthetic biology patent applications, there are significant variations among the leading countries. Denmark, Switzerland and Japan have higher rates of synthetic biology patenting relative to their synthetic biology publication authorships. The USA and the Netherlands patent at rates only slighly below their level of publications. Synthetic biology publishing by assignees located in Great Britain is low (.20) relative to the high rate of synthetic biology publishing by UK researchers.

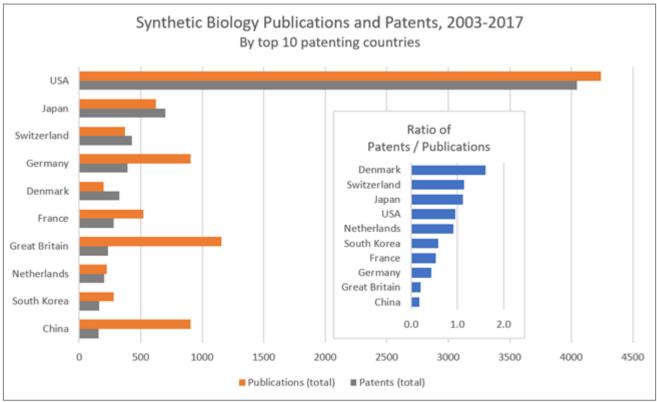


Figure 10. Synthetic Biology Publications and Patents, 2003-2017

Source: Publications – analysis of Web of Science publication records (2000 to mid-July 2018), Shapira et al. 2017 synthetic biology search strategy, N=11,369. Patents – analysis of PATSTAT patent records (2003 to August 3, 2018), Kwon et al. 2016 synthetic biology patent search strategy, N=8,460. VantagePoint used for data cleaning and analysis.

Leading Patent Assignees

Companies are most frequent among the world's leading patent assignees in the synthetic biology domain, with 27 companies present among the top 41 assignees. This top group also contains universities and non-profit research organizations, particularly in the US and to a lesser extent in Japan, France, and Singapore. The US is the leading location for patent assignees, with 26 organizations, followed by Denmark and Japan (each with three) and France and Switzerland (two each). (Figure 11.) The leading British patent assignee is the Glaxo Group / GlaxoSmithKline (76th globally). There are six companies among the top (11) British patent assignees, four universities and one governmental non-profit research organization. (Figure 12). When reviewing these results, keep in mind our previous caveats about limitations and trade-offs in precision and recall in identifying synthetic biology patents.

Assignee	Assignee Type	Country	Patents	Assignee	Assignee Type	Country	Patents
1 NOVOZYMES AS	COMPANY	DK	275	21 MONSANTO TECHNOLOGY LLC	COMPANY	US	51
2 HOFFMANN LA ROCHE	COMPANY	СН	133	22 UNIV PENNSYLVANIA	UNIVERSITY	US	47
3 CELLECTIS	COMPANY	FR	108	23 UNIV TEXAS	UNIVERSITY	US	46
4 GENENTECH INC	COMPANY	US	108	24 GEN HOSPITAL CORP	UNIVERSITY	US	45
5 UNIV KYOTO	UNIVERSITY	JP	105	25 CENTRE NAT RECH SCIENT	GOV NON-PROFIT	FR	44
6 NOVARTIS AG	COMPANY	СН	104	26 DU PONT	COMPANY	US	43
7 MASSACHUSETTS INST TECHNOLOGY	UNIVERSITY	US	103	27 MDRNA INC	COMPANY	US	42
8 DANISCO US INC	COMPANY	US	98	28 MERCK SHARP & DOHME	COMPANY	DK	39
9 DOW AGROSCIENCES LLC	COMPANY	US	91	=29 UNIV LELAND STANFORD JUNIOR	UNIVERSITY	US	38
10 HARVARD COLLEGE	UNIVERSITY	US	88	=29 UNIV OHIO STATE RES FOUND	UNIVERSITY	US	38
11 UNIV CALIFORNIA	UNIVERSITY	US	87	=29 UNIV TOKYO	UNIVERSITY	US	38
12 REGENERON PHARMA	COMPANY	US	85	=32 BIOGEN IDEC INC	COMPANY	US	34
=13 ALNYLAM PHARMACEUTICALS INC	COMPANY	US	84	=32 SCRIPPS RESEARCH INST	GOV NON-PROFIT	JP	34
=13 SANGAMO BIOSCIENCES INC	COMPANY	US	84	=34 BAYER CROPSCIENCE NV	COMPANY	BE	32
15 ISIS PHARMACEUTICALS INC	COMPANY	US	73	=34 DSM IP ASSETS BV	COMPANY	NL	32
16 CHUGAI PHARMACEUTICAL CO LTD	COMPANY	JP	63	36 MODERNA THERAPEUTICS INC	COMPANY	US	31
17 PIONEER HI BRED INT	COMPANY	US	60	37 SANTARIS PHARMA AS	COMPANY	DK	30
=18 AMGEN INC	COMPANY	US	58	=38 AGENCY SCIENCE TECH & RES	GOV NON-PROFIT	SG	28
=18 BROAD INST INC	GOV NON-PROFIT	US	58	=38 CUREVAC GMBH	COMPANY	DE	28
20 GENOMATICA INC	COMPANY	US	53	=38 EVOGENE LTD	COMPANY	IL	28
				=38 JANSSEN BIOTECH INC	COMPANY	US	28

