

Comprehensive analysis of commercial fragment libraries

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Table S1: List and annotation of analyzed commercial libraries

Table S2: Summary of non-chemically biased commercial libraries properties.

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Table S1: List and annotation of analyzed commercial libraries

Supplier	Chemical Libraries		
	Small ($\leq 2\,000$)	Intermediate	Large ($>10\,000$)
General	BIONET 2nd Generation Premium Fragment Library – KeyOrganics * Purity > 90% 1 166 fragments on 22/02/2021 Drug-Fragment Library – Prestwick * Purity $\geq 95\%$ 1 463 fragments on 22/02/2021	Chembridge Fragment Library Part 2 – Chembridge * Purity $\geq 90\%$ 2 942 fragments on 22/02/2021 Fragment-Based Library – Timtec * 3 032 fragments on 22/02/2021 All Purpose Fragment Library – FCH Group * Purity $\geq 90\%$ 8 969 fragments on 24/02/2021	Fragments Library – ChemDiv * Purity $\geq 92\%$ 11 269 fragments on 24/02/2021 General Fragment Library – OTAVACHemicals * Purity $\geq 95\%$ 11 726 fragments on 22/02/2021 Chembridge Fragment Library Part 1 – Chembridge * Purity $\geq 90\%$ 13 475 fragments on 22/02/2021 Advanced Subset General Fragment Library – LifeChemicals * Purity > 90% 16 774 fragments on 22/02/2021 Allium – Vitasmlab * 18 505 fragments on 22/02/2021 Asinex Fragments – Asinex * Purity > 90% 20 061 fragments on 22/02/2021 Fragment Collection – Maybridge Purity $\geq 90\%$ 30 099 fragments on 29/01/2019 General Fragment Library – LifeChemicals * Purity > 90% 49 236 fragments on 22/02/2021 Ro3 Library – Enamine * Purity $\geq 90\%$ 172 723 fragments on 22/02/2021
Diverse	Fragment Diversity Set 3 – LifeChemicals * Purity > 90% 320 fragments on 22/02/2021 Fragment Diversity Set 2 – LifeChemicals * Purity > 90% 960 fragments on 22/02/2021 Broad Spectrum Fragment Library – Reaxense * Purity > 90% 1 226 fragments on 23/02/2021 Fragment Diversity Set 1 – LifeChemicals * Purity > 90% 1 280 fragments on 22/02/2021 Selcia Fragment Library – Bioascent *	Ultimate Fragment Library – LifeChemicals * Purity > 90% 8 187 fragments on 22/02/2021	

	Purity > 95% 1 366 fragments on 22/02/2021 High Fidelity Fragments – Enamine * Purity ≥ 90% 1 920 fragments on 22/02/2021 Ro3 diversity Sets – Maybridge * Purity ≥ 90% 2 000 fragments on 22/02/2021		
Natural Product-Like	BIONET Fragments from Nature – KeyOrganics * Purity ≥ 95% 183 fragments on 22/02/2021 Natural Fragment Library – Reaxense * Purity > 90% 250 fragments on 23/02/2019	Natural Product Like Fragment Library – LifeChemicals * Purity > 90% 3 148 fragments on 22/02/2021 Natural Product-like Fragments – Enamine * Purity ≥ 90% 4 160 fragments on 22/02/2021	
3D shape	Spiro Fragments – FCH Group * Purity ≥ 90% 189 fragments on 24/02/2021 3D Shape Diverse Fragments – Enamine * Purity ≥ 90% 1 200 fragments on 22/02/2021 Stereogenic Centers Fragment Library – OTAVACHemicals * Purity ≥ 95% 1 902 fragments on 22/02/2021	3D-shaped Fragment Library – LifeChemicals * Purity > 90% 3 186 fragments on 22/02/2021	
sp3	High Fsp3 Fragment Library – FCH Group * Purity ≥ 90% 1 975 fragments on 24/02/2021	High Fsp3 Fragment Library – OTAVACHemicals * Purity ≥ 95% 2 662 fragments on 22/02/2021 Advanced Subset of Fsp3-Enriched Fragment Library – LifeChemicals * Purity > 90% 8 536 fragments on 22/02/2021	Fsp3 Enriched Fragment Library – LifeChemicals * Purity > 90% 17 862 fragments on 22/02/2021 Special sp3-rich Fragment Set – Enamine * Purity ≥ 90% 50 272 fragments on 22/02/2021
Metal	Chelator Fragment Library – LifeChemicals * Purity > 90% 1 584 fragments on 22/02/2021 Fragment Library Chelators 2019 subset – Reaxense * Purity > 90% 1 602 fragments on 23/02/2021 Chelator Fragment Library – OTAVACHemicals * Purity ≥ 95% 1 774 fragments on 22/02/2021		
PPI	Fragment-Like Aminoacids – FCH Group Purity ≥ 90% 48 fragments on 24/02/2021	PPI Fragment Library – Enamine Purity ≥ 90% 3 600 fragments on 22/02/2021 PPI Fragment Library – LifeChemicals Purity > 90% 3 882 fragments on 22/02/2021 PPI Fragment Library – Reaxense Purity > 90%	

