Supporting Information:
Radical Scavenging Could Answer the Challenge
Posed by Electron-Electron Dipolar Interactions
in the Cryptochrome Compass Model

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Spin dynamics simulations

Dynamics of the spin density $\hat{\rho}(t)$ are described by the Liouville-von Neumann equation,

$$\frac{d}{dt}\hat{\rho}(t) = -\frac{i}{\hbar} \left[ \hat{H}, \hat{\rho}(t) \right] - k_X \hat{\rho}(t) - \frac{k_f}{2} \left\{ \hat{P}_{ab}, \hat{\rho}(t) \right\}, \quad (S1)$$

where the time-independent Hamiltonian may be written as sum of energy operators:

$$\hat{H} = \hat{H}_{\text{Zee}} + \hat{H}_{\text{dip}} + \hat{H}_{\text{hf}} + \hat{H}_{\text{ex}}, \quad (S2)$$

including magnetic Zeeman effects $\hat{H}_{\text{Zee}}$, electron-electron dipolar (EED) interactions $\hat{H}_{\text{dip}}$, electron-nuclear “hyperfine” coupling $\hat{H}_{\text{hf}}$, and electron-electron exchange $\hat{H}_{\text{ex}}$. We neglect decoherence processes, assumed slow relative to the lifetime of the radical pair, as reflected in the rate constants for scavenging $k_X$ and escape $k_f$. As usual, square brackets $[,]$ denote commutation, whereas brace brackets $\{,\}$ indicate anti-commutation of the enclosed terms.

In detail, the Zeeman Hamiltonian $\hat{H}_{\text{Zee}} = \sum_i g_i \mu_B \hat{S}_i \cdot \vec{B}$ describes interaction of the magnetic field denoted $\vec{B}$ with each radical $i$’s spin angular momentum (expressed as unitless vector operators $\hat{S}_i$), where $\mu_B$ is the Bohr magneton. The dipolar Hamiltonian $\hat{H}_{\text{dip}}$ defines the energy of the EED interactions,

$$\hat{H}_{\text{dip}} = -\sum_{i>j}^m D_{ij}(r_{ij}) \left( 3(\hat{S}_i \cdot \vec{u}_{ij})(\hat{S}_j \cdot \vec{u}_{ij}) - (\hat{S}_i \cdot \hat{S}_j) \right) \quad (S3)$$

where $D_{ij}(r_{ij}) = \mu_0 g_i g_j \mu_B^2 / (4\pi |\vec{r}_{ij}|^3)$, $\vec{r}_{ij} = \vec{r}_j - \vec{r}_i$ gives the displacement from radical $i$ to $j$ where $\vec{u}_{ij} = \vec{r}_{ij} / |\vec{r}_{ij}|$ is the corresponding unit vector, $g_i$ and $g_j$ designate electronic $g$-factors, and $\mu_0$ denotes the magnetic permeability of free space. The hyperfine Hamiltonian $\hat{H}_{\text{hf}}$ defines the energy of interaction of the $i$th electron spin with the $n_i$ magnetic nuclei (enumerated as $\ell_i$) within the radical $i$:

$$\hat{H}_{\text{hf}} = \sum_i \hat{\mathbf{S}}_i \cdot \left( \sum_{\ell_i=1}^{n_i} A_{i\ell} \cdot \hat{I}_{\ell_i} \right). \quad (S4)$$
The anisotropic hyperfine coupling tensors $A_{iℓ}$ define the electron-nuclear magnetic couplings where they are present. The exchange Hamiltonian is of the form

$$\hat{H}_{\text{ex}} = \sum_{i>j} J_{ij} \left( 2\hat{S}_i \cdot \hat{S}_j + \frac{1}{2} \right).$$

The projector $P_{S}^{ab}$ defines the singlet state of any two radicals $a$ and $b$. Recombination is recovered in the R3M case where $(a, b) = (1, 2)$, whereas scavenging of either of either member of the radical pair is modeled otherwise, i.e., either $(a, b) = (1, 3)$ or $(a, b) = (2, 3)$.

