

Supplemental Materials

Contents:

Figure S1: The values of the radius of gyration at different temperatures in the coarse-grained “Go”-like model.

Figure S2: The correlation coefficients between the torsional angles and the “length of the knot tails” as a function of the time extension Δt .

Figure S3: The average correlation coefficients between the torsional angles and the “length of knot tails” as a function of the number of simulation replicas at different residues.

Figure S4: The average correlation coefficients of the virtual angles with “the length of knot tails” in the folding simulation with coarse-grained “Go”-like model.

Figure S5: The evolution curve of the “length of knot tails” at the unfolding point of the AMD simulation with coarse-grained “Go”-like model.

Figure S6: The evolutions of the virtual bond angle κ and virtual torsional angle τ during the unfolding process in coarse-grained “Go”-like model.

Figure S7: The average correlation coefficients of the virtual angles with “the length of knot tails” in the unfolding simulation with coarse-grained “Go”-like model.

Figure S8: The evolution of RMSD in the unfolding simulation in all-atom model.

Figure S9: The evolution curve of the “length of knot tails” at the unfolding point of the AMD simulation with all-atom model.

Figure S10: The evolution of virtual bond angle κ and virtual torsional angle τ during the unfolding process in all-atom model.

Figure S11: The average correlation coefficients of the virtual angles with “the length of knot tails” in the unfolding simulation with all-atom model.

Figure S12: Comparison on the rankings results of the residues between two different temperature settings in the AMD simulations

Figure S13: Comparison on the ranking results of the residues between two different simulation time settings in the AMD simulations

Figure S14: Comparison on the rankings of the residues with correlation coefficients calculated from Eq. 2 and Eq. 4.

Figure S15: The ROC curve of key residue for knotting according to the predictions from Eq. 4.

Table S1: The ranking of residues according to correlation coefficients between “length of knot tails” and virtual torsional angle τ for knotting in coarse-grained “Go”-like model, unknotting in coarse-grained “Go”-like model and unknotting in all-atom model, respectively.

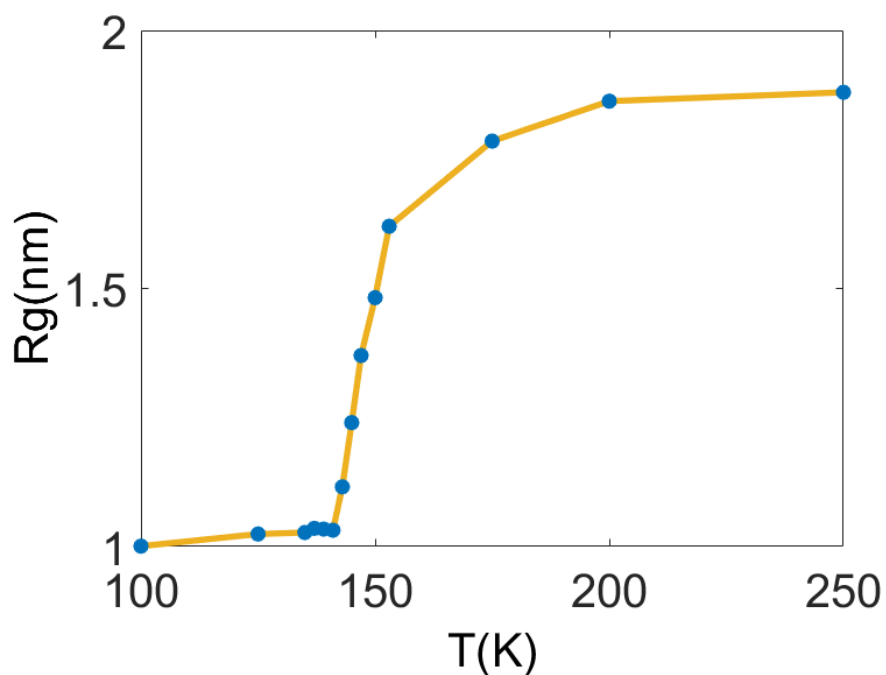


Figure S1: The average values of the radius of gyration at different temperatures in the coarse-grained “Go”-like model. The melting temperature T_m is labelled.

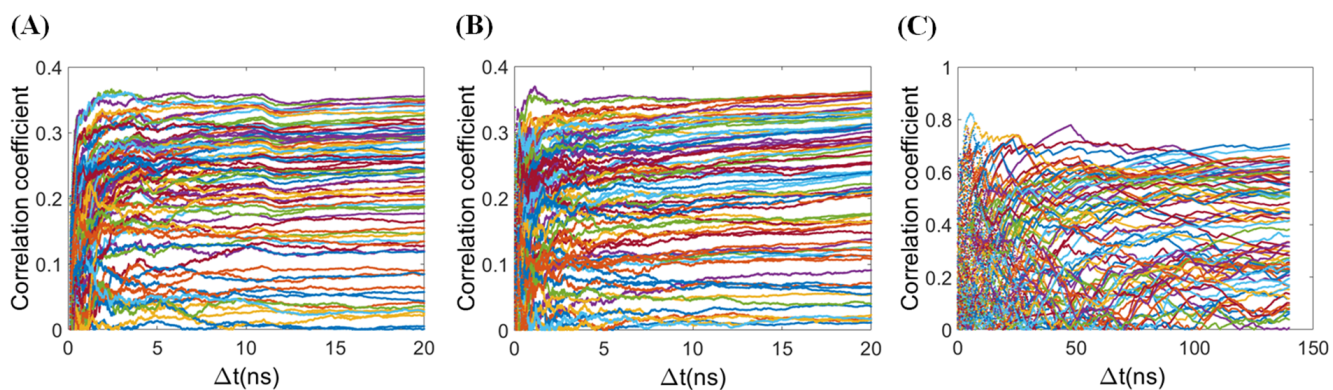


Figure S2: The correlation coefficients between the torsional angles and the “length of the knot tails” as a function of the time extension Δt . Panels (A), (B), (C) are for the cases of knotting in coarse-grained “Go”-like model, unknotting in coarse-grained “Go”-like model and unknotting in all-atom model, respectively. Each line in the figure represents the correlation coefficient at a residue in the protein.

