# Supplemental Table 1: Eterna100 Benchmark

This table provides details of the Eterna100 benchmark, with puzzle number, name, Eterna ID, author, and secondary structure string. The solvers column indicates how many participants of the study were able to solve the problem under specific user-defined constraints, as of July 22, 2015. As the six tested algorithms ignored these constraints, the number of solvers might not be an accurate measure of the overall problem difficulty. The Teslagon puzzle only has 1 solver, as no participants other than the puzzle's original creator have yet found a solution. Additionally, sample solutions can be found in Dataset S2.

#	Puzzle Name	Eterna ID	Author	Secondary Structure	Solvers
1	Simple Hairpin	20111	Sneh	(((((.....)))))	59723
2	Arabidopsis Thaliana 6 RNA - Difficulty Level 0	215430	Sneh	((((((...((.......))((((((((....((((((((((((...((((....)))))).)))))).)))))))..)))))) ..))))))	22230
3	Prion Pseudoknot - Difficulty Level 0	15819	Sneh	((((((.((((....)))))).)))........	15727
4	Human Integrated Adenovirus - Difficulty Level 0	15886	Sneh	(((((((((((((.(((((.......(((((((((....(((((((...((((((((....))))))))).....)))))))...)))).))))...))))...((((((((.....))))).))))...))).)..	13427
5	The Gammaretrovirus Signal - Difficulty Level 0	15847	Sneh	..(.(.(((((((....))))).).)......((((.(((((((((((....))))))))))).(((((((....))))))..	10304
6	Saccharomyces Cerevisiae - Difficulty Level 0	17811	Sneh	(((((((((......))).((...............)...(((((......)).....(((((....)))))).....)))((((......))))(((.........))((((.((((......)))))(((((((......))))...((((((.(((((....))))).)))))).(((((......)))))((((......))))....	3252
7	Fractal 2	13687	pkinney	....(((((((....((((((((((.((((((.......))).((((........))).(((((.......)))...((((((((......)))))..(((((((((....(.((((......)).(((((.......)))....((((........))))....	365

#	Title	ID	User	Structure	Length
8	G-C Placement	1074756	hoglahoo6	(((...))).	247
9	The Sun	13840	pkinney	(((((((((((...))))..))))...(((((((((...))))..)))))...(((((((((...))))...)))))...(((((((...))))..(((((((((...)))))...((((((((...))))))...(((((...)))))..)))).))))...(((((((((...)))))...(((((...))))))))	241
10	Frog Foot	426871	kmcole	......(((..)))((((...)))((((...)))	175
11	InfoRNA test 16	816170	paramodic	((((((.((((((...)))))).).)))))	174
12	Mat - Martian 2	399912	mat747	((((...))))...((((((..((((((...))))))))))...((((((..(((((((...)))))))))...(((((...)))))))...(((((((((((...)))))...((((((((...)))))))).))...(((...))))	172
13	square	756881	jboanmit	((((((((((((((((((((((((...))))))...)))))...)))))...))))))	156
14	Six legd turtle 2	446042	Eli Fisker	...((..((..))..((...))..((...))..((...))..((...))..)	146
15	Small and Easy 6	727172	Brourd	(((((.....)).(.........))))	144
16	Fractile	443196	penguian	........((...))..((.(..(..)..).((.(..)..).((..)..).((....)))	143
17	Six legd Turtle	445593	Eli Fisker	...(..(..(..))..(..(....)..(..(..)..(..(..))..(...))..)	142
18	snoRNA SNORD64 2	1427482	ribonucleic	(((((....((...((((...(((((.........))))...)))..))).))))))	142
19	Chalk Outline	461984	Quasispecies	....(((((.(((((..).))).((((...)))).(((((...)))).))).))))	141
20	InfoRNA bulge test 9	775904	paramodic	(((((((.(.(.(((((....)))))))))	141
21	Tilted Russian Cross	601331	paramodic	...((((((...)))(((((.((((...)))((((...))))(((((....))))	140
22	This is ACTUALLY Small And Easy 6	3084759	steven123505	....	136
23	Shortie 4	997382	Eli Fisker	((....)).((....))	132
24	Shape Test	472029	Brourd	...(.((((.......)))).((.((((.((((...)))).((((...)))).)))).)......	123
25	The Minitsry	427350	penguian	(((....((....((....(((.....))).))).))).)))	122
26	stickshift	852950	janderso	..(((((((.....)))))))...	122

#	Title	ID	Author	Structure	Score
			nlee		
27	U	426038	Joshua Weitzman	....((((((.(.(.(.(((((((((....))))))))))))))).....	118
28	Still Life (Sunflower In A Vase)	404191	boganis	..((((((((....))))).((((...))))...((((....))))).((((....))))).((((....)))).((.... (((((((((....)))).))))))((((.... .))))..((((....)))).((((.....)))).)))..	110