We modeled hyperfine (HF) coupling interactions up to a total of four magnetic nuclei. For the [FAD$^{•-}$ / W$^{•+}$] simulations, two hyperfine interactions were retained each for the FAD and W radical sites. For DmCry, we have used the following previously-calculated hyperfine tensors:\footnote{\textsuperscript{1}}

\begin{align*}
A_{\text{FAD} N_5} &= \begin{bmatrix}
-0.099 & 0.003 & 0 \\
0.003 & -0.087 & 0 \\
0 & 0 & 1.757
\end{bmatrix} \text{ mT}, \\
A_{\text{FAD} N_{10}} &= \begin{bmatrix}
-0.015 & 0.002 & 0 \\
0.002 & -0.024 & 0 \\
0 & 0 & 0.605
\end{bmatrix} \text{ mT}, \\
A_{\text{W} C_{11}} &= \begin{bmatrix}
-0.034 & 0.092 & -0.135 \\
0.092 & 0.330 & -0.532 \\
-0.135 & -0.532 & 0.668
\end{bmatrix} \text{ mT}, \\
A_{\text{W} C_{11}} &= \begin{bmatrix}
-0.992 & -0.209 & -0.200 \\
-0.209 & -0.263 & 0.280 \\
-0.200 & 0.280 & -0.540
\end{bmatrix} \text{ mT}, \\
A_{\text{W} D_{11}} &= \begin{bmatrix}
-0.048 & 0.132 & 0.013 \\
0.132 & 1.056 & 0.103 \\
0.0134 & 0.103 & -0.043
\end{bmatrix} \text{ mT}, \\
A_{\text{W} D_{11}} &= \begin{bmatrix}
-0.678 & -0.050 & 0.516 \\
-0.050 & -0.693 & -0.081 \\
0.516 & -0.081 & -0.425
\end{bmatrix} \text{ mT}.
\end{align*}
For ClCry4, the flavin hyperfine tensors were as given above, whereas the tryptophan
tensors were rotated to reflect its altered relative orientation in this protein:

\[
\mathbf{A}_{WC N_1} = \begin{bmatrix}
-0.053 & -0.059 & 0.046 \\
-0.059 & 0.564 & -0.565 \\
0.046 & -0.565 & 0.453
\end{bmatrix} \text{ mT,}
\]

\[
\mathbf{A}_{WC H_1} = \begin{bmatrix}
-1.000 & -0.206 & -0.193 \\
-0.206 & -0.442 & 0.307 \\
-0.193 & 0.307 & -0.352
\end{bmatrix} \text{ mT,}
\]

\[
\mathbf{A}_{WD N_1} = \begin{bmatrix}
-0.063 & -0.0141 & -0.001 \\
-0.014 & 1.064 & 0.138 \\
-0.001 & 0.138 & -0.036
\end{bmatrix} \text{ mT,}
\]

\[
\mathbf{A}_{WD H_1} = \begin{bmatrix}
-0.697 & -0.062 & 0.512 \\
-0.062 & -0.704 & -0.026 \\
0.512 & -0.026 & -0.394
\end{bmatrix} \text{ mT.}
\]

For the flavin semiquinone, the following three tensors were used:

\[
\mathbf{A}_{FAD N_5} = \begin{bmatrix}
-2.431 & -0.068 & -0.363 \\
-0.068 & -2.445 & 0.306 \\
-0.363 & 0.306 & 43.53
\end{bmatrix} \text{ MHz,}
\]

\[
\mathbf{A}_{FAD N_{10}} = \begin{bmatrix}
0.494 & 0.068 & 2.101 \\
0.068 & -0.016 & -0.209 \\
2.101 & -0.209 & 23.10
\end{bmatrix} \text{ MHz,}
\]

\[
\mathbf{A}_{FAD H_5} = \begin{bmatrix}
-2.380 & 1.872 & 0.167 \\
1.872 & -40.64 & 0.081 \\
0.167 & 0.081 & -27.87
\end{bmatrix} \text{ MHz.}
\]

The position of the scavenger radical was varied in three dimensions by assuming a
virtual “shell” of possible locations on the vertices of a sphere-like geodesic polyhedron of
radius \( R \), while varying \( R \). For each type of scavenger reaction (scavenging of the anion
or cation of the primary radical pair), the polyhedron was centred around the scavenger’s
target radical. We initially sampled scavenger coordinates at \( \Delta R = 1 \text{ Å} \) radial increments,
recursively adjusting the radius increment and number of vertices to generate a smooth
MFE function $\Gamma$ for each tunneling decay constant $\beta$ tested. The “R3M”\textsuperscript{1} recombination-based systems were approximated by simulating primary-pair recombination with a third, unreactive “bystander” radical nearby.

