Supporting Information

For "Automated Event Detection and Activity Monitoring in Long Molecular Dynamics Simulations," by Willy Wriggers, Kate A. Stafford, Yibing Shan, Stefano Piana, Paul Maragakis, Kresten Lindorff-Larsen, Patrick J. Miller, Justin Gullingsrud, Charles A. Rendleman, Michael P. Eastwood, Ron O. Dror, and David E. Shaw

System and Simulation Parameters

Trajectory 1 (Fig. 1 in the main text) is based on the catalytic domain of c-Src kinase (unphosphorylated) solvated in a 61×64×72 $Å^3$ periodic box with 7,871 SPC water molecules, 32 Na^+ ions, and 28 Cl^- ions. The total system size was 28,089 atoms. The protein force field parameters were derived from OPLS_AA. The calculations were performed with Desmond[1] version 1.7.3 using SHAKE bond distance constraints for water and protein hydrogen atoms. An NPT ensemble at temperature 300K (Berendsen) and at pressure 1 bar (Berendsen; isotropic pressure tensor) was simulated using a RESPA integrator with Fourier-space electrostatics computed every 5 fs and all remaining interactions computed every 2.5 fs. A 10 Å cutoff was applied to van der Waals and electrostatics interactions with long-range electrostatics computed by Gaussian Split Ewald. The Src kinase simulation was started from PDB entry 1Y57 with the regulatory SH2/SH3 domains removed.

Trajectories 2–4 (Fig. 1 in the main text) are based on the fast folding mutant K65(NLE), N68H, K70(NLE) of chicken villin subdomain HP-35.[2] The protein was modeled at pH 4.8 without peptide capping groups in a $(51\ Å)^3$ periodic box using 4,211 TIP3P water molecules, one Na^+ ion, and two Cl^- ions. The total system size was 13,213 atoms. The protein and solvent force field parameters were derived from AMBER03 (trajectory 4) and CHARMM27 with CMAP (trajectories 2 and 3). Non-standard norleucine side-chain parameters were adapted from corresponding methyl and (neutral) lysine parameters in these force fields. The villin runs were performed with Desmond[1] versions 1.7.3 (trajectory 4) and 1.8.4.4 (trajectories 2 and 3) using SHAKE bond distance constraints for water and protein hydrogen atoms. An NVT ensemble at temperature 300K was simulated using a RESPA integrator, with Fourier-space electrostatics computed every 5.2 fs, pairwise electrostatic and van der Waals interactions computed every 2.6 fs, and bonded interactions computed every 1.3 fs. An 8 Å cutoff was applied to van der Waals and electrostatics interactions with longer-range electrostatics simulated by Particle Mesh Ewald. Trajectory 2 started from PDB entry 2F4K (using the "A" variants of dual occupancy rotamers) subject to 2.6 ns equilibration at 300K in the NPT ensemble. Trajectories 3 and 4 started from unequilibrated, fully extended main chains modeled with Maestro.[3]

Implementation of the Recrossing Filter

Figure 6 in the main text illustrates the nine possible paths crossing the buffer. The non-trivial formation of a contact is defined as an incoming path originating either from the non-contact zone or from the initial ($t = 0$) buffer. The non-trivial breaking of a contact is defined as an outgoing path ending either in the non-contact zone or in the final ($t = t_{max}$) buffer. All other paths are ignored. To identify the paths it is necessary to assign labels $l(t)$, which are arbitrary numbers identifying which of the nine paths is travelled. There are many ways to implement this; our rule is based on a forward and backward processing of the time series.

Initially, our scheme assigns start label values of $l = 5$ for contacts, $l = -5$ for non-contacts, and $l = 0$ for the buffer. Then the following two rules are applied in succession:

- For $t = 1, 2, \cdots, t_{max} - 1$:
  if $\left(l(t) = 0 \text{ and } l(t-1) > 0\right)$ then $l(t) = +1$
  if $\left(l(t) = 0 \text{ and } l(t-1) < 0\right)$ then $l(t) = -1$