29	Quasispecies 2-2 Loop Challenge	552663	Quasispecies	....(((((((.((((...)))).))))((((.(.(...).)))))...))))))).))))))	110
30	Corner bulge training	1452086	Eli Fisker	.(((((((((...))))).....))))).	110
31	Spiral	535777	MindofScience3	....((((.((((((.(.(.(.(.(.(.(......)))))))))))))))))).....	108
32	InfoRNA bulge test	736567	paramodic	............................((((....(((.-((((.(((((((....))).))).).)))....))).)))... ..)).)).	108
33	Worm 1	1569272	ribonucleic	......(.(.(.(.(.((.(....).))).).).).)	105
34	just down to 1 bulge	742530	Edward Lane	....((((.((((....))))-.((((....))).))-...((((((....))).)))...............))))))..	101
35	Iron Cross	530172	MindofScience3	.(((.((((...((.(((...)).(((....)))))...(((((....))).)))-.(((((.(((...)))))))...).(((...)).)))...	96
36	loops and stems	1487670	Owen0990	....(((((...(((.(.((((....)))))....)))..(((.......))))...((((.....)))).-.(((....... .))).-))).-))).-((.....))))......	96
37	Water Strider	460087	Quasispecies	....((.((((((....)))))))((....)))(((((...))))((((...)))(((...)).)((((...)).))).)............	95
38	The Turtle(s) Move(s)	401904	boganis	..((...))....((((((.....))))))....(((....)))....-(((((....)))))...-(((-.((....))...(((.....)))...-(((.......)))).-(((((.....-(((((....))))))..)))))......	85
39	Adenine	2463193	Eli Fisker	(((((.(((((.(.(((((.(((((((((....)))).)))).-((((((...)))))).)))))))))))))))))).((((((((((.....))))))-.))))).)))))))...-.)))))....))))....)))))....)))))))...-...))))....-..)))).)))))).))))))	85

40	Tripod5	903842	janderso nlee	..((((((((....))))((((....))))))..	84
41	Shortie 6	997391	Eli Fisker	((....)).((....).((....)).((....))	80
42	Runner	888104	Yoshi789	...((((((....)))))-(((((...))))-.(((((((....)))...))))((((...))).))...((-(((....))).))).....	78
43	Recoil	969361	largevee	...((((((.(.-(.((.(((.((..(.-.))).)))))))).)))))...............	78
44	[CloudBeta] An Arm and a Leg 1.0	2320259	kcabral28	...((-(.((((...)).)))(((.((.....))))..)).))...............	78
45	[CloudBeta] 5 Adjacent Stack Multi-Branch Loop	2322879	Brourd	(((((((((...)))))((((...)))))(((((...)))))(((((...)))))).	78
46	Triple Y	481598	Quasispe cies	...((((((((((....))))((((....))))))((((((...)))))))))...............	76
47	Misfolded Aptamer	683941	starryjess	((((....((((...)).((....))........))....))))	72
48	Flower power	1884959	ariel19_8 9	...(((((((...)))).)-((((((...))))..(((((...)))..((((...))))))).(((...))))...............	72
49	Kudzu	458872	Quasispe cies	...((((-(.(-((((.((((...))))))(((((((...)))).((((...)))..))).).)))..)))...).).)))...............	59
50	1,2,3and4bulges	737448	Edward Lane	...((((.(((((....)))).((((...))))...((((((...)...)))((((....))))).)))...............	58
51	medallion	1398974	mspano	((((((.(((((....))))).((((....))).(((((....)))).((((((....)))))).(((.....)))))).(((...)))).((((((...-..)))).((((((...-))).(((((((...-.))))).((((((....-.)))))).((((((....-))))).((((....)...)))))).(((...))))	55
52	[RNA] Repetitious Sequences 8/10	3144144	paramodi c	.((......((.....))......((......((......))....))......))....	52
53	Documenting	319498	paramodi	......((.........((...........((.........((.........((.........((	51

#	repetitious behavior	0	c	(structure)
54	7 multiloop	256987	wateronthemoon	48
55	Kyurem 7	550435	Freywa	47
56	JF1	458607	Quasispecies	46
57	multilooping fun	2493932	ribonucleic	46
58	Multiloop...	4238942	qwed117	42
59	hard Y	422821	Joshua Weitzman	41
60	Mat - Elements & Sections	479654	mat747	40
61	Chicken feet	457731	Eli Fisker	38
62	Bug 18	970812	jandersonlee	38
63	Fractal star x5	3676828	Crul	36
64	Crop circle 2	448277	Eli Fisker	33
65	Branching Loop	459030	Brourd	33
66	Bug 38	1005956	jandersonlee	33
67	Simple Single	457023	starryjess	31

	Bond				
68	Taraxacum officinale	1887121	ariel19_89	30	(((((....))))).((((...)))).((((...).))).((((...).))).((((((((((((((... .)))).))))))).(((((....))))))).(((((...)))))).((((((((...)).))))))))))). (((((....)))).(((((....)))).(((....).))))
