Supporting Information

Toward the Accuracy and Speed of Protein Side-Chain Packing: A Systematic Study on Rotamer Libraries

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Supporting Texts

Text S1. The EvoEF energy function.

EvoEF is a physics-based energy function designed to describe the atomic interactions in proteins for design scoring and was first implemented in our protein design protocol EvoDesign[1]. In general, it consists of five energy terms:

$$E_{EvoEF} = E_{VDW} + E_{ELEC} + E_{HB} + E_{DESOLV} - E_{REF} \quad \text{(S1)}$$

$$E_{VDW} = \sum_{i,j} w_{vdw} E_{vdw}(i,j) \quad \text{(S2)}$$

$$E_{ELEC} = \sum_{i,j} w_{elec} E_{elec}(i,j) \quad \text{(S3)}$$

$$E_{HB} = \sum_{i,j} w_{hb} E_{hb}(i,j) \quad \text{(S4)}$$

$$E_{DESOLV} = \sum_{i,j} w_{desolv} E_{desolv}(i,j) \quad \text{(S5)}$$

$$E_{REF} = \sum_{l=1}^{L} E_{ref}(aa_l) \quad \text{(S6)}$$

Here, E_{VDW}, E_{ELEC}, E_{HB}, E_{DESOLV}, and E_{REF} are the total van der Waals, electrostatic, hydrogen bonding, desolvation and reference energies for a protein. $E_{vdw}(i,j)$, $E_{elec}(i,j)$, $E_{hb}(i,j)$, and $E_{desolv}(i,j)$ are the pairwise interactions between non-bonded atoms i and j, and w_{vdw}, w_{elec}, w_{hb} and w_{desolv} are the relative weights for the corresponding energy terms. $E_{ref}(aa_l)$ is the amino acid-specific reference energy used to model the energy of an amino acid in the unfolded state, and the reference energy of a protein (E_{REF}) is assumed to be the summation of the amino acid-specific $E_{ref}(aa_l)$ values at position l across the whole protein chain with length L, where $E_{ref}(aa_l)$ is a parameter that was determined for each amino acid aa.

$E_{vdw}(i,j)$, is the van der Waals energy between atoms i and j, which was modified from the Lennard-Jones (LJ) 12-6 potential[2,3] and describes atomic packing interactions:

$$E_{vdw}(i,j) = \begin{cases} min\left\{5.0\varepsilon_{ij}, \varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{d_{ij}}\right)^{12} - 2\left(\frac{\sigma_{ij}}{d_{ij}}\right)^{6}\right]\right\}, & if\ d_{ij} < 0.8909\sigma_{ij} \\ \varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{d_{ij}}\right)^{12} - 2\left(\frac{\sigma_{ij}}{d_{ij}}\right)^{6}\right], & if\ 0.8909\sigma_{ij} \le d_{ij} < 5.0 \\ A * d_{ij}^3 + B * d_{ij}^2 + C * d_{ij} + D, & if\ 5.0 \le d_{ij} < 6.0 \\ 0, & if\ d_{ij} \ge 6.0 \end{cases} \quad \text{(S7)}$$

$$\begin{cases} A = -0.4\varepsilon_{ij}\left(\frac{\sigma_{ij}}{5.0}\right)^{12} - 1.6\varepsilon_{ij}\left(\frac{\sigma_{ij}}{5.0}\right)^{6} \\ B = 7.8\varepsilon_{ij}\left(\frac{\sigma_{ij}}{5.0}\right)^{12} + 25.2\varepsilon_{ij}\left(\frac{\sigma_{ij}}{5.0}\right)^{6} \\ C = -50.4\varepsilon_{ij}\left(\frac{\sigma_{ij}}{5.0}\right)^{12} + 129.6\varepsilon_{ij}\left(\frac{\sigma_{ij}}{5.0}\right)^{6} \\ D = 108\varepsilon_{ij}\left(\frac{\sigma_{ij}}{5.0}\right)^{12} + 216\varepsilon_{ij}\left(\frac{\sigma_{ij}}{5.0}\right)^{6} \end{cases} \quad (S8)$$

where d_{ij} is the distance between the two atoms i and j, $\sigma_{ij} = \sigma_i + \sigma_j$ is the sum of their van der Waals atomic radii and ε_{ij} is the combined well-depth for atoms i and j, which is taken from the CHARMM19 force field[4]. The attractive and repulsive components of the van der Waals energy are split at $\mathrm{d}_{ij} = 0.8909\sigma_{ij}$. A maximum distance cutoff of 6.0 Å is set to increase the computational efficiency of EvoEF, and a cubic function is used to continuously connect the LJ energy from its value at 5.0 Å to zero at the cutoff distance (6.0 Å). For the repulsive component of the LJ potential, the maximum energy cutoff is set to $5.0\varepsilon_{ij}$, which helps alleviate possible clashes, while not overly penalizing them due to the discrete rotameric conformations used in protein design. The weights for the attractive and repulsive energies were separately determined.

$E_{elec}(i,j)$ is used to determine the electrostatic interactions between partially charged, non-bonded atoms i and j in a protein:

$$E_{elec}(i,j) = \begin{cases} \frac{C_0 q_i q_j}{\varepsilon(0.8\sigma_{ij})}\frac{1}{0.8\sigma_{ij}}, & if\ d_{ij} < 0.8\sigma_{ij} \\ \frac{C_0 q_i q_j}{\varepsilon(d_{ij})}\frac{1}{d_{ij}}, & if\ 0.8\sigma_{ij} < d_{ij} < 6.0 \\ 0, & if\ d_{ij} \geq 6.0 \end{cases} \quad (S9)$$

where q_i and q_j are the CHARMM19 atomic charges[4]. Furthermore, $C_0 = 332$ Å kcal mol$^{-1}e^{-2}$, where e is the elementary charge, and $\varepsilon(d_{ij})$ is the distance-dependent dielectric constant, defined as $\varepsilon(d_{ij}) = 40d_{ij}$. The distance d_{ij} is set to $0.8\,\sigma_{ij}$ if d_{ij} is less than $0.8\,\sigma_{ij}$ when calculating the electrostatics term and dielectric constant. This avoids an infinite electrostatic energy value when d_{ij} is close to zero. Again, for the sake of computational efficiency, the electrostatics energy is set to zero if d_{ij} is beyond the maximum distance cutoff of 6.0 Å.

$E_{hb}(i,j)$ is used to calculate the hydrogen-bonding interactions between potential hydrogen bond donor/acceptor pairs for atoms i and j, one of which should be a polar hydrogen. $E_{hb}(i,j)$ is a linear combination of three energy terms that depend on the hydrogen-acceptor distance (d_{ij}^{HA}), the angle between the donor atom, hydrogen and acceptor (θ_{ij}^{DHA}), and the angle between the hydrogen, acceptor and base atom (φ_{ij}^{HAB}):

$$E_{hb}(i,j) = w_{d_{HA}}E\left(d_{ij}^{HA}\right) + w_{\theta_{DHA}}E\left(\theta_{ij}^{DHA}\right) + w_{\varphi_{HAB}}E\left(\varphi_{ij}^{HAB}\right) \quad (S10)$$

where:

$$\begin{cases} E\left(d_{ij}^{HA}\right) = \begin{cases} -cos\left[\frac{\pi}{2}\left(d_{ij}^{HA} - 1.9\right)/(1.9 - d_{min})\right], d_{min} \le d_{HA} \le 1.9 \\ -0.5\,cos\left[\pi\left(d_{ij}^{HA} - 1.9\right)/(d_{max} - 1.9)\right] - 0.5, \;\; 1.9\text{ Å} < \; d_{HA} \le \; d_{max} \\ 0 \qquad\qquad\qquad\qquad , \quad otherwise \end{cases} \\ E\left(\theta_{ij}^{DHA}\right) = -cos^4\left(\theta_{ij}^{DHA}\right),\ \theta_{ij}^{DHA} \ge 90° \\ E\left(\varphi_{ij}^{HAB}\right) = \begin{cases} -cos^4\left(\varphi_{ij}^{HAB} - 150°\right), \varphi_{ij}^{HAB} \ge 80° \quad for\ BBHB\ \ and\ for\ sp^2\ in\ SBHB\ or\ SSHB \\ -cos^4\left(\varphi_{ij}^{HAB} - 135°\right), \varphi_{ij}^{HAB} \ge 80° \quad for\ sp^3\ in\ SBHB\ or\ SSHB \end{cases} \end{cases} \tag{S11}$$

The optimal distance between the hydrogen and its acceptor is set to 1.9 Å, which was taken from Kortemme *et al.*[5]. Additionally, $d_{min} = 1.4$ Å and $d_{max} = 3.0$ Å are the lower and upper bounds on the distance between the hydrogen-acceptor pair. The optimal φ_{ij}^{HAB} value is set to either 150 °or 135 °, depending on the acceptor hybridization (sp^2 or sp^3) and the locations of the donor and acceptor atoms (BBHB: Backbone-Backbone Hydrogen Bond; SBHB: Sidechain-Backbone Hydrogen Bond; SSHB: Sidechain-Sidechain Hydrogen Bond).