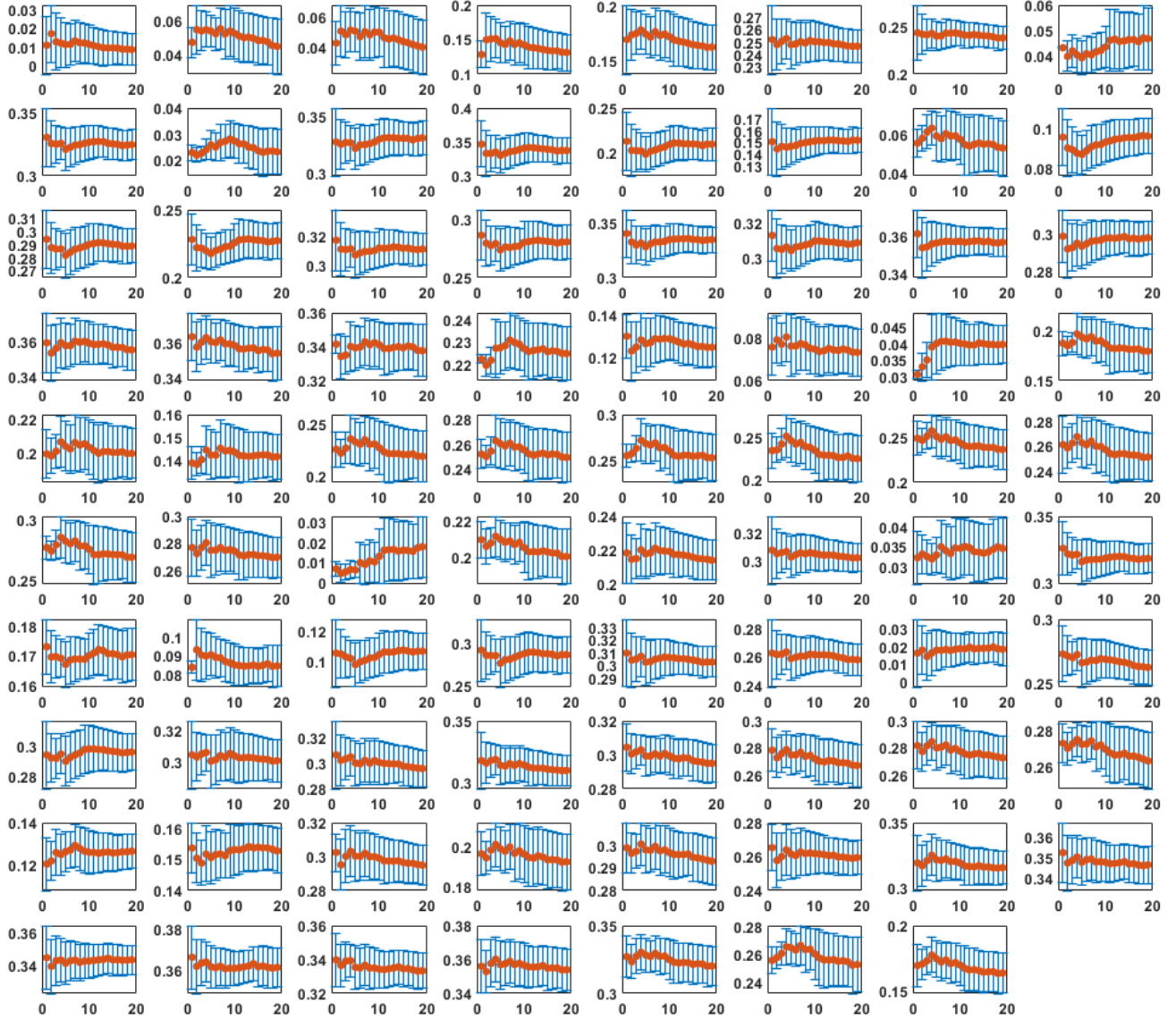


Figure S3: The average correlation coefficients between the torsional angles and the “length of knot tails” as a function of the number of simulation replicas at different residues. The red dots are the average values and the blue error bars denote the standard deviations. The x- and y-axis represents the number of replicas and the value of correlation coefficient, respectively. Each panel shows the correlation coefficients for a residue. The corresponding residue index for each panel (from 7 to 85) increases from left to right and top to bottom.