		6 298 fragments on 23/02/2021	
Fluor	F19 Library – Maybridge Purity ≥ 90% 387 fragments on 22/02/2021 BIONET Fluorine Fragment Set – KeyOrganics Purity ≥ 95% 462 fragments on 22/02/2021 Fluorinated Fragments Diversity Set – Enamine Purity ≥ 90% 1 000 fragments on 22/02/2021 19F NMR Fluorine containing Fragment Library – OTAVACchemicals Purity ≥ 95% 1 151 fragments on 22/02/2021 Fluorine Fragment Cocktail – LifeChemicals Purity > 90% 1 340 fragments on 22/02/2021 Advanced Subset of Fluorine Fragment Library – LifeChemicals Purity > 90% 1 762 fragments on 22/02/2021 Fluorine Fragment Library – FCH Group Purity ≥ 90% 1 821 fragments on 24/02/2021	Chembridge Fragment Fluor Library – Chembridge Purity ≥ 90% 2 321 fragments on 22/02/2021 Fluorine Fragment Library – LifeChemicals Purity > 90% 5 808 fragments on 22/02/2021 Fluorinated Fragments – Enamine Purity ≥ 90% 6 377 fragments on 22/02/2021	Fluoro Fragments – Maybridge Purity ≥ 90% 27 045 fragments on 22/02/2021
Halogen	BIONET Bromine Fragments – KeyOrganics Purity > 90% 275 fragments on 22/02/2021 Halogen-Enriched Fragment Library – OTAVACchemicals Purity ≥ 95% 596 fragments on 22/02/2021 Advanced Subset of Bromine – LifeChemicals Purity > 90% 1 314 fragments on 22/02/2021	Bromine Fragment Library – Life Chemicals Purity > 90% 2 031 fragments on 22/02/2021 Chembridge Fragment Bromo Library – Chembridge Purity ≥ 90% 2 378 fragments on 22/02/2021 Halogen-Enriched Fragment Library – Reaxense Purity > 90% 2 659 fragments on 23/02/2021 Bromo Fragments – Maybridge Purity ≥ 90% 7 270 fragments on 22/02/2021	
Covalent	Specific Covalent Fragments – LifeChemicals Purity > 90% 598 fragments on 22/02/2021 BIONET Covalent Fragments – KeyOrganics Purity > 90% 687 fragments on 22/02/2021 Serine Focused Covalent Fragments – Enamine Purity ≥ 90% 1 280 fragments on 22/02/2021	Covalent Fragment Library – Reaxense Purity > 90% 2 506 fragments on 23/02/2021 Advance Subset of Covalent Fragment Library – LifeChemicals Purity > 90% 2 851 fragments on 22/02/2021 Cystein Focused Covalent Fragments – Enamine Purity ≥ 90% 3 200 fragments on 22/02/2021 Covalent Fragment Library – LifeChemicals	