$E_{desolv}(i,j)$ is used to describe the desolvation energy using the pairwise gaussian volume-excluded implicit solvation model developed by Lazaridis and Karplus[6]. The pairwise $E_{desolv}(i,j)$ is calculated as the sum of the desolvation energies for atom i desolvating j ($f_{desov}(i,j)$) and for j desolvating i ($f_{desov}(j,i)$), as shown in Eq. S12:

$$E_{desolv}(i,j) = f_{desov}(i,j) + f_{desov}(j,i) \tag{S12}$$

$$f_{desolv}(i,j) = -V_j \frac{\Delta G_i^{free}}{2\pi^{\frac{3}{2}}\lambda_i d_{ij}^2} \exp\left[-\left(\frac{d_{ij} - \sigma_i}{\lambda_i}\right)^2\right] \tag{S13}$$

$$f_{desolv}(j,i) = -V_i \frac{\Delta G_j^{free}}{2\pi^{\frac{3}{2}}\lambda_j d_{ij}^2} \exp\left[-\left(\frac{d_{ij} - \sigma_j}{\lambda_j}\right)^2\right] \tag{S14}$$

where $V_{i,j}$, $\Delta G_{i,j}^{free}$, and $\lambda_{i,j}$ are the volumes, reference solvation energies, and correlation lengths for atoms i and j, respectively. All types of carbon and sulfur atoms are considered as nonpolar, while oxygen and nitrogen atoms are polar. The desolvation energy for hydrogen atoms is ignored in the Larzaridis-Karplus model, while the desolvation energy for other polar and nonpolar atoms are separately calculated and weighted. Specifically, $E_{DESOLV} = \sum w_{desolvPolar} f_{desolvPolar} + \sum w_{desolvNonP} f_{desolvNonP}$.

Supporting Tables

Table S1. Summary of the EvoEF2 energy weights for BBDRLs and BBIRLs.

Classification	Energy terms	BBDRL	BBIRL
Intra-residue interactions	Van der Waals attractive	0.43	0.00
	Van der Waals repulsive	0.06	0.55
	Coulomb's electrostatics	0.29	0.96
	desolvP	0.00	0.08
	desolvH	0.34	0.06
	HBsb_dist	0.83	0.00
	HBsb_theta	0.28	1.01
	HBsb_phi	0.00	0.00
	Amino_acid_propensity	0.59	0.63
	Ramachandran	0.42	0.48
	DunbrackRot	0.35	0.00
Inter-residue interactions in the same chain	Van der Waals attractive	1.21	1.34
	Van der Waals repulsive	1.28	1.43
	Coulomb's electrostatics	2.31	1.95
	desolvP	0.75	0.94
	desolvH	4.59	4.00
	SSbond	2.72	3.88
	HBbb_dist	1.02	1.05
	HBbb_theta	1.01	1.02
	HBbb_phi	1.07	1.08
	HBsb_dist	0.85	0.48
	HBsb_theta	0.91	1.18
	HBsb_phi	0.17	0.39
	HBss_dist	1.19	1.00
	HBss_theta	0.71	0.89
	HBss_phi	0.00	0.00
Inter-residue interactions in different chains	Van der Waals attractive	1.06	1.49
	Van der Waals repulsive	0.80	1.14
	Coulomb's electrostatics	2.44	1.92
	desolvP	0.68	1.30
	desolvH	4.79	3.90
	SSbond	1.07	1.11
	HBbb_dist	1.01	1.00
	HBbb_theta	1.01	1.00
	HBbb_phi	1.02	1.01
	HBsb_dist	0.94	1.23
	HBsb_theta	0.70	0.94
	HBsb_phi	0.32	0.09
	HBss_dist	0.94	1.15
	HBss_theta	0.97	0.62
	HBss_phi	0.00	0.00

Table S2. Summary of the EvoEF2 reference energies for BBDRLs and BBIRLs.

Amino acid	BBDRL	BBIRL
ALA	-0.408	-1.094
CYS	-0.111	-0.671
ASP	-0.802	-1.256
GLU	-1.225	-0.519
PHE	0.679	1.217
GLY	-2.093	-2.397
HIS	-0.295	0.504
ILE	2.330	1.283
LYS	-1.250	-1.043
LEU	1.613	1.129
MET	0.759	1.347
ASN	-2.155	-1.937
PRO	-0.647	-0.754
GLN	-1.936	-1.131
ARG	-1.322	-1.279
SER	-1.978	-2.300
THR	-0.416	-1.501
VAL	1.700	0.435
TRP	2.004	2.363
TYR	0.700	0.986

Table S3. Sequence identities between the native and designed sequences using libraries L1-L6.

PDB ID	Sequence identity (%)					
	L1	L2	L3	L4	L5	L6
1AGY	40.1	34.5	40.6	26.9	27.4	32.0
1AKY	33.0	33.5	28.0	24.8	26.1	28.0
1AMM	29.9	31.0	27.6	20.7	28.7	27.0
1AQB	28.6	24.6	29.1	22.3	22.3	22.9
1BDO	41.3	38.8	42.5	31.3	30.0	30.0
1BK7	33.2	33.2	30.5	21.1	23.2	24.2
1BKF	38.3	39.3	42.1	32.7	37.4	32.7
1C3D	35.4	33.7	33.0	23.8	28.2	29.9
1CKA	29.8	28.1	26.3	22.8	22.8	26.3
1CTF	32.4	33.8	42.6	26.5	38.2	20.6
1CTJ	41.6	36.0	33.7	25.8	31.5	37.1
1CYO	35.2	35.2	35.2	25.0	30.7	29.5
1DAD	39.3	30.8	35.7	25.4	23.2	26.8
1EW4	32.1	34.9	33.0	27.4	29.2	31.1
1FNC	26.0	27.7	29.4	22.0	22.3	23.3
1HFC	36.9	40.8	35.7	32.5	27.4	32.5
1IC6	43.7	40.5	41.2	33.7	33.3	29.7
1IFC	29.0	28.2	30.5	27.5	28.2	29.8
1IGD	36.1	29.5	24.6	31.1	31.1	24.6
1JBC	35.0	32.9	33.3	31.6	31.6	27.8
1KF5	30.6	33.9	29.0	20.2	24.2	21.0
1KNB	37.6	36.0	34.4	26.9	33.9	25.8
1KUH	39.4	37.9	34.8	31.8	34.8	30.3
1LTU	29.1	29.5	29.1	22.2	24.4	22.2
1MC2	23.0	23.0	24.6	22.1	23.8	23.0
1MD6	37.0	33.8	35.7	21.4	29.9	31.8
1NOA	39.8	39.8	32.7	26.5	32.7	31.9
1NWA	38.9	38.3	37.1	31.1	34.1	36.5
1O8X	28.7	31.5	27.3	22.4	21.0	20.3
1OPD	37.6	40.0	47.1	25.9	32.9	36.5
1P3C	39.5	31.6	34.9	32.1	25.6	32.1
1PGV	28.7	38.3	29.9	28.1	25.7	19.2
1PLC	43.4	40.4	43.4	32.3	33.3	38.4
1PPN	36.3	32.1	36.3	29.7	34.4	32.5
1PS4	36.5	39.2	43.9	32.8	28.6	33.9
1R12	32.7	32.7	28.3	25.1	26.3	27.1
1RA9	23.3	29.6	25.2	26.4	29.6	20.1
1RCF	34.3	31.4	30.8	25.4	26.0	27.8
1RRO	30.6	42.6	36.1	35.2	29.6	26.9
1RWZ	35.2	30.7	34.0	25.8	24.2	27.9

