Patterns, Volume *3*

Supplemental information

Antibody structure prediction using interpretable deep learning

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Supplemental Information

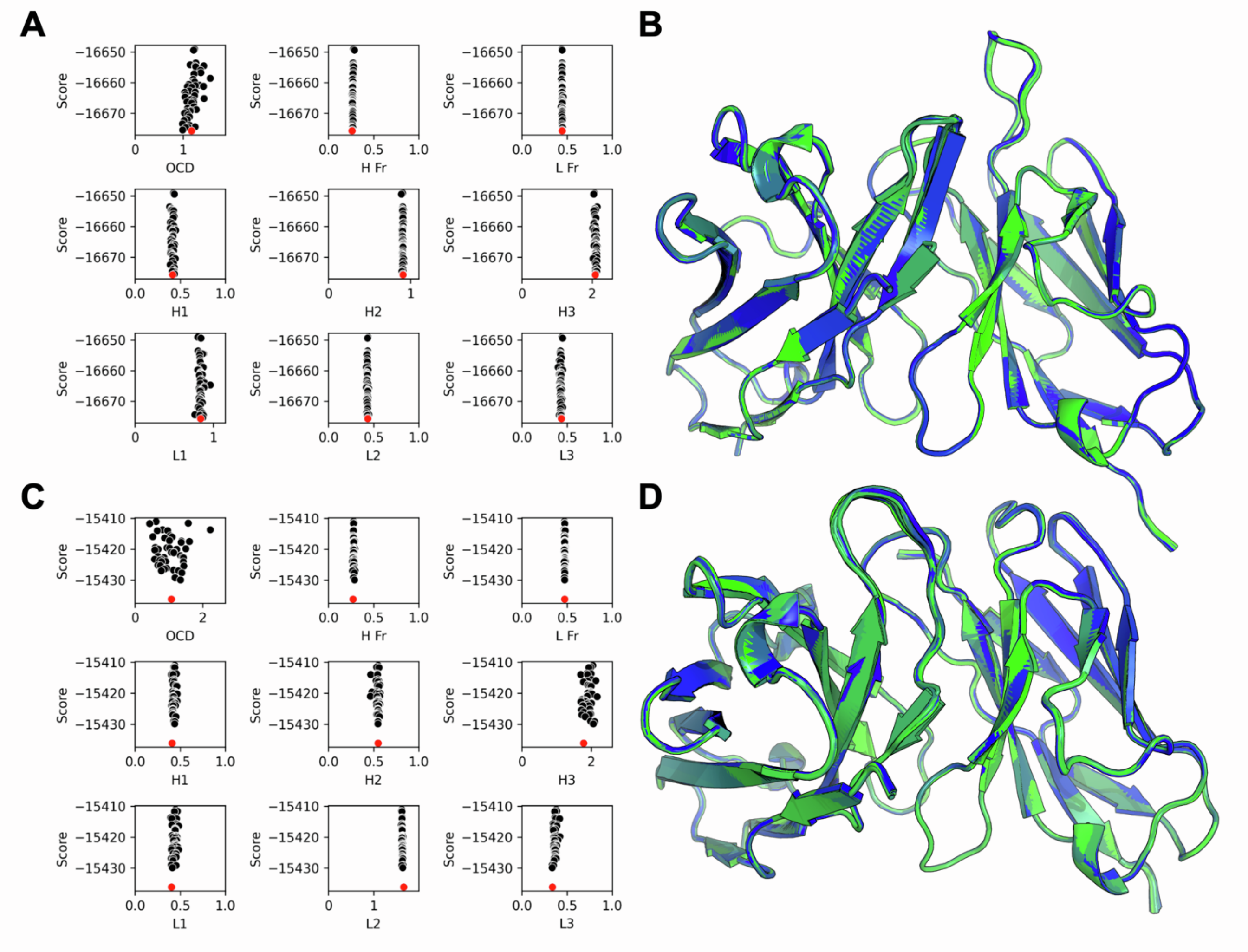

Figure S1. Convergence of predicted structures for two benchmark examples. (A) Funnel plots showing accuracy (OCD, RMSD) versus score for 50 DeepAb decoys for target 3PP3 (therapeutic benchmark), with low-scoring structure in red. (B) Superimposed decoy structures for target 3PP3. (C) Funnel plots showing accuracy (OCD, RMSD) versus score for 50 DeepAb decoys for target 3I9G (RosettaAntibody benchmark), with low-scoring structure in red. (D) Superimposed decoy structures for target 3I9G.

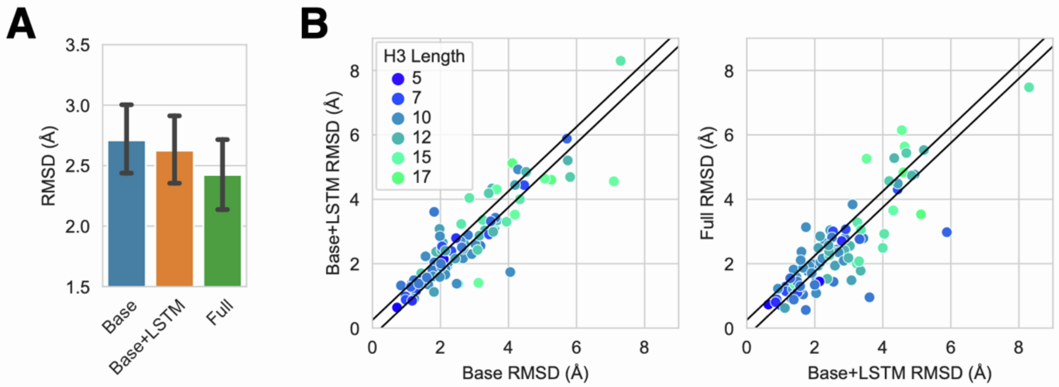

Figure S2. Impact of architecture additions on H3 loop accuracy. (A) Average RMSD of H3 loops predicted by baseline model (without LSTM features or CCA), baseline model with LSTM features, and full model. Error bars show standard deviations for each model on each benchmark. (B) Direct comparison of H3 RMSD for each target as architecture is expanded, with diagonal bands indicating predictions that were within ± 0.25 Å. Point color indicates H3 loop length for each target.