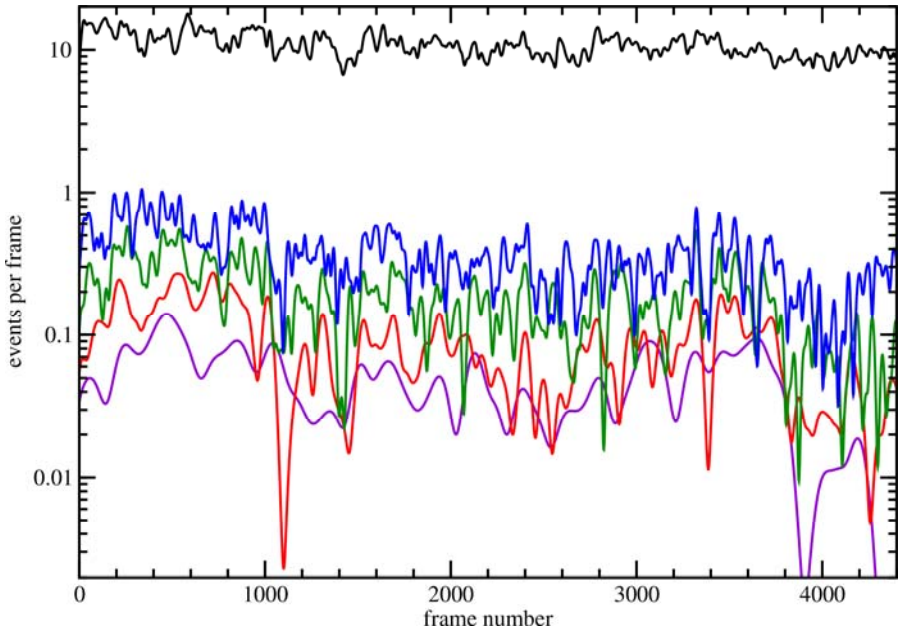
- For $t = t_{max} - 1, t_{max} - 2, \cdots, 1$:
  if $\left(|l(t)| \le 1 \text{ and } l(t+1) > +1\right)$ then $l(t) = l(t) + 3$
  if $\left(|l(t)| \le 1 \text{ and } l(t+1) < -1\right)$ then $l(t) = l(t) - 3$

As shown in Figure 6 in the main text, the final labels achieved with this scheme identify the nine paths and allow the assignment of non-trivial contact formation and breaking times.

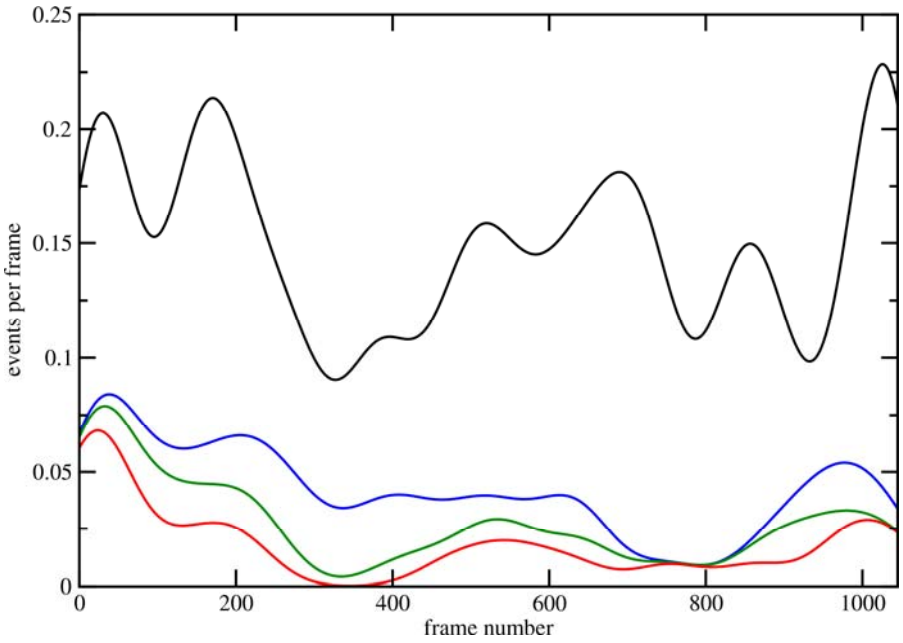
Supporting Movie Animation

The additional supporting AVI file (using the Indeo® video 5 codec which is widely available on the internet) shows an animation of the diffusive trajectory 3 with combination plot of activity levels. On the right side, eight consecutive frames (one frame equals 0.962 ns) are shown as a function of simulation time to visualize conformational variability. The corresponding time line in the combination plot on the left side identifies GMD- and cutoff-based activity levels.