1SAU	42.1	42.1	43.0	36.8	36.0	27.2
1SEN	38.1	41.8	36.6	29.9	35.1	29.9
1SMX	44.8	40.2	42.5	29.9	35.6	35.6
1SNC	28.1	28.1	26.7	28.1	28.1	28.1
1T2I	37.5	36.5	36.5	29.2	31.3	30.2
1T3Y	26.7	34.4	30.5	16.8	19.8	21.4
1THV	37.2	41.5	39.1	35.7	30.9	31.9
1TTA	39.4	33.1	33.9	28.3	25.2	24.4
1UAI	35.0	34.5	32.3	27.4	28.3	24.7
1V05	41.9	37.6	41.9	38.7	40.9	37.6
1V7Q	39.1	38.5	35.5	29.0	32.5	28.4
1V8E	45.6	38.2	39.6	28.1	32.7	30.4
1VIE	33.3	33.3	28.3	23.3	31.7	36.7
1WC2	32.2	35.0	31.1	30.6	32.2	26.7
1WHI	45.1	43.4	43.4	38.5	37.7	37.7
1X1E	41.4	39.3	39.7	31.4	34.3	31.0
1X6X	35.3	30.3	28.6	27.7	28.6	26.9
1YCK	29.3	30.5	26.9	24.6	24.0	22.8
1YHH	33.2	31.0	31.0	26.2	31.4	27.1
1YU5	28.4	25.4	31.3	25.4	34.3	26.9
1YW5	36.2	32.2	28.8	25.4	29.9	27.1
1Z2U	32.7	32.7	34.7	29.9	30.6	29.9
1ZEQ	32.5	27.3	40.3	27.3	29.9	26.0
1ZZK	36.3	33.8	37.5	27.5	33.8	21.3
2A8F	25.5	27.6	25.5	22.4	25.5	21.4
2AYH	35.0	36.0	36.9	28.5	28.0	32.2
2B0A	36.6	35.5	32.3	26.9	36.0	31.2
2BK8	35.1	39.2	32.0	18.6	28.9	23.7
2BOP	24.7	28.2	30.6	18.8	23.5	27.1
2BV9	34.9	35.6	31.3	23.9	27.5	25.7
2CBA	38.0	39.9	35.3	26.0	25.6	27.5
2CG7	36.7	33.3	32.2	27.8	34.4	32.2
2CPL	39.6	36.0	43.3	28.0	31.7	29.9
2CWR	45.4	37.1	38.1	34.0	36.1	36.1
2D4P	40.2	37.6	46.2	34.2	30.8	30.8
2DFB	36.0	33.3	41.3	35.4	32.3	37.0
2DRI	36.2	33.2	38.4	29.2	29.9	35.4
2E8F	22.0	19.0	20.0	22.0	20.0	14.0
2E8G	36.7	35.0	34.2	26.3	32.9	28.8
2END	29.9	34.3	36.5	32.8	28.5	31.4
2FBQ	25.8	27.7	26.3	23.0	19.2	21.1
2FI1	34.8	38.0	32.6	21.9	30.5	21.4
2FI9	47.5	46.6	40.7	33.9	33.9	29.7
2FJ8	31.7	35.8	23.3	30.8	32.5	31.7
2FJZ	25.4	32.2	28.8	11.9	23.7	20.3

2FL4	22.4	26.9	23.1	19.4	20.9	19.4
2FQ3	23.5	27.1	23.5	23.5	27.1	25.9
2FRG	31.1	34.9	35.8	21.7	32.1	23.6
2G69	34.3	44.4	35.4	27.3	30.3	21.2
2H2R	28.1	30.4	31.1	28.9	23.7	24.4
2I24	23.0	26.5	29.2	26.5	29.2	23.0
2I3F	33.0	30.6	32.0	28.2	27.7	25.2
2I4A	29.9	32.7	32.7	29.9	30.8	23.4
2I6V	27.6	25.3	34.5	24.1	28.7	26.4
2IBL	24.1	18.5	28.7	20.4	17.6	20.4
2IGD	37.7	31.1	34.4	31.1	31.1	29.5
2JEK	34.3	37.1	40.7	30.7	34.3	32.1
2MHR	27.1	26.3	29.7	16.9	22.9	13.6
2NR7	35.1	35.6	34.6	20.9	26.7	24.6
2NWD	36.9	42.3	38.5	33.8	20.8	27.7
2OEB	30.3	32.2	25.7	24.3	30.9	23.0
2OHW	35.2	39.8	35.2	25.0	30.5	34.4
2OL7	38.4	35.2	31.2	31.2	31.6	26.0
2OSA	33.7	32.1	30.6	21.9	21.9	19.4
2OSS	38.6	35.4	33.9	29.9	22.0	26.8
2OVO	39.3	41.1	33.9	21.4	14.3	21.4
2PBP	30.6	34.5	30.6	25.5	25.9	21.2
2PET	33.3	32.5	35.1	26.4	27.7	29.4
2PHY	36.0	32.8	33.6	25.6	23.2	25.6
2PMR	21.1	22.4	23.7	27.6	21.1	25.0
2PND	25.2	21.8	37.0	29.4	31.9	28.6
2PPP	43.0	43.9	39.3	35.5	35.5	32.7
2QSK	43.2	44.2	42.1	33.7	34.7	36.8
2RIK	30.2	35.6	29.2	31.0	26.0	25.6
2RN2	27.7	24.5	31.6	20.6	21.9	26.5
2TGI	26.8	26.8	25.9	25.9	22.3	23.2
2VC8	27.8	33.3	30.6	23.6	26.4	33.3
2VQ4	34.9	33.0	31.1	29.2	37.7	30.2
2VWR	32.3	29.0	39.8	36.6	28.0	38.7
2WWE	35.6	35.6	31.7	14.4	24.0	26.0
2YXF	30.3	33.3	33.3	27.3	26.3	20.2
2Z37	38.1	36.1	34.0	29.5	29.9	31.6
2ZIB	23.8	21.5	16.2	20.8	26.9	25.4
3BN6	38.0	38.0	35.4	30.4	32.9	27.8
3CHY	32.8	35.9	35.2	30.5	38.3	33.6
3CO1	33.8	33.8	33.8	24.6	24.6	26.2
3EY6	39.0	39.0	37.3	35.6	34.7	31.4
3ICH	39.4	47.8	47.2	33.9	38.9	37.2
3KLR	36.8	30.4	29.6	27.2	24.0	31.2
3LZM	33.5	31.1	37.8	23.8	30.5	28.0

3Q6L	27.5	27.5	35.1	19.8	21.4	22.9
3VUB	33.7	28.7	30.7	24.8	25.7	22.8
4FGF	37.1	37.1	41.9	30.6	24.2	29.8
4LZT	33.3	39.5	38.0	27.1	32.6	28.7
4PTI	32.8	27.6	24.1	25.9	25.9	34.5
5P21	32.5	34.9	25.9	27.7	27.7	24.1

Table S4. TM-scores between the native structures and the I-TASSER models of the designed sequences using libraries L1-L6.