Figure S1: Graphical representation of $Dm$Cry4 (PDB ID: 4GU5)\textsuperscript{2} as a ribbon diagram.\textsuperscript{3} Labels indicate the FAD prosthetic group and Trp terad residues, superimposed on the protein ribbon to illustrate their positions in the molecule.
Figure S2: Pertinent residues in the crystal structure of ClCry4 (red) and the homology model of ErCry4 from Ref. [4] (blue). The root-mean-square displacement (RMSD) of the relevant part of both of these structures amounts to only 1.2 Å and the differences in inter-radical distances are negligible (compared to their fluctuations as assessed in molecular dynamics simulation). Note in particular that DmCry and ClCry4 too differ by a RMSD of 1.2 Å, while the simulated MFEs of these systems are practically identical (cf. Fig. 2 and S8). No intrinsic enhancement of magnetosensitivity is expected for ErCry4 within the constraints of the suggested model. The superiority recently established for ErCry4 in vitro appears to be the result of tuned rate constants. However, the rate constants established there do not permit substantial magnetosensitivity in the geomagnetic field. Changes in the relative radical orientation are likewise not expected to dramatically boost the magnetosensitivity.

Table S1: Summary of three-radical reactions. The table shows the initial spin configuration of the geminate radical pair, the charge recombination mechanism, and the reaction scheme as given in the main manuscript. Bystander-enhanced schemes (in the top two rows) recover the RPM in the large-distance limit of the distance from the primary pair to bystander B•.

| Radical Trio Notation | Geminate Pair | Mechanism | Scheme |
|-----------------------|--------------|-----------|--------|
| (FAD•− / W•+) / B•    | Singlet      | Recombination | 2      |
| (FAD• / Z•−) / B•     | Triplet      | Recombination | 2      |
| FAD•− / (W•+ / S•)    | Singlet      | Scavenging  | 3      |
| (S• / FAD•−) / W•+    | Singlet      | Scavenging  | 3      |
| FADH• / (Z•− / S•)    | Triplet      | Scavenging  | 3      |
| (S• / FADH•) / Z•−    | Triplet      | Scavenging  | 3      |
Unconstrained models

We began by carrying out a systematic exploration of the reaction phase space, setting $k_{12} = 0$ and independently varying $k_{13}$ and $k_{23}$ for a scavenger radical positioned at one of a few choice locations around the surface of $Dm$Cry, but preliminary results did not suggest a likelihood of finding a single, joint optimum MFE for some specific values of $\{k_{13}, k_{23}\}$. So, as an alternative approach, we next set $k_{12} = k_{23} = 0$ for the $(S^*/FAD^*)/W^*$ reaction in $Dm$Cry, systematically considering a wide range of possible values for $k_{13}$ while exploring possible scavenger positions over the whole volume of space within 200 Å of the FAD cofactor. To our surprise, a global maximum MFE anisotropy $\Gamma_{\text{max}}$ was obtained using the value $k_{13} \approx 0.03 \text{ ns}^{-1}$ in the asymptotic limit as $R \to \infty$.