69	Headless Bug on Windshield	461805	Quasispecies	29	.((.((....(((((...((((..............))))..))).)))).((((....(((((....(((....)))).......(((.....)))))).).((((((...((((...((((.....((....)))).)))).)).)))))))))).)).
70	Pokeball	2418507	rnjensen45	29	..((((((((....((.(.((.((.(.((.((.((.))).(((.))).).))).)))))))))).))))).......((((((....(((. .((.((.(.((.((.((.)).)..)))).)......))).....
71	Variation of a crop circle	972844	jboanmit	28	....((..((..(((.((.(.)..)..)......)............).............
72	Loop next to a Multiloop	472262	Brourd	27	..(((((((....(.(((....))))).(((((....).))))).......))))))..
73	Snowflake 4	415914	Ding	26	(((((...)))))(((((....))))((((((((....))))).((((...)))))).(((((....))))(((((...))).(((((...)))).-(((((....)))).(((((...))))((((...)).-(((....).))))))((((....)))))(((....))))((....))))(((...)))
74	Mat - Cuboid	450940	mat747	26	(.((.((.((.((.((..((.((.((..((.((.((..((.((.((.((.(((.((.((.((.((.((..((.((.((..((.((.((..((.(.....))-))-))-))-)) .)))-)).))).))))-)).))))).....)).))))-)).))))-))).-)))).))))).))).)))((.((...))))((((....)))).)).)).)).))
75	Misfolded Aptamer 6	708346	starryjess	24	.....((((....(((....(((....)))...)....))))........
76	Snowflake 3	415093	Ding	23	(((((....)).((((((....).))(((....)))((((....)).)).(((.(((...))((((....))((((....)))((((....))))((((.(....(((.((.((...)))).-))).)))))((((.(....))))((((...))(((((.(....)))-((...))))((....)).)))(((....)))(((...)))))...((....))))
77	Hard Y and a bit more	443518	Joshua Weitzman	23	....(((((((.(((((...)))))((((((((.(((.(((...))).-(((.....)))).).)))))))._ ....
78	Mat - Lot 2-2 B	451142	mat747	23	(.((((.((((..((...))-(((....(((((..((..((((....((...)))).)))...)))))(.((.((.((.((...)))).)))...)))).)).))).)).))((.((

#	Name	ID	Author	Structure	Score
79	Shapes and Energy	480112	Brourd	....((.(((.(..(...))).).)....).).)).)).).).).	22
80	Spiral of 5's	474410	Brourd	(....(((((...(((((...(((((....(((((...(((((...((((...((((...(((((..(((((..((((...((((...)))).....))))....))))....))))...)))))...)....	21
81	Campfire	547104	starryjess	....((((.((((((...((((((..(((((...((((((....).)))))(((((.((.((.(....)))))((((((...))))))))))))((((((...)))))))).)).))))))).))).....	21
82	Anemone	3058638	wateronthemoon	..(((((...))))))((((...((((..((((...))))..((((((((...))))((((((((((...)))))))))).))))((((((...))))))	18
83	Fractal 3	460166	Eli Fisker	....((((.(((.(....)))(((.(....)))).(((.(.....))))(((.(....))(((.(....)).).)).).))......	17
84	Kyurem 5	545680	Freywa	...(((((((.(...)))((...((((((..((((...)))))(((...))))))).)))....	16
85	Snowflake Necklace (or v2.0)	624517	Wobble Dynx	((((((((((((((...(((...)).((....).)((((...))).)(((((...))))((((((....)).((....)).(((((((((...)).((....)).(((((...)).((....)).(((((((((...)).((....)).))))))))))))))	15
