# **Development of Phage Display Technology: A Bibliometric Assessment**

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Corresponding Author: Vadim Gureyev Vector State Research Center of Virology and Biotechnology, Koltsovo, Novosibirsk Region, Russia, 630559, Russia Email: GureyevVN@ipgg.sbras.ru Abstract: The paper presents results of bibliometric analysis of papers on phage display technology written in the past 30 years. More than 2000 Scopus-indexed papers have been published in 638 journals. 73.95% papers were published by 10 most productive countries out of 58: The USA, China, Great Britain, Germany, Japan, the Netherlands, Switzerland, Italy, France and Australia. Rapid growth in scholarly output began in 1993, i.e., 8 years after discovery of phage display in 1985 and up to 2000 was equal to 26.85% per year. Later, the number of papers stabilized. In some countries, number of studies is decreasing: The USA, Great Britain, the Netherlands, Switzerland, Italy and Australia; the other countries show increase in the number of annually published papers: Germany, Japan, France and China. Average number of citations per paper in 3-year citation window is 5.09. Swiss papers are the most cited: 9.09 citations per paper, whereas Chinese papers are lowly cited ranking 2nd: 2.51 citations per paper. Results of studies on phage display are published in 11 languages with two leading ones: English (92.19%) and Chinese (6.29%). Biochemistry, genetics and molecular biology subject area uses phage display technology more intensively (61.04% papers), followed by immunology and microbiology (31.06%) and medicine (24.09%). The core of serials published the majority of papers on phage display began to lose strong borders. Only PLoS One shows obvious growth in the number of papers describing phage display studies.

**Keywords:** Phage Display, Peptide Library, Bibliometric Analysis, Citation Analysis, Scopus

## Introduction

In 2015 phage display technology celebrated its 30year anniversary. In conditions of rapid changes and emergence of new achievements in biotechnology, this term seems to be sufficient to conduct retrospective analysis of phage display in order to make some conclusions and to detect further possible trends. To date, several dozens of reviews have been published showing different aspect in the use of the technique. However, there have not been any bibliometric studies on the subject. We believe, such a study can also be useful in evaluating phage display efficiency in prior years and its future applications.

The first mention of phage display is traditionally referred to the paper of J.P. Smith, for the time a

researcher of Biological Department of the Missouri phage: University: "Filamentous fusion Novel expression vectors that display cloned antigens on the virion surface" published in 1985 in Science (Smith, 1985). The second paper came from Vector State Research Center of Virology and Biotechnology (Novosibirsk, Russia) in Doklady Akademii nauk USSR in 1989 and demonstrated possibility to expose foreign peptides on the surface of filamentous bacteriophage M13 using the main coat protein (Il'ichev et al., 1989). In 1985, J.P. Smith for the first time showed that polypeptides can be exposed on the surface of phage capsids. It should be noted, that in the case of correct selection of site of insertion chimeric phage particle continues to be infectious and can be reproduced in appropriate bacterial strain. Furthermore, it was



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demonstrated that phage carrying certain peptide, can be isolated from a number of phages of wild type using affine selection or biopanning (Parmley and Smith, 1988). Rotation of selection and reproduction causes formation of phage mix comprising big amount of phage particles exposing the same peptide. Application of this principle resulted in construction of large collections of chimeric phages where each phage exposed peptide that differed from other peptides, i.e., peptide phage libraries (Cwirla et al., 1990; Devlin et al., 1990; Felici et al., 1991; Scott and Smith, 1990). In theory, such peptide repertoire can serve as a source of ligands for all receptors. After isolation of phage carrying necessary ligand amino acid sequence of selected peptides is defined by sequencing of chimeric capsid genes. Comparative analysis of amino acid compound of selected peptides enables to identify consensus sequence, i.e., conservative amino acid residues necessary for binding of this receptor.

Using phage display technique specific ligands were detected for antibodies, enzymes, proteins for transmission of cell signals, surface cell receptors and non-protein molecules (carbohydrates, polymers or other surface materials, as well as DNA) (Smith and Petrenko, 1997). Affordability of experiments and availability of affine selection technique enabled phage display to become significant tool in molecular biology, especially in the field of protein engineering and functional genomics.