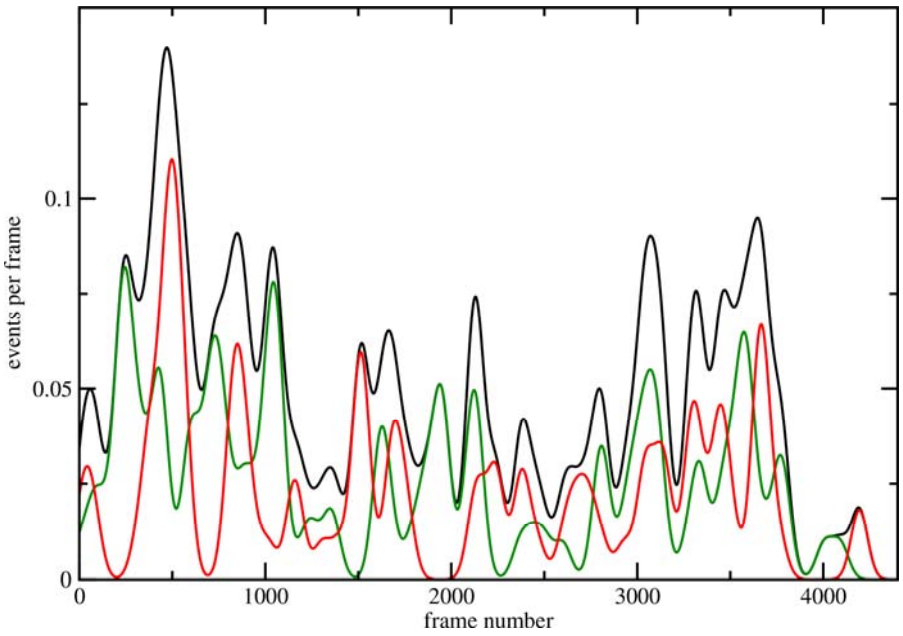
Supporting Figures



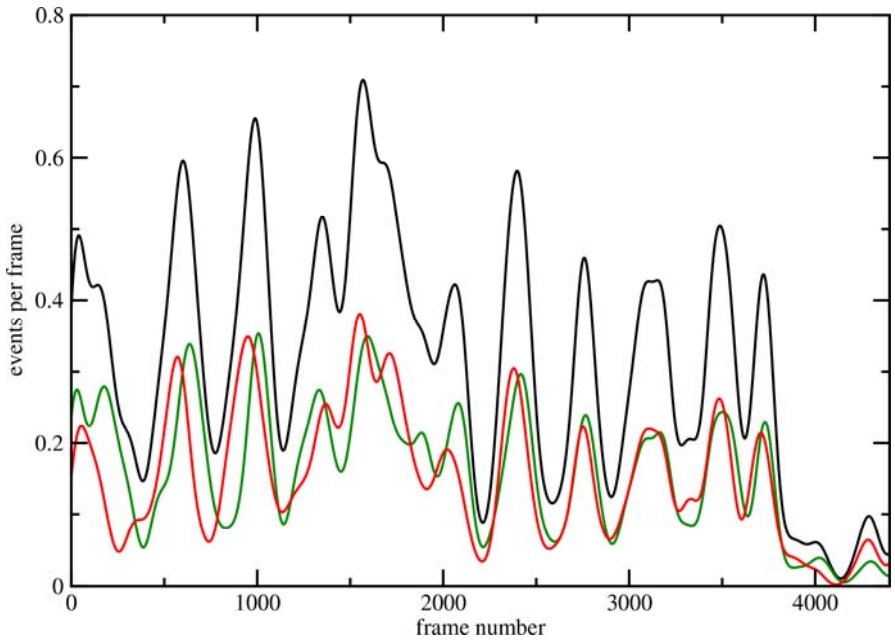
Supporting Figure 1. Effect of median filtering (see text) on trajectory 3 activity levels: no filter (black); half width 13 frames (blue); 26 frames (green); 52 frames (red); 104 frames (purple). Shown are cutoff-based activities using a crossing buffer of 6.0–7.0 Å (see text). One frame equals 0.962 ns.



Supporting Figure 2. Effect of recrossing suppression on trajectory 2 activity levels: no buffer at cutoff 7.5 Å (black); buffer 7.5–7.8 Å (blue); buffer 7.5–8.0 Å (green); buffer 7.5–8.5 Å (red). A median filter was applied using a half width of 104 frames. One frame equals 0.962 ns.



Supporting Figure 3. Contributions of forming (green) and breaking (red) contacts to total cutoff activity (black). The time series was extracted from trajectory 3 with a median filter (half width 104 frames), and with a crossing buffer of 6.0–7.0 Å. One frame equals 0.962 ns.



Supporting Figure 4. Contributions of forming (green) and breaking (red) contacts to total GMD activity (black). The time series was extracted from trajectory 3 with a median filter (half width 104 frames), and with a $k = 3$ crossing buffer. One frame equals 0.962 ns.