86	Methaqualone C16H14N2O Structural Representation	4891834	Malcolm	......((((.((((.((((....)).((.......)))((((.((((...))))))).((((((....))(((((((...))))).))).))).))))(((((((....)))(((((((...))))((((((...)).(((((((...))))).)))....)))))...)))).)))...	14
87	Cat's Toy 2	474564	merryskies	...(((((((((..((.(.........).((..((.((..))....))))))))).....	13
88	Zigzag Semicircle	477402	Brourd	...((((((((.(....)).).)))).....	13
89	Short String 4	505782	Brourd	....((.(.(.(..(((((....)))).).(.(.((...)).).).)).)).)))................	11
90	Gladius	944766	Quasispecies	(....).(...(.....(.(((((((...((((((....)))).(..(.((((((((....)))).((((.....((((((((...)))))).((((((.(..(((((.....)))))...)))))).))).)).))))..((((...)).).).)).))....).(....)	11
91	Thunderbolt	908660	Quasispe	((..(((((......(.(..((.(.....(....)((((((((((......(....)))))...)).(.((......(.(.....)...	11

#	Name	ID	cies	Structure	Score
92	Mutated chicken feet	787674	Eli Fisker	).(.((...(...).(((...(.((.(.(.).).).)---))((....-(.((.(.)).).)-....)-)((((....-.(.-.)))))--....-))))))-....)))).))).-....(....).)))).)).	8
93	Chicken Tracks	965314	hoglahoo	......(((.(.(...))-)(((...)-..))((((....))).-(((((..)).-((((...))))-.......	7
94	Looking Back Again	726696	Brourd	......((((((((((...)))))-..((((...))).-((((....)))).(((((...))).-.((((...	6
95	Multilooping 6	3526038	jnicol	..(((((((((((....))))((((((....)))(((((....).)))))..	5
96	Cesspool	911841	hoglahoo	(.(.(...).((.(.(.((...).).-.(-.(.-.)-.))((-...)).).)))..(.-(.(.-.).).-(-...-).).(....).).((.(.)-.).)-((.(.(.((...))).).))).-(...(..).).))	4
97	Hoglafractal	1632102	hoglahoo	.((.((.((((.-.((((....-.(((((....-.((((.(((...)))).-.((((....-...)))))))((.....)))(((....-)))((....-))))....-......))).).).)-....(.(.(...))((....-.)))(((....))).)))))..	3
98	Bullseye	965280	hoglahoo	.-.((((((..))).-.(((.....)))).((((....)))).....(((((...)))))......((....))(((....))).-((.(...)))(...))...	3
99	Shooting Star	913357	Brourd	((((((((((....))))))((((..-.(.((((((((....)))).).-.).-..))((((....)))).).-.((...)((....))((((...).).)).(-...).((((((....)))))))((....)))).((.-.(.(.(((((.((((.-.((((.(...).))))((....)))).).-....))).-.)))).	2
100	Teslagon	6050904 1	wawan151	......((.(....(((.....).......-((......((((....-)......))-)((.(.....(((....-)).((...-....)).)-))).((-....-)).(((....-))((((.....))).)((....-.))))))))-.).).-......((-....-.......(....-..)))-....-)).))(-........)).)).......))......	0

Supplemental Figure 1: Secondary structures for each of the design challenges in the EteRNA100 benchmark are shown below, where orange and blue represent unpaired and paired nucleotides, repsectively. Each design challenge's id is displayed at the top left for reference, along with part of the design challenge's name. The 5' end is always directly to the left of the 3' end.