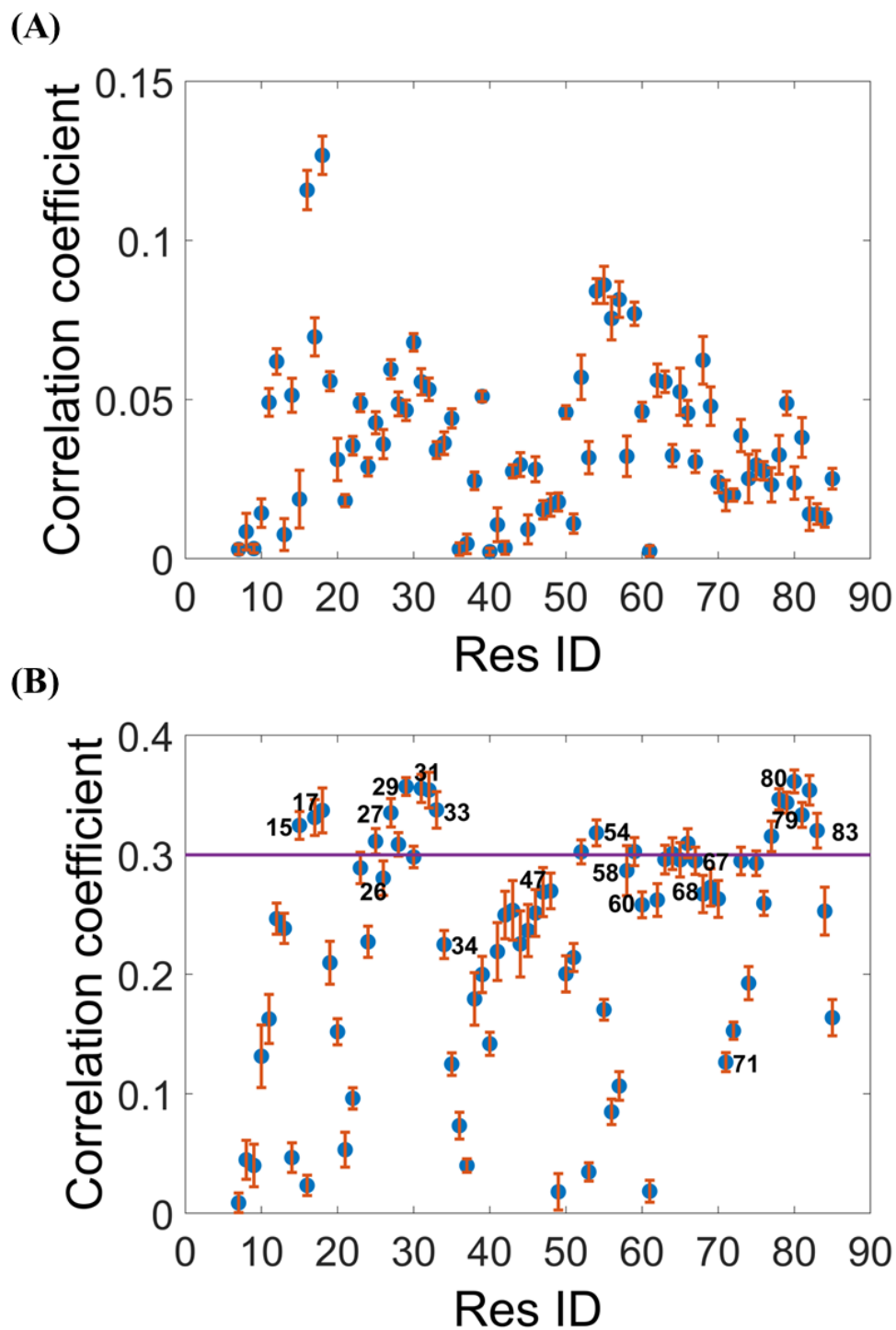


Figure S4: The average correlation coefficients of the virtual angles with “the length of knot tails” in the folding simulation with coarse-grained “Go”-like model. (A) The correlation coefficients between “length of knot tails” and κ . (B) The correlation coefficients between “length of knot tails” and τ . The key residues verified by experiment are labeled in the figure. The blue dots are the average values and the red error bars denote the standard deviations.

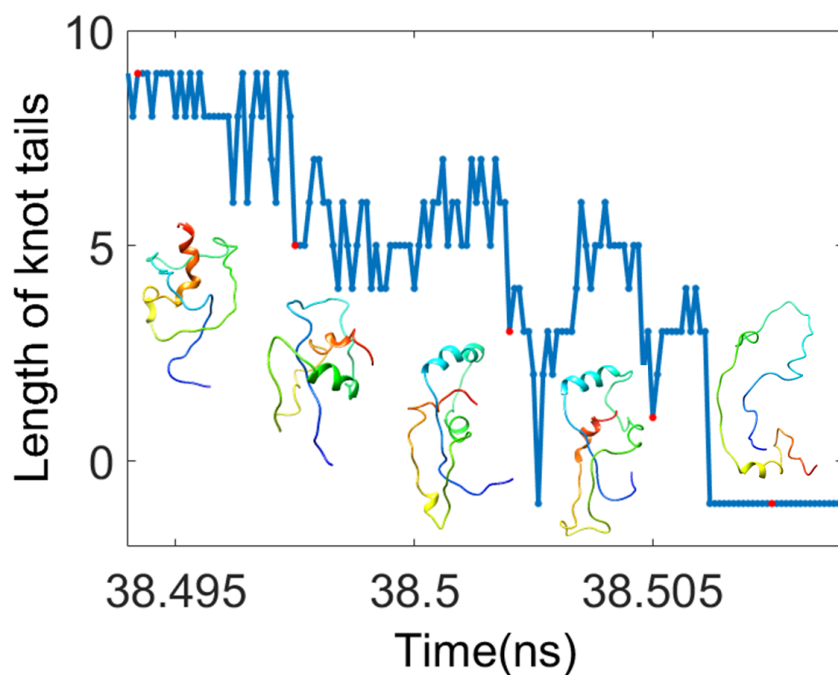


Figure S5: The evolution curve of the “length of knot tails” at the unfolding point of the AMD simulation with coarse-grained “Go”-like model. The snapshots corresponding to different “length of knot tails” (red points on the curve) are shown as insets.

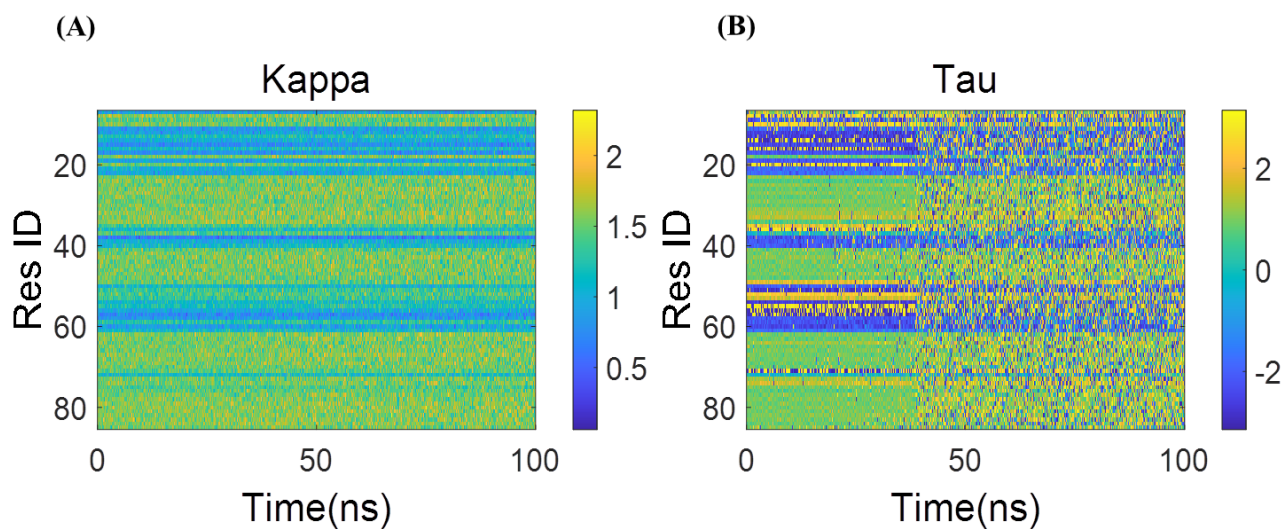


Figure S6: The evolutions of the virtual bond angle κ (Panel A) and virtual torsional angle τ (Panel B) during the unfolding process in coarse-grained “Go”-like model.