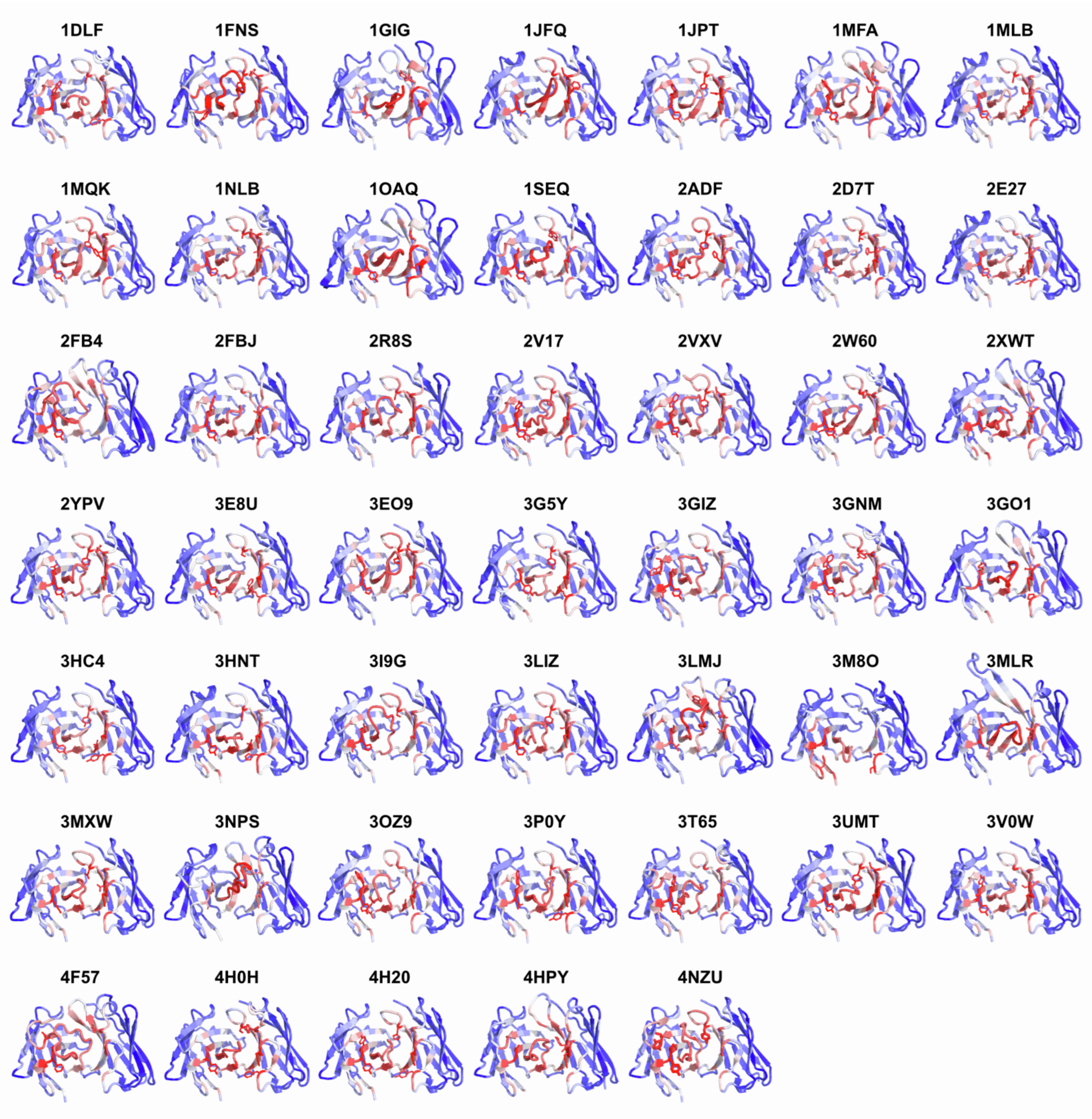

Figure S3. H3 loop attention for RosettaAntibody benchmark targets. Model C_α attention while predicting H3 loop structures for each of the 47 targets in the RosettaAntibody benchmark. Attention values increase from blue to red. For each target, the side chains of the five most attended non-H3 residues are represented as sticks.

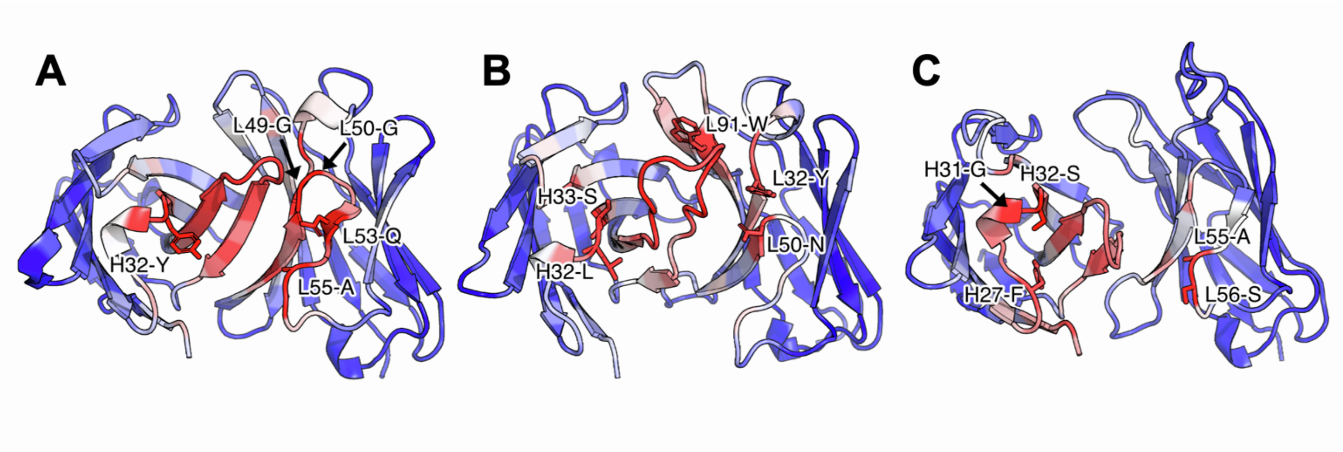

Figure S4. Variability of key residues identified by attention mechanism. Model C_α attention while predicting H3 loop structures for three targets in the RosettaAntibody benchmark. Attention values increase from blue to red. For each target, the side chains of the five most attended non-H3 residues are represented as sticks. (A) H3 attention for 1OAQ prediction. (B) H3 attention for 3MLJ prediction. (C) H3 attention for 3M8O prediction.

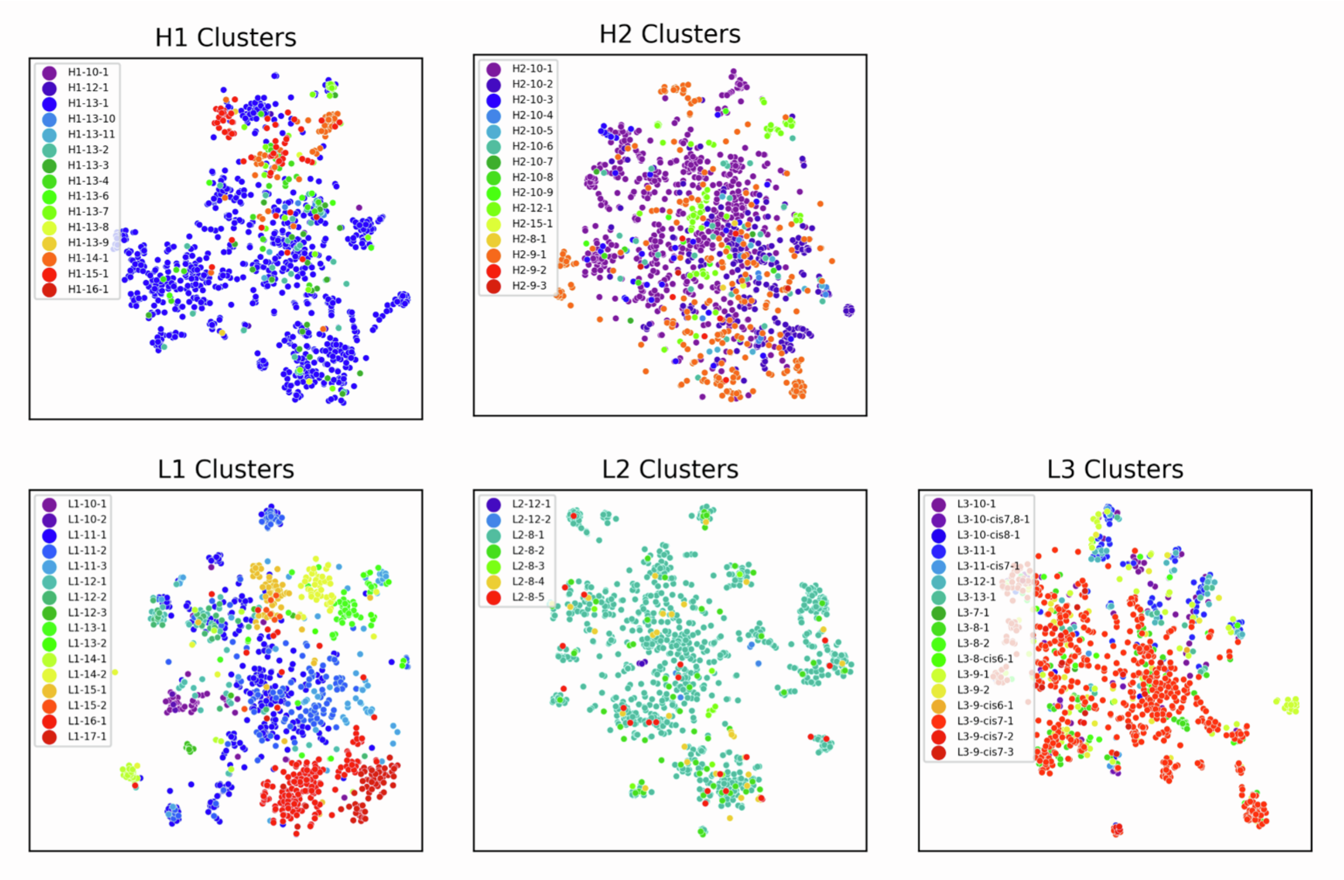

Figure S5. Non-H3 CDR loop t-SNE embeddings labeled by structural clusters. CDR-specific embeddings are created by averaging the bi-LSTM encoder hidden states of residues for each CDR loop.