1. Simple Hairpin	2. Arabidopsis Thaliana...	3. Prion Psuedoknot...	4. Human Integrated...
5. The Gammaretrovir...	6. Saccharomyces...	7. Fractal 2	8. G-C Placement
9. The Sun	10. Frog Foot	11. InfoRNA test 16	12. Mat - Martian 2
13. square	14. Six legd turtle 2	15. Small and Easy 6	16. Fractile
17. Six legd turtle	18. snoRNA SNORD64	19. Chalk Outline	20. InfoRNA bulge test 9
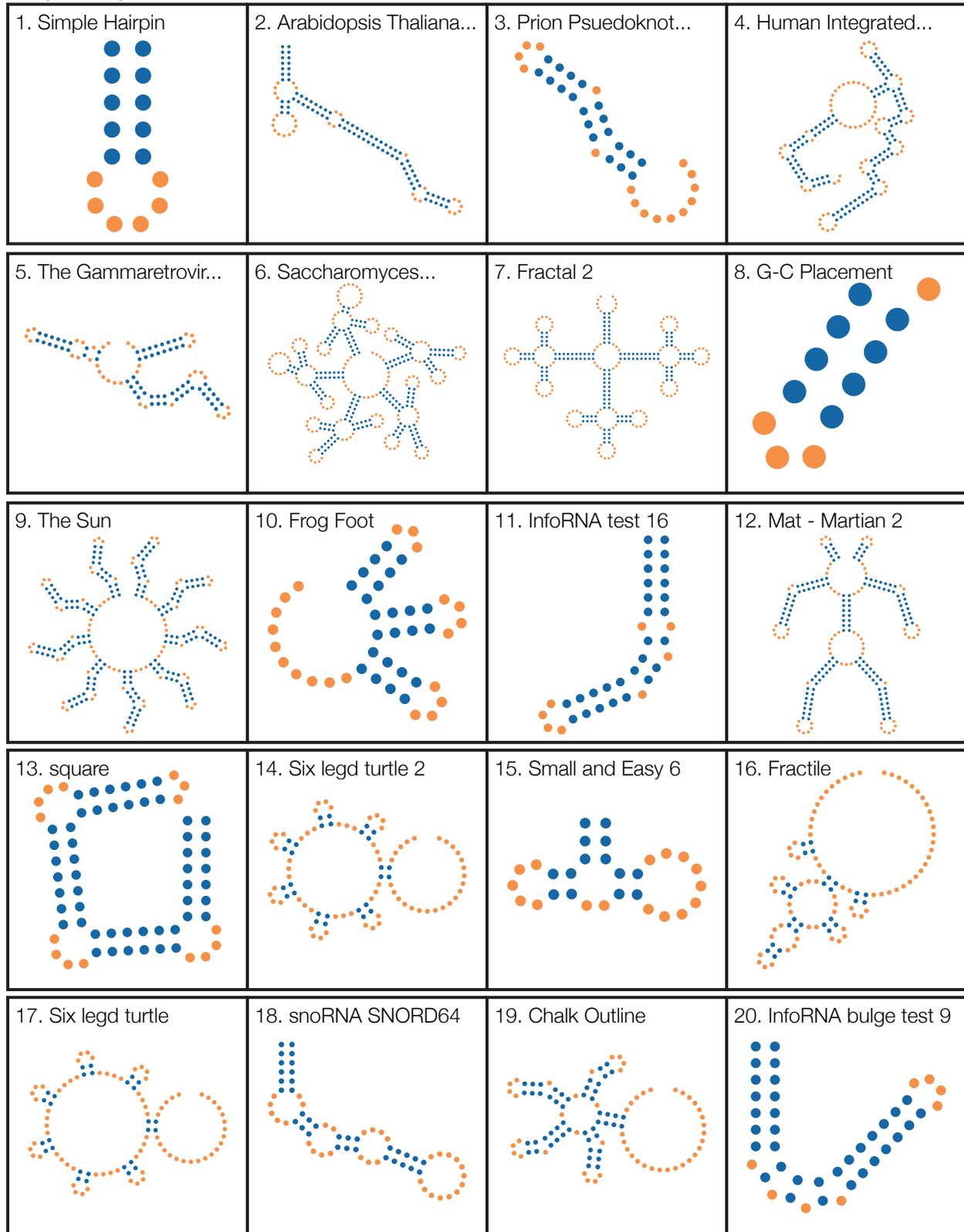
21. Tilted Russian Cross	22. This is ACTUALLY...	23. Shortie 4	24. Shape Test
25. The Minitsry	26. stickshift	27. U	28. Still Life...
29. Quasispecies 2-2...	30. Corner bulge training	31. Spiral	32. InfoRNA bulge test
33. Worm 1	34. just down to 1 bulge	35. Iron Cross	36. loops and stems
37. Water Strider	38. The Turtle(s) Move(s)	39. Adenine	40. Tripod5
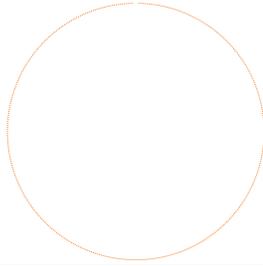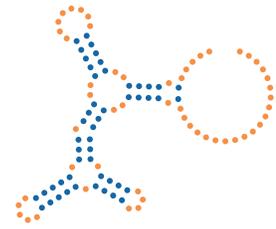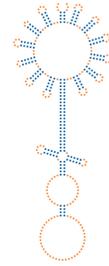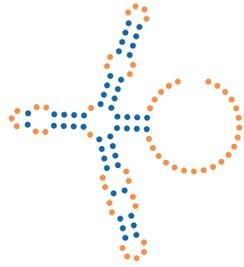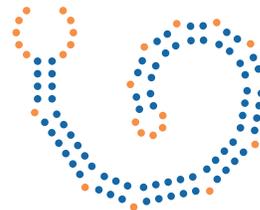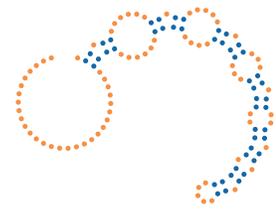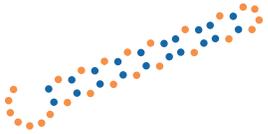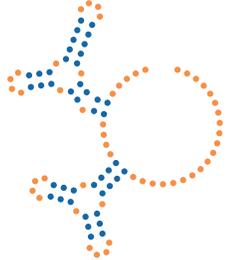