

S2 Table. : Trajectory and cross validation overview for all protein targets. Each row shows the trajectory name, the cross-validation fold assignment, the number of snapshots per trajectory, the total number of sampling runs and the absolute number of sampled improved, no-change and decreased states.

| Traj. Name | Fold | # Snap. | # Traj. | I | N | D |
|-----------------|------|---------|---------|------|------|-------|
| TR759_dist_rst | 0 | 12008 | 8 | 7401 | 1995 | 2612 |
| TR759_no_rst | 0 | 11208 | 8 | 4260 | 2231 | 4717 |
| TR759_point_rst | 0 | 11208 | 8 | 5517 | 1701 | 3990 |
| TR782_no_rst | 0 | 11208 | 8 | 30 | 171 | 11007 |
| TR782_point_rst | 0 | 11208 | 8 | 149 | 948 | 10111 |
| TR810_dist_rst | 0 | 12008 | 8 | 18 | 474 | 11516 |
| TR810_no_rst | 0 | 11208 | 8 | 55 | 690 | 10463 |
| TR810_point_rst | 0 | 11208 | 8 | 92 | 7104 | 4012 |
| TR856_dist_rst | 0 | 12008 | 8 | 0 | 1 | 12007 |
| TR856_no_rst | 0 | 11208 | 8 | 0 | 3 | 11205 |
| TR856_point_rst | 0 | 11208 | 8 | 0 | 267 | 10941 |
| TR869_cm_excl | 0 | 24505 | 5 | 18 | 3077 | 21410 |
| TR869_cm_min | 0 | 24505 | 5 | 3 | 882 | 23620 |
| TR869_point_rst | 0 | 11208 | 8 | 35 | 2599 | 8574 |
| TR891_cm_excl | 0 | 24505 | 5 | 4 | 1895 | 22606 |
| TR891_cm_min | 0 | 24505 | 5 | 28 | 2622 | 21855 |
| TR891_point_rst | 0 | 11208 | 8 | 12 | 2230 | 8966 |
| TR283_dist_rst | 1 | 12008 | 8 | 318 | 1074 | 10616 |
| TR283_no_rst | 1 | 11208 | 8 | 19 | 531 | 10658 |
| TR283_point_rst | 1 | 11208 | 8 | 0 | 8 | 11200 |
| TR780_dist_rst | 1 | 12008 | 8 | 4242 | 1940 | 5826 |
| TR780_no_rst | 1 | 11208 | 8 | 1167 | 1191 | 8850 |
| TR780_point_rst | 1 | 11208 | 8 | 5729 | 4651 | 828 |
| TR837_dist_rst | 1 | 12008 | 8 | 1268 | 886 | 9854 |
| TR837_no_rst | 1 | 11208 | 8 | 1329 | 1448 | 8431 |
| TR837_point_rst | 1 | 11208 | 8 | 727 | 1336 | 9145 |
| TR854_dist_rst | 1 | 12008 | 8 | 329 | 991 | 10688 |
| TR854_no_rst | 1 | 11208 | 8 | 376 | 1084 | 9748 |
| TR854_point_rst | 1 | 11208 | 8 | 2943 | 6376 | 1889 |
| TR879_cm_excl | 1 | 24505 | 5 | 0 | 11 | 24494 |
| TR879_cm_min | 1 | 24505 | 5 | 0 | 27 | 24478 |
| TR879_point_rst | 1 | 11208 | 8 | 0 | 40 | 11168 |
| TR921_cm_excl | 1 | 24505 | 5 | 17 | 6751 | 17737 |
| TR921_cm_min | 1 | 24505 | 5 | 27 | 9337 | 15141 |
| TR921_point_rst | 1 | 11208 | 8 | 13 | 6552 | 4643 |
| TR217_dist_rst | 2 | 12008 | 8 | 0 | 13 | 11995 |
| TR217_no_rst | 2 | 11208 | 8 | 0 | 15 | 11193 |
| TR217_point_rst | 2 | 11208 | 8 | 583 | 6864 | 3761 |
| TR760_dist_rst | 2 | 12008 | 8 | 0 | 8 | 12000 |
| TR760_no_rst | 2 | 11208 | 8 | 0 | 8 | 11200 |
| TR760_point_rst | 2 | 11208 | 8 | 381 | 5509 | 5318 |
| TR786_dist_rst | 2 | 12008 | 8 | 2 | 74 | 11932 |
| TR786_no_rst | 2 | 11208 | 8 | 1 | 60 | 11147 |
| TR786_point_rst | 2 | 11208 | 8 | 3451 | 4746 | 3011 |
| TR816_dist_rst | 2 | 12008 | 8 | 1017 | 488 | 10503 |
| TR816_no_rst | 2 | 11208 | 8 | 1598 | 1024 | 8586 |
| TR816_point_rst | 2 | 11208 | 8 | 1409 | 1754 | 8045 |
| TR862_cm_excl | 2 | 24505 | 5 | 422 | 3323 | 20760 |
| TR862_cm_min | 2 | 24505 | 5 | 2444 | 4205 | 17856 |
| TR862_point_rst | 2 | 11208 | 8 | 595 | 2900 | 7713 |
| TR872_cm_excl | 2 | 24505 | 5 | 2201 | 6844 | 15460 |
| TR872_cm_min | 2 | 24505 | 5 | 1488 | 4055 | 18962 |
| TR872_point_rst | 2 | 11208 | 8 | 767 | 3268 | 7173 |
| TR762_dist_rst | 3 | 12008 | 8 | 0 | 8 | 12000 |
| TR762_no_rst | 3 | 11208 | 8 | 0 | 8 | 11200 |