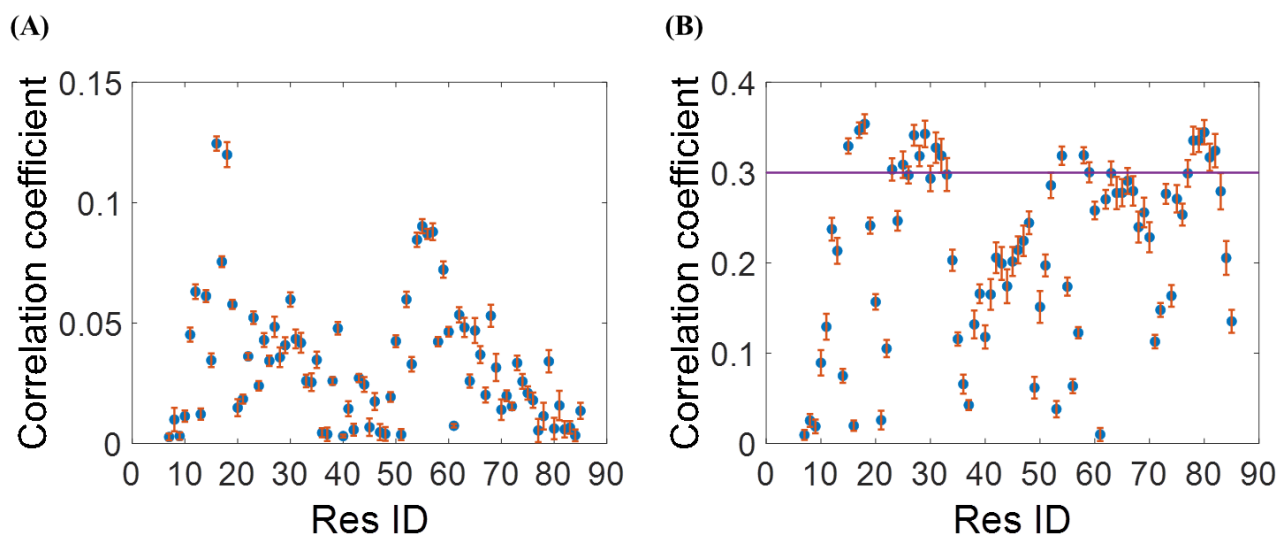


Figure S7: The average correlation coefficients of the virtual angles with “the length of knot tails” in the unfolding simulation with coarse-grained “Go”-like model. (A) The correlation coefficients between “length of knot tails” and κ . (B) The correlation coefficients between “length of knot tails” and τ . The red dots are the average value and the blue error bars denote the standard deviations.

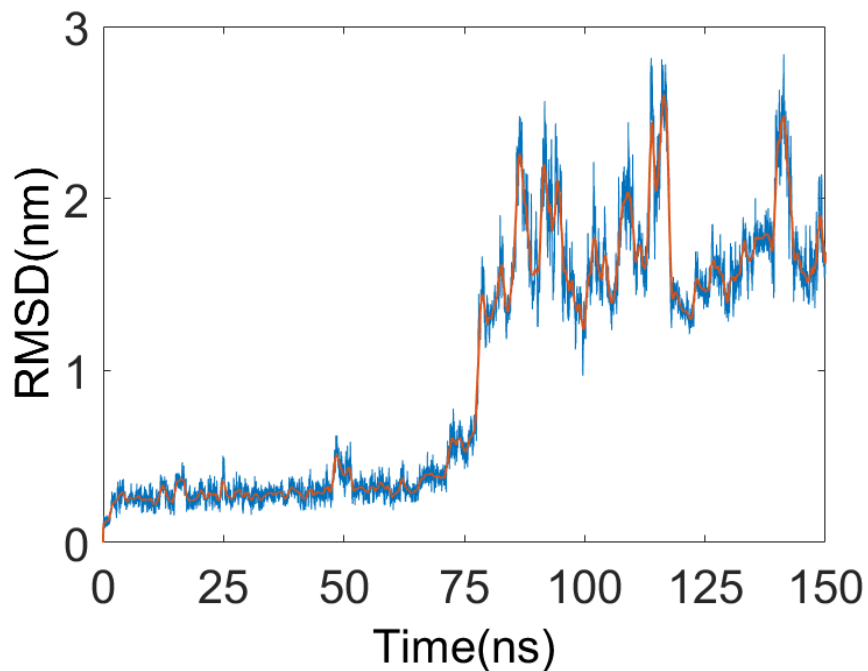


Figure S8: The evolution of RMSD in the unfolding simulation in all-atom model.