	Lysine Focused Covalent Fragments – Enamine Purity ≥ 90% 1 600 fragments on 22/02/2021	Purity > 90% 4 077 fragments on 22/02/2021 Covalent Fragments Library Plated – Enamine Purity ≥ 90% 6 120 fragments on 22/02/2021	
Miscellaneous	Mini-Fragment Library – Enamine * Purity ≥ 90% 80 fragments on 22/02/2021 BIONET MiniFrag – KeyOrganics * Purity > 90% 81 fragments on 22/02/2021 Essential Fragments – Enamine * Purity ≥ 90% 320 fragments on 22/02/2021 Boronic Acids Fragments – KeyOrganics Purity > 90% 514 fragments on 22/02/2021 Special Selection Fragment Library – FCH Group * Purity ≥ 90% 864 fragments on 24/02/21 DSI-POISED Library Plated – Enamine * Purity ≥ 90% 896 fragments on 22/02/2021 Solubility Fragment Library – OTAVACHemicals * Purity ≥ 95% 957 fragments on 22/02/2021 Single Pharmacophore Fragments – Enamine * Purity ≥ 90% 1 500 fragments on 22/02/2021	Fragment-Like Amines – FCH Group Purity ≥ 90% 2 155 fragments on 24/02/2021 Ro3 Compliant for CherryPicking – Maybridge * Purity ≥ 95% 2 733 fragments on 22/02/2021 Fragment-Like Acids – FCH Group Purity ≥ 90% 2 898 fragments on 24/02/2021 High Solubility Fragment Subset – LifeChemicals * Purity > 90% 3 783 fragments on 22/02/2021 Carboxylic Acids Fragments – Enamine Purity ≥ 90% 4 000 fragments on 22/02/2021 Advanced Subset of Low MW Fragment Library – LifeChemicals * Purity > 90% 4 949 fragments on 22/02/2021 Low MW Fragment Library – LifeChemicals * Purity > 90% 6 323 fragments on 22/02/2021	Fragment Library with Experimental Solubility Data – LifeChemicals * Purity > 90% 18 027 fragments on 22/02/2021 Tangible Fragments –LifeChemicals * Purity > 90% 123 026 fragments on 22/02/2021

* Non-chemically biased libraries.

Purity has been determined by HPLC and/or 1H-NMR

Table S2: Summary of non-chemically biased commercial libraries properties.