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| Traj. Name | Fold | # Snap. | # Traj. | I | N | D |
|-----------------|------|---------|---------|-------|-------|-------|
| TR762_point_rst | 3 | 11208 | 8 | 0 | 1656 | 9552 |
| TR765_dist_rst | 3 | 12008 | 8 | 11107 | 551 | 350 |
| TR765_no_rst | 3 | 11208 | 8 | 8259 | 963 | 1986 |
| TR765_point_rst | 3 | 11208 | 8 | 10719 | 425 | 64 |
| TR828_dist_rst | 3 | 12008 | 8 | 3 | 13 | 11992 |
| TR828_no_rst | 3 | 11208 | 8 | 1 | 15 | 11192 |
| TR828_point_rst | 3 | 11208 | 8 | 7 | 57 | 11144 |
| TR833_dist_rst | 3 | 12008 | 8 | 2 | 83 | 11923 |
| TR833_no_rst | 3 | 11208 | 8 | 1 | 64 | 11143 |
| TR833_point_rst | 3 | 11208 | 8 | 1232 | 4336 | 5640 |
| TR928_cm_excl | 3 | 24505 | 5 | 0 | 0 | 24505 |
| TR928_cm_min | 3 | 24505 | 5 | 0 | 0 | 24505 |
| TR928_point_rst | 3 | 11208 | 8 | 0 | 0 | 11208 |
| TR945_cm_excl | 3 | 24505 | 5 | 139 | 13368 | 10998 |
| TR945_cm_min | 3 | 24505 | 5 | 116 | 10678 | 13711 |
| TR945_point_rst | 3 | 11208 | 8 | 265 | 7400 | 3543 |
| TR817_dist_rst | 4 | 12008 | 8 | 843 | 958 | 10207 |
| TR817_no_rst | 4 | 11208 | 8 | 326 | 576 | 10306 |
| TR817_point_rst | 4 | 11208 | 8 | 73 | 6538 | 4597 |
| TR821_dist_rst | 4 | 12008 | 8 | 5115 | 1530 | 5363 |
| TR821_no_rst | 4 | 11208 | 8 | 5235 | 1458 | 4515 |
| TR829_dist_rst | 4 | 12008 | 8 | 84 | 425 | 11499 |
| TR829_no_rst | 4 | 11208 | 8 | 41 | 371 | 10796 |
| TR829_point_rst | 4 | 11208 | 8 | 3213 | 4337 | 3658 |
| TR857_dist_rst | 4 | 12008 | 8 | 1933 | 2781 | 7294 |
| TR857_no_rst | 4 | 11208 | 8 | 1734 | 1944 | 7530 |
| TR857_point_rst | 4 | 11208 | 8 | 1870 | 3345 | 5993 |
| TR870_cm_excl | 4 | 24505 | 5 | 17 | 343 | 24145 |
| TR870_cm_min | 4 | 24505 | 5 | 617 | 2950 | 20938 |
| TR870_point_rst | 4 | 11208 | 8 | 153 | 1718 | 9337 |
| TR944_cm_excl | 4 | 24505 | 5 | 86 | 2461 | 21958 |
| TR944_cm_min | 4 | 24505 | 5 | 578 | 3006 | 20921 |
| TR944_point_rst | 4 | 11208 | 8 | 59 | 2130 | 9019 |
| TR769_dist_rst | 5 | 12008 | 8 | 2004 | 1537 | 8467 |
