

# Supporting Information

**Time-dependent dielectric relaxation** To probe the time dependency of dielectric relaxation in the protein, we consider the electrostatic potential  $V(t)$  on the heme nitrogens (averaged over the four sites) after the redox electron is abruptly removed from the reduced protein. Averaging over a large number of starting structures gives the ensemble average  $\langle V(t) \rangle_R$  (R for “reduced” state average). Here, perturbing charges (+0.25e on each heme nitrogen, representing the redox electron) were inserted into 24 structures drawn from a 2.3-ns simulation of the reduced protein, and 24 simulations were run, each of 30 ps length, with Nosé Hoover conditions, as above (although strictly speaking, constant energy simulations should be used to study the time-dependent relaxation). Fig. 4 shows  $\langle V(t) \rangle_R$ . Three different estimates are reported. The first (grey dots) is the average over the 24 non-equilibrium simulations. The second and third are linear response estimates, based on the equilibrium fluctuations of the potential  $V(t)$  in the oxidized state. Indeed, one can show [1–4] that

$$\langle V(t) \rangle_R = \langle V(0) \rangle_O - \beta(\langle V(0)V(t) \rangle_O - \langle V(0) \rangle_O^2) + O(V)^3$$

The brackets  $\langle \rangle_O$  represent an ensemble average over the oxidized state, approximated here by averaging over a molecular dynamics (MD) simulation. Linear response neglects the last term. Two MD simulations are used: the first (2.3 ns; black line) simulation of run 1 and the last (1.5 ns; dashed line) simulation of run 2. Fig. 4 shows that the direct and linear response estimates agree well for short times,  $\leq 10$  ps (by which time the relaxation is almost complete). For longer times, nonlinearities  $O(V)^3$  contribute, and the linear response prediction for  $\langle V(t) \rangle_R$  is no longer accurate.

## References

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