Events Log File

In the following we show a typical events log file that lists formation and breaking of contacts and corresponding trajectory frame numbers. The data was extracted from trajectory 2. A cutoff of 7.5 Å was used (no crossing buffer was applied to emphasize trivial recrossings, see text). A median filter was applied using a half width of 104 frames.

```
+++ initial contact at step 0: (NLE   1 - SER   2) - starting with 83 contacts
+++ initial contact at step 0: (NLE   1 - ASP   5) - starting with 83 contacts
+++ initial contact at step 0: (NLE   1 - PHE   6) - starting with 83 contacts
+++ initial contact at step 0: (NLE   1 - VAL   9) - starting with 83 contacts
+++ initial contact at step 0: (NLE   1 - LEU  34) - starting with 83 contacts
+++ initial contact at step 0: (SER   2 - ASP   3) - starting with 83 contacts
+++ initial contact at step 0: (SER   2 - GLU   4) - starting with 83 contacts
+++ initial contact at step 0: (SER   2 - ASP   5) - starting with 83 contacts
+++ initial contact at step 0: (SER   2 - ARG  14) - starting with 83 contacts
+++ initial contact at step 0: (ASP   3 - PHE   6) - starting with 83 contacts
+++ initial contact at step 0: (ASP   3 - THR  13) - starting with 83 contacts
+++ initial contact at step 0: (ASP   3 - ARG  14) - starting with 83 contacts
+++ initial contact at step 0: (GLU   4 - LYP   7) - starting with 83 contacts
+++ initial contact at step 0: (ASP   5 - PHE   6) - starting with 83 contacts
+++ initial contact at step 0: (ASP   5 - ALA   8) - starting with 83 contacts
+++ initial contact at step 0: (PHE   6 - VAL   9) - starting with 83 contacts
+++ initial contact at step 0: (PHE   6 - PHE  10) - starting with 83 contacts
+++ initial contact at step 0: (PHE   6 - THR  13) - starting with 83 contacts
+++ initial contact at step 0: (PHE   6 - ARG  14) - starting with 83 contacts
+++ initial contact at step 0: (PHE   6 - PHE  17) - starting with 83 contacts
+++ initial contact at step 0: (LYP   7 - ALA   8) - starting with 83 contacts
+++ initial contact at step 0: (LYP   7 - GLY  11) - starting with 83 contacts
+++ initial contact at step 0: (LYP   7 - THR  13) - starting with 83 contacts
+++ initial contact at step 0: (ALA   8 - VAL   9) - starting with 83 contacts
+++ initial contact at step 0: (ALA   8 - GLY  11) - starting with 83 contacts
+++ initial contact at step 0: (VAL   9 - PHE  10) - starting with 83 contacts
+++ initial contact at step 0: (VAL   9 - GLY  11) - starting with 83 contacts
+++ initial contact at step 0: (VAL   9 - LYP  32) - starting with 83 contacts
+++ initial contact at step 0: (VAL   9 - LEU  34) - starting with 83 contacts
+++ initial contact at step 0: (PHE  10 - GLY  11) - starting with 83 contacts
+++ initial contact at step 0: (PHE  10 - MET  12) - starting with 83 contacts
+++ initial contact at step 0: (PHE  10 - PHE  17) - starting with 83 contacts
+++ initial contact at step 0: (PHE  10 - LEU  28) - starting with 83 contacts
+++ initial contact at step 0: (PHE  10 - LYP  32) - starting with 83 contacts
+++ initial contact at step 0: (PHE  10 - LEU  34) - starting with 83 contacts
+++ initial contact at step 0: (GLY  11 - MET  12) - starting with 83 contacts
+++ initial contact at step 0: (MET  12 - THR  13) - starting with 83 contacts
+++ initial contact at step 0: (MET  12 - ALA  16) - starting with 83 contacts
+++ initial contact at step 0: (MET  12 - PHE  17) - starting with 83 contacts
+++ initial contact at step 0: (MET  12 - LEU  20) - starting with 83 contacts
+++ initial contact at step 0: (MET  12 - LEU  28) - starting with 83 contacts
+++ initial contact at step 0: (THR  13 - SER  15) - starting with 83 contacts
+++ initial contact at step 0: (THR  13 - ALA  16) - starting with 83 contacts
+++ initial contact at step 0: (SER  15 - ALA  16) - starting with 83 contacts
+++ initial contact at step 0: (SER  15 - ALA  18) - starting with 83 contacts
+++ initial contact at step 0: (SER  15 - ASN  19) - starting with 83 contacts
+++ initial contact at step 0: (ALA  16 - PHE  17) - starting with 83 contacts