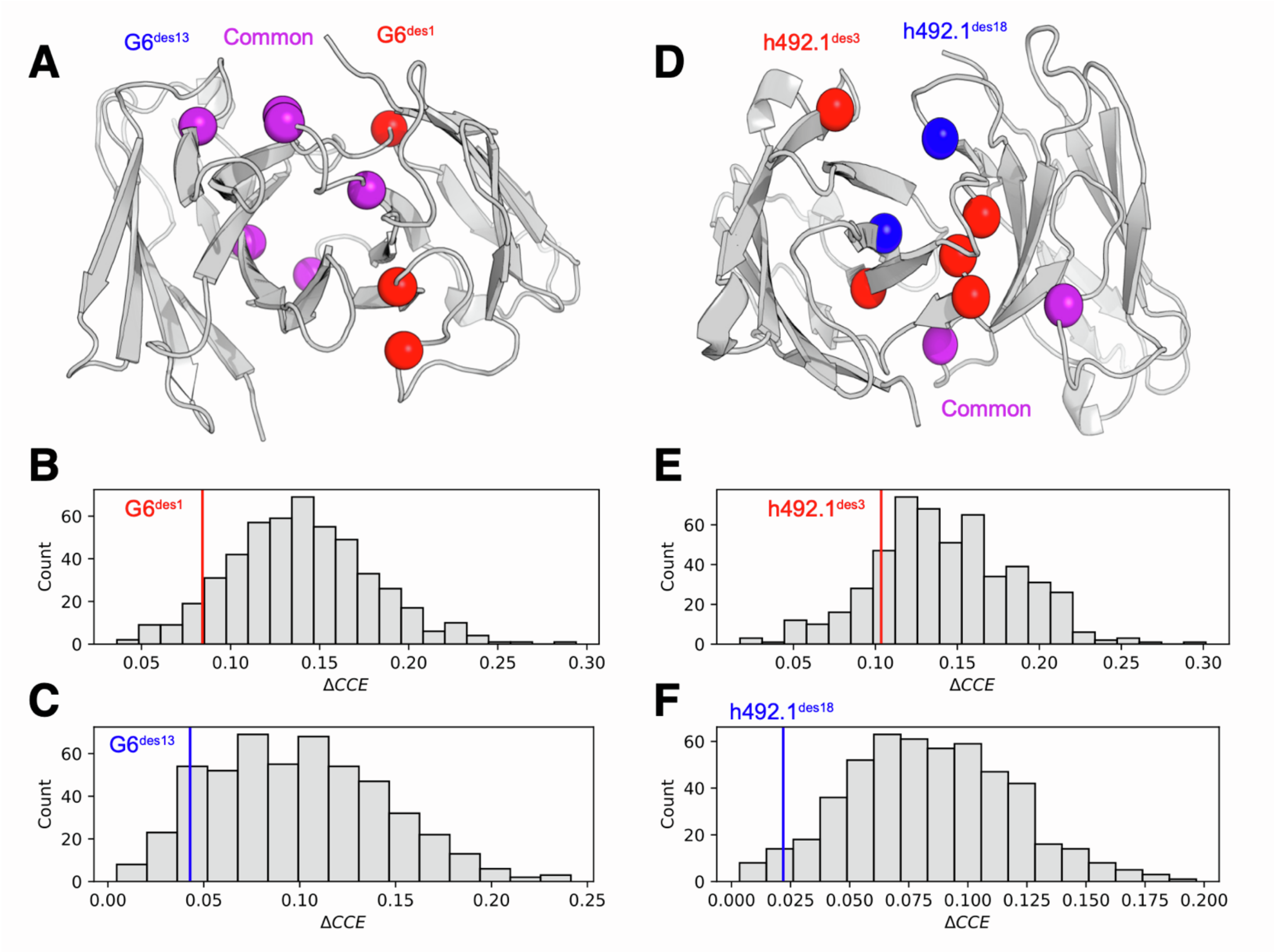

Figure S6. Identification of stable multi-point variants for two AbLIFT designs. Both wild type structures were present in the training dataset, resulting in a slight bias for the native sequence. (A) Mutation positions for two anti-VEGF multi-point variants presented by Warszawski *et al*[1]. (B) Comparison of ΔCCE values for G6^{des1} (nine-point variant) and random nine-point variants at the same positions. (C) Comparison of ΔCCE values for G6^{des13} (six-point variant) and random six-point variants at the same positions. (D) Mutation positions for two anti-QSOX1 multi-point variants. (E) Comparison of ΔCCE values for h492.1^{des3} (seven-point variant) and random seven-point variants at the same positions. (F) Comparison of ΔCCE values for h492.1^{des18} (four-point variant) and random four-point variants at the same positions.

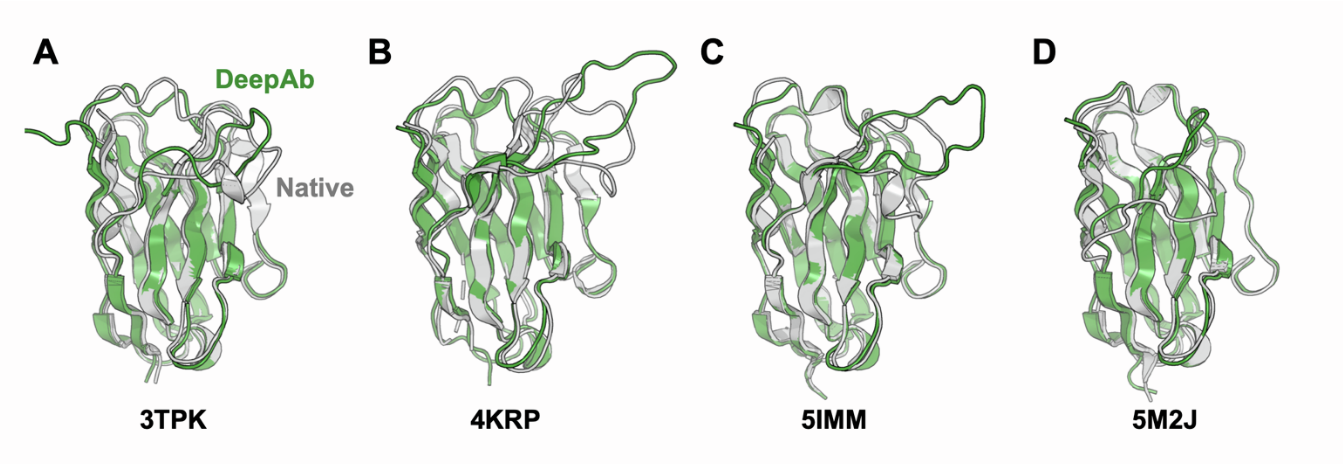

Figure S7. Nanobody structures predicted by DeepAb. Four nanobody structures predicted by DeepAb (green) aligned to native structures (gray). Prediction accuracy is reported as RMSDs over the framework region and the three CDR loops. (A) Predicted structure for nanobody 3TPK (framework: 0.58 Å, CDR1: 3.29 Å, CDR2: 1.07 Å, CDR3: 4.73 Å). (B) Predicted structure for nanobody 4KRP (framework: 0.82 Å, CDR1: 2.36 Å, CDR2: 2.07 Å, CDR3: 5.56 Å). (C) Predicted structure for nanobody 5IMM (framework: 0.46 Å, CDR1: 1.89 Å, CDR2: 0.58 Å, CDR3: 7.60 Å). (D) Predicted structure for nanobody 5M2J (framework: 1.01 Å, CDR1: 1.12 Å, CDR2: 0.86 Å, CDR3: 8.34 Å)

Table S1. CDR loop RMSD and OCD results for DeepAb on RosettaAntibody benchmark.