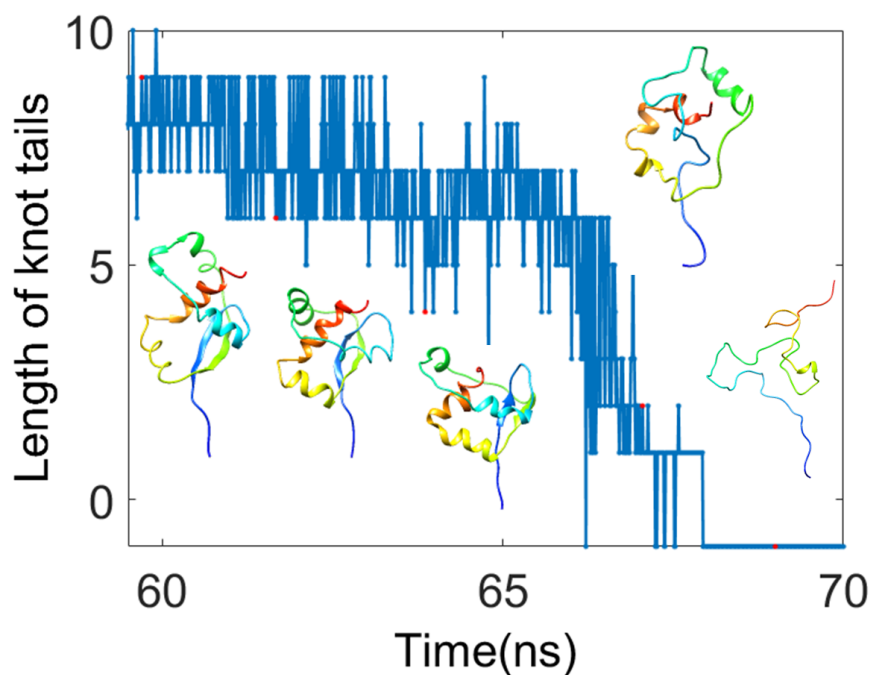


Figure S9: The evolution curve of the “length of knot tails” at the unfolding point of the AMD simulation with all-atom model. Some snapshots corresponding to different “length of knot tails” (red points on the curve) are shown as insets.

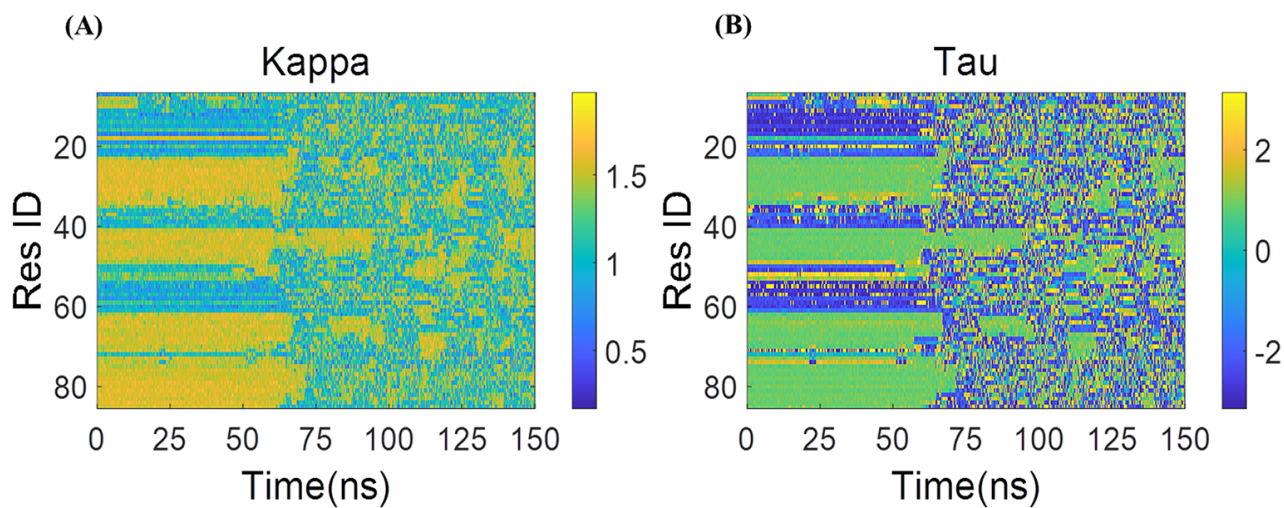


Figure S10: The evolution of virtual bond angle κ (panel A) and virtual torsional angle τ (panel B) during the unfolding process in all-atom model.

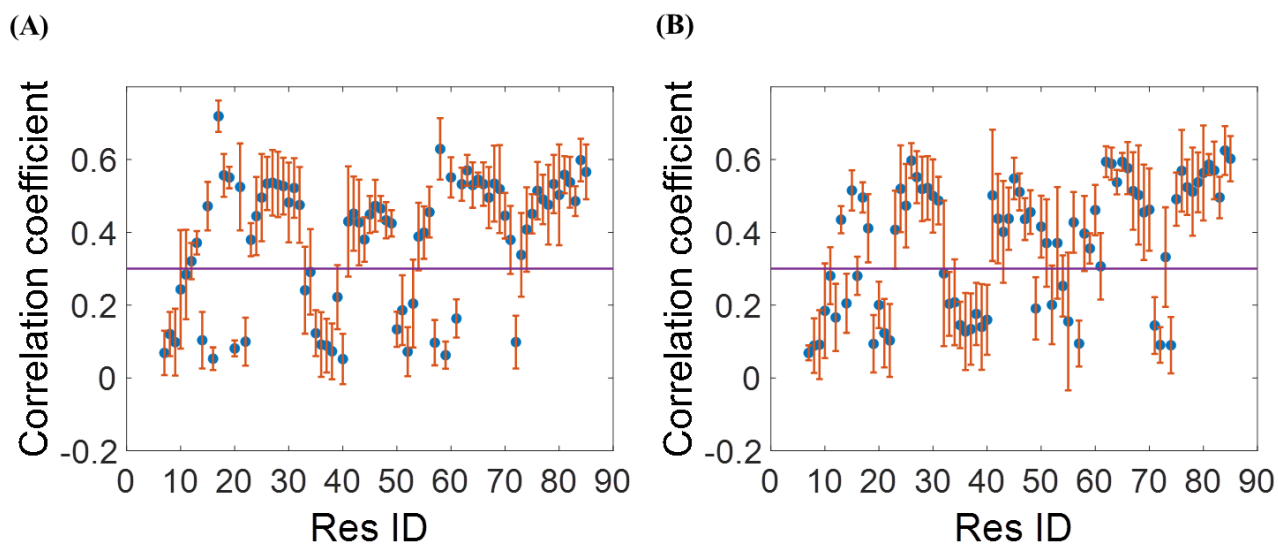


Figure S11: The average correlation coefficients of the virtual angles with “the length of knot tails” in the unfolding simulation with all-atom model. (A) The correlation coefficients between “length of knot tails” and κ . (B) The correlation coefficients between “length of knot tails” and τ . The blue dots are the average value and the red error bars denote the standard deviations.