PDB ID	TM-score					
	L1	L2	L3	L4	L5	L6
1AGY	0.997	0.997	0.996	0.997	0.997	0.996
1AKY	0.986	0.991	0.981	0.987	0.988	0.987
1AMM	0.970	0.981	0.983	0.988	0.981	0.977
1AQB	0.992	0.991	0.994	0.991	0.989	0.987
1BDO	0.963	0.962	0.962	0.948	0.950	0.935
1BK7	0.997	0.997	0.951	0.932	0.994	0.996
1BKF	0.970	0.979	0.966	0.968	0.972	0.973
1C3D	0.972	0.968	0.958	0.940	0.982	0.988
1CKA	0.922	0.951	0.933	0.922	0.919	0.924
1CTF	0.925	0.921	0.924	0.937	0.941	0.909
1CTJ	0.983	0.990	0.984	0.985	0.992	0.989
1CYO	0.950	0.937	0.936	0.958	0.956	0.949
1DAD	0.994	0.996	0.995	0.996	0.992	0.992
1EW4	0.978	0.975	0.970	0.971	0.963	0.972
1FNC	0.992	0.991	0.990	0.992	0.991	0.990
1HFC	0.988	0.986	0.986	0.984	0.985	0.986
1IC6	0.998	0.998	0.998	0.997	0.998	0.998
1IFC	0.985	0.978	0.986	0.980	0.984	0.984
1IGD	0.922	0.941	0.873	0.949	0.941	0.943
1JBC	0.995	0.995	0.977	0.982	0.996	0.995
1KF5	0.974	0.972	0.976	0.973	0.973	0.900
1KNB	0.990	0.992	0.984	0.925	0.985	0.988
1KUH	0.994	0.992	0.994	0.991	0.992	0.990
1LTU	0.988	0.951	0.963	0.930	0.955	0.971
1MC2	0.947	0.946	0.960	0.957	0.952	0.966
1MD6	0.979	0.975	0.979	0.914	0.991	0.977
1NOA	0.946	0.931	0.947	0.945	0.946	0.955
1NWA	0.990	0.976	0.995	0.998	0.987	0.996
1O8X	0.980	0.973	0.981	0.936	0.970	0.954
1OPD	0.982	0.990	0.974	0.948	0.974	0.979
1P3C	0.997	0.997	0.999	0.998	0.998	0.998
1PGV	0.932	0.939	0.949	0.948	0.953	0.956
1PLC	0.979	0.980	0.979	0.975	0.977	0.978
1PPN	0.994	0.995	0.995	0.994	0.980	0.993
1PS4	0.988	0.990	0.987	0.990	0.986	0.962
1R12	0.997	0.997	0.997	0.975	0.997	0.989
1RA9	0.959	0.971	0.968	0.965	0.974	0.975
1RCF	0.981	0.981	0.981	0.980	0.980	0.980
1RRO	0.953	0.973	0.967	0.966	0.966	0.975
1RWZ	0.987	0.986	0.985	0.995	0.988	0.979
1SAU	0.989	0.855	0.962	0.995	0.947	0.928

1SEN	0.848	0.859	0.854	0.855	0.869	0.916
1SMX	0.890	0.893	0.884	0.867	0.867	0.879
1SNC	0.959	0.963	0.978	0.964	0.965	0.974
1T2I	0.973	0.973	0.976	0.974	0.964	0.971
1T3Y	0.960	0.950	0.951	0.935	0.956	0.953
1THV	0.991	0.993	0.993	0.992	0.978	0.992
1TTA	0.981	0.976	0.984	0.982	0.983	0.982
1UAI	0.996	0.998	0.996	0.997	0.996	0.996
1V05	0.967	0.966	0.976	0.930	0.968	0.970
1V7Q	0.976	0.980	0.990	0.974	0.986	0.987
1V8E	0.996	0.997	0.987	0.998	0.981	0.998
1VIE	0.930	0.946	0.980	0.947	0.935	0.942
1WC2	0.997	0.997	0.997	0.972	0.998	0.996
1WHI	0.977	0.979	0.980	0.974	0.973	0.965
1X1E	0.995	0.994	0.993	0.995	0.988	0.996
1X6X	0.922	0.964	0.945	0.955	0.957	0.970
1YCK	0.986	0.989	0.975	0.986	0.989	0.967
1YHH	0.986	0.989	0.981	0.987	0.986	0.989
1YU5	0.977	0.965	0.965	0.978	0.963	0.949
1YW5	0.998	0.998	0.998	0.998	0.996	0.998
1Z2U	0.936	0.956	0.953	0.959	0.956	0.947
1ZEQ	0.948	0.943	0.983	0.954	0.971	0.980
1ZZK	0.861	0.855	0.887	0.863	0.889	0.868
2A8F	0.966	0.979	0.950	0.974	0.970	0.976
2AYH	0.988	0.988	0.988	0.989	0.988	0.989
2B0A	0.996	0.997	0.996	0.998	0.994	0.954
2BK8	0.872	0.900	0.904	0.873	0.912	0.974
2BOP	0.892	0.872	0.864	0.880	0.902	0.904
2BV9	0.999	0.999	0.998	0.999	0.999	0.999
2CBA	0.995	0.995	0.995	0.994	0.995	0.994
2CG7	0.978	0.969	0.968	0.974	0.962	0.986
2CPL	0.995	0.995	0.995	0.992	0.994	0.995
2CWR	0.950	0.948	0.954	0.955	0.960	0.962
2D4P	0.987	0.982	0.984	0.993	0.973	0.992
2DFB	0.993	0.993	0.992	0.992	0.991	0.992
2DRI	0.633	0.988	0.990	0.996	0.985	0.995
2E8F	0.980	0.356	0.639	0.992	0.982	0.744
2E8G	0.999	0.999	0.999	0.999	0.999	0.999
2END	0.996	0.993	0.993	0.995	0.992	0.993
2FBQ	0.998	0.999	0.994	0.999	0.998	0.999
2FI1	0.678	0.996	0.998	0.998	0.998	0.998
2FI9	0.996	0.997	0.997	0.996	0.996	0.995
2FJ8	0.993	0.983	0.994	0.990	0.992	0.983
2FJZ	0.887	0.924	0.907	0.298	0.898	0.306
2FL4	0.931	0.993	0.943	0.992	0.997	0.960

2FQ3	0.988	0.993	0.992	0.974	0.985	0.992
2FRG	0.988	0.963	0.974	0.654	0.945	0.973
2G69	0.925	0.931	0.924	0.919	0.922	0.941
2H2R	0.797	0.802	0.851	0.820	0.766	0.814
2I24	0.943	0.914	0.936	0.903	0.946	0.949
2I3F	0.998	0.999	0.998	0.999	0.999	0.998
2I4A	0.968	0.970	0.972	0.973	0.974	0.976
2I6V	0.810	0.809	0.810	0.842	0.806	0.830
2IBL	0.868	0.445	0.681	0.636	0.503	0.636
2IGD	0.941	0.948	0.947	0.965	0.924	0.924
2JEK	0.997	0.997	0.998	0.997	0.998	0.996
2MHR	0.995	0.996	0.995	0.992	0.993	0.973
2NR7	0.997	0.985	0.971	0.996	0.810	0.996
2NWD	0.994	0.994	0.994	0.994	0.992	0.988
2OEB	0.997	0.996	0.997	0.996	0.997	0.991
2OHW	0.994	0.994	0.995	0.994	0.994	0.992
2OL7	0.895	0.897	0.875	0.871	0.899	0.877
2OSA	0.980	0.981	0.980	0.979	0.976	0.929
2OSS	0.963	0.949	0.949	0.955	0.934	0.956
2OVO	0.924	0.899	0.922	0.572	0.475	0.903
2PBP	0.962	0.974	0.956	0.962	0.949	0.957
2PET	0.993	0.997	0.997	0.993	0.997	0.997
2PHY	0.989	0.990	0.960	0.652	0.991	0.990
2PMR	0.981	0.992	0.993	0.983	0.752	0.517
2PND	0.966	0.880	0.974	0.952	0.923	0.953
2PPP	0.973	0.972	0.973	0.972	0.972	0.974
2QSK	0.984	0.968	0.982	0.365	0.356	0.361
2RIK	0.759	0.858	0.833	0.917	0.831	0.711
2RN2	0.953	0.942	0.933	0.948	0.935	0.953
2TGI	0.933	0.950	0.934	0.730	0.970	0.935
2VC8	0.967	0.977	0.985	0.721	0.951	0.975
2VQ4	0.973	0.967	0.963	0.973	0.969	0.851
2VWR	0.974	0.988	0.977	0.969	0.823	0.960
2WWE	0.994	0.979	0.993	0.928	0.989	0.985
2YXF	0.863	0.862	0.869	0.868	0.867	0.871
2Z37	0.993	0.993	0.994	0.993	0.993	0.995
2ZIB	0.974	0.941	0.956	0.993	0.906	0.984
3BN6	0.979	0.981	0.988	0.981	0.984	0.987
3CHY	0.910	0.893	0.962	0.857	0.902	0.925
3CO1	0.956	0.959	0.959	0.953	0.947	0.960
3EY6	0.956	0.951	0.936	0.963	0.951	0.956
3ICH	0.985	0.982	0.964	0.986	0.987	0.984
3KLR	0.965	0.962	0.964	0.964	0.961	0.965
3LZM	0.979	0.934	0.931	0.953	0.941	0.877
3Q6L	0.981	0.977	0.990	0.979	0.984	0.987

3VUB	0.985	0.985	0.985	0.898	0.985	0.991
4FGF	0.991	0.991	0.969	0.990	0.990	0.990
4LZT	0.960	0.977	0.975	0.980	0.982	0.976
4PTI	0.950	0.941	0.944	0.947	0.943	0.952
5P21	0.983	0.977	0.965	0.985	0.983	0.986

Table S5. RMSDs between the native structures and the I-TASSER models of the designed sequences using libraries L1-L6.