Target	OCD	H Fr (Å)	H1 (Å)	H2 (Å)	H3 (Å)	L Fr (Å)	L1 (Å)	L2 (Å)	L3 (Å)
1dlf	6.04	0.65	0.92	0.82	3.84	0.51	0.37	0.64	0.32
1fns	1.72	0.37	0.62	1.15	2.01	0.32	0.51	0.27	0.51
1gig	1.95	0.39	0.64	0.47	2.49	0.47	0.36	0.99	1.14
1jfq	3.20	0.49	0.49	1.07	1.10	0.33	0.43	0.21	0.54
1jpt	1.42	0.43	0.36	0.67	1.29	0.24	0.72	0.41	0.37
1mfa	2.08	0.45	0.50	0.69	1.45	0.29	0.89	0.41	1.24
1mlb	5.36	0.46	0.42	0.60	1.14	0.42	0.44	0.76	0.64
1mqk	2.68	0.24	0.29	0.34	1.04	0.48	0.46	0.38	1.76
1nlb	3.21	0.27	0.21	0.59	0.56	0.50	0.77	0.33	0.35
1oaq	1.33	0.39	0.37	0.67	1.93	0.38	0.58	0.39	0.40
1seq	2.45	0.39	0.66	0.58	2.93	0.36	0.41	0.20	0.40
2adf	2.87	0.42	0.48	0.61	1.77	0.53	0.75	0.28	0.59
2d7t	15.91	0.65	0.80	0.78	2.27	0.44	0.42	0.36	1.00
2e27	3.29	0.34	0.54	0.53	4.30	0.58	0.71	0.49	1.90
2fb4	5.83	0.34	0.30	0.34	3.53	0.88	0.91	0.47	0.63
2fbj	6.73	0.46	0.57	1.01	1.44	0.45	1.02	0.62	1.99
2r8s	2.59	0.48	0.64	1.83	2.55	0.37	0.32	0.41	0.49
2v17	2.12	0.36	0.44	1.26	2.44	0.67	0.69	0.35	0.86
2vxv	1.95	0.35	0.65	1.09	5.28	0.35	0.26	0.90	1.77
2w60	4.64	0.29	0.36	0.54	1.97	0.36	0.43	0.30	0.49
2xwt	0.46	0.43	1.24	0.54	3.13	0.32	0.61	1.07	0.99
2ypv	3.73	0.82	0.69	0.70	2.36	0.33	0.68	0.39	0.55
3e8u	3.26	0.48	0.56	0.59	1.30	0.37	0.51	0.42	0.35
3eo9	4.42	0.36	0.53	0.68	2.42	0.34	0.41	0.39	0.79
3g5y	3.75	0.29	0.52	0.37	0.72	0.60	0.24	0.35	0.42
3giz	2.10	0.37	0.56	0.43	1.95	0.31	0.25	0.28	0.25
3gnm	0.81	0.29	0.44	0.30	2.78	0.40	0.63	0.19	0.47
3go1	2.13	0.36	1.47	1.22	3.28	0.47	0.95	0.83	1.83
3hc4	4.13	1.02	0.49	0.99	0.89	0.41	0.46	0.30	0.37
3hnt	3.28	0.39	0.19	0.66	1.19	0.49	0.36	0.90	0.93
3i9g	1.24	0.27	0.41	0.55	1.78	0.47	0.40	1.66	0.34
3liz	1.67	0.33	0.52	0.37	4.77	0.50	0.66	0.32	0.30
3lmj	3.20	0.40	3.16	5.81	5.26	0.27	0.46	0.35	1.68
3m8o	4.42	0.56	1.48	1.19	2.98	0.48	1.49	0.32	1.08
3mlr	2.36	0.51	0.57	0.53	3.65	0.43	0.50	0.34	-
3mxw	1.03	0.41	0.59	0.56	1.08	0.32	0.30	0.25	0.68
3nps	21.84	1.19	3.24	1.76	4.84	0.45	0.67	0.48	1.01
3oz9	2.89	0.48	0.53	0.90	1.21	0.46	0.85	0.21	1.52
3p0y	2.10	0.37	0.70	0.98	1.53	0.21	0.39	0.30	1.53
3t65	1.91	0.28	0.36	0.40	1.48	0.39	0.49	0.36	0.39
3umt	2.52	0.36	0.60	0.73	2.05	0.47	0.79	0.47	0.30
3v0w	4.87	0.42	0.86	0.53	0.91	0.44	0.34	0.33	0.44
4f57	2.22	0.27	0.32	1.08	1.36	0.23	0.34	0.23	0.73
4h0h	3.06	0.30	0.33	0.62	1.22	0.47	0.35	0.37	0.29
4h20	3.81	0.52	0.26	0.60	2.63	0.35	0.34	0.29	0.83
4hpy	3.71	0.33	2.58	0.29	1.94	0.27	0.66	0.34	2.23
4nzu	4.35	0.31	0.27	0.73	5.64	0.40	0.26	0.42	0.37
Mean	3.67	0.43	0.72	0.85	2.33	0.42	0.55	0.45	0.86
SD	3.58	0.18	0.66	0.81	1.32	0.12	0.25	0.28	0.58

Table S2. CDR loop RMSD and OCD results for DeepAb on therapeutic benchmark.

Target	OCD	H Fr (Å)	H1 (Å)	H2 (Å)	H3 (Å)	L Fr (Å)	L1 (Å)	L2 (Å)	L3 (Å)
1bey	1.64	0.58	1.45	0.86	2.35	0.62	0.73	0.55	0.65
1cz8	1.92	0.30	0.64	0.76	1.65	0.24	0.30	0.28	0.38
1mim	1.60	0.49	0.54	0.49	1.01	0.36	0.61	0.48	0.81
1sy6	1.78	0.32	0.46	0.62	2.16	0.40	0.32	0.31	0.90
1yy8	1.78	0.98	0.49	0.68	0.62	0.42	0.57	0.49	0.74
2hwz	3.17	0.25	0.50	0.35	1.93	0.46	0.70	0.37	2.40
3eo0	2.50	0.31	3.25	1.05	4.49	0.27	1.27	0.23	0.44
3gkw	9.94	1.24	2.79	1.08	7.48	0.42	0.72	0.35	0.91
3nfs	3.88	0.46	0.44	0.54	1.10	0.39	0.65	0.36	0.84
3o2d	5.31	0.38	0.39	0.71	2.26	0.24	0.54	0.27	0.40
3pp3	1.18	0.26	0.42	0.91	2.09	0.45	0.84	0.43	0.44
3qwo	2.37	0.32	0.65	1.24	1.58	0.27	0.39	0.43	0.54
3u0t	9.53	0.58	1.60	0.79	3.07	0.50	0.83	0.54	1.01
4cni	3.76	0.32	0.31	1.02	2.79	0.44	0.33	0.39	0.63
4dn3	2.61	0.40	2.29	0.79	1.82	0.35	1.27	0.34	1.26
4g5z	3.98	0.30	0.36	0.44	1.45	0.47	0.30	0.57	0.46
4g6k	5.89	0.30	0.40	1.05	1.87	0.46	0.73	0.27	1.06
4hkz	4.03	0.25	0.43	0.46	3.04	0.26	0.27	0.28	0.56
4i77	3.24	0.41	0.89	1.04	2.37	0.29	0.80	0.27	0.60
4irz	1.77	0.38	0.43	0.52	3.05	0.41	1.00	0.41	1.38
4kaq	3.63	0.54	0.45	0.58	2.38	0.37	0.49	0.32	0.38
4m6n	6.05	0.35	0.70	0.40	2.76	0.28	1.32	0.29	2.02
4nyl	5.31	0.52	0.35	0.56	4.74	0.55	0.52	0.46	0.78
4od2	1.38	0.44	0.42	0.61	5.53	0.45	0.78	1.36	2.14
4ojf	1.35	0.36	0.28	1.09	1.71	0.24	0.42	0.32	0.55
4qxg	0.95	0.37	0.37	0.47	1.55	0.36	0.44	0.46	1.67
4x7s	1.99	0.37	1.43	0.65	2.18	0.29	0.39	0.22	0.55
4ypg	3.94	0.38	0.62	0.45	3.00	0.37	0.45	0.66	0.86
5csz	5.58	0.23	0.34	0.38	2.11	0.30	0.89	0.36	0.98
5dk3	4.00	0.32	0.54	0.58	2.49	0.33	0.32	0.55	0.52
5ggq	2.13	0.31	0.34	0.54	1.45	0.28	0.18	0.31	0.20
5ggu	5.51	0.24	0.43	0.46	6.14	0.32	0.27	0.25	0.34
5i5k	8.73	0.73	0.63	0.79	4.57	0.84	0.78	0.64	0.95
5jxe	3.98	0.29	0.67	0.46	2.85	0.59	0.49	0.58	0.77
5kmv	6.17	0.52	0.62	0.71	0.73	0.34	0.58	0.45	0.51
5l6y	3.89	0.25	0.47	0.54	5.44	0.21	0.28	0.52	2.29
5n2k	2.78	0.24	0.35	0.29	2.70	0.35	0.51	0.32	4.55
5nhw	2.43	0.29	0.69	0.48	0.80	0.26	0.76	0.37	4.34
5sx4	0.46	0.46	0.94	0.69	0.88	0.33	0.26	0.34	0.57
5tru	3.00	0.33	0.40	0.43	1.34	0.30	1.01	0.25	1.22
5vh3	3.95	0.31	0.67	0.36	0.95	0.40	0.32	0.38	0.42
5wuv	2.83	0.43	0.69	0.87	2.82	0.24	0.22	0.32	0.56
5xxy	2.99	0.38	0.54	0.94	1.30	0.37	1.10	0.56	0.44
5y9k	1.98	0.38	2.29	0.98	2.07	0.29	0.72	0.63	1.21
6and	1.56	0.33	0.58	0.80	2.57	0.32	0.52	0.38	0.51
Mean	3.52	0.40	0.77	0.68	2.52	0.37	0.60	0.42	1.02
SD	2.16	0.19	0.67	0.24	1.50	0.12	0.30	0.19	0.92