Objectives of this paper are the following:

- To analyze phage display papers at the level of publication types, languages, countries of studies, subject areas and journals
- To reveal rate of citations and their distribution according to countries and subject areas
- To detect the most frequent keywords in phage display publications to precise themes of studies using phage display technology
- To reveal trends in phage display technology development globally and in certain countries using the data concerning research output, citation impact and their ratios

Detailed data are shown for 10 most productive countries studying phage display and using the technology.

## **Materials and Methods**

To carry out bibliometric analysis international multidisciplinary database Scopus was used (Scopus, 2015). Query "phage display" was conducted in Document search tab using Article Title field. Analyzed period includes papers published from 1985 (year of the 1st article) to 2013. Papers of 2014 were excluded due to

incomplete data in Scopus by the time this work was being carried out.

We did not refine search results using any subject areas or document type restrictions; thus, all Scopus databases and all types of papers were considered. To study subject distribution of papers over disciplines Scopus Subject Areas were used. When addressing citation count, 3-year citation window was considered: The year of publication and two following years. This paper methodology was partially based on approaches offered by (Gupta *et al.*, 2015).

# **Results and Discussion**

## Phage Display Research Output

From 1985 to 2013, researchers published 2194 Scopus-indexed papers directly devoted to phage display technology. Figure 1 demonstrates distribution of scholarly output across a date of publishing.

Figure 1 shows almost 10-year timeout between the 1st paper in Science describing new technology and the beginning of rapid growth in the number of research papers. Interestingly, this paper was unnoticed for the initial few years. Having been cited almost 2000 times by 2015, Smith's article was firstly cited only 3 years after its publishing.

It should be noted that phage display technology was developed concurrently in the USA and in Russia at Vector State Research Center of Virology and Biotechnology. Later publishing date (1989) of the Russian paper (Il'ichev *et al.*, 1989) can be explained by blackout of Vector's studies. From the late 1980s onwards researchers have published 24 papers on phage display technology affiliated with SCR VB Vector. Total number of papers published by Vector's researchers exceeds 100; a lot of them are affiliated with foreign organizations due to emigration of Russian scientists in the early 1990s. This list includes highly cited papers with some papers published in co-authorship with founder of technology J.P. Smith.

Significant increase in phage display scholarly output began in 1993 when Elsevier's Gene published the issue devoted to the new technology. The journal covered proceedings of the conference held in Cold Spring Harbor, USA, by J.P. Smith. After that, the term "phage display" came into scientific use, although its first mention date from the early 1980s. From 1993 to 2000, high steady growth in the number of papers on numerous aspects of phage display was observed. Annual average growth in the number of publications in that 7-year period achieved 27%. Since 2000s, the technology has firmly established itself in a number of biomedicine areas and steadily used by researchers worldwide according to low equal fluctuations in the number of papers.

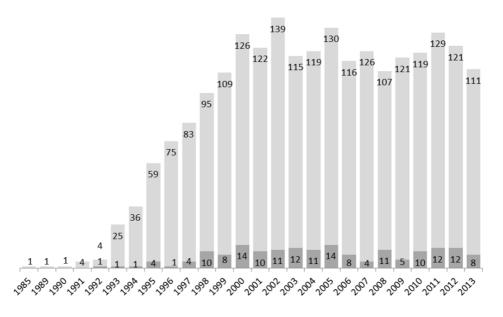


Fig. 1. Distribution of papers across the years. Top numbers mean absolute number of papers (light gray) while bottom numbers point at the number of reviews (dark gray)

### Types of Publications

Distribution of document types in analyzed period was the following: 1869 (85.26%) articles, 172 (7.84%) reviews, 82 (3.74%) conference papers, 22 (1%) erratums and 22 (1%) short surveys. Interestingly, this distribution lacks book chapters, letters, notes, editorials, or business articles. Reviews ranked the 2nd next to articles; Fig. 1 shows incomplete correspondence in the number of reviews and articles that possibly points to insufficient amount of reviews.