+++ initial contact at step 0: (ALA  16 - ALA  18) - starting with 83 contacts
+++ initial contact at step 0: (ALA  16 - ASN  19) - starting with 83 contacts
+++ initial contact at step 0: (ALA  16 - LEU  20) - starting with 83 contacts
+++ initial contact at step 0: (PHE  17 - ALA  18) - starting with 83 contacts
+++ initial contact at step 0: (PHE  17 - LEU  20) - starting with 83 contacts
+++ initial contact at step 0: (PHE  17 - GLN  25) - starting with 83 contacts
+++ initial contact at step 0: (PHE  17 - LEU  28) - starting with 83 contacts
+++ initial contact at step 0: (PHE  17 - NLE  29) - starting with 83 contacts
+++ initial contact at step 0: (ALA  18 - ASN  19) - starting with 83 contacts
+++ initial contact at step 0: (ALA  18 - LEU  20) - starting with 83 contacts
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+++ initial contact at step 0: (ALA  18 - GLN  25) - starting with 83 contacts
+++ initial contact at step 0: (ASN  19 - LEU  20) - starting with 83 contacts
+++ initial contact at step 0: (LEU  20 - PRO  21) - starting with 83 contacts
+++ initial contact at step 0: (LEU  20 - NLE  24) - starting with 83 contacts
+++ initial contact at step 0: (LEU  20 - GLN  25) - starting with 83 contacts
+++ initial contact at step 0: (LEU  20 - LEU  28) - starting with 83 contacts
+++ initial contact at step 0: (PRO  21 - TRP  23) - starting with 83 contacts
+++ initial contact at step 0: (PRO  21 - NLE  24) - starting with 83 contacts
+++ initial contact at step 0: (LEU  22 - GLN  25) - starting with 83 contacts
+++ initial contact at step 0: (LEU  22 - GLN  26) - starting with 83 contacts
+++ initial contact at step 0: (TRP  23 - NLE  24) - starting with 83 contacts
+++ initial contact at step 0: (NLE  24 - LEU  28) - starting with 83 contacts
+++ initial contact at step 0: (GLN  25 - NLE  29) - starting with 83 contacts
+++ initial contact at step 0: (GLN  26 - HIP  27) - starting with 83 contacts
+++ initial contact at step 0: (GLN  26 - NLE  29) - starting with 83 contacts
+++ initial contact at step 0: (GLN  26 - CPH  35) - starting with 83 contacts
+++ initial contact at step 0: (HIP  27 - LEU  28) - starting with 83 contacts
+++ initial contact at step 0: (HIP  27 - LYP  30) - starting with 83 contacts
+++ initial contact at step 0: (LEU  28 - GLU  31) - starting with 83 contacts
+++ initial contact at step 0: (LEU  28 - LYP  32) - starting with 83 contacts
+++ initial contact at step 0: (NLE  29 - LEU  34) - starting with 83 contacts
+++ initial contact at step 0: (NLE  29 - CPH  35) - starting with 83 contacts
+++ initial contact at step 0: (LYP  30 - CPH  35) - starting with 83 contacts
+++ initial contact at step 0: (GLU  31 - LYP  32) - starting with 83 contacts
+++ initial contact at step 0: (GLY  33 - LEU  34) - starting with 83 contacts
+++ initial contact at step 0: (GLY  33 - CPH  35) - starting with 83 contacts
--- contact broken at step 1: (HIP  27 - LYP  30) - now have 82 contacts
+++ contact formed at step 6: (ALA  8 - PHE  10) - now have 84 contacts
+++ contact formed at step 6: (HIP  27 - LYP  30) - now have 84 contacts
--- contact broken at step 7: (ALA  8 - PHE  10) - now have 82 contacts
--- contact broken at step 7: (HIP  27 - LYP  30) - now have 82 contacts
+++ contact formed at step 10: (ASP  3 - SER  15) - now have 83 contacts
+++ contact formed at step 16: (GLU  4 - ASP  5) - now have 84 contacts
--- contact broken at step 19: (GLU  4 - ASP  5) - now have 83 contacts
+++ contact formed at step 20: (GLU  4 - ASP  5) - now have 84 contacts
--- contact broken at step 21: (GLU  4 - ASP  5) - now have 83 contacts
--- contact broken at step 27: (NLE  1 - LEU  34) - now have 81 contacts
--- contact broken at step 27: (GLN  26 - HIP  27) - now have 81 contacts
+++ contact formed at step 30: (GLU  4 - ASP  5) - now have 84 contacts
+++ contact formed at step 30: (TRP  23 - HIP  27) - now have 84 contacts
+++ contact formed at step 30: (HIP  27 - LYP  30) - now have 84 contacts
--- contact broken at step 31: (HIP  27 - LYP  30) - now have 83 contacts