Table S3. CDR loop RMSD and OCD results for RosettaAntibody-G on RosettaAntibody benchmark.

Target	OCD	H Fr (Å)	H1 (Å)	H2 (Å)	H3 (Å)	L Fr (Å)	L1 (Å)	L2 (Å)	L3 (Å)
1dlf	9.61	0.69	1.17	1.14	4.92	0.61	0.67	1.00	0.64
1fns	3.22	0.58	0.79	1.20	4.32	0.35	0.67	0.44	1.13
1gig	8.70	0.59	0.68	0.86	4.35	0.90	0.78	2.29	1.00
1jfq	5.07	0.67	0.97	1.07	1.34	0.51	0.40	0.83	0.74
1jpt	6.69	0.52	1.62	0.99	1.48	0.30	0.67	0.90	0.75
1mfa	7.30	0.76	0.82	1.07	3.39	0.93	2.37	0.98	1.29
1mlb	4.15	0.59	1.23	0.58	5.45	0.59	0.54	1.18	0.85
1mqk	6.21	0.41	0.71	0.88	1.78	0.71	0.79	0.81	1.95
1nlb	4.41	0.52	0.62	0.52	1.47	0.55	0.54	0.79	0.89
1oaq	7.46	0.76	1.22	0.85	1.96	0.88	0.64	1.72	1.21
1seq	2.73	0.46	1.04	1.61	6.57	0.45	0.48	1.20	0.81
2adf	6.20	0.39	0.78	0.56	2.11	0.39	0.42	0.91	0.43
2d7t	13.32	0.82	1.07	0.87	5.90	0.53	0.56	0.79	0.98
2e27	4.19	0.33	0.47	0.36	3.03	0.57	0.30	0.63	1.46
2fb4	2.54	0.42	1.17	0.58	8.25	1.15	1.26	0.78	0.64
2fbj	12.86	0.48	0.83	0.57	1.38	0.48	1.15	0.89	2.18
2r8s	6.83	0.62	1.93	1.76	2.76	0.52	3.04	0.38	0.57
2v17	9.30	0.58	0.86	1.60	1.72	0.68	0.63	0.63	0.63
2vxv	0.86	0.37	0.90	1.00	4.40	0.42	0.30	0.64	0.62
2w60	2.59	0.54	1.17	0.62	0.77	0.74	0.59	1.25	0.37
2xwt	4.50	0.44	1.41	0.43	2.48	0.57	0.74	0.54	2.08
2ypv	5.19	0.71	1.03	0.84	6.09	0.48	0.35	0.84	0.59
3e8u	2.87	0.61	0.84	0.66	2.32	0.41	0.67	0.71	0.67
3eo9	5.22	0.49	1.47	0.91	2.06	0.43	0.36	0.78	0.69
3g5y	2.18	0.29	0.75	0.39	0.42	0.73	0.48	0.78	0.46
3giz	2.69	0.48	0.74	0.55	4.86	0.48	1.98	0.79	0.68
3gnm	1.96	0.31	0.62	0.51	2.45	0.44	0.66	0.70	0.79
3go1	6.31	0.47	1.61	2.44	6.56	0.38	0.60	0.82	2.89
3hc4	7.98	1.03	0.57	1.13	1.39	0.46	0.55	0.32	0.26
3hnt	0.36	0.62	1.24	0.74	3.27	0.63	0.43	1.05	0.90
3i9g	5.75	0.52	0.44	1.06	2.93	0.61	0.75	0.78	0.80
3liz	2.71	0.58	1.41	0.34	4.57	0.75	0.34	0.58	0.37
3lmj	0.75	0.73	3.21	6.59	6.60	0.48	0.58	0.77	1.71
3m8o	8.76	0.64	2.22	1.04	8.38	0.46	1.27	1.03	1.10
3mlr	3.72	0.57	0.70	1.12	3.04	5.30	3.16	1.63	-
3mxw	2.71	1.21	1.31	1.29	1.72	0.41	0.74	0.66	0.80
3nps	3.59	1.27	3.74	2.99	5.53	0.61	1.02	0.87	2.64
3oz9	10.17	0.54	0.79	0.88	2.16	0.61	0.98	0.94	2.15
3p0y	3.34	0.38	2.74	2.61	2.60	0.54	0.30	0.71	1.77
3t65	1.81	0.35	0.93	0.75	0.44	0.41	0.67	0.50	0.69
3umt	7.46	0.59	1.59	0.97	4.04	0.55	0.50	0.67	0.83
3v0w	7.14	0.56	1.53	1.59	1.74	0.41	0.51	0.63	0.99
4f57	4.10	0.58	1.17	2.46	8.28	0.69	1.01	0.92	1.41
4h0h	5.66	0.52	0.65	0.67	2.67	0.58	0.61	0.76	0.74
4h20	3.67	0.54	0.86	0.35	1.75	0.58	0.50	0.86	1.57
4hpy	3.78	0.38	2.77	0.61	0.61	0.54	0.75	0.97	1.18
4nzu	5.55	0.47	0.83	0.77	7.16	0.71	0.45	1.12	0.82
Mean	5.19	0.57	1.22	1.14	3.48	0.67	0.80	0.87	1.06
SD	2.96	0.20	0.71	1.01	2.21	0.71	0.63	0.34	0.61

Table S4. CDR loop RMSD and OCD results for RosettaAntibody-G on therapeutic benchmark.