**Figure S3:** This plot shows the maximum anisotropic magnetic field effect $\Gamma$ as a function the distance from the scavenger to its target FAD in the molecule $Dm$Cry.
Table S2: Unconstrained optimal relative MFEs $\Gamma_{\text{opt}}^{\text{max}}$, with corresponding scavenger-radical distances $R_{\text{opt}}^{\text{max}} \leq 100\ang$ and rates $k_{X}^{\text{opt}}$. For the FAD$^{\bullet-}$ / W$^{\bullet+}$ radical pairs, we have studied the relative orientations as found in ClCry4 and DmCry. The FADH$^{\bullet-}$ / Z$^{\bullet+}$ models are applicable to both species. ET rates are given in GHz. Brackets indicate which radical is being scavenged by S$^{\bullet}$ (cf Table S1). For comparison, see also Figures S2 - S5.

| Radical Trio | DmCry | ClCry4 |
|-------------|-------|--------|
|              | $\Gamma_{\text{opt}}^{\text{max}}$ | $R_{\text{opt}}^{\text{max}}$ | $k_{X}$ | $\Gamma_{\text{opt}}^{\text{max}}$ | $R_{\text{opt}}^{\text{max}}$ | $k_{X}$ |
| FAD$^{\bullet-}$ / ( W$_{C}^{\bullet+}$ / S$^{\bullet}$ ) | 45% | 70\ang | 0.03 | 44% | 75\ang | 0.03 |
| FAD$^{\bullet-}$ / ( W$_{D}^{\bullet+}$ / S$^{\bullet}$ ) | 53% | 80\ang | 0.03 | 52% | 90\ang | 0.03 |
| FADH$^{\bullet-}$ / ( Z$_{\text{near}}^{\bullet+}$ / S$^{\bullet}$ ) | 107% | 100\ang | 0.03 | 107% | 100\ang | 0.03 |
| FADH$^{\bullet-}$ / ( Z$_{\text{par}}^{\bullet+}$ / S$^{\bullet}$ ) | 147% | 45\ang | 0.03 | 147% | 45\ang | 0.03 |
| ( S$^{\bullet}$ / FAD$^{\bullet-}$ ) / W$_{C}^{\bullet+}$ | 162% | 100\ang | 0.03 | 158% | 100\ang | 0.03 |
| ( S$^{\bullet}$ / FAD$^{\bullet-}$ ) / W$_{D}^{\bullet+}$ | 181% | 100\ang | 0.03 | 179% | 100\ang | 0.03 |
| ( S$^{\bullet}$ / FADH$^{\bullet-}$ ) / Z$_{\text{near}}^{\bullet+}$ | 104% | 100\ang | 0.03 | 104% | 100\ang | 0.03 |
| ( S$^{\bullet}$ / FADH$^{\bullet-}$ ) / Z$_{\text{par}}^{\bullet+}$ | 89% | 100\ang | 0.03 | 89% | 100\ang | 0.03 |

Subsequently, we developed a rough three-parameter approximation of the optimal $k_{13}^{\text{opt}}$, intended to optimize the resulting $\Gamma$ over all space for the reaction ( S$^{\bullet}$ / FAD$^{\bullet-}$ ) / W$^{\bullet+}$ in the DmCry system:

$$k_{13}^{\text{opt}} \approx [0.03 + 6 \cdot \exp(-2 \cdot R/9)] \text{ns}^{-1}.$$  \hspace{1cm} (S5)

Although the expression for $k_{13}^{\text{opt}}$ given in eq. (S5) cannot be characterized as an exactly optimized function for all $R$s, we found that it nevertheless provided a sense of asymptotically optimal behavior in the MFE, while delivering large MFEs at modest values of $R$.

When eq. (S5) was applied as the ET rate constant in the other scavenger-reaction systems listed in Table S2, it uniformly predicted large “optimal” values of the resulting MFEs in the asymptotic limit $R \to \infty$, where substantial scavenger-mediated ET rates could not be considered plausible indicators of MFE-mediating scavenging rates in realistic biological systems. Ad hoc preliminary findings obtained from applying eq. (S5) in the other model systems indicated that unconstrained optimizations of the scavenging rate in the asymptotic distance limit would not lead to realistic MFE predictions—a hypothesis which
was later borne out in the results of the studies we performed as a consequence using ET rates bounded by Marcus theory (viz. Figs. S3, S4, S5).