Figure 11. Top Patent Assignees in the Synthetic Biology Domain, Worldwide

Analysis of PATSTAT patent records (2003 to August 3, 2018), Kwon et al. 2016 synthetic biology patent search strategy, N=8,460 [7,847 with identified assignee country locations]

Assignee	Assignee Type	Country	Patents
1 GLAXO GROUP LTD	COMPANY	GB	20
2 UCL BUSINESS PLC	UNIVERSITY	GB	19
3 KYMAB LTD	COMPANY	GB	18
4 OXFORD NANOPORE TECH LTD	COMPANY	GB	18
5 MEDIMMUNE	COMPANY	GB	10
6 ISIS INNOVATION	UNIVERSITY	GB	7
=7 MEDICAL RES COUNCIL	GOV NON-PROFIT	GB	5
=7 OXITEC LTD	COMPANY	GB	5
=7 UNIV EDINBURGH	UNIVERSITY	GB	5
=10 CAMBRIDGE ENTPR LTD	UNIVERSITY	GB	4
=10 FUJIFILM DIOSYNTH BIOTECHNOLOGIES UK	COMPANY	GB	4

Figure 12. Top Patent Assignees in the Synthetic Biology Domain, Great Britain

Analysis of PATSTAT patent records (2003 to August 3, 2018), Kwon et al. 2016 synthetic biology patent search strategy, N=8,460 [7,847 with identified assignee country locations]

Synthetic Biology Patenting Visualized on the Map of Patents

Synthetic biology patenting covers a broad range of technological and application areas. Just over 100 International Patent Classification (IPC) subclasses (or about 16% of all IPC subclasses) are represented in our synthetic biology patent data set, with the largest patent subclasses including mutation or genetic engineering (C12N), measuring or testing processes involving enzymes, nucleic acids or microorganisms (C12Q), and medicinal preparations containing genetic material (A61K). An individual patent may be classed under multiple IPCs. To visualize the distribution of synthetic biology patents, we have mapped the worldwide synthetic biology patent set onto a base map of patents, organized into 35 major technological groups (Figure 13). This highlights major clusters in areas of biotechnology, drugs, instrumentation, pesticides, and catalysts, with smaller groups in food, detergents, information technology, and filtration and fibers. A mapping of patents with assignees located in Great Britain is shown, on the same base map of patents, is also shown (Figure 14).

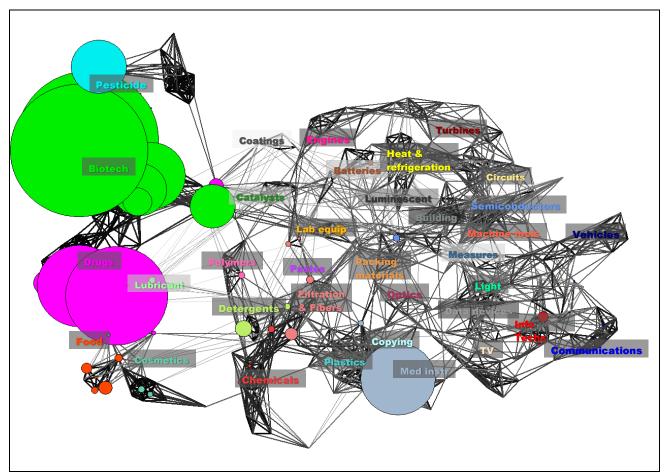


Figure 13. Synthetic Biology Patents on Map of Patents, Worldwide, 2003-2018

Source: Analysis of PATSTAT patent records (2003 to August 3, 2018), Kwon et al. 2016 synthetic biology patent search strategy, N=8,460. Overlaid on visual map of patents comprising 466 technological classifications and 35 technological groups (see Kay et al. 2014).¹³ PATSTAT IPC classifications. The size of nodes is proportional to the number of patent applications in the corresponding technology group. On the base map, lines represent relationships between technological categories (the darker the line, the shorter the technological distance between categories).

