

Method S3

Detailed protocol of the simulation of molecular dynamics

A 5.0 ns simulation of the tandem BRCT of NBS1 in explicit solvent is presented in this study. The modelled structure of the protein was introduced in a box of water (i) ions were introduced to obtain a neutral system (ii) the system was minimized in two steps, first water minimization and then entire system minimization (iii) the system was warmed to 300K with a simulated annealing (iv) the 5.0 ns dynamic at 300K was performed.

The molecular dynamic simulation was conducted using the GROMACS v3.2 molecular dynamics simulation package with parameter set opl. The production simulation was performed in the NVT ensemble. The system temperature was coupled using the Berendsen algorithm at 300 K with coupling constant $\tau_T = 0.1$ ps. Electrostatic interactions were calculated using the particle mesh Ewald with a real space cutoff of 0.9 nm. Cutoff for van der Waals interactions was set at 0.9 nm. Time-step for integration was 2 fs, coordinates and velocities were saved every 2 ps.

The box size was determined so as to be 10Å around the protein. The global system was sized 417 nm³ and contained 41667 atoms: 3482 atoms representing the 223 residues of the tandem BRCT of NBS1, 38160 atoms representing solvent (12720 H₂O molecules), 13 Na⁺ and 12 Cl⁻. As the charge of the protein was -1e, the global system was neutral.

The system was subjected to 1000 steps of conjugate gradient energy minimization. The coordinates of the protein were frozen, allowing the solvent molecules to relax. A second 1000 steps of conjugate gradient energy minimization was then performed without freezing the protein in order to remove clashes often found in modelled protein structures.

The entire system was subjected to a simulated annealing. The temperature was linearly increased from 0K to 300K in 600ps. The resulting system was used in a 5.0 ns simulation at 300K.

Simulations were analyzed using GROMACS routines. Secondary structures were analyzed using DSSP.