Figure S4: Top figures show \( \text{FAD}^{−}/(W_{C}^{+}/S^{*}) \) [left] and \( \text{FAD}^{−}/(W_{D}^{+}/S^{*}) \) [right]. Bottom figures show \( (S^{*}/\text{FAD}^{−})/W_{C}^{+} \) [left] and \( (S^{*}/\text{FAD}^{−})/W_{D}^{+} \) [right].

Plots show the maximal \( \Gamma \) as a function of the inter-radical distance \( R \) obtained for \( \text{DmCry} \) using eq. (S5) (green), superimposed on the maximal \( \Gamma \) realizable for activationless ET for four tunneling media: covalently-bound (blue), typical protein (red), “soft” vacuum (yellow), and “hard” vacuum (purple), shown up close in each inset plot.
Figure S5: Top figures show $\text{FAD}^\ast$−/$(\text{W}^\ast_C / \text{S}^\ast)$ [left] and $\text{FAD}^\ast$−/$(\text{W}^\ast_D / \text{S}^\ast)$ [right]. Bottom figures show $(\text{S}^\ast / \text{FAD}^\ast$−$)/\text{W}^\ast_C$ [left] and $(\text{S}^\ast / \text{FAD}^\ast$−$)/\text{W}^\ast_D$ [right].

Plots show estimates of $\Gamma$ predicted for ClCry4 using eq. (S5) (green), laid over the values fit for the various parameters based on activationless ET for four tunneling media: covalently-bound (blue), typical protein (red), “soft” vacuum (yellow), and “hard” vacuum (purple), shown up close in each inset plot.
Figure S6: Top figures show $\text{FADH}^\bullet / (Z_{\text{near}}^- / S^\bullet)$ [left] and $\text{FADH}^\bullet / (Z_{\text{far}}^- / S^\bullet)$ [right]. Bottom figures show $(S^\bullet / \text{FADH}^\bullet) / Z_{\text{far}}^\bullet$ [left] and $(S^\bullet / \text{FADH}^\bullet) / Z_{\text{far}}^\bullet$ [right].

Plots show estimates of $\Gamma$ obtained by using eq. (S5) (green), laid over the values fit for the various parameters based on activationless ET for four tunneling media: covalently-bound (blue), typical protein (red), “soft” vacuum (yellow), and “hard” vacuum (purple), shown up close in each inset plot.
Figure S7: In order to compare the original RPM and its derivative the R3M to the scavenging-mediated mechanism on equal footing, we carried out an additional set of simulations of recombination-based MFEs in cryptochrome employing ET constraints like those used to bound the model of scavenger-mediated MFEs. These are based on activationless ET through three tunneling media: covalently-linked (CB, $\beta = 0.9\text{Å}^{-1}$) shown in blue, typical protein (MD, $\beta = 1.4\text{Å}^{-1}$) in red, and “soft” vacuum (TV, $\beta = 2.8\text{Å}^{-1}$) in yellow. The RPM model proper is recovered from the R3M as the bystander is placed sufficiently far away from the spin-polarized radical-pair to render the bystander’s influence negligible, where the resulting MFE generally becomes negligible as well. The panels give the maximal relative anisotropy as a function of the bystander-flavin distance for a) $\frac{\text{FAD}^\bullet^- / \text{W}_{C}^{\bullet+}}{\text{B}^\bullet}$; b) $\frac{\text{FAD}^\bullet^- / \text{W}_{D}^{\bullet+}}{\text{B}^\bullet}$; c) $\frac{\text{FADH}^\bullet / \text{Z}_{\text{near}}^{\bullet-}}{\text{B}^\bullet}$; and d) $\frac{\text{FADH}^\bullet / \text{Z}_{\text{far}}^{\bullet-}}{\text{B}^\bullet}$.
Scavenger-mediated Relative MFEs in *DmCry*