Type	Index of library	Number of fragments	Number of scaffolds ^a	MW (Mean $\pm$ SD)	logP (Mean $\pm$ SD)	PBF (Mean $\pm$ SD)	QED (Mean $\pm$ SD)
GEN	1	1 163	339 (15)	176.57 $\pm$ 34.57	1.06 $\pm$ 1.05	0.29 $\pm$ 0.27	0.66 $\pm$ 0.10
	2	1 463	340 (50)	195.17 $\pm$ 48.02	1.00 $\pm$ 1.46	0.42 $\pm$ 0.29	0.66 $\pm$ 0.13
	3	2 936	1 565 (867)	256.25 $\pm$ 24.66	0.59 $\pm$ 1.25	0.65 $\pm$ 0.19	0.78 $\pm$ 0.09
	4	3 032	974 (211)	217.05 $\pm$ 40.88	0.88 $\pm$ 1.30	0.38 $\pm$ 0.28	0.70 $\pm$ 0.12
	5	8 968	1 986 (307)	245.78 $\pm$ 42.68	0.35 $\pm$ 1.12	0.62 $\pm$ 0.26	0.76 $\pm$ 0.11
	6	11 268	2 387 (631)	250.27 $\pm$ 38.54	1.56 $\pm$ 1.23	0.45 $\pm$ 0.29	0.77 $\pm$ 0.12
	7	11 724	1 349 (364)	220.60 $\pm$ 45.35	1.38 $\pm$ 1.18	0.40 $\pm$ 0.30	0.72 $\pm$ 0.12
	8	13 475	1 910 (278)	244.33 $\pm$ 48.98	1.48 $\pm$ 1.29	0.50 $\pm$ 0.26	0.75 $\pm$ 0.12
	9	16 774	3 779 (837)	226.46 $\pm$ 45.58	0.88 $\pm$ 1.20	0.51 $\pm$ 0.25	0.74 $\pm$ 0.11
	10	18 473	3 431 (1 191)	236.18 $\pm$ 46.49	1.83 $\pm$ 1.20	0.43 $\pm$ 0.28	0.73 $\pm$ 0.13
	11	20 061	4 656 (1 722)	252.27 $\pm$ 36.25	0.85 $\pm$ 1.43	0.54 $\pm$ 0.27	0.75 $\pm$ 0.12
	12	49 234	11 804 (5 454)	253.56 $\pm$ 42.32	1.12 $\pm$ 1.22	0.54 $\pm$ 0.26	0.76 $\pm$ 0.12
	13	172 631	29 672 (16 553)	246.45 $\pm$ 41.48	0.83 $\pm$ 1.28	0.60 $\pm$ 0.25	0.77 $\pm$ 0.10
DIV	1	320	247 (20)	196.12 $\pm$ 46.68	0.84 $\pm$ 1.31	0.40 $\pm$ 0.28	0.69 $\pm$ 0.12
	2	960	602 (48)	211.91 $\pm$ 45.21	0.98 $\pm$ 1.16	0.46 $\pm$ 0.26	0.72 $\pm$ 0.11
	3	1 226	501 (59)	224.58 $\pm$ 45.12	1.31 $\pm$ 1.22	0.42 $\pm$ 0.32	0.73 $\pm$ 0.11
	4	1 280	776 (68)	207.96 $\pm$ 46.10	0.94 $\pm$ 1.20	0.44 $\pm$ 0.27	0.72 $\pm$ 0.12
	5	1 366	288 (46)	169.86 $\pm$ 32.58	0.70 $\pm$ 1.23	0.26 $\pm$ 0.27	0.60 $\pm$ 0.12
	6	1 920	620 (28)	176.40 $\pm$ 26.89	0.25 $\pm$ 1.06	0.45 $\pm$ 0.23	0.65 $\pm$ 0.09
	7	2 000	399 (28)	180.00 $\pm$ 38.92	1.25 $\pm$ 1.13	0.32 $\pm$ 0.27	0.66 $\pm$ 0.11
	8	8 187	2 153 (299)	219.22 $\pm$ 38.38	0.80 $\pm$ 1.16	0.52 $\pm$ 0.23	0.74 $\pm$ 0.10
NP	1	183	83 (23)	249.04 $\pm$ 35.80	-1.14 $\pm$ 1.63	0.66 $\pm$ 0.17	0.64 $\pm$ 0.14
	2	249	96 (12)	195.97 $\pm$ 29.63	0.43 $\pm$ 1.28	0.46 $\pm$ 0.27	0.60 $\pm$ 0.12
	3	3 148	512 (149)	253.07 $\pm$ 41.92	1.09 $\pm$ 1.21	0.51 $\pm$ 0.28	0.74 $\pm$ 0.11
	4	4 152	1 307 (382)	229.24 $\pm$ 52.72	0.77 $\pm$ 1.34	0.60 $\pm$ 0.26	0.72 $\pm$ 0.11
3D	1	189	121 (30)	264.15 $\pm$ 29.44	0.35 $\pm$ 1.17	0.73 $\pm$ 0.16	0.76 $\pm$ 0.10
	2	1 199	557 (53)	209.25 $\pm$ 44.52	0.41 $\pm$ 1.29	0.70 $\pm$ 0.19	0.69 $\pm$ 0.14
	3	1 894	473 (86)	232.46 $\pm$ 43.17	0.97 $\pm$ 1.27	0.63 $\pm$ 0.21	0.73 $\pm$ 0.12
	4	3 186	1 182 (272)	237.02 $\pm$ 45.39	0.65 $\pm$ 1.32	0.64 $\pm$ 0.16	0.73 $\pm$ 0.12