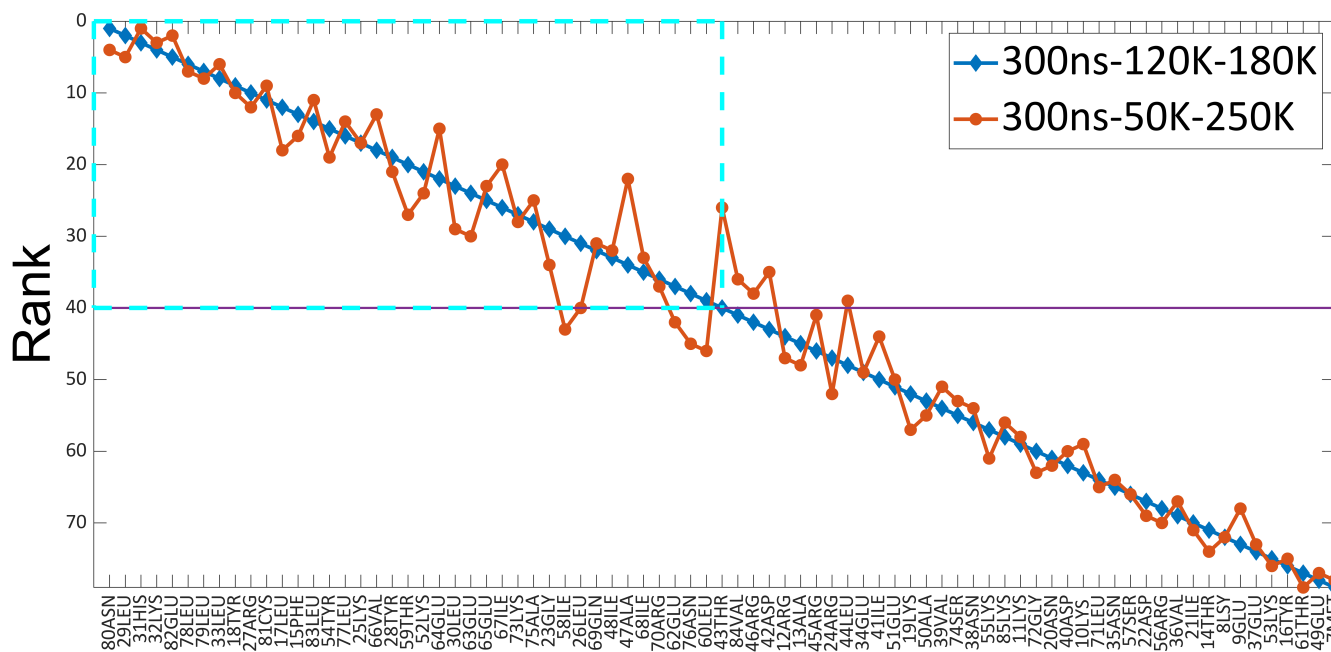


Figure S12: Comparison on the rankings results of the residues between two different temperature settings in the AMD simulations.

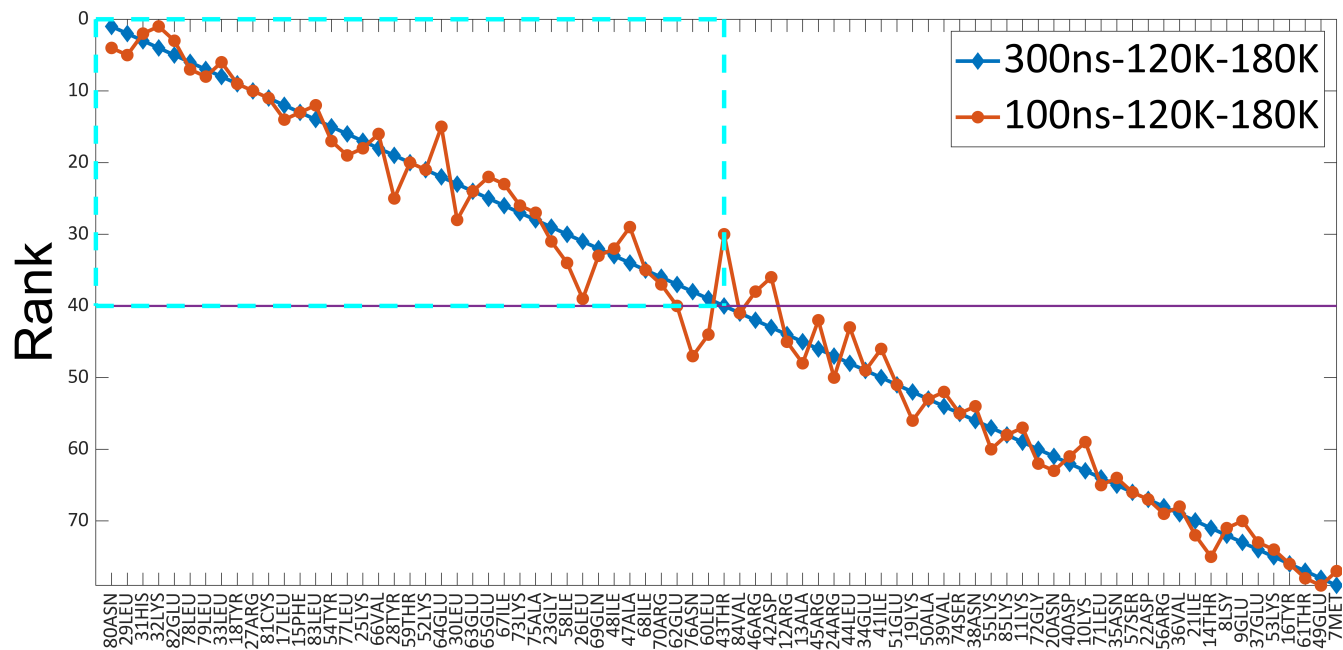


Figure S13: Comparison on the rankings results of the residues between two different time settings in the AMD simulations.