#### Distribution of Languages of Research Papers

Studies on phage display were published in 11 languages:

- English-2021 papers (92.19%)
- Chinese-138 papers (6.29%)
- Russian-11 papers (0.50%)
- Japanese-11 papers (0.50%)
- French-5 papers (0.22%)
- Korean-3 papers (0.13%)
- Portuguese-2 papers (0.09%)
- Finnish, German and Polish-each published one paper (0.04%)

It should be noted that list of the most usable languages is inconsistent with distribution of papers across countries. For instance, only one paper was published in German, although total number of papers written by German researchers is 165. There were no papers in Italian; however, Italy is in the top 10 countries according to the number of papers on phage display. At the same time Russian ranks third according to paper count and the majority of papers from Russia is written in Russian; however, the Russian Federation is absent in the top list of countries. This phenomenon can be explained by the fact that many scientists from Vector State Research Center of Virology and Biotechnology emigrated in the early 1990s into European countries and the USA. In these countries, Russian researchers began to indicate their new affiliations in their paper on phage display causing increase in bibliometric indexes in new organizations.

When analyzing language distribution, it is necessary to consider language bias in international bibliometric databases and their focus on English that was described in a number of studies (Archambault et al., 2005; Leydesdorff and Milojević, 2014). For instance, query "phage display" in the Russian Science Citation Index (RSCI, 2015) in analyzed period delivers 148 papers, although Scopus indexes only 16 Russian papers. Such great difference is explained not only by small number of Russian journals indexed in Scopus (332 items in 2014 (LRJIS, 2014)), but also by the fact that several Russian journals with translated English version de jure belong to other countries gaining author rights. Thus, a part of Russian papers belongs to other countries. Such inconsistencies cannot significantly affect statistical data in countries with big number of papers, but they can influence in case of countries with small number of publications. Of note, in the last few years Scopus covers more than 55% of all published Russian papers (Gureyev and Mazov, 2013). At the same time, archival part of papers is weakly covered.

## Citation Count

Total number of citations of 2194 papers using 3-year citation windows is 11,176. Table 1 shows distribution of citations across the years, as well as average number of citations per paper in a certain year.

Citation count lacks of significant leaps or dramatic fluctuations across years. The highest values of citations per paper were observed in the initial years of development of phage display technology, i.e., 1991, 1994 and 1996. Significant share in high values of citation count in those years accrues to a smaller part of the highly cited papers in some cases with 1000 or more citations. As a rule, they are reviews or papers in multidisciplinary journals with high impact factors. For example, in 1991 two of four papers were published in Nature and Nature Biotechnology; in 1994 only one paper in Annual Review of Immunology gained 22% citations; in 1996 the most cited papers were published Nature, Science, Nature Biotechnology and in Proceedings of the National Academy of Sciences of the United States of America.

At the bottom of Table 1 distribution of publications and citations across the three 7-years periods is shown, starting from 1993 when consistent increase in paper count began. Presented data enable to conclude that during the 1st period phage display was theoretically explained and methodological basis of its application was developed. Peak of practical application was observed in the early 2000s. After that, phage display technology can be considered as a common tool in biotechnology, since in certain periods a slight decrease in paper count was registered and citedness of papers declined. There has been lack of breakthrough discoveries in this technology, according to slowing down the rate of citedness since 2000s.

The total number of citations of 2194 papers in 2015 is 50,645. One paper is cited at average 23.10 times. Furthermore, near 20% all citations accrues to only 19 highly cited papers published in 1990s in multidisciplinary journals with high impact factors. Detailed distribution of citations is shown in Table 2.

Table 2 demonstrates that papers on phage display are highly cited, since there is lack of uncited papers and there are many papers with more than 50 citations.

## Distribution of Scholarly Output over Subject Areas

Table 3 shows data concerning the most frequent keywords in papers on phage display.

Analysis of Table 3 data enables to detect some trends in development of phage display technology. Bibliometric indicators show growing interest to peptide libraries and to the use of animals in the experiments with application of phage display technology. Significant increase in number of papers devoted to design of medicinal drugs based on phage display and studies on protein binding is shown.

The top seven subject areas (more than 100 papers per each area) according to Scopus classification system are shown in Table 4-6.