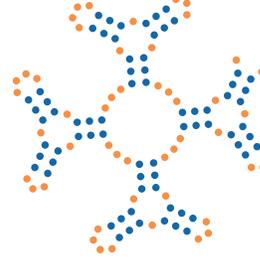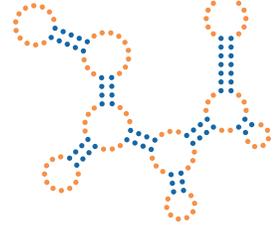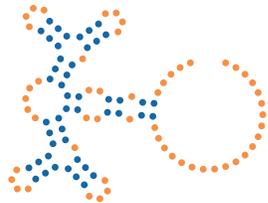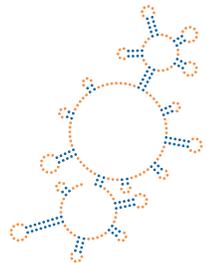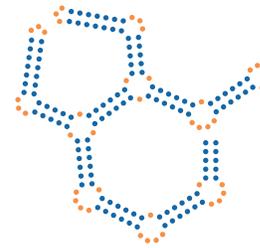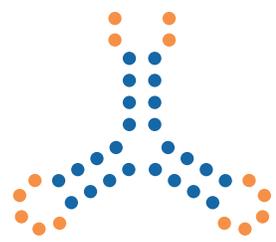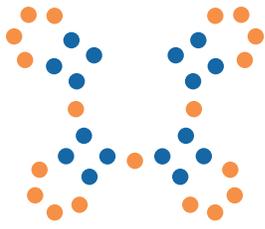
41. Shortie 6	42. Runner	43. Recoil	44. [CloudBeta] An Arm...
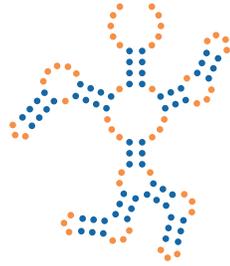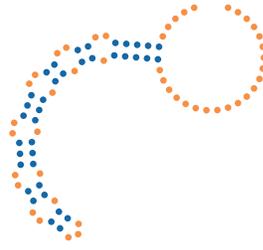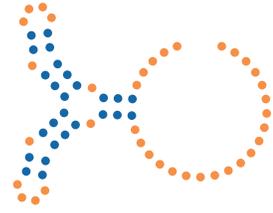
45. [CloudBeta] 5 Adj...	46. Triple Y	47. Misfolded Aptamer	48. Flower power
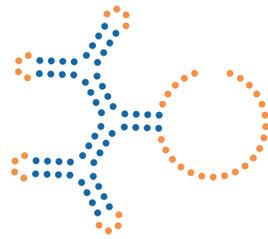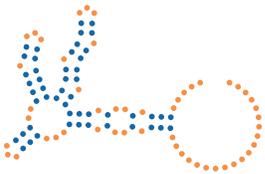
49. Kudzu	50. 1,2,3and4bulges	51. medallion	52. [RNA] Repetitious...
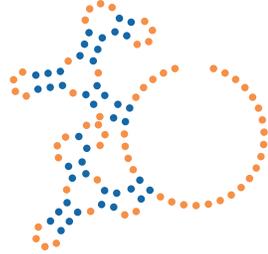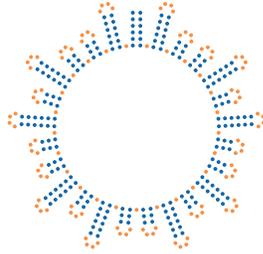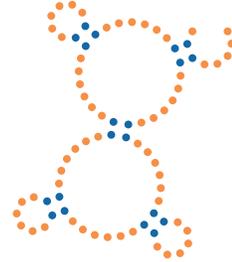
53. Documenting repe...	54. 7 multiloop	55. Kyurem 7	56. JF1
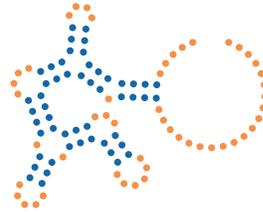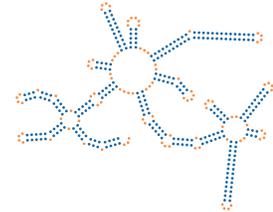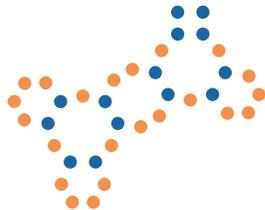
57. multilooping fun	58. Multiloop...	59. hard Y	60. Mat - Elements...