PDB ID	RMSD (Å)					
	L1	L2	L3	L4	L5	L6
1AGY	0.269	0.288	0.336	0.272	0.275	0.332
1AKY	0.666	0.523	0.794	0.661	0.611	0.657
1AMM	0.900	0.687	0.654	0.546	0.693	0.773
1AQB	0.448	0.476	0.380	0.468	0.526	0.565
1BDO	0.712	0.731	0.712	0.893	0.902	0.993
1BK7	0.297	0.300	1.533	2.001	0.398	0.339
1BKF	0.698	0.571	0.745	0.724	0.670	0.649
1C3D	1.224	1.291	1.532	1.927	0.923	0.702
1CKA	0.878	0.680	0.748	0.900	0.932	0.930
1CTF	0.866	0.900	0.886	0.797	0.776	0.973
1CTJ	0.543	0.385	0.488	0.535	0.322	0.419
1CYO	1.336	1.460	1.938	1.309	1.324	1.385
1DAD	0.457	0.376	0.400	0.347	0.552	0.512
1EW4	0.612	0.715	0.798	0.710	0.937	0.695
1FNC	0.570	0.598	0.631	0.593	0.626	0.651
1HFC	0.534	0.568	0.579	0.621	0.589	0.575
1IC6	0.302	0.305	0.266	0.383	0.252	0.310
1IFC	0.530	0.648	0.519	0.624	0.549	0.550
1IGD	0.812	0.677	2.480	0.657	0.682	0.669
1JBC	0.429	0.422	0.923	0.826	0.374	0.429
1KF5	0.749	0.779	0.687	0.762	0.733	1.959
1KNB	0.529	0.473	0.719	2.005	0.691	0.577
1KUH	0.339	0.376	0.340	0.439	0.391	0.442
1LTU	0.704	1.826	1.493	2.106	1.871	1.227
1MC2	1.099	1.116	0.937	0.983	1.061	0.873
1MD6	0.705	0.781	0.728	2.247	0.447	0.757
1NOA	1.066	1.186	1.054	1.005	1.061	1.035
1NWA	0.491	0.864	0.336	0.237	0.572	0.292
1O8X	0.725	0.868	0.689	1.365	0.899	1.160
1OPD	0.452	0.344	0.561	0.860	0.557	0.494
1P3C	0.279	0.322	0.202	0.230	0.234	0.275
1PGV	1.394	1.293	1.184	1.175	1.124	1.082
1PLC	0.546	0.532	0.551	0.608	0.582	0.561
1PPN	0.411	0.403	0.370	0.423	0.942	0.505
1PS4	0.687	0.615	0.720	0.565	0.729	1.210
1R12	0.303	0.337	0.320	1.107	0.307	0.661
1RA9	1.068	0.885	0.971	0.988	0.836	0.781
1RCF	0.878	0.886	0.912	0.892	0.889	0.915
1RRO	0.928	0.661	0.741	0.778	0.789	0.641
1RWZ	0.682	0.715	0.820	0.451	0.677	1.043
1SAU	0.429	2.659	0.824	0.272	1.083	1.318

1SEN	2.008	1.908	1.937	1.948	1.823	1.358
1SMX	1.590	1.717	1.747	2.059	1.950	1.921
1SNC	1.074	0.973	0.717	1.032	0.917	0.811
1T2I	0.611	0.615	0.572	0.601	0.748	0.639
1T3Y	0.964	1.163	1.139	1.311	1.001	1.062
1THV	0.636	0.587	0.575	0.611	0.958	0.619
1TTA	0.646	0.726	0.575	0.624	0.602	0.626
1UAI	0.339	0.269	0.336	0.327	0.337	0.338
1V05	0.702	0.661	0.560	1.103	0.649	0.641
1V7Q	0.805	0.715	0.501	0.838	0.602	0.569
1V8E	0.341	0.332	0.650	0.265	0.776	0.257
1VIE	0.890	0.700	0.402	0.944	0.762	1.134
1WC2	0.293	0.298	0.266	1.117	0.239	0.309
1WHI	0.631	0.604	0.590	0.679	0.685	0.794
1X1E	0.435	0.510	0.521	0.466	0.682	0.428
1X6X	1.428	1.081	1.256	1.170	1.141	1.050
1YCK	0.589	0.529	0.832	0.612	0.520	1.015
1YHH	0.743	0.650	0.937	0.678	0.713	0.635
1YU5	0.461	0.602	0.780	0.455	0.917	1.825
1YW5	0.237	0.248	0.242	0.228	0.298	0.245
1Z2U	1.247	1.006	1.044	0.961	0.993	1.100
1ZEQ	0.837	0.869	0.434	0.720	0.610	0.475
1ZZK	2.898	2.957	2.548	2.848	2.601	2.783
2A8F	0.691	0.535	0.882	0.607	0.648	0.577
2AYH	0.649	0.649	0.659	0.631	0.638	0.630
2B0A	0.320	0.300	0.325	0.255	0.399	1.334
2BK8	1.890	1.689	1.507	1.692	1.412	0.597
2BOP	1.609	1.871	1.796	1.829	2.275	1.461
2BV9	0.238	0.243	0.275	0.197	0.202	0.198
2CBA	0.507	0.491	0.495	0.491	0.513	0.545
2CG7	0.526	0.620	0.647	0.565	0.698	0.409
2CPL	0.339	0.344	0.338	0.447	0.378	0.357
2CWR	1.074	1.091	1.074	1.056	0.982	0.755
2D4P	0.460	0.548	0.515	0.348	0.684	0.361
2DFB	0.442	0.454	0.466	0.477	0.484	0.471
2DRI	5.496	0.676	0.612	0.379	0.761	0.423
2E8F	0.539	6.945	3.375	0.340	0.513	3.611
2E8G	0.155	0.179	0.164	0.180	0.188	0.168
2END	0.287	0.365	0.356	0.310	0.383	0.377
2FBQ	0.245	0.188	0.426	0.182	0.218	0.187
2FI1	4.785	0.315	0.240	0.207	0.254	0.218
2FI9	0.258	0.220	0.236	0.267	0.264	0.277
2FJ8	0.339	0.543	0.309	0.411	0.372	0.537
2FJZ	1.463	0.799	0.919	6.505	0.994	9.675
2FL4	1.620	0.376	1.233	0.385	0.261	0.985

2FQ3	0.372	0.286	0.299	0.585	0.410	0.297
2FRG	0.427	0.785	0.646	4.271	1.087	0.662
2G69	1.287	1.234	1.319	1.343	1.246	1.103
2H2R	3.842	3.755	2.584	3.364	4.010	3.703
2I24	1.242	1.441	1.285	2.026	1.116	1.091
2I3F	0.240	0.184	0.243	0.166	0.209	0.225
2I4A	0.738	0.692	0.671	0.655	0.643	0.618
2I6V	1.932	1.912	1.965	1.701	1.895	1.821
2IBL	1.730	5.625	4.961	3.999	6.861	3.999
2IGD	0.694	0.649	0.651	0.516	0.851	0.780
2JEK	0.243	0.239	0.199	0.226	0.213	0.273
2MHR	0.300	0.260	0.288	0.379	0.331	0.768
2NR7	0.293	0.711	1.041	0.343	9.208	0.313
2NWD	0.334	0.320	0.320	0.318	0.390	0.480
2OEB	0.260	0.296	0.274	0.288	0.245	0.446
2OHW	0.335	0.323	0.308	0.337	0.339	0.391
2OL7	2.806	2.354	2.843	2.937	2.166	2.849
2OSA	0.851	0.814	0.877	0.898	1.025	1.662
2OSS	1.007	1.372	1.409	1.092	2.046	1.288
2OVO	1.237	1.281	1.348	5.881	4.527	1.520
2PBP	1.405	1.081	1.554	1.407	1.726	1.562
2PET	0.471	0.291	0.314	0.494	0.328	0.298
2PHY	0.456	0.431	0.895	7.884	0.400	0.415
2PMR	0.449	0.282	0.267	0.407	2.103	5.955
2PND	0.804	2.224	0.690	0.946	1.355	0.962
2PPP	0.653	0.669	0.651	0.674	0.676	0.642
2QSK	0.499	0.661	0.513	8.381	8.375	8.358
2RIK	3.777	2.730	2.987	1.910	2.976	4.452
2RN2	1.520	1.635	1.797	1.585	1.656	1.453
2TGI	1.118	0.941	1.161	3.828	0.715	1.148
2VC8	0.638	0.465	0.367	2.633	0.708	0.481
2VQ4	0.686	0.749	0.852	0.693	0.710	2.489
2VWR	0.638	0.405	0.553	0.739	2.255	0.978
2WWE	0.305	0.561	0.323	1.075	0.408	0.476
2YXF	2.891	2.895	2.986	3.019	3.038	3.043
2Z37	0.513	0.514	0.444	0.513	0.506	0.433
2ZIB	0.785	1.271	1.034	0.379	1.706	0.543
3BN6	0.717	0.743	0.526	0.688	0.614	0.543
3CHY	1.604	1.870	0.896	2.083	1.677	1.435
3CO1	0.989	0.919	0.919	1.002	1.081	0.905
3EY6	1.007	1.022	1.246	0.870	1.019	0.967
3ICH	0.714	0.837	1.180	0.654	0.601	0.727
3KLR	1.077	1.054	1.035	1.090	1.121	1.072
3LZM	0.731	1.397	1.332	1.106	1.286	1.887
3Q6L	0.600	0.666	0.443	0.636	0.553	0.486