Target	OCD	H Fr (Å)	H1 (Å)	H2 (Å)	H3 (Å)	L Fr (Å)	L1 (Å)	L2 (Å)	L3 (Å)
1bey	4.23	0.96	1.81	2.06	3.58	0.67	0.72	1.20	1.22
1cz8	3.32	0.35	2.82	0.30	0.40	0.45	0.75	0.96	0.61
1mim	13.64	0.63	1.00	0.74	0.85	0.63	1.35	0.98	2.36
1sy6	3.53	0.32	0.88	0.46	1.62	0.49	0.52	0.80	0.84
1yy8	5.26	1.17	0.99	1.04	4.84	0.55	0.58	0.77	0.71
2hwz	1.74	0.31	1.05	0.42	1.79	0.56	0.58	1.06	2.23
3eo0	5.58	0.72	2.81	1.61	9.58	0.39	1.57	1.13	0.83
3gkw	10.31	1.23	2.68	0.94	7.81	0.65	1.53	1.15	0.94
3nfs	4.31	0.84	1.80	1.65	3.34	0.46	1.00	0.91	1.38
3o2d	4.18	0.56	0.86	0.94	4.71	0.55	0.82	0.83	0.40
3pp3	2.22	0.53	0.90	1.30	4.15	0.54	1.06	0.90	0.92
3qwo	4.57	0.35	0.66	1.32	1.73	0.56	0.71	1.18	2.22
3u0t	17.22	0.66	2.22	1.15	5.15	0.71	1.17	0.96	1.40
4cni	9.41	0.58	0.64	1.30	3.42	0.52	0.34	0.79	0.81
4dn3	7.94	0.68	3.74	1.30	2.66	0.41	1.44	0.89	1.02
4g5z	4.56	0.38	0.79	0.40	0.56	0.50	0.31	0.73	0.53
4g6k	4.11	0.38	0.76	1.24	2.33	0.59	0.73	0.69	0.53
4hkz	4.75	1.07	1.01	1.00	3.55	0.59	0.43	0.46	0.65
4i77	4.27	0.87	0.90	1.09	3.10	0.35	1.10	0.66	0.53
4irz	2.62	0.64	1.02	1.26	3.33	0.58	0.70	0.80	1.30
4kaq	3.65	1.02	1.12	0.79	2.82	0.48	0.36	0.61	0.94
4m6n	4.57	0.31	0.66	0.66	3.81	0.66	1.27	0.88	1.57
4nyl	3.47	0.54	1.02	0.76	4.36	0.77	0.98	0.77	0.82
4od2	5.18	0.69	0.88	0.60	8.60	0.63	0.74	0.96	1.72
4ojf	4.80	0.45	1.05	1.22	4.98	0.48	0.27	1.12	0.73
4qxg	3.26	0.54	0.97	0.79	1.76	0.44	0.39	0.48	2.14
4x7s	5.23	0.62	1.52	3.26	2.46	0.57	0.60	0.60	0.60
4ypg	2.84	0.47	1.18	1.20	4.51	0.34	0.54	0.63	1.23
5csz	5.96	0.59	0.71	1.32	2.69	0.39	0.75	0.38	1.31
5dk3	1.27	0.56	2.54	0.73	0.94	0.34	0.85	0.52	0.33
5ggq	1.15	0.46	0.89	0.75	2.17	0.46	1.93	0.89	0.38
5ggu	6.62	0.97	1.20	1.00	8.20	0.43	0.43	0.81	0.61
5i5k	8.32	1.10	0.92	0.96	5.21	0.89	0.99	0.74	1.57
5jxe	3.75	0.50	3.68	1.66	5.74	0.68	1.23	0.68	0.73
5kmv	11.64	0.60	1.57	0.87	1.28	0.48	0.86	1.07	0.53
5l6y	11.90	0.36	0.72	0.97	12.57	0.50	0.58	0.82	1.87
5n2k	4.14	0.47	0.78	0.49	3.91	0.62	1.08	1.01	6.54
5nhw	3.48	0.46	2.54	0.68	1.24	0.68	0.81	0.82	5.18
5sx4	7.47	1.09	1.32	1.03	1.42	1.13	1.58	0.89	10.26
5tru	4.89	0.46	0.70	0.51	3.24	0.36	1.84	0.59	1.55
5vh3	2.71	0.51	1.41	0.70	3.10	0.56	0.70	0.76	0.40
5wuv	2.54	0.42	0.90	0.74	3.70	0.38	0.46	0.48	1.19
5xxy	3.82	0.55	1.46	2.02	2.63	0.55	1.19	0.49	0.53
5y9k	7.84	0.76	2.97	1.20	7.23	0.70	1.12	1.68	1.63
6and	6.16	0.44	1.62	0.79	2.69	0.53	1.07	0.91	0.67
Mean	5.43	0.63	1.42	1.05	3.77	0.55	0.89	0.83	1.48
SD	3.32	0.25	0.83	0.52	2.53	0.15	0.41	0.24	1.76

Table S5. CDR loop RMSD and OCD results for RepertoireBuilder on RosettaAntibody benchmark.

Target	OCD	H Fr (Å)	H1 (Å)	H2 (Å)	H3 (Å)	L Fr (Å)	L1 (Å)	L2 (Å)	L3 (Å)
1dlf	10.60	0.86	0.84	1.02	2.93	0.60	0.39	0.51	0.40
1fns	5.37	0.51	0.54	1.45	3.99	0.55	0.53	0.24	0.42
1gig	5.07	0.60	0.58	0.85	3.11	0.40	0.59	1.09	0.93
1jfq	3.60	0.65	0.51	1.15	1.88	0.34	0.36	0.41	0.28
1jpt	1.47	0.51	0.37	0.72	0.53	0.40	0.59	0.55	0.38
1mfa	7.63	0.61	0.52	0.82	0.41	0.45	0.70	0.56	0.49
1mlb	4.94	0.58	0.52	1.68	0.65	0.57	0.56	0.90	0.60
1mqk	4.48	0.34	0.53	0.83	1.92	0.46	0.55	0.50	2.04
1nlb	9.29	0.46	0.72	0.50	1.79	0.66	0.44	0.49	0.72
1oaq	5.63	0.55	0.50	0.58	2.14	0.50	0.58	0.63	1.02
1seq	7.46	0.62	0.65	0.72	3.71	0.37	0.66	0.35	0.86
2adf	4.67	0.31	0.60	0.86	2.51	0.34	0.46	0.49	0.32
2d7t	8.09	0.71	1.13	0.65	3.73	0.54	0.76	0.42	1.06
2e27	8.15	0.66	0.63	0.51	4.62	0.48	0.36	0.52	2.40
2fb4	1.45	0.43	0.43	0.64	5.29	0.98	0.79	0.50	1.45
2fbj	7.51	0.51	0.94	0.87	2.37	0.38	1.16	0.87	2.10
2r8s	1.50	0.50	0.88	1.86	2.50	0.45	0.88	0.62	1.04
2v17	9.98	0.42	0.50	1.20	2.34	0.78	1.03	0.62	0.65
2vxv	1.91	0.22	0.72	0.74	3.92	0.53	0.39	0.92	2.62
2w60	4.14	0.48	0.74	0.50	2.46	0.42	0.69	0.25	0.63
2xwt	8.67	0.39	1.43	0.44	3.63	0.53	0.36	0.87	1.51
2ypv	6.75	1.04	0.74	0.92	3.88	0.69	0.91	0.39	0.70
3e8u	4.91	0.73	0.50	0.66	1.54	0.42	0.65	0.45	0.68
3eo9	5.64	0.39	0.87	0.58	3.39	0.48	0.50	0.52	0.70
3g5y	7.72	0.60	0.48	0.36	1.04	0.67	0.48	0.43	0.47
3giz	4.82	0.67	0.80	0.56	2.58	0.48	0.47	0.57	0.55
3gnm	3.65	0.76	0.58	0.99	1.41	0.47	0.70	0.27	0.71
3go1	3.17	0.43	2.23	0.95	3.48	0.65	1.05	0.95	3.52
3hc4	3.15	1.05	0.46	1.13	0.92	0.53	0.52	0.37	0.20
3hnt	4.28	0.59	0.65	0.84	1.68	0.59	0.40	0.93	1.87
3i9g	2.80	0.29	0.50	0.55	3.85	0.57	0.64	0.46	1.00
3liz	5.59	0.29	0.73	0.50	4.43	0.69	0.33	0.36	0.40
3lmj	2.61	0.99	3.21	7.12	6.56	0.45	0.49	0.43	2.40
3m8o	11.24	0.65	1.92	1.15	7.45	0.79	1.64	0.44	0.67
3mlr	5.69	0.52	0.25	1.27	5.60	0.59	0.82	0.47	-
3mxw	4.49	0.92	0.80	1.30	1.94	0.30	0.39	0.38	0.66
3nps	4.87	0.73	2.83	0.92	4.31	0.68	1.24	0.50	1.45
3oz9	4.49	0.62	0.52	1.70	2.98	0.54	0.62	0.24	1.76
3p0y	6.18	0.52	1.15	1.60	3.11	0.38	0.58	0.25	1.40
3t65	3.02	0.42	0.27	0.66	0.43	0.36	0.75	1.04	0.40
3umt	8.31	0.74	1.22	0.59	3.47	0.44	0.52	0.27	0.42
3v0w	4.86	0.49	0.80	0.67	2.12	0.46	0.60	0.51	0.79
4f57	3.20	0.28	0.45	0.76	0.57	0.22	0.44	0.21	0.50
4h0h	5.21	0.64	0.51	0.68	3.01	0.62	0.36	0.38	0.36
4h20	3.30	0.79	0.51	0.50	4.45	0.33	0.67	0.73	1.51
4hpy	2.38	0.64	2.61	0.56	2.45	0.30	0.50	0.35	1.42
4nzu	3.24	0.59	0.65	1.03	5.11	0.49	0.49	0.41	0.91
Mean	5.26	0.58	0.86	1.00	2.94	0.51	0.63	0.52	1.03
SD	2.46	0.20	0.65	0.98	1.59	0.15	0.26	0.23	0.73

Table S6. CDR loop RMSD and OCD results for RepertoireBuilder on therapeutic benchmark.