Table 4-6 demonstrate 30-year changes taking place from the discovery of phage display technique: In recent years, this technology actively used in Medicine, Chemistry and Pharmaceutics, i.e., applied significance can be observed. In contrast, in basic sciences, e.g., Immunology or Microbiology, publication and citation counts are constantly decreasing due to completion of theoretical feasibility demonstration of this technology. In the last period, ranks of groups of papers have been changed depending on subject areas: Medicine has ranked second according to publication count and Chemical Engineering has outranked Agricultural and Biological Sciences. Average citations per paper is increasing Pharmacology, Toxicology in and Pharmaceutics, Agricultural and Biological Sciences, as well as in Chemical Engineering. As for medicine papers, average citations per paper is decreasing despite significant growth in publication count.

Table 1. Distribution of citations in 3-year citation window across the years; average number of citations per paper

			Citations				Citations
Year	Papers	Citations	per paper	Year	Papers	Citations	per paper
1985	1	0	0	2003	115	531	4.61
1989	1	1	0.33	2004	119	545	4.57
1990	1	1	0.33	2005	130	599	4.60
1991	4	73	18.25	2006	116	543	4.68
1992	4	14	3.50	2007	126	558	4.42
1993	25	141	5.64	2008	107	463	4.32
1994	36	364	10.11	2009	121	404	3.33
1995	59	464	7.86	2010	119	616	5.17
1996	75	619	8.25	2011	129	590	4.57
1997	83	414	4.98	2012	121	524	4.33
1998	95	597	6.28	2013	111	265	2.38
1999	109	762	6.99	1993-1999	482	3361	6.97
2000	126	761	6.03	2000-2006	867	4308	4.96
2001	122	558	4.57	2007-2013	834	3420	4.10
2002	139	771	5.54	1985-2013	2192	11176	5.09

Table 2. Distribution of citations. Numbers in parentheses point at a share of papers and citations	Table 2 Distribution of sitetions Noushans in	mananthanan maint at a shana af	a a mana a mala aikaki a ma
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Distribution of citations	Cited papers	Total number of citations (1985–2015)
0	297 (13.55%)	0
1–10	865 (39.46%)	4040 (7.98%)
11-20	393 (17.93%)	5783 (11.42%)
21-30	213 (9.72%)	5321 (10.51%)
31-40	134 (6.11%)	4621 (9.12%)
41-50	68 (3.10%)	3076 (6.07%)
51-100	143 (6.52%)	10143 (20.03%)
101-200	61 (2.78%)	8258 (16.31%)
201-1815	18 (0.82%)	9403 (18.57%)
Total:	2192 (100%)	50645 (100%)

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Table 3. The most frequent keywords in	papers on phage display	V Share of naners with cor	responding keyword is sho	um in narenthecec
1 able 5. The most neguent keywords in	papers on phage display	. Share of papers with con	responding Reyword is sho	with in parenuleses

	Number of papers with certain keywords					
Keyword	All years	1993–1999	2000–2006	2007–2013		
Peptide library ↑	1426	150 (31.1%)	671 (77.4%)	604 (72.4%)		
Human	1110	249 (51.7%)	458 (52.8%)	400 (48.0%)		
Nonhuman ↑	1016	205 (42.5%)	402 (46.4%)	404 (48.4%)		
Amino acid sequence ↓	962	246 (51.0%)	393 (45.3%)	318 (38.1%)		
Bacteriophage ↓	903	314 (65.1%)	317 (36.6%)	259 (31.1%)		
Animals ↑	761	146 (30.3%)	307 (35.4%)	306 (36.7%)		
Controlled study ↑	719	85 (17.6%)	309 (35.6%)	325 (39.0%)		
Molecular sequence data ↓	707	235 (48.8%)	269 (31.0%)	198 (23.7%)		
ELISA	611	123 (25.5%)	256 (29.5%)	232 (27.8%)		
Peptide ↑	581	79 (16.4%)	235 (27.1%)	266 (31.9%)		
Molecular cloning ↓	523	153 (31.7%)	217 (25.0%)	125 (15.0%)		
Protein binding ↑	491	68 (14.1%)	201 (23.2%)	222 (26.6%)		
Unclassified drug ↑	488	30 (6.2%)	193 (22.3%)	264 (31.7%)		
Mice ↑	450	89 (18.5%)	171 (19.7%)	188 (22.5%)		
Monoclonal antibodies ↓	443	129 (26.8%)	185 (21.3%)	128 (15.3%)		
Base sequence ↓	308	148 (30.7%)	110 (12.7%)	45 (5.4%)		
Gene library ↓	299	136 (28.2%)	89 (10.3%)	72 (8.6%)		