3VUB	0.457	0.465	0.462	1.896	0.468	0.358
4FGF	0.403	0.407	0.859	0.412	0.421	0.408
4LZT	0.964	0.664	0.711	0.634	0.601	0.689
4PTI	0.977	1.125	0.833	0.750	0.763	0.777
5P21	0.651	0.767	0.984	0.603	0.672	0.589

Table S6. Sequence identities achieved between the native and designed sequences using libraries L1-L3 when the rotamer probability term was disabled.

PDB ID	Sequence identity (%)		
	L1	L2	L3
1AGY	32.5	27.4	25.9
1AKY	20.6	22.5	30.7
1AMM	23.6	22.4	23.0
1AQB	18.3	24.6	20.6
1BDO	23.8	35.0	30.0
1BK7	17.9	23.2	17.9
1BKF	30.8	31.8	37.4
1C3D	26.9	29.3	31.3
1CKA	22.8	26.3	26.3
1CTF	22.1	23.5	29.4
1CTJ	27.0	30.3	31.5
1CYO	30.7	19.3	28.4
1DAD	19.6	29.5	30.8
1EW4	17.9	22.6	21.7
1FNC	21.3	24.3	25.7
1HFC	20.4	30.6	33.1
1IC6	31.2	36.9	37.3
1IFC	21.4	20.6	22.9
1IGD	27.9	29.5	32.8
1JBC	26.2	26.6	30.4
1KF5	19.4	23.4	24.2
1KNB	24.2	26.3	25.3
1KUH	28.0	27.3	33.3
1LTU	19.6	19.3	19.6
1MC2	21.3	28.7	23.8
1MD6	17.5	24.7	23.4
1NOA	23.9	26.5	28.3
1NWA	23.4	31.1	29.9
1O8X	25.9	21.0	26.6
1OPD	31.8	30.6	28.2
1P3C	24.7	31.2	31.6
1PGV	25.1	21.0	31.7
1PLC	26.3	29.3	31.3
1PPN	22.6	25.9	27.4
1PS4	27.0	26.5	31.2
1R12	23.1	23.5	25.1
1RA9	19.5	22.6	20.8
1RCF	20.7	24.3	32.5
1RRO	25.0	32.4	27.8
1RWZ	27.0	24.6	31.1
1SAU	33.3	36.0	33.3

1SEN	24.6	29.1	26.1
1SMX	31.0	35.6	33.3
1SNC	20.0	23.7	25.9
1T2I	27.1	28.1	31.3
1T3Y	17.6	16.8	14.5
1THV	18.4	27.5	33.3
1TTA	21.3	26.8	26.8
1UAI	26.9	27.4	27.8
1V05	23.7	25.8	39.8
1V7Q	27.8	32.0	28.4
1V8E	29.0	31.8	34.6
1VIE	20.0	28.3	21.7
1WC2	28.9	25.0	30.6
1WHI	28.7	25.4	39.3
1X1E	29.3	34.3	31.4
1X6X	23.5	21.0	31.9
1YCK	24.0	19.8	24.6
1YHH	15.7	22.7	25.3
1YU5	23.9	20.9	23.9
1YW5	27.7	29.4	26.6
1Z2U	21.8	25.9	29.3
1ZEQ	19.5	19.5	27.3
1ZZK	22.5	33.8	28.8
2A8F	10.2	16.3	18.4
2AYH	22.9	24.8	30.4
2B0A	25.8	25.3	29.6
2BK8	19.6	20.6	27.8
2BOP	15.3	12.9	27.1
2BV9	23.9	26.8	28.5
2CBA	23.3	24.4	28.3
2CG7	20.0	23.3	30.0
2CPL	29.3	32.3	33.5
2CWR	19.6	28.9	22.7
2D4P	31.6	34.2	34.2
2DFB	28.0	30.2	29.1
2DRI	24.0	27.7	23.6
2E8F	14.0	15.0	18.0
2E8G	21.7	25.4	33.3
2END	24.1	22.6	28.5
2FBQ	16.0	15.0	21.1
2FI1	21.4	31.6	33.2
2FI9	29.7	36.4	31.4
2FJ8	26.7	21.7	20.0
2FJZ	18.6	18.6	22.0
2FL4	13.4	18.7	23.1

2FQ3	17.6	21.2	15.3
2FRG	20.8	21.7	25.5
2G69	20.2	25.3	25.3
2H2R	22.2	25.2	22.2
2I24	15.9	23.0	23.9
2I3F	23.3	24.8	25.2
2I4A	18.7	27.1	22.4
2I6V	16.1	21.8	19.5
2IBL	16.7	18.5	17.6
2IGD	21.3	27.9	27.9
2JEK	20.7	29.3	26.4
2MHR	14.4	16.9	24.6
2NR7	24.1	26.2	23.0
2NWD	26.2	30.0	33.8
2OEB	22.4	22.4	21.7
2OHW	27.3	28.1	32.8
2OL7	25.6	22.4	28.4
2OSA	20.4	21.9	27.6
2OSS	19.7	24.4	29.1
2OVO	15.4	19.6	16.1
2PBP	20.0	22.4	27.5
2PET	22.9	27.7	29.9
2PHY	22.4	22.4	16.0
2PMR	18.4	25.0	25.0
2PND	21.0	20.2	26.1
2PPP	29.0	32.7	33.6
2QSK	31.6	31.6	32.6
2RIK	17.8	25.3	28.5
2RN2	21.9	24.5	24.5
2TGI	16.1	21.4	24.1
2VC8	25.0	23.6	23.6
2VQ4	30.2	29.2	28.3
2VWR	22.6	35.5	31.2
2WWE	22.1	19.2	10.6
2YXF	26.3	21.2	27.3
2Z37	22.1	25.8	28.3
2ZIB	18.5	20.0	20.0
3BN6	25.9	31.6	30.4
3CHY	22.7	31.3	33.6
3CO1	21.5	30.8	29.2
3EY6	25.4	18.6	29.7
3ICH	33.3	35.0	37.2
3KLR	30.4	28.8	28.8
3LZM	28.7	25.0	30.5
3Q6L	20.6	19.8	16.8

3VUB	12.9	21.8	18.8
4FGF	28.2	25.8	37.1
4LZT	30.2	31.8	33.3
4PTI	25.9	20.7	24.1
5P21	21.7	22.9	25.3

Table S7. Sequence identities between the native and designed sequences using libraries L1-L6 with native rotamers included.