Target	OCD	H Fr (Å)	H1 (Å)	H2 (Å)	H3 (Å)	L Fr (Å)	L1 (Å)	L2 (Å)	L3 (Å)
1bey	2.80	0.54	1.49	0.91	3.96	0.68	0.91	0.70	0.61
1cz8	0.59	0.26	0.82	0.75	3.66	0.39	0.35	0.36	0.42
1mim	3.42	0.56	0.64	0.92	0.63	0.38	0.83	0.62	1.14
1sy6	3.71	0.71	0.99	1.04	3.17	0.41	0.26	0.48	0.37
1yy8	6.38	0.61	0.54	0.55	4.21	0.35	0.45	0.52	0.91
2hwz	4.98	0.28	0.89	1.31	2.33	0.44	0.90	0.59	2.27
3eo0	3.96	0.34	3.13	1.15	4.38	0.30	1.43	0.30	0.74
3gkw	15.79	1.40	2.74	1.62	9.66	0.56	1.64	0.67	0.60
3nfs	2.53	0.57	0.60	0.69	1.91	0.54	0.56	0.61	0.60
3o2d	10.03	0.93	0.71	0.97	2.75	0.46	0.47	0.30	0.43
3pp3	4.02	0.29	0.46	1.17	3.36	0.64	0.62	0.59	0.81
3qwo	3.14	0.36	0.34	1.34	2.77	0.38	0.76	0.54	0.66
3u0t	10.10	0.67	1.62	0.91	2.29	0.50	1.05	0.47	0.93
4cni	1.46	0.60	0.89	1.26	1.28	0.63	0.51	0.52	0.59
4dn3	2.36	0.49	1.54	0.93	1.74	0.33	1.36	0.52	1.44
4g5z	6.55	0.49	0.84	0.57	1.51	0.61	0.40	0.69	0.68
4g6k	2.36	0.62	0.51	1.22	2.95	0.67	0.57	0.46	0.93
4hkz	2.29	0.26	0.42	0.83	2.98	0.37	0.38	0.48	0.61
4i77	5.19	0.29	1.22	0.87	3.39	0.40	0.49	0.48	0.68
4irz	3.99	0.99	1.26	0.60	3.98	0.46	0.71	0.40	1.55
4kaq	4.21	0.75	0.47	0.89	2.79	0.70	0.80	0.57	0.80
4m6n	4.11	0.31	0.76	0.36	2.51	0.34	1.88	0.35	1.65
4nyl	7.73	0.74	0.45	0.67	5.12	0.71	0.63	0.69	1.05
4od2	0.89	0.63	0.49	0.76	6.49	0.51	1.11	1.25	2.14
4ojf	6.62	0.76	0.59	1.32	3.84	0.39	0.58	0.40	0.57
4qxg	0.82	0.42	0.45	0.76	2.06	0.47	0.52	0.66	1.81
4x7s	6.16	0.77	1.72	1.18	2.71	0.45	0.45	0.28	0.69
4ypg	4.22	1.05	1.15	1.09	2.87	0.49	0.33	0.93	0.82
5csz	2.55	0.56	0.74	0.66	2.67	0.26	0.50	0.33	1.43
5dk3	5.32	0.80	0.61	1.20	2.80	0.49	0.46	0.70	0.40
5ggq	1.88	0.64	0.47	0.73	0.55	0.51	0.36	0.63	0.51
5ggu	4.40	0.38	0.52	0.48	6.34	0.51	0.49	0.35	0.92
5i5k	3.29	1.16	0.62	1.03	4.87	0.90	0.87	0.61	1.10
5jxe	3.76	0.79	0.57	1.50	2.86	0.66	0.54	0.61	0.62
5kmv	3.52	0.35	0.66	0.54	0.56	0.22	0.44	0.37	0.40
5l6y	1.88	0.96	0.91	0.63	5.61	0.32	0.31	0.53	1.99
5n2k	1.65	0.62	0.94	0.88	3.28	0.48	0.69	0.21	4.27
5nhw	3.38	0.99	0.66	0.84	1.22	0.27	1.08	0.21	4.76
5sx4	7.62	1.29	0.94	1.40	2.49	0.46	0.61	0.62	0.79
5tru	1.95	0.36	0.32	0.98	2.32	0.33	1.72	0.33	0.96
5vh3	4.22	0.27	0.60	0.63	1.62	0.56	0.48	0.58	0.70
5wuv	1.98	0.63	0.88	0.78	3.00	0.38	0.23	0.34	0.41
5xxy	4.89	0.51	0.66	2.10	2.37	0.46	1.07	0.62	0.43
5y9k	7.48	0.59	2.79	0.74	4.13	0.34	0.32	0.35	1.90
6and	6.29	0.45	0.52	1.48	2.80	0.47	0.95	0.37	0.41
Mean	4.37	0.62	0.91	0.96	3.13	0.47	0.71	0.52	1.08
SD	2.85	0.28	0.63	0.35	1.68	0.14	0.40	0.19	0.90

Table S7. CDR loop RMSD and OCD results for ABodyBuilder on RosettaAntibody benchmark.