Table 4. Distribution of papers across the subject areas

	Distribution of papers in three periods				
Subject area	all years	1993–1999	2000–2006	2007–2013	
Biochemistry, Genetics and Molecular Biology↓	1338 (61.04%)	309 (64.11%)	515 (59.40%)	508 (60.91%)	
Immunology and Microbiology ↓	681 (31.06%)	180 (37.34%)	277 (31.95%)	222 (26.62%)	
Medicine ↑	528 (24.09%)	70 (14.52%)	192 (22.15%)	266 (31.89%)	
Chemistry ↑	233 (10.63%)	22 (4.56%)	90 (10.38%)	121 (14.51%)	
Pharmacology, Toxicology and Pharmaceutics	198 (9.03%)	14 (2.90%)	82 (9.46%)	99 (11.87%)	
Agricultural and Biological Sciences↑	131 (5.98%)	22 (4.56%)	34 (3.92%)	75 (8.99%)	
Chemical Engineering↑	121 (5.52%)	12 (2.49%)	29 (3.34%)	80 (9.59%)	
Total	2192 (100%)	482 (100%)	867 (100%)	834 (100%)	

Table 5. Distribution of citation across the subject areas (3-year citation window)
Distribution of citations in three periods

	Distribution of citations in three periods					
Subject area	All years	1993–1999	2000–2006	2007–2013		
Biochemistry, Genetics and Molecular Biology ↑	7097 (63.50%)	2030 (60.40%)	2722 (63.18%)	2292 (67.02%)		
Immunology and Microbiology ↓	3491 (31.24%)	1319 (39.24%)	1394 (32.36%)	763 (22.31%)		
Medicine ↑	2209 (19.77%)	376 (11.19%)	852 (19.78%)	981 (28.68%)		
Chemistry ↑	1206 (10.79%)	132 (3.93%)	457 (10.61%)	617 (18.04%)		
Pharmacology, Toxicology and Pharmaceutics ↑	989 (8.85%)	58 (1.73%)	404 (9.38%)	527 (15.41%)		
Agricultural and Biological Sciences ↑	362 (3.24%)	39 (1.16%)	94 (2.18%)	229 (6.70%)		
Chemical Engineering ↑	619 (5.54%)	34 (1.01%)	169 (3.92%)	416 (12.16%)		
Total	11176	3361	4308	3420		

	Distribution	of citations in th	nree periods		
Subject area	All years	1993–1999	2000–2006	2007–2013	Uncited papers All years
Biochemistry, Genetics and Molecular Biology ↓	5.30	6.57	4.41	4.51	125 (9.34%)
Immunology and Microbiology ↓	5.13	7.33	5.03	3.44	74 (10.87%)
Medicine ↓	4.18	5.37	4.44	3.69	106 (20.08%)
Chemistry ↓	5.18	6.00	5.07	5.10	19 (8.15%)
Pharmacology, Toxicology and Pharmaceutics ↑	4.99	4.14	4.93	5.32	14 (7.07%)
Agricultural and Biological Sciences ↑	2.76	1.77	2.76	3.05	32 (24.43%)
Chemical Engineering ↑	5.12	2.83	5.83	5.20	11 (9.09%)
Total	5.10	6.97	4.97	4.10	297 (13.55%)

	Table 6. Average number of citations	per paper in different subject areas
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Table 7. Distribution of	papers on phage	display over the countries
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	Paper count			
Country	Total	1993–1999	2000–2006	2007–2013
USA↓	714 (32.57%)	196 (40.66%)	281 (32.41%)	231 (27.70%)
China ↑	273 (12.45%)	13 (2.70%)	91 (10.50%)	169 (20.26%)
United Kingdom ↓	177 (8.07%)	60 (12.45%)	81 (9.34%)	35 (4.20%)
Germany ↑	165 (7.53%)	32 (6.64%)	73 (8.42%)	60 (7.19%)
Japan ↑	125 (5.70%)	21 (4.36%)	47 (5.42%)	57 (6.83%)
Netherlands ↓	99 (4.52%)	29 (6.02%)	50 (5.77%)	20 (2.40%)
Switzerland ↓	82 (3.74%)	28 (5.81%)	41 (4.73%)	13 (1.56%)
Italy↓	77 (3.42%)	30 (6.22%)	27 (3.11%)	19 (2.28%)
France ↑	75 (3.42%)	10 (2.07%)	41 (4.73%)	24 (2.88%)
Australia ↓	69 (3.15%)	17 (3.53%)	29 (3.34%)	23 (2.76%)
Total ↑	2192 (100%)	482	867	834

# Countries Contribution to Scholarly Output and Citations

Distribution of papers on phage display across 58 countries is also of interest. The top ten countries published 1621 papers (73.95%). Table 7-9 show ranked list of countries according to number of published papers, citations and average citations per paper.