| TR769_no_rst | 5 | 11208 | 8 | 3089 | 1880 | 6239 |
| TR774_dist_rst | 5 | 12008 | 8 | 1 | 46 | 11961 |
| TR774_no_rst | 5 | 11208 | 8 | 1 | 44 | 11163 |
| TR774_point_rst | 5 | 11208 | 8 | 6 | 1028 | 10174 |
| TR792_dist_rst | 5 | 12008 | 8 | 2815 | 2383 | 6810 |
| TR792_no_rst | 5 | 11208 | 8 | 3906 | 2620 | 4682 |
| TR792_point_rst | 5 | 11208 | 8 | 2811 | 4515 | 3882 |
| TR795_dist_rst | 5 | 12008 | 8 | 373 | 1367 | 10268 |
| TR795_point_rst | 5 | 11208 | 8 | 1956 | 7702 | 1550 |
| TR848_dist_rst | 5 | 12008 | 8 | 1 | 22 | 11985 |
| TR848_no_rst | 5 | 11208 | 8 | 2 | 53 | 11153 |
| TR848_point_rst | 5 | 11208 | 8 | 77 | 1541 | 9590 |
| TR893_cm_excl | 5 | 24505 | 5 | 0 | 121 | 24384 |
| TR893_cm_min | 5 | 24505 | 5 | 0 | 21 | 24484 |
| TR893_point_rst | 5 | 11208 | 8 | 0 | 45 | 11163 |
| TR228_dist_rst | 6 | 12008 | 8 | 3073 | 3563 | 5372 |
| TR228_no_rst | 6 | 11208 | 8 | 4852 | 2362 | 3994 |
| TR228_point_rst | 6 | 11208 | 8 | 5893 | 2875 | 2440 |
| TR768_dist_rst | 6 | 12008 | 8 | 50 | 591 | 11367 |
| TR768_no_rst | 6 | 11208 | 8 | 59 | 491 | 10658 |
| TR768_point_rst | 6 | 11208 | 8 | 1190 | 4161 | 5857 |
| TR776_dist_rst | 6 | 12008 | 8 | 0 | 20 | 11988 |
| TR776_no_rst | 6 | 11208 | 8 | 0 | 15 | 11193 |

S2 Table. : Trajectory and cross validation overview for all protein targets.

| Traj. Name | Fold | # Snap. | # Traj. | I | N | D |
|-------------------|-------------|----------------|----------------|----------|----------|----------|
| TR776_point_rst | 6 | 11208 | 8 | 312 | 7811 | 3085 |
| TR783_dist_rst | 6 | 12008 | 8 | 10 | 49 | 11949 |
| TR783_no_rst | 6 | 11208 | 8 | 0 | 55 | 11153 |
| TR783_point_rst | 6 | 11208 | 8 | 93 | 1640 | 9475 |
| TR803_dist_rst | 6 | 12008 | 8 | 215 | 1387 | 10406 |
| TR803_no_rst | 6 | 11208 | 8 | 8 | 351 | 10849 |
| TR803_point_rst | 6 | 11208 | 8 | 228 | 1006 | 9974 |
| TR868_cm_excl | 6 | 24505 | 5 | 329 | 542 | 23634 |
| TR868_cm_min | 6 | 24505 | 5 | 76 | 503 | 23926 |
| TR868_point_rst | 6 | 11208 | 8 | 592 | 1293 | 9323 |