+++ contact formed at step 32: (GLN  26 - HIP  27) - now have 84 contacts
--- contact broken at step 33: (GLN  26 - HIP  27) - now have 83 contacts
+++ contact formed at step 36: (HIP  27 - LYP  30) - now have 84 contacts
--- contact broken at step 37: (HIP  27 - LYP  30) - now have 83 contacts
+++ contact formed at step 38: (HIP  27 - LYP  30) - now have 84 contacts
--- contact broken at step 59: (PRO  21 - TRP  23) - now have 82 contacts
--- contact broken at step 59: (HIP  27 - LYP  30) - now have 82 contacts
--- contact broken at step 83: (NLE  1 - VAL  9) - now have 81 contacts
--- contact broken at step 93: (TRP  23 - NLE  24) - now have 80 contacts
+++ contact formed at step 128: (HIP  27 - GLU  31) - now have 81 contacts
--- contact broken at step 132: (TRP  23 - HIP  27) - now have 80 contacts
+++ contact formed at step 136: (GLY  11 - LYP  32) - now have 81 contacts
--- contact broken at step 146: (GLN  26 - NLE  29) - now have 80 contacts
--- contact broken at step 147: (GLY  11 - LYP  32) - now have 80 contacts
+++ contact formed at step 147: (TRP  23 - HIP  27) - now have 80 contacts
+++ contact formed at step 148: (GLY  11 - LYP  32) - now have 81 contacts
+++ contact formed at step 154: (THR  13 - ARG  14) - now have 82 contacts
--- contact broken at step 157: (HIP  27 - GLU  31) - now have 81 contacts
--- contact broken at step 159: (GLY  33 - CPH  35) - now have 80 contacts
+++ contact formed at step 162: (GLY  33 - CPH  35) - now have 81 contacts
--- contact broken at step 163: (ASP  5 - PHE  6) - now have 80 contacts
+++ contact formed at step 164: (HIP  27 - GLU  31) - now have 81 contacts
--- contact broken at step 166: (GLY  33 - CPH  35) - now have 80 contacts
+++ contact formed at step 167: (GLY  33 - CPH  35) - now have 81 contacts
--- contact broken at step 168: (GLY  33 - CPH  35) - now have 80 contacts
+++ contact formed at step 171: (GLY  33 - CPH  35) - now have 81 contacts
--- contact broken at step 172: (GLY  33 - CPH  35) - now have 80 contacts
--- contact broken at step 183: (ASN  19 - LEU  20) - now have 79 contacts
+++ contact formed at step 201: (PHE  10 - NLE  29) - now have 80 contacts
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+++ contact formed at step 207: (ASN  19 - LEU  20) - now have 81 contacts
--- contact broken at step 208: (ASN  19 - LEU  20) - now have 79 contacts
--- contact broken at step 208: (NLE  24 - LEU  28) - now have 79 contacts
+++ contact formed at step 209: (TRP  23 - NLE  24) - now have 80 contacts
+++ contact formed at step 210: (GLY  33 - CPH  35) - now have 81 contacts
--- contact broken at step 212: (TRP  23 - HIP  27) - now have 80 contacts
+++ contact formed at step 249: (PRO  21 - TRP  23) - now have 81 contacts
+++ contact formed at step 257: (NLE  24 - LEU  28) - now have 82 contacts
--- contact broken at step 258: (THR  13 - ARG  14) - now have 81 contacts
--- contact broken at step 264: (GLY  11 - LYP  32) - now have 80 contacts
+++ contact formed at step 266: (GLY  11 - LYP  32) - now have 81 contacts
--- contact broken at step 267: (GLY  11 - LYP  32) - now have 80 contacts
+++ contact formed at step 270: (ASN  19 - LEU  20) - now have 81 contacts
+++ contact formed at step 286: (GLY  11 - LYP  32) - now have 82 contacts
+++ contact formed at step 289: (NLE   1 - VAL   9) - now have 82 contacts
--- contact broken at step 289: (ASN  19 - LEU  20) - now have 82 contacts
--- contact broken at step 344: (PRO  21 - TRP  23) - now have 81 contacts
+++ contact formed at step 367: (ASN  19 - LEU  20) - now have 83 contacts
+++ contact formed at step 367: (PRO  21 - TRP  23) - now have 83 contacts
--- contact broken at step 372: (NLE   1 - VAL   9) - now have 82 contacts
--- contact broken at step 378: (ASN  19 - LEU  20) - now have 81 contacts
+++ contact formed at step 380: (ASN  19 - LEU  20) - now have 82 contacts
--- contact broken at step 383: (ASN  19 - LEU  20) - now have 81 contacts
+++ contact formed at step 392: (ASN  19 - LEU  20) - now have 82 contacts
+++ contact formed at step 400: (NLE   1 - VAL   9) - now have 83 contacts