PDB ID	Sequence identity (%)					
	L1	L2	L3	L4	L5	L6
1AGY	60.9	58.4	60.9	40.6	32.5	34.5
1AKY	51.4	51.8	53.7	29.4	27.1	24.3
1AMM	61.5	60.9	66.7	36.2	27.6	29.3
1AQB	58.3	54.9	52.0	32.6	28.0	24.6
1BDO	52.5	53.8	51.3	33.8	31.3	27.5
1BK7	53.7	60.0	55.8	35.8	28.4	27.4
1BKF	67.3	57.9	64.5	39.3	30.8	35.5
1C3D	55.8	58.5	57.8	34.7	35.7	26.9
1CKA	61.4	64.9	56.1	42.1	35.1	29.8
1CTF	57.4	54.4	63.2	30.9	27.9	33.8
1CTJ	56.2	56.2	59.6	33.7	32.6	28.1
1CYO	59.1	56.8	59.1	23.9	25.0	31.8
1DAD	57.6	53.1	56.3	37.5	32.1	26.8
1EW4	51.9	56.6	48.1	36.8	32.1	33.0
1FNC	51.4	51.4	51.7	33.1	28.7	24.3
1HFC	65.0	64.3	64.3	42.7	37.6	39.5
1IC6	68.1	67.0	67.0	44.1	37.3	38.7
1IFC	52.7	51.9	50.4	29.0	32.8	28.2
1IGD	52.5	50.8	52.5	32.8	42.6	37.7
1JBC	59.1	61.6	61.6	38.0	30.8	29.5
1KF5	58.9	51.6	57.3	29.8	31.5	24.2
1KNB	54.3	51.1	54.8	36.6	29.6	31.7
1KUH	64.4	66.7	57.6	45.5	34.1	35.6
1LTU	53.1	60.0	59.3	29.1	24.0	25.5
1MC2	54.9	54.1	54.1	27.9	26.2	24.6
1MD6	57.1	55.2	59.1	29.2	28.6	26.0
1NOA	58.4	54.0	51.3	38.1	34.5	31.9
1NWA	64.1	65.3	67.7	44.3	39.5	37.1
1O8X	63.6	62.9	65.0	48.3	30.1	28.0
1OPD	56.5	58.8	67.1	42.4	31.8	34.1
1P3C	61.4	64.7	63.3	43.3	32.6	32.6
1PGV	52.7	46.7	50.9	27.5	28.1	27.5
1PLC	68.7	70.7	67.7	46.5	41.4	33.3
1PPN	59.4	59.9	64.2	38.2	36.3	34.4
1PS4	54.5	56.6	54.5	37.0	31.7	33.3
1R12	55.4	51.4	51.8	31.5	22.7	26.7
1RA9	54.7	49.1	53.5	32.1	27.7	28.9
1RCF	61.5	56.8	62.1	35.5	37.9	31.4
1RRO	65.7	61.1	63.9	50.0	32.4	32.4
1RWZ	56.6	54.9	57.8	36.1	24.2	27.9
1SAU	72.8	72.8	67.5	48.2	36.8	43.9

1SEN	67.2	64.2	67.2	32.1	29.9	32.1
1SMX	62.1	69.0	60.9	37.9	35.6	46.0
1SNC	50.4	50.4	52.6	32.6	31.9	25.9
1T2I	58.3	57.3	56.3	37.5	35.4	29.2
1T3Y	58.8	53.4	63.4	38.2	22.9	20.6
1THV	59.4	59.4	59.4	37.7	32.4	33.8
1TTA	47.2	47.2	48.8	36.2	31.5	31.5
1UAI	55.6	63.2	57.8	36.3	30.5	30.0
1V05	64.5	57.0	66.7	48.4	41.9	40.9
1V7Q	55.6	59.8	62.1	41.4	37.9	32.0
1V8E	66.8	67.3	63.1	35.9	38.7	32.3
1VIE	56.7	51.7	55.0	28.3	30.0	21.7
1WC2	67.8	68.3	70.0	39.4	37.2	32.8
1WHI	67.2	68.0	69.7	43.4	42.6	30.3
1X1E	61.5	61.5	61.5	42.7	34.7	36.0
1X6X	57.1	65.5	54.6	38.7	35.3	31.1
1YCK	55.1	53.9	53.3	38.3	34.1	29.3
1YHH	51.1	57.2	54.1	32.3	26.2	28.4
1YU5	53.7	61.2	47.8	40.3	41.8	26.9
1YW5	55.9	54.8	59.3	39.5	38.4	29.4
1Z2U	66.0	58.5	57.1	43.5	37.4	27.9
1ZEQ	57.1	51.9	58.4	29.9	31.2	33.8
1ZZK	63.8	63.8	58.8	40.0	36.3	28.8
2A8F	61.2	54.1	50.0	26.5	25.5	18.4
2AYH	65.0	63.6	59.8	42.1	31.8	31.8
2B0A	56.5	58.6	60.2	35.5	34.4	34.9
2BK8	55.7	58.8	55.7	33.0	28.9	28.9
2BOP	52.9	43.5	47.1	34.1	29.4	28.2
2BV9	56.7	64.4	63.4	38.7	30.3	30.6
2CBA	62.4	65.5	63.2	36.4	31.8	33.3
2CG7	66.7	63.3	66.7	44.4	33.3	32.2
2CPL	68.9	73.2	71.3	40.9	32.3	36.0
2CWR	70.1	58.8	59.8	54.6	46.4	46.4
2D4P	64.1	64.1	56.4	27.4	35.0	37.6
2DFB	66.7	72.0	61.9	47.6	38.1	38.1
2DRI	54.2	52.0	54.2	36.2	29.9	30.6
2E8F	45.0	40.0	51.0	20.0	19.0	23.0
2E8G	60.4	60.4	65.0	36.3	33.8	27.5
2END	59.9	58.4	58.4	40.9	32.8	29.9
2FBQ	44.1	42.3	42.7	26.8	23.5	22.5
2FI1	55.1	57.8	57.8	37.4	27.3	25.7
2FI9	60.2	59.3	59.3	41.5	40.7	34.7
2FJ8	60.8	55.0	54.2	47.5	31.7	33.3
2FJZ	59.3	42.4	55.9	28.8	16.9	18.6
2FL4	45.5	46.3	51.5	25.4	23.1	21.6

2FQ3	58.8	49.4	55.3	27.1	20.0	25.9
2FRG	55.7	58.5	55.7	30.2	34.9	26.4
2G69	61.6	62.6	62.6	29.3	28.3	30.3
2H2R	39.6	39.6	41.8	35.6	34.8	25.9
2I24	58.5	60.7	58.5	38.1	31.9	26.5
2I3F	61.1	57.5	50.4	33.5	33.0	26.2
2I4A	63.6	60.7	63.1	36.4	30.8	30.8
2I6V	56.1	55.1	60.7	29.9	29.9	24.1
2IBL	66.7	57.5	59.8	25.0	21.3	19.4
2IGD	26.4	29.1	34.5	32.8	32.8	44.3
2JEK	38.9	38.9	40.7	43.6	31.4	32.1
2MHR	50.8	55.7	55.7	33.9	26.3	22.9
2NR7	66.4	60.7	60.7	38.7	29.8	28.3
2NWD	50.8	55.9	56.8	43.1	35.4	31.5
2OEB	56.5	64.9	68.6	36.2	30.9	23.0
2OHW	70.8	61.5	66.9	41.4	37.5	35.2
2OL7	56.6	57.2	56.6	33.2	30.8	28.8
2OSA	57.8	61.7	62.5	35.7	28.1	27.6
2OSS	46.0	52.8	47.2	44.1	38.6	32.3
2OVO	37.6	36.5	39.2	41.1	25.0	23.2
2PBP	57.7	56.1	59.7	29.8	28.6	27.1
2PET	66.9	64.6	63.0	30.7	27.7	25.5
2PHY	69.6	62.5	64.3	35.2	32.8	28.0
2PMR	42.4	49.0	49.0	18.4	26.3	25.0
2PND	52.8	53.7	55.4	34.5	27.7	35.3
2PPP	65.6	62.4	67.2	46.7	29.9	41.1
2QSK	50.0	51.3	46.1	57.9	45.3	42.1
2RIK	64.7	53.8	63.0	31.0	25.3	28.1
2RN2	72.0	63.6	71.0	29.7	27.7	23.2
2TGI	71.6	67.4	64.2	30.4	33.9	27.7
2VC8	46.3	49.1	48.4	29.2	30.6	25.0
2VQ4	47.7	46.5	51.6	49.1	41.5	44.3
2VWR	61.6	59.8	58.0	29.0	33.3	29.0
2WWE	47.2	56.9	47.2	26.0	27.9	24.0
2YXF	65.1	65.1	61.3	36.4	28.3	31.3
2Z37	65.6	60.2	62.4	42.2	34.0	32.0
2ZIB	57.7	63.5	59.6	33.1	27.7	23.1
3BN6	60.6	53.5	57.6	44.9	48.1	34.8
3CHY	63.5	61.9	65.6	38.3	37.5	37.5
3CO1	52.3	53.8	52.3	32.3	26.2	31.5
3EY6	65.2	65.2	65.2	34.7	35.6	33.9
3ICH	59.4	54.7	58.6	45.6	38.9	36.7
3KLR	65.4	63.8	57.7	38.4	33.6	27.2
3LZM	35.6	34.4	28.8	40.9	34.1	32.9
3Q6L	53.4	50.8	50.0	30.5	26.0	29.0