Represented data show that phage display technology has passed into practical stage, as we mentioned above. It is proved by increasing paper count and decreasing number of citations both in absolute terms and in normalized numbers, e.g., citations per paper. Furthermore, applied studies using phage display seem to be developed in Asian countries since they demonstrate growth in publication and citation counts. In European countries, the USA and Australia decrease in research activity was detected compared to initial period in 1990s when basic papers were published giving impetus to rapid growth in the use of phage display technology. Only in Germany and France researchers show sustained interest: Publication activity in these countries lacks of sharp fluctuations.

Switzerland takes leading position according to citations per paper value (9.09 citations) and has the lowest share of uncited papers. At the same time, there has been a reduction of interest to phage display in this country. Switzerland is followed by the Netherlands (7.87), the United Kingdom (7.35), the USA (7.03), Germany (6.30), Italy (5.49), Australia (4.64), France (4.28), Japan (3.51) and China (2.51).

The most rapid growth in paper count was registered in China that got close to the USA in 2013: 30 papers in China and 31-in the USA. However, Chinese papers are cited significantly more rarely, although Chinese scholarly output is constantly growing. Substantial part of uncited papers (30.04%) is another interesting fact concerning Chinese studies on phage display. Of note, this value is twice as much as global average index (13.55%). This can be explained both by language barrier and probably by lower quality of these papers (Novikov, 2015; Hvistendahl, 2013).

#### Collaboration

The considerable part of studies on phage display in different countries has been carried out without any international collaboration. Table 10 shows absolute number of papers and a share of papers published without international collaboration in the top ten countries.

Chinese, Japanese and American scientists are the most independent of international collaboration. In the majority of European countries share of international collaboration ranges from 43% (Italy) to 56% (the United Kingdom) due to a number of common scientific programs in Europe.

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Table 8. Distribution of citations over the countries	(3-vear citation window)	
	(5 year entancen (index)	

Country	Citation count					
	Total	1993–1999	2000–2006	2007–2013		
USA↓	5018 (44.90%)	1701 (50.61%)	1994 (46.29%)	1272 (37.19%)		
China ↑	684 (6.12%)	7 (0.21%)	189 (4.39%)	488 (14.27%)		
United Kingdom↓	1301 (11.64%)	658 (19.58%)	453 (10.52%)	157 (4.59%)		
Germany –	1039 (9.30%)	213 (6.34%)	503 (11.68%)	323 (9.44%)		
Japan ↑	439 (3.93%)	83 (2.47%)	171 (3.97%)	185 (5.41%)		
Netherlands ↓	779 (6.97%)	272 (8.09%)	376 (8.73%)	131 (3.83%)		
Switzerland ↓	745 (6.67%)	355 (10.56%)	299 (6.94%)	91 (2.66%)		
Italy ↓	423 (3.78%)	187 (5.56%)	152 (3.53%)	82 (2.40%)		
France ↑	321 (2.87%)	55 (1.64%)	185 (4.29%)	81 (2.37%)		
Australia ↓	320 (2.86%)	111 (3.30%)	126 (2.92%)	83 (2.43%)		
Total ↓	11176	3361	4308	3420		