Target	OCD	H Fr (Å)	H1 (Å)	H2 (Å)	H3 (Å)	L Fr (Å)	L1 (Å)	L2 (Å)	L3 (Å)
1dlf	8.05	0.66	0.93	0.47	4.19	0.63	1.10	0.49	0.80
1fns	3.07	0.38	0.52	0.52	5.44	0.55	0.83	0.42	0.84
1gig	11.80	0.54	0.99	0.62	4.02	0.44	0.55	1.09	0.54
1jfq	5.43	0.64	0.53	1.17	1.25	0.49	0.24	0.23	0.27
1jpt	3.00	0.60	0.76	1.32	1.28	0.40	1.05	0.50	0.69
1mfa	2.28	0.42	0.38	0.38	0.17	0.23	0.70	0.23	0.37
1mlb	4.00	0.57	0.72	1.01	0.84	0.41	0.47	0.65	0.56
1mqk	4.24	0.37	0.43	0.44	2.37	0.42	1.02	0.42	2.13
1nlb	3.54	0.31	0.50	0.31	2.42	0.42	1.05	0.21	0.88
1oaq	3.29	0.62	0.54	0.66	1.83	0.42	0.55	0.51	1.27
1seq	9.24	0.33	0.55	1.02	5.12	0.32	0.80	0.26	1.17
2adf	4.38	0.21	0.73	0.74	2.07	0.54	0.60	0.33	0.53
2d7t	13.72	0.76	0.69	0.82	2.88	0.48	0.73	0.37	1.26
2e27	4.52	0.31	0.49	0.42	4.56	0.64	0.38	0.61	2.37
2fb4	2.92	0.51	0.50	0.46	5.63	0.77	0.92	0.49	1.31
2fbj	6.53	0.40	0.43	0.53	1.99	0.49	1.18	0.92	2.24
2r8s	1.63	0.70	4.01	2.25	6.93	0.45	0.42	0.62	0.58
2v17	3.25	0.46	0.49	1.20	2.66	0.72	0.89	0.60	0.91
2vxv	1.52	0.25	0.79	0.71	4.68	0.54	0.59	0.91	3.48
2w60	10.18	0.30	0.46	0.65	2.49	0.60	0.57	0.66	0.35
2xwt	8.91	0.54	1.21	0.60	3.51	0.34	0.40	0.90	0.82
2ypv	5.96	0.51	0.86	0.90	2.67	0.61	0.33	0.28	0.78
3e8u	1.81	0.56	0.58	0.98	2.24	0.31	0.53	0.50	0.40
3eo9	5.51	0.42	0.57	1.51	3.04	0.54	0.57	0.59	1.49
3g5y	4.70	0.24	0.39	0.38	0.94	0.71	0.28	0.49	0.60
3giz	2.92	0.40	0.38	0.51	2.94	0.52	0.55	0.53	0.56
3gnm	5.54	0.57	0.69	0.46	2.17	0.33	0.67	0.24	0.75
3go1	6.19	0.53	1.45	0.87	3.23	0.65	1.74	0.90	3.59
3hc4	5.45	1.13	2.54	1.38	3.59	0.32	0.53	0.35	0.65
3hnt	2.20	0.58	0.29	0.49	2.27	0.56	0.69	1.09	1.29
3i9g	1.47	0.25	0.58	0.90	3.32	0.38	0.83	0.44	0.55
3liz	2.68	0.48	0.65	0.54	4.38	0.61	0.37	0.27	0.72
3lmj	4.17	0.50	3.10	2.78	4.88	0.60	0.59	0.81	1.02
3m8o	3.18	0.93	2.31	0.86	5.67	0.74	3.00	0.56	2.19
3mlr	3.98	0.51	0.80	1.24	4.93	0.54	0.75	0.74	-
3mxw	2.70	0.92	2.07	1.26	2.74	0.57	0.61	0.55	0.97
3nps	2.86	0.86	3.35	1.71	5.10	0.58	1.01	0.45	1.77
3oz9	6.12	0.49	0.63	0.55	2.63	0.68	0.75	0.69	2.52
3p0y	4.34	0.40	0.91	1.76	2.57	0.35	0.46	0.22	1.58
3t65	1.47	0.23	0.26	0.32	0.26	0.37	0.50	0.41	0.33
3umt	4.64	0.44	0.82	0.92	2.67	0.47	0.95	0.51	0.43
3v0w	5.99	0.43	0.83	0.83	1.53	0.26	0.36	0.25	0.38
4f57	3.85	0.28	0.40	0.78	0.60	0.22	0.52	0.21	0.50
4h0h	5.76	0.80	0.50	1.18	1.47	0.66	0.64	0.74	0.46
4h20	5.12	0.64	1.76	0.42	2.73	0.52	0.44	0.38	0.94
4hpy	2.87	0.30	2.80	0.61	0.62	0.39	0.55	0.36	1.28
4nzu	3.43	0.27	0.51	0.72	2.53	0.46	0.36	0.42	0.85
Mean	4.69	0.50	0.99	0.88	2.94	0.49	0.72	0.52	1.09
SD	2.66	0.20	0.88	0.51	1.58	0.14	0.44	0.23	0.79

Table S8. CDR loop RMSD and OCD results for ABodyBuilder on therapeutic benchmark.

Target	OCD	H Fr (Å)	H1 (Å)	H2 (Å)	H3 (Å)	L Fr (Å)	L1 (Å)	L2 (Å)	L3 (Å)
1bey	2.81	0.56	1.07	1.31	3.37	0.66	0.75	0.82	1.08
1cz8	1.09	0.19	0.26	0.26	0.33	0.19	0.36	0.23	0.27
1mim	4.83	0.54	0.76	0.60	0.71	0.41	0.84	0.49	2.77
1sy6	2.03	0.84	0.76	0.77	7.12	0.42	0.41	0.43	0.44
1yy8	0.93	0.15	0.14	0.15	0.12	0.28	0.16	0.13	0.13
2hwz	1.31	0.27	0.67	1.31	1.77	0.47	0.79	0.61	2.20
3eo0	2.15	0.33	3.51	1.18	9.54	0.27	1.45	0.22	3.46
3gkw	20.52	1.40	3.19	4.76	7.82	0.72	1.21	0.39	0.84
3nfs	2.89	0.51	0.58	0.91	1.52	0.34	0.75	0.55	0.91
3o2d	3.42	0.39	0.66	0.55	3.88	0.49	0.80	0.38	0.94
3pp3	3.15	0.28	0.83	0.98	3.30	0.50	0.93	0.51	1.38
3qwo	1.39	0.27	0.67	1.31	1.77	0.47	0.79	0.61	2.20
3u0t	10.88	0.72	1.74	0.96	3.69	0.55	0.80	0.87	1.39
4cni	2.52	0.36	0.58	1.08	1.09	0.51	0.40	0.45	0.86
4dn3	3.15	0.48	2.52	1.94	1.93	0.48	1.34	0.47	1.63
4g5z	4.89	0.43	0.37	0.52	2.15	0.65	0.87	0.76	0.71
4g6k	7.37	0.55	2.57	1.30	1.38	0.73	0.79	0.26	1.53
4hkz	1.50	0.33	0.41	0.74	0.15	0.36	0.37	0.35	0.74
4i77	1.89	0.29	1.48	1.19	2.28	0.37	0.60	0.50	1.12
4irz	0.94	0.57	2.81	1.06	5.16	0.55	1.03	0.48	1.61
4kaq	4.46	0.94	0.33	0.94	5.19	0.41	0.50	0.42	0.67
4m6n	10.07	0.31	0.52	0.54	3.54	0.62	1.35	0.42	2.63
4nyl	5.47	0.53	0.61	0.77	4.14	0.69	0.60	0.44	0.68
4od2	2.30	0.53	0.51	0.67	5.41	0.58	1.60	1.51	2.19
4ojf	3.17	0.48	0.46	2.13	2.70	0.33	0.88	0.60	0.60
4qxg	3.87	0.41	0.66	0.71	1.64	0.46	1.81	0.77	1.31
4x7s	12.37	0.66	1.63	1.09	2.94	0.36	5.18	0.38	1.28
4ypg	2.70	0.42	0.81	0.64	4.17	0.40	3.29	0.86	0.79
5csz	2.19	0.30	0.51	0.48	3.69	0.43	1.82	0.48	0.74
5dk3	3.00	0.37	0.81	1.08	2.34	0.34	1.04	0.54	0.49
5ggq	3.80	0.40	0.43	0.65	2.40	0.41	0.33	0.28	0.92
5ggu	2.19	0.27	0.28	0.49	4.30	0.30	0.27	0.23	0.43
5i5k	7.23	1.09	1.62	2.41	2.17	0.83	1.02	0.67	1.07
5jxe	3.65	0.35	0.58	0.84	2.43	0.63	0.97	0.64	0.80
5kmv	6.28	0.62	0.89	1.08	0.71	0.38	0.77	0.54	1.30
5l6y	3.69	0.28	0.70	0.62	3.76	0.27	0.24	0.28	2.16
5n2k	2.24	0.36	0.20	0.38	2.52	0.44	0.44	0.40	5.24
5nhw	3.76	0.27	0.74	0.61	0.64	0.27	0.84	0.21	4.69
5sx4	4.30	1.25	1.70	1.11	3.88	0.35	0.30	0.71	0.51
5tru	5.56	0.34	0.52	0.47	2.07	0.28	1.68	0.41	1.26
5vh3	4.05	0.43	0.71	0.72	3.35	0.44	0.70	0.39	0.52
5wuv	4.97	0.58	1.20	1.21	4.54	0.34	0.44	0.39	0.56
5xxy	10.94	0.61	1.15	1.07	3.15	0.48	1.25	0.58	1.45
5y9k	2.39	0.56	3.11	0.76	1.18	0.39	3.46	0.55	1.62
6and	2.16	0.32	0.97	1.54	2.87	0.44	0.63	0.39	0.65
Mean	4.37	0.49	1.05	1.02	3.00	0.45	1.04	0.50	1.35
SD	3.67	0.26	0.86	0.73	1.97	0.14	0.92	0.23	1.06

Note S1. RosettaAntibody grafting command.

```
antibody.linuxgccrelease -fasta 1dlf.fasta -exclude_pdbs 1dlf 1c5c 2dlf 1wz1
1c5b
```

References

1. Warszawski, S., Borenstein Katz, A., Lipsh, R., Khmelnitsky, L., Ben Nissan, G., Javitt, G., Dym, O., Unger, T., Knop, O., Albeck, S., et al. (2019). Optimizing antibody affinity and stability by the automated design of the variable light-heavy chain interfaces. PLOS Comput. Biol. *15*, e1007207. 10.1371/journal.pcbi.1007207.