¹³ Kay, L., Newman, N., Youtie, J., Porter, A. L. and Rafols, I. (2014), Patent Overlay Mapping: Visualizing Technological Distance. *J Assn Inf Sci Tec*, 65: 2432-2443. doi:<u>10.1002/asi.23146</u>

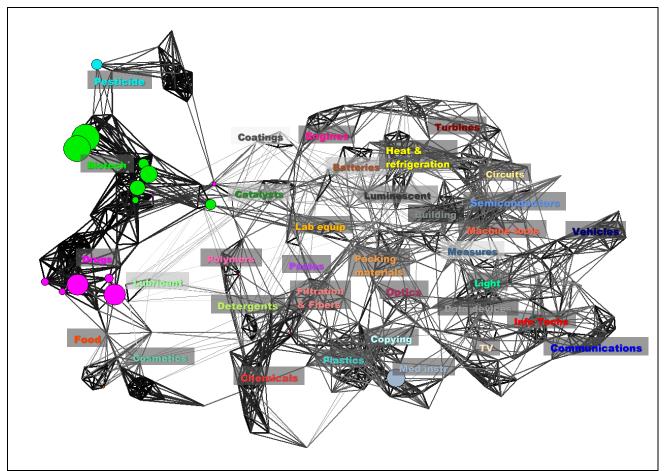


Figure 14. Synthetic Biology Patents on Map of Patents, Great Britain, 2003-2018

Source: Analysis of PATSTAT patent records (2003 to August 3, 2018), Kwon et al. 2016 synthetic biology patent search strategy, N=231 (assignees in Great Britain). Overlaid on visual map of patents comprising 466 technological classifications and 35 technological groups (see Kay et al. 2014). PATSTAT IPC classifications. The size of nodes is proportional to the number of patent applications in the corresponding technology group. On the base map, lines represent relationships between technological categories (the darker the line, the shorter the technological distance between categories).

Appendix

This appendix compares publication counts returned using the Shapira et al 2017 "expanded" search with a simple topic search for "synthetic biology." A topic search captures the use of a term in the title, abstract, or key words or a publication. While broadly these searches track one another in terms of growth rates, the expanded search captures publications in the domain even where the topic term "synthetic biology" is not used. A third search for the use of "engineering biology" as a topic returns relatively few publications.

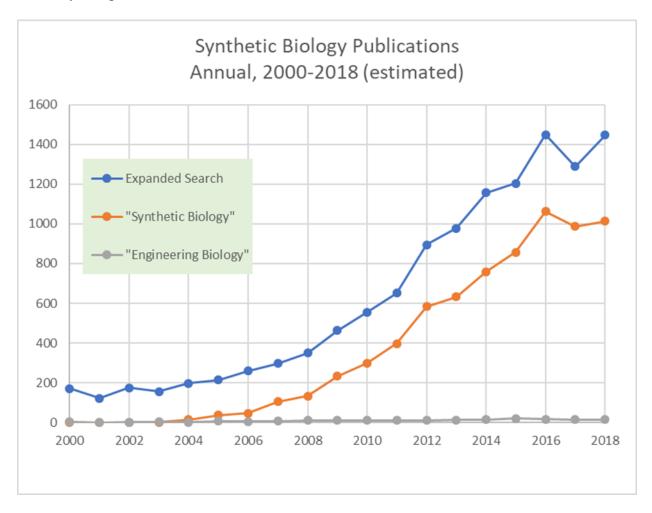


Figure A1. Worldwide Synthetic Biology Publications

Source: Analysis of Web of Science (WoS) publication records. Expanded search from Shapira et al. 2017 synthetic biology search strategy, 2000 to mid-July 2018, N=11,369. WoS topic searches (title, abstract, or key words containing exact term), 2000 to mid-October 2018 for "Synthetic Biology" N= 7,000, and "Engineering Biology" N=173. Annualized totals for 2018 estimated from part-year 2018 publication trends. The WoS databases searched comprised SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH, and A&HCI (document type: all).

Added statistics	Publication counts (actual), 2000-2018*
	(*see dates in source notes)
Expanded search	11,369
"Synthetic Biology"	7,000
"Engineering Biology"	173
"Synthetic Biology" OR "Engineering Biology"	7,142
"Synthetic Biology" AND "Engineering Biology"	31

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