--- contact broken at step 402: (NLE   1 - VAL   9) - now have 82 contacts
--- contact broken at step 408: (ASN  19 - LEU  20) - now have 81 contacts
--- contact broken at step 431: (HIP  27 - GLU  31) - now have 80 contacts
+++ contact formed at step 472: (TRP  23 - HIP  27) - now have 81 contacts
--- contact broken at step 473: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 474: (NLE  24 - LEU  28) - now have 81 contacts
--- contact broken at step 478: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 482: (NLE  24 - LEU  28) - now have 81 contacts
--- contact broken at step 490: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 498: (THR  13 - ARG  14) - now have 81 contacts
--- contact broken at step 504: (THR  13 - ARG  14) - now have 80 contacts
+++ contact formed at step 507: (NLE  24 - LEU  28) - now have 81 contacts
--- contact broken at step 510: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 518: (NLE  24 - LEU  28) - now have 81 contacts
--- contact broken at step 520: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 526: (THR  13 - ARG  14) - now have 82 contacts
+++ contact formed at step 526: (NLE  24 - LEU  28) - now have 82 contacts
--- contact broken at step 528: (THR  13 - ARG  14) - now have 80 contacts
--- contact broken at step 528: (TRP  23 - HIP  27) - now have 80 contacts
--- contact broken at step 559: (NLE  24 - LEU  28) - now have 79 contacts
+++ contact formed at step 568: (NLE   1 - ARG  14) - now have 80 contacts
--- contact broken at step 571: (NLE   1 - ARG  14) - now have 79 contacts
+++ contact formed at step 572: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 576: (NLE   1 - ARG  14) - now have 80 contacts
--- contact broken at step 576: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 602: (GLN  26 - NLE  29) - now have 81 contacts
+++ contact formed at step 607: (HIP  27 - GLU  31) - now have 82 contacts
--- contact broken at step 629: (GLN  26 - NLE  29) - now have 81 contacts
--- contact broken at step 631: (NLE   1 - ARG  14) - now have 81 contacts
+++ contact formed at step 631: (NLE  24 - LEU  28) - now have 81 contacts
+++ contact formed at step 633: (GLN  26 - NLE  29) - now have 82 contacts
--- contact broken at step 634: (GLN  26 - NLE  29) - now have 81 contacts
+++ contact formed at step 635: (GLN  26 - NLE  29) - now have 82 contacts
+++ contact formed at step 637: (NLE   1 - VAL   9) - now have 83 contacts
+++ contact formed at step 652: (ASN  19 - LEU  20) - now have 84 contacts
--- contact broken at step 658: (GLY  33 - CPH  35) - now have 83 contacts
--- contact broken at step 659: (GLN  26 - NLE  29) - now have 82 contacts
+++ contact formed at step 679: (GLN  26 - NLE  29) - now have 83 contacts
--- contact broken at step 686: (GLN  26 - NLE  29) - now have 82 contacts
--- contact broken at step 694: (ASN  19 - LEU  20) - now have 81 contacts
+++ contact formed at step 695: (GLY  33 - CPH  35) - now have 82 contacts
--- contact broken at step 702: (GLY  33 - CPH  35) - now have 81 contacts
+++ contact formed at step 703: (GLY  33 - CPH  35) - now have 82 contacts
+++ contact formed at step 705: (GLN  26 - NLE  29) - now have 83 contacts
--- contact broken at step 711: (GLY  33 - CPH  35) - now have 82 contacts
+++ contact formed at step 712: (GLY  33 - CPH  35) - now have 83 contacts
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--- contact broken at step 714: (GLN  26 - NLE  29) - now have 82 contacts
--- contact broken at step 715: (GLY  33 - CPH  35) - now have 81 contacts
+++ contact formed at step 716: (ASN  19 - LEU  20) - now have 82 contacts
--- contact broken at step 725: (ASN  19 - LEU  20) - now have 81 contacts
+++ contact formed at step 732: (GLY  33 - CPH  35) - now have 82 contacts
+++ contact formed at step 737: (ASN  19 - LEU  20) - now have 83 contacts
--- contact broken at step 750: (GLY  33 - CPH  35) - now have 82 contacts
--- contact broken at step 752: (ASN  19 - LEU  20) - now have 82 contacts
+++ contact formed at step 752: (GLY  33 - CPH  35) - now have 82 contacts