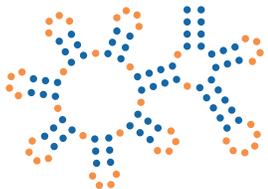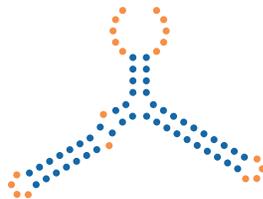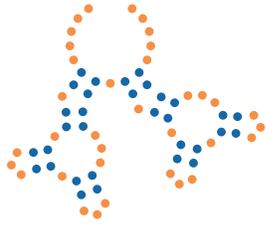
61. Chicken feet	62. Bug 18	63. Fractal star x5	64. Crop circle 2
65. Branching Loop	66. Bug 38	67. Simple Single Bond	68. Taraxacum...
69. Headless Bug on...	70. Pokeball	71. Variation of a crop...	72. Loop next to a...
73. Snowflake 4	74. Mat - Cuboid	75. Misfolded Aptamer 6	76. Snowflake 3
77. Hard Y and a bit more	78. Mat - Lot 2-2 B	79. Shapes and Energy	80. Spiral of 5's
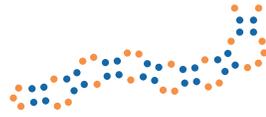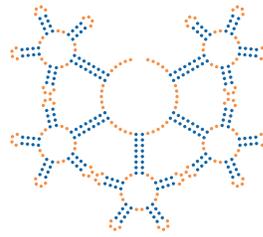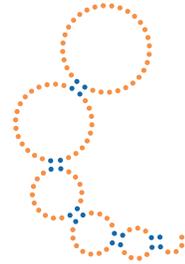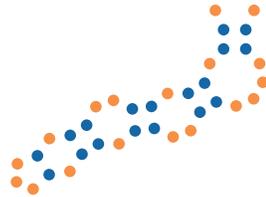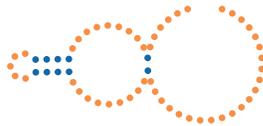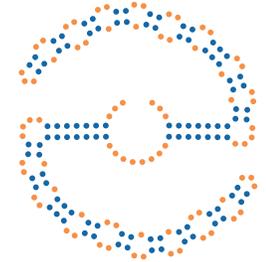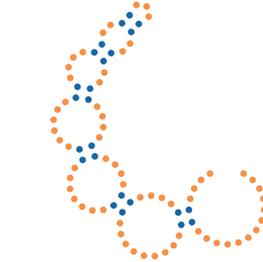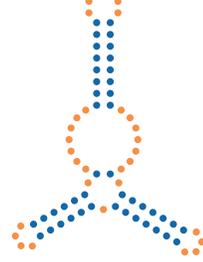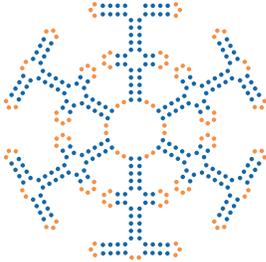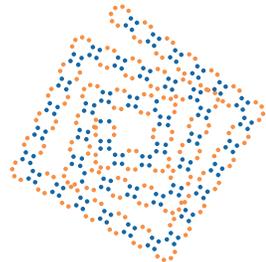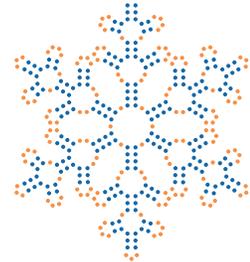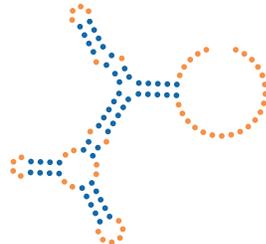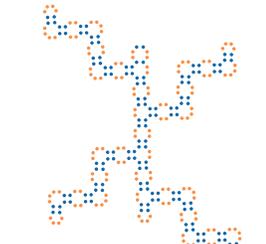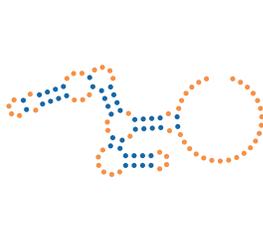