#### Table 9. Average citations per paper in the top ten countries

	Citations per				
		1002 1000	2000.2006		Uncited papers
Country	Total	1993–1999	2000-2006	2007-2013	Total
USA↓	7.03	8.68	7.10	5.51	49 (6.82%)
China ↑	2.51	0.54	2.08	2.89	82 (30.04%)
United Kingdom↓	7.35	10.97	5.92	4.49	12 (6.78%)
Germany ↓	6.30	6.66	6.89	5.38	11 (6.66%)
Japan —	3.51	3.95	3.64	3.26	9 (7.20%)
Netherlands ↓	7.87	9.37	7.52	6.55	5 (5.05%)
Switzerland ↓	9.09	12.68	7.29	7.00	2 (2.44%)
Italy ↓	5.49	6.23	5.63	4.32	5 (6.49%)
France ↓	4.28	5.56	4.51	3.38	3 (4.00%)
Australia ↓	4.64	6.53	4.34	3.61	2 (2.90%)
Total ↓	5.10	6.97	4.97	4.10	297 (13.55%)

Table 10. Papers without international collaboration

	Papers without	Share of papers without
Country	international collaboration	international collaboration (percent)
USA	520	72.82
China	230	84.24
United Kingdom	100	56.49
Germany	88	53.33
Japan	94	75.20
Netherlands	99	50.50
Switzerland	82	48.78
Italy	77	42.86
France	75	52.00
Australia	69	50.72

Researchers from the United States published the majority of papers with international links-119 collaborative papers with the 9 other top countries. Distribution of the other countries according to the number of collaborative papers is as follows:

- Germany-61 papers/9 countries
- United Kingdom-58 papers/9 countries
- Netherlands-38 papers/8 countries
- China-36 papers/7 countries
- Switzerland-35 papers/7 countries
- Italy-30 papers/6 countries

- Australia-25 papers/9 countries
- France-23 papers/7 countries
- Japan-21 papers/6 countries

## Phage Display Papers in Scholarly Journals

Analyzed papers on phage display were published in 638 serials. Table 11 shows the top ten journals published more than 20% of papers (447 items).

From the middle 2000s, wider distribution of papers in different journals has been observed. Thus, boundaries of core of journals publishing papers on phage display have begun to dissolve. Growth in the number of papers on phage display was detected only in PLoS One.

Table 11. The top journals published papers on phage display technology

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Journals	Papers count
Journal of immunological methods	99 (4.52%)
Journal of biological chemistry	61 (2.78%)
Journal of molecular biology	57 (2.60%)
Methods in molecular biology clifton N J	53 (2.42%)
Gene	37 (1.69%)
PLoS One	33 (1.51%)
Biochemical and biophysical	32 (1.46%)
research communications	
Biotechniques	27 (1.23%)
Biochemistry	24 (1.09%)
Journal of immunology	24 (1.09%)

The majority of highly cited papers were published in journals with high impact factors. Thus, five Nature Publishing Group journals: Nature. Nature Biotechnology, Nature Structural Biology, Nature Protocols and Nature Medicine published 29 papers with 4012 citations from a total value of 50,645, i.e., 7.92%. Proceedings of the National Academy of Sciences of the United States of America published 17 papers with 1375 citations, i.e., 2.71%. Science journal published three papers (including the first one) cited 2216 times, i.e., 4.38%. Thus, those 49 papers (2.24%) have been cited 7603 times (15.01%). Papers published in the top 10 journals (Table 11) have been cited 10,809 times (21.34%). This value corresponds to share of phage display papers in these journals (20.39%).

## Conclusion

This paper enables us to trace the history of phage display studies through the last 30 years in terms of bibliometrics. Researchers published 2194 papers in 638 serials registered in Scopus database. The USA, China, Great Britain, Germany, Japan, the Netherlands, Switzerland, Italy, France and Australia were the most productive countries and accounted for 74% of scholarly output. In 1993-2000 there was the most significant increase in the number of papers, registering 27% per year. In the last 15 years slowdown in the growth was observed. Research activity was shifted from the USA and the European countries to Asian research organization. However, Western papers continue to obtain the majority of citations. Distribution of journals publishing studies on phage display is increasing; therefore, now we can observe that the core of journals with papers on phage display is dissolving its boundaries.

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## **Author's Contributions**

All authors have read and approved the final manuscript.

Alexander Ilyichev and Larisa Karpenko: Analyzed and discussed obtained results.

**Vadim Gureyev:** Collected and processed bibliometric data and wrote the manuscript.

**Nikolay Mazov:** Designed bibliometric study, structured and planned the paper.

## Ethics

The paper contains unpublished material. The corresponding author confirms that there were no ethical issues concerning the manuscript.

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