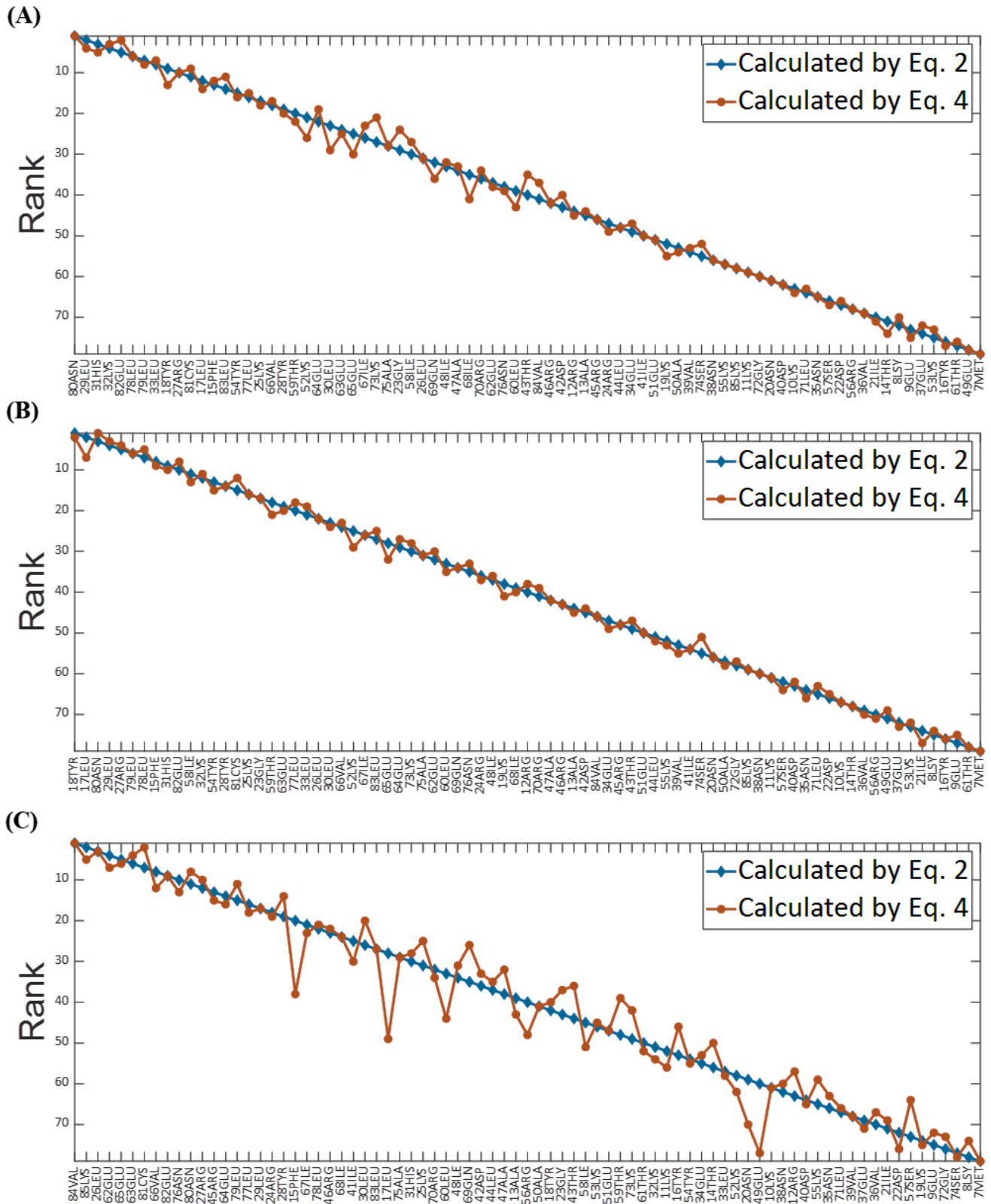


Figure S14: Comparison on the rankings of each residue with correlation coefficients calculated from Eq. 2 and Eq. 4. Panels (A), (B), (C) are for the cases of knotting in coarse-grained "Go"-like model, unknotting in coarse-grained "Go"-like model and unknotting in all-atom model, respectively.