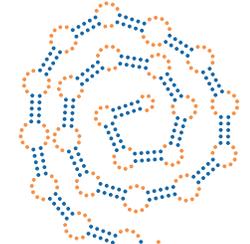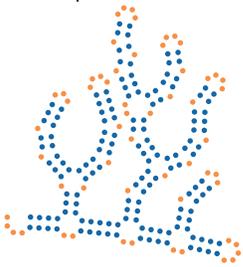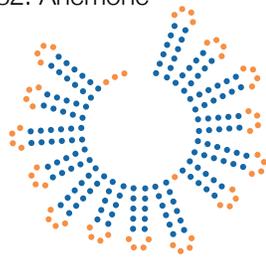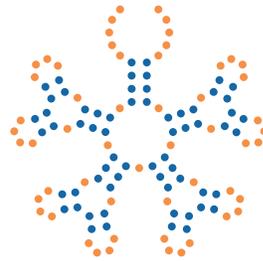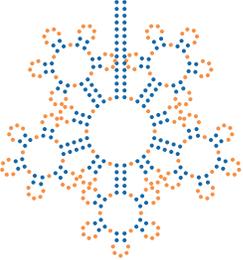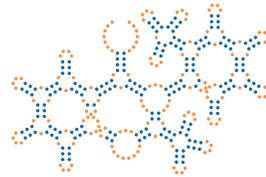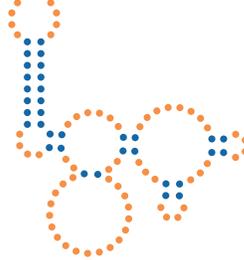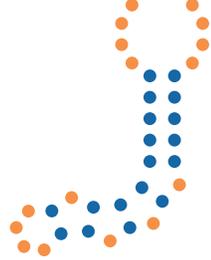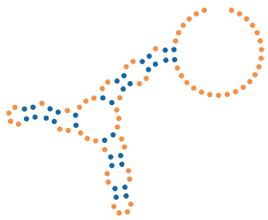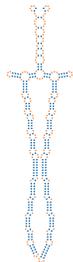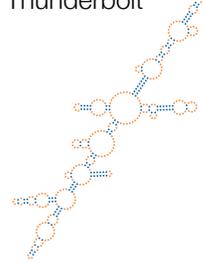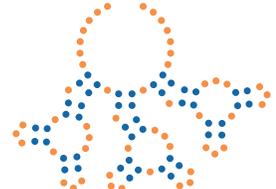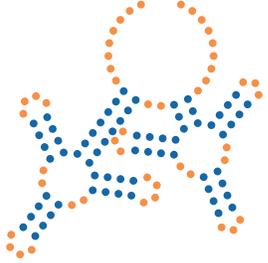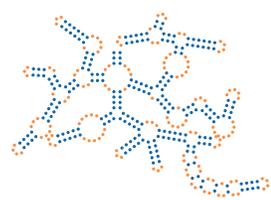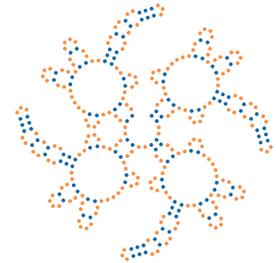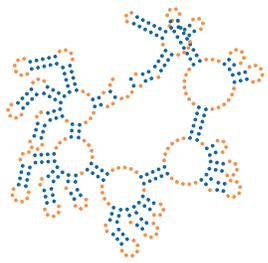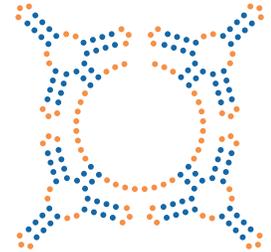
| 81. Campfire	82. Anemone	83. Fractal 3	84. Kyurem 5
85. Snowflake Necklace...	86. Methaqualone...	87. Cat's Toy 2	88. Zigzag Semicircle
89. Short String 4	90. Gladius	91. Thunderbolt	92. Mutated chicken...
93. Chicken Tracks	94. Looking Back Again	95. Multilooping 6	96. Cesspool
97. Hoglafractal	98. Bullseye	99. Shooting Star	100. Teslagon