3VUB	34.4	36.7	27.8	36.6	27.7	26.7
4FGF	64.4	73.9	68.3	36.3	33.1	33.9
4LZT	55.2	57.6	60.0	39.5	40.3	31.0
4PTI	51.2	56.1	53.7	41.4	43.1	31.0
5P21	44.6	38.6	41.6	38.6	24.7	29.5

Supporting Figures

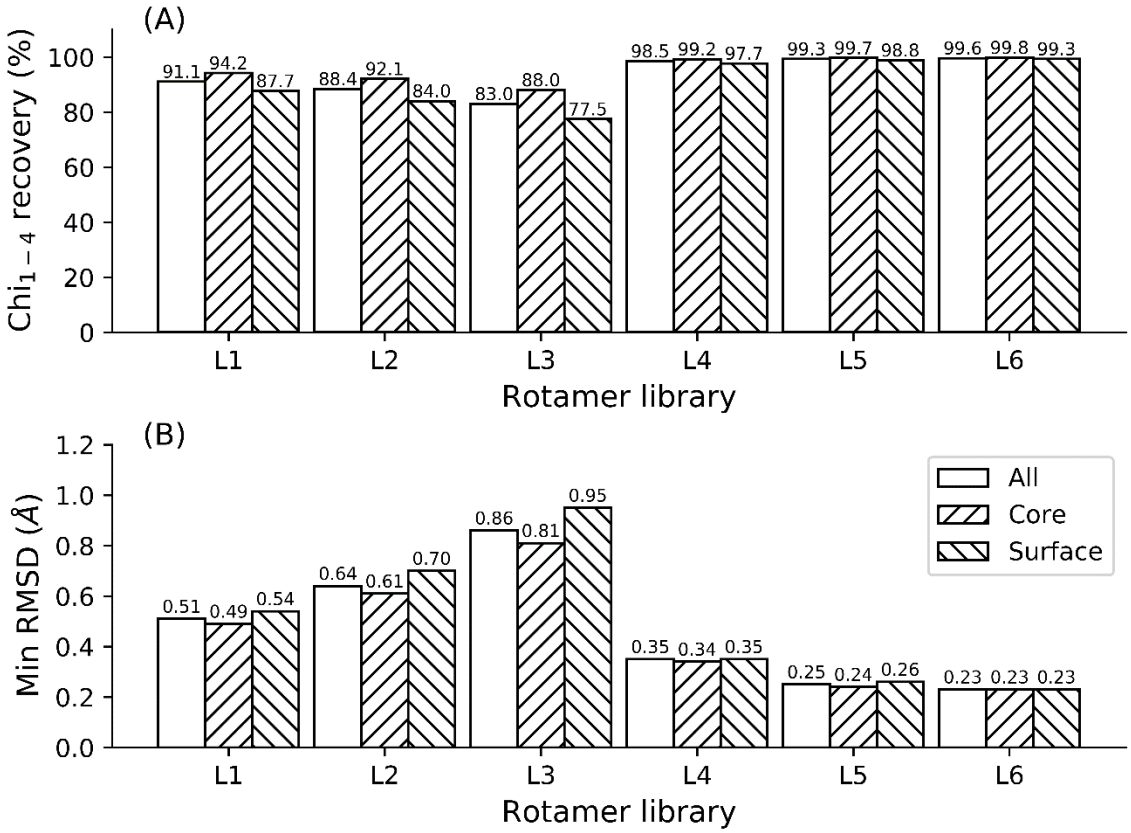

Figure S1. The dihedral angle ($\chi_{1\text{-}4}$) reproduction rates (a) and the minimal side-chain RMSDs achievable (b) using rotamer libraries L1-L6 on 3719 protein chains.

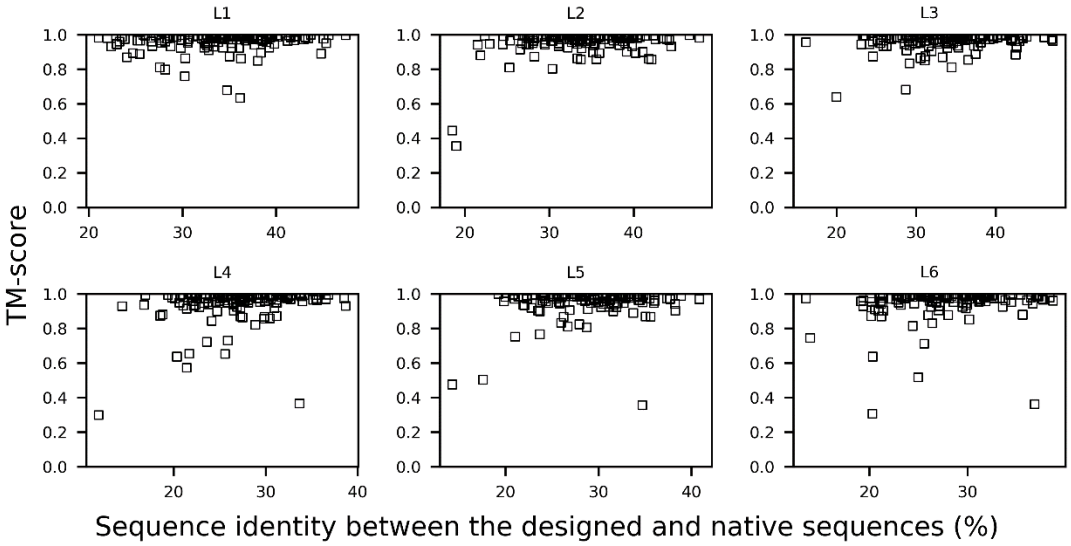

Figure S2. TM-scores of the predicted I-TASSER models to the native structures as a function of sequence identity between the native and designed sequences using libraries L1-L6.

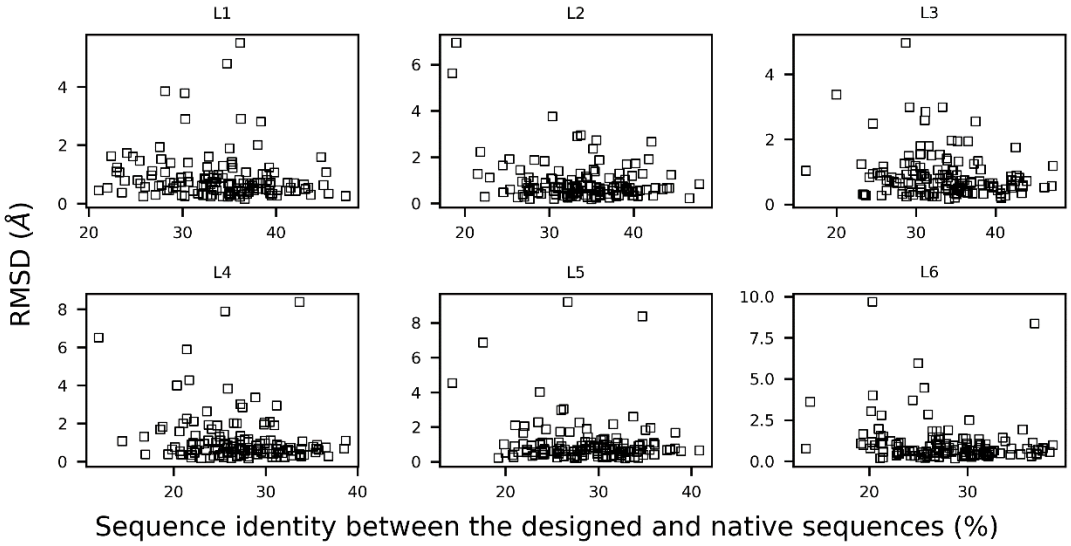

Figure S3. RMSDs of the predicted I-TASSER models to the native structures as a function of sequence identity between the native and designed sequences using libraries L1-L6.

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