--- contact broken at step 800: (NLE  24 - LEU  28) - now have 81 contacts
+++ contact formed at step 824: (NLE  24 - LEU  28) - now have 82 contacts
--- contact broken at step 833: (NLE  24 - LEU  28) - now have 81 contacts
+++ contact formed at step 836: (NLE  24 - LEU  28) - now have 82 contacts
--- contact broken at step 838: (NLE  24 - LEU  28) - now have 81 contacts
--- contact broken at step 843: (NLE  1 - VAL  9) - now have 80 contacts
+++ contact formed at step 849: (NLE  1 - VAL  9) - now have 81 contacts
+++ contact formed at step 853: (NLE  24 - LEU  28) - now have 82 contacts
--- contact broken at step 854: (NLE  24 - LEU  28) - now have 81 contacts
+++ contact formed at step 855: (NLE  24 - LEU  28) - now have 82 contacts
--- contact broken at step 856: (NLE  1 - VAL  9) - now have 81 contacts
+++ contact formed at step 861: (NLE  1 - VAL  9) - now have 82 contacts
--- contact broken at step 863: (NLE  1 - VAL  9) - now have 81 contacts
--- contact broken at step 870: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 884: (NLE  24 - LEU  28) - now have 81 contacts
--- contact broken at step 886: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 889: (NLE  24 - LEU  28) - now have 81 contacts
--- contact broken at step 899: (PRO  21 - TRP  23) - now have 80 contacts
+++ contact formed at step 933: (TRP  23 - HIP  27) - now have 81 contacts
--- contact broken at step 934: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 976: (ASP  5 - PHE  6) - now have 81 contacts
--- contact broken at step 977: (ASP  5 - PHE  6) - now have 80 contacts
--- contact broken at step 979: (TRP  23 - HIP  27) - now have 79 contacts
+++ contact formed at step 1014: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 1018: (GLN  26 - NLE  29) - now have 81 contacts
--- contact broken at step 1019: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 1020: (NLE  24 - LEU  28) - now have 81 contacts
--- contact broken at step 1021: (NLE  24 - LEU  28) - now have 80 contacts
+++ contact formed at step 1022: (NLE  24 - LEU  28) - now have 81 contacts
--- contact broken at step 1023: (NLE  24 - LEU  28) - now have 79 contacts
--- contact broken at step 1023: (GLN  26 - NLE  29) - now have 79 contacts
+++ contact formed at step 1024: (GLN  26 - NLE  29) - now have 80 contacts
+++ contact formed at step 1028: (NLE  24 - LEU  28) - now have 81 contacts
--- contact broken at step 1029: (NLE  24 - LEU  28) - now have 80 contacts
--- contact broken at step 1031: (TRP  23 - NLE  24) - now have 79 contacts
+++ contact formed at step 1032: (NLE  24 - LEU  28) - now have 80 contacts
--- contact broken at step 1033: (NLE  24 - LEU  28) - now have 79 contacts
+++ contact formed at step 1034: (NLE  24 - LEU  28) - now have 80 contacts
--- contact broken at step 1035: (NLE  24 - LEU  28) - now have 79 contacts
+++ contact formed at step 1036: (NLE  24 - LEU  28) - now have 80 contacts
--- contact broken at step 1037: (NLE  24 - LEU  28) - now have 79 contacts
+++ contact formed at step 1038: (NLE  24 - LEU  28) - now have 80 contacts
--- contact broken at step 1041: (NLE  24 - LEU  28) - now have 79 contacts
+++ contact formed at step 1042: (NLE  24 - LEU  28) - now have 80 contacts
--- contact broken at step 1043: (NLE  24 - LEU  28) - now have 78 contacts
--- contact broken at step 1043: (GLN  26 - NLE  29) - now have 78 contacts
+++ contact formed at step 1046: (GLN  26 - NLE  29) - now have 79 contacts
```

Supporting References

[1] Bowers, K. J.; Chow, E.; Xu, H.; Dror, R. O.; Eastwood, M. P.; Gregersen, B. A.; Klepeis, J. L.; Kolossváry, I.; Moraes, M. A.; Sacerdoti, F. D.; Salmon, J. K.; Shan, Y.; Shaw, D. E. Scalable Algorithms for Molecular Dynamics Simulations on Commodity Clusters, *Proceedings of the 2006 ACM/IEEE Conference on Supercomputing*, Tampa, FL, 2006; ACM Press: New York, NY, 2006.

[2] Kubelka, J.; Chiu, T. K.; Davies, D. R.; Eaton, W. A.; Hofrichter, J. Sub-Microsecond Protein Folding. *J. Mol. Biol.* **2006**, *359*, 546–553.

[3] *Maestro*, version 8.0; Schrödinger, LLC: New York, NY, 2007.