**Supporting protocol S1.** *In silico* analyses of BvgS-p dynamics and associated references.

Normal mode analyses

Normal mode analyses (NMA) were performed using the standalone version of the HingeProt program [1], using cut-off values of 1.0 nm in the Gaussian Network Model [2].

Molecular dynamics simulations

To prepare the MD simulations, missing side-chain atoms were constructed using the program ‘profix’ of the Jackal package (<http://wiki.c2b2.columbia.edu/honiglab_public/index.php/Software:Jackal>) [3]. The resulting structure file was immersed in a truncated dodecahedron box consisting of SPC water molecules [4], keeping a minimum distance of 1.0 nm from the protein to the edges of the box. Overlapping water molecules were removed, and 22 random water molecules were replaced by Na+ atoms to ensure electrostatic neutrality. The resulting system box (volume of 1074.8 nm3) contained BvgS, 22 Na+ atoms and 30657 water molecules, totaling 102097 particles. The system was equilibrated using 2000 steps of steepest descent energy minimization followed by 100-ps molecular dynamics simulation with weak position restraints on all protein atoms, excluding hydrogens. The calculations were performed with the Gromacs suite of programs [5], version 4.5.4, using the Gromos96 43a2 parameter set [6]. A time step of 2 fs was employed, updating the neighbor list every 5 steps. The system was coupled to a temperature bath at 310 K with a coupling constant of 0.1 ps [7]. Pressure was maintained at 1 bar using isotropic pressure coupling with a coupling constant of 1 ps. Van der Waals interactions were cut off at a distance of 1.0 nm, and electrostatic interactions were calculated with the particle mesh Ewald method [8], using fourth-order splining and a grid spacing of 0.12 nm. Equations of motion for the water molecules were solved analytically with the SETTLE algorithm [9]. All bonds were constrained using the LinCS algorithm[10],and the rotational motion involving CH3 groups was slowed down using virtual sites [11]. For the production runs, the time step was increased to 4 fs and the velocity rescaling procedure was used for the temperature coupling [12]. Three production runs were made, one of 400 ns and two of 300 ns. All simulations were run on in-house parallel computing hardware.

Construction of a model of BvgSE113C/N177C with S-S bonded VFT1s

Residues Glu113 and Asn177 were mutated *in silico* to Cys residues, and the distance between the sulfur atoms was measured. A disulfide bond was created in the molecular topology, and by use of a slow-growth molecular dynamics simulation the bond was slowly decreased to its desired length of 2.04 Å at a rate of 1 Å/ns. A time step of 2 fs was employed. In order to avoid distortion of the protein, initial N-O hydrogen bond donor-acceptor distances *d*N-O in α and β secondary structure elements were measured and subjected to distance-dependent additional restraints by applying a harmonic penalty potential (force constant *k*dr) above a chosen threshold distance *d*r. For strong hydrogen bonds (*d*N-O < 2.76 Å), a threshold distance *d*r of 2.76 Å with *k*dr = 3 106 kJ/mol/nm was employed, while for weaker hydrogen bonds (2.76 Å < *d*N-O < 3.50 Å) *d*r was increased to 3.50 Å and *k*dr was reduced to 106 kJ/mol/nm. A linear force penalty was applied for distances exceeding 3.4 Å and 5.0 Å for strong and weak hydrogen bonding, respectively. All other simulation parameters were as in the production runs.

**Supporting References**

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