SP3	1	1 975	927 (298)	231.67 $\pm$ 48.88	-0.22 $\pm$ 1.30	0.67 $\pm$ 0.18	0.69 $\pm$ 0.12
	2	2 660	703 (128)	223.23 $\pm$ 47.26	0.87 $\pm$ 1.37	0.58 $\pm$ 0.24	0.71 $\pm$ 0.13
	3	8 536	2 333 (503)	224.20 $\pm$ 46.17	0.65 $\pm$ 1.32	0.60 $\pm$ 0.17	0.72 $\pm$ 0.12
	4	17 862	4 759 (1 850)	247.24 $\pm$ 44.58	0.71 $\pm$ 1.28	0.61 $\pm$ 0.19	0.75 $\pm$ 0.12
	5	50 268	612 721 (6 090)	257.61 $\pm$ 25.74	0.34 $\pm$ 1.37	0.69 $\pm$ 0.18	0.76 $\pm$ 0.10
CHE	1	1 584	449 (48)	207.36 $\pm$ 46.58	0.64 $\pm$ 1.31	0.38 $\pm$ 0.30	0.70 $\pm$ 0.12
	2	1 602	429 (28)	200.97 $\pm$ 44.30	0.36 $\pm$ 1.33	0.38 $\pm$ 0.29	0.68 $\pm$ 0.12
	3	1 774	419 (51)	218.78 $\pm$ 46.34	0.96 $\pm$ 1.24	0.32 $\pm$ 0.28	0.71 $\pm$ 0.13
MIS	1	80	52 (21)	94.05 $\pm$ 15.66	-0.64 $\pm$ 1.10	0.15 $\pm$ 0.19	0.43 $\pm$ 0.06
	2	81	53 (21)	94.33 $\pm$ 16.63	-0.60 $\pm$ 1.15	0.17 $\pm$ 0.19	0.43 $\pm$ 0.06
	3	320	86 (0)	166.46 $\pm$ 29.55	0.63 $\pm$ 1.11	0.22 $\pm$ 0.26	0.62 $\pm$ 0.10
	4	864	311 (72)	178.83 $\pm$ 28.58	-0.31 $\pm$ 1.06	0.40 $\pm$ 0.27	0.63 $\pm$ 0.09
	5	896	375 (22)	205.43 $\pm$ 31.84	0.70 $\pm$ 1.35	0.48 $\pm$ 0.23	0.72 $\pm$ 0.11
	6	957	298 (9)	195.19 $\pm$ 39.61	1.00 $\pm$ 1.01	0.33 $\pm$ 0.28	0.69 $\pm$ 0.10
	7	1 500	634 (32)	171.40 $\pm$ 22.55	0.52 $\pm$ 0.93	0.39 $\pm$ 0.24	0.65 $\pm$ 0.08
	8	2 732	497 (51)	179.77 $\pm$ 39.10	1.24 $\pm$ 1.19	0.34 $\pm$ 0.27	0.65 $\pm$ 0.11
	9	3 783	1 311 (215)	224.33 $\pm$ 43.13	1.05 $\pm$ 1.04	0.54 $\pm$ 0.23	0.75 $\pm$ 0.10
	10	4 949	1 462 (103)	184.76 $\pm$ 25.66	0.47 $\pm$ 1.22	0.40 $\pm$ 0.24	0.66 $\pm$ 0.09
	11	6 321	1 782 (141)	185.70 $\pm$ 25.96	0.55 $\pm$ 1.23	0.39 $\pm$ 0.25	0.65 $\pm$ 0.09
	12	18 004	4 761 (1 359)	236.63 $\pm$ 45.22	1.08 $\pm$ 1.20	0.53 $\pm$ 0.25	0.75 $\pm$ 0.11
	13	123 026	15 642 (6 394)	252.58 $\pm$ 33.99	1.20 $\pm$ 1.23	0.58 $\pm$ 0.24	0.79 $\pm$ 0.09

^aThe number of scaffolds which are present in a single copy in the full set of unique fragments is indicated in brackets

Table S3: Fifty most common scaffolds in all libraries and in small-sized libraries.

Most popular scaffolds in all libraries					Most popular scaffolds in small-sized libraries				
 21660	 4987	 4625	 4374	 4371	 2461	 782	 331	 322	 310
 4308	 3104	 3064	 3030	 2489	 274	 255	 183	 182	 174
 2461	 2294	 2267	 2195	 2162	 165	 155	 151	 138	 118
 2092	 2010	 1960	 1854	 1781	 112	 110	 109	 108	 108
 1752	 1703	 1695	 1665	 1632	 107	 106	 105	 103	 102
 1558	 1535	 1518	 1486	 1470	 102	 95	 91	 90	 90
 1381	 1370	 1335	 1334	 1307	 89	 88	 87	 84	 81
 1277	 1227	 1177	 1133	 1129	 81	 79	 79	 77	 72
 1107	 1105	 1094	 1070	 1022	 72	 72	 68	 68	 67
 1004	 944	 917	 867	 866	 67	 66	 64	 62	 62

The numbers below the structures correspond to the number of molecules containing the scaffold