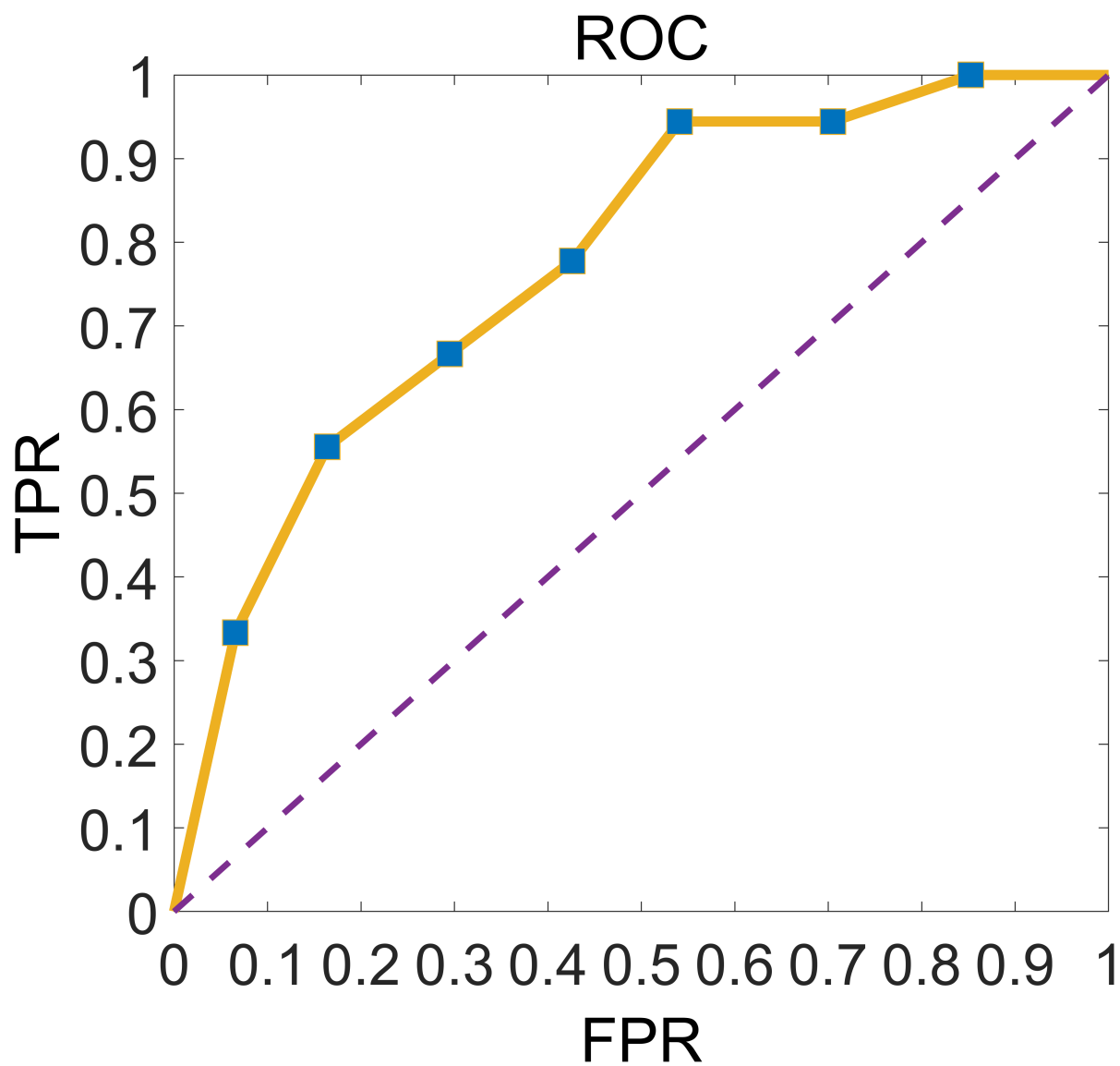


Figure S15: The ROC curve of key residue for knotting according to the predictions from Eq. 4.

Table S1: The ranking of residues according to correlation coefficients between “length of knot tails” and virtual torsional angle τ for knotting in coarse-grained “Go”-like model, unknotting in coarse-grained “Go”-like model and unknotting in all-atom model, respectively. The first column represents the index of residues, second to fourth columns represent the ranking for knotting in coarse-grained “Go”-like model, unknotting in coarse-grained “Go”-like model and unknotting in all-atom model, respectively.

| Res ID | Go-fold | Go-unfold | AA-unfold | Res ID | Go-fold | Go-unfold | AA-unfold |
|--------|---------|-----------|-----------|--------|---------|-----------|-----------|
| 7 | 79 | 79 | 79 | 47 | 34 | 42 | 38 |
| 8 | 72 | 75 | 78 | 48 | 33 | 37 | 34 |
| 9 | 73 | 77 | 75 | 49 | 78 | 71 | 60 |
| 10 | 63 | 67 | 61 | 50 | 53 | 57 | 41 |
| 11 | 59 | 61 | 52 | 51 | 51 | 50 | 47 |
| 12 | 44 | 40 | 63 | 52 | 21 | 25 | 58 |
| 13 | 45 | 44 | 39 | 53 | 75 | 73 | 46 |
| 14 | 71 | 68 | 56 | 54 | 15 | 13 | 54 |
| 15 | 13 | 8 | 20 | 55 | 57 | 52 | 65 |
| 16 | 76 | 76 | 53 | 56 | 68 | 70 | 40 |
| 17 | 12 | 2 | 28 | 57 | 66 | 62 | 73 |
| 18 | 9 | 1 | 42 | 58 | 30 | 11 | 45 |
| 19 | 52 | 38 | 74 | 59 | 20 | 18 | 48 |
| 20 | 61 | 56 | 59 | 60 | 39 | 33 | 33 |
| 21 | 70 | 74 | 71 | 61 | 77 | 78 | 50 |
| 22 | 67 | 66 | 72 | 62 | 37 | 32 | 4 |
| 23 | 29 | 17 | 43 | 63 | 24 | 19 | 6 |
| 24 | 47 | 36 | 18 | 64 | 22 | 29 | 14 |
| 25 | 17 | 16 | 31 | 65 | 25 | 28 | 5 |
| 26 | 31 | 22 | 3 | 66 | 18 | 24 | 8 |
| 27 | 10 | 5 | 12 | 67 | 26 | 26 | 21 |
| 28 | 19 | 14 | 19 | 68 | 35 | 39 | 24 |
| 29 | 2 | 4 | 17 | 69 | 32 | 34 | 35 |
| 30 | 23 | 23 | 26 | 70 | 36 | 41 | 32 |
| 31 | 3 | 9 | 30 | 71 | 64 | 65 | 67 |
| 32 | 4 | 12 | 51 | 72 | 60 | 58 | 76 |
| 33 | 8 | 21 | 57 | 73 | 27 | 30 | 49 |
| 34 | 49 | 47 | 55 | 74 | 55 | 55 | 77 |
| 35 | 65 | 64 | 66 | 75 | 28 | 31 | 29 |
| 36 | 69 | 69 | 70 | 76 | 38 | 35 | 10 |
| 37 | 74 | 72 | 69 | 77 | 16 | 20 | 16 |
| 38 | 56 | 60 | 62 | 78 | 6 | 7 | 22 |
| 39 | 54 | 53 | 68 | 79 | 7 | 6 | 15 |
| 40 | 62 | 63 | 64 | 80 | 1 | 3 | 11 |
| 41 | 50 | 54 | 25 | 81 | 11 | 15 | 7 |
| 42 | 43 | 45 | 36 | 82 | 5 | 10 | 9 |
| 43 | 40 | 49 | 44 | 83 | 14 | 27 | 27 |
| 44 | 48 | 51 | 37 | 84 | 41 | 46 | 1 |
| 45 | 46 | 48 | 13 | 85 | 58 | 59 | 2 |
| 46 | 42 | 43 | 23 | | | | |