Figure S8: Maximum relative MFE (Γ) by distance from the scavenged radical S•, for models of FAD•−/W•+ primary-pair types in *DmCry* based on activationless ET through four tunneling media: covalently-bound (blue), typical protein (red), “soft” vacuum (yellow), and “hard” vacuum (purple). Subfigures a and c show MFEs from simulations wherein W•+ was scavenged by S•, whereas subfigures b and d show results for FAD•− scavenged by S•. Tunneling decay parameters are indicated by colour, in figure. Brackets are used in the subfigure labels to indicate the radicals involved in the scavenging process. Note that the anisotropic MFE becomes negligible in the large scavenging-radius limit as ET with the scavenger approaches zero and the primary radical recombination has been neglected.
Figure S9: Maximum relative MFE (Γ) by distance from the scavenger radical S*, for models of FAD•−/Z•− born with random spin configuration (i.e., as F-pairs), assuming activationless ET through protein media (β = 1.4 Å). The legend specifies the identity of the scavenged radical, where brackets indicate the pair involved in the scavenging process. Note that the anisotropic MFE becomes negligible in the large scavenging-distance limit as the ET with the scavenger approaches zero and the primary radical recombination has been neglected.
Figure S10: Maximum absolute MFE ($\Delta \Phi_f$) by scavenger distance $R$ from the scavenged radical $S^*$, for models of FAD$^{•−}/W^{•+}$ primary-pair types in ClCry4 based on activation-less ET through four tunneling media: covalently-bound (blue), typical protein (red), “soft” vacuum (yellow), and “hard” vacuum (purple). Subfigures a and c show MFEs from simulations wherein $W^{•+}$ was scavenged by $S^*$, whereas subfigures b and d show results for FAD$^{•−}$ scavenged by $S^*$. Tunneling decay parameters are indicated by colour, in figure. Brackets in the subfigure labels indicate which radical is involved in the scavenging process. Note that the anisotropic MFE becomes negligible in the large scavenging-radius limit as ET with the scavenger approaches zero, and that the primary radical recombination has been neglected.
Free Scavenger-mediated Absolute Anisotropies

Figure S11: Maximum absolute MFE ($\Delta \Phi_i$) by distance $R$ from the scavenger $S^*$ for each FADH*/$Z^*$− model, based on activationless ET through four tunneling media: covalently-coupled (blue), typical protein (red), “soft” vacuum (yellow), and “hard” vacuum (purple). Subfigures a and b show results from simulations of $Z^*$− scavenged by $S^*$, whereas subfigures c and d show MFEs from simulations of FADH* scavenged by $S^*$. Tunneling decay parameters are indicated by colour, in figure. Brackets are used in the subfigure labels to indicate which radical is being scavenged. These free radical predictions may be similar to those for ClCry4.
Scavenging-mediated Absolute Anisotropies in *DmCry*

Figure S12: Maximum absolute MFE (ΔΦ₁) by scavenger distance R from the scavenged radical S•, for models of FAD•−/W•+ primary-pair types in *DmCry*, based on activation-less ET through four tunneling media: covalently-bound (blue), typical protein (red), “soft” vacuum (yellow), and “hard” vacuum (purple). Subfigures a and c show MFEs from simulations wherein W•+ was scavenged by S•, whereas subfigures b and d show results for FAD•− scavenged by S•. Tunneling decay parameters are indicated by colour, in figure. Brackets in the subfigure labels indicate which radical is involved in the scavenging process. Note that the anisotropic MFE becomes negligible in the large scavenging-radius limit as ET with the scavenger approaches zero, and that the primary radical recombination has been neglected.
Description of scavenger locations leading to enhanced Relative MFEs for \textit{DmCry}

Scavenging of TrpH\textsuperscript{+} by Radical S\textsuperscript{*}

For the FAD\textsuperscript{*−} / ( W\textsubscript{C}\textsuperscript{−} / S\textsuperscript{*} ) reaction in \textit{DmCry} the through-vacuum models predicted optimal scavenger locations placed within 7 Å of W\textsubscript{C}, just outside the protein surface, with a maximum MFEs of 18\% (for \( \beta = 4.0 \, \text{Å}^{-1} \)) in close proximity to Ser396, and bimodal maxima of 16\% (for \( \beta = 2.8 \, \text{Å}^{-1} \)) for scavengers located 5 Å apart, at positions either abutted next to Met331 or tucked between Pro341 and Lys344. Likewise, the typical protein-coupled model predicted bimodal maxima approaching 17\% for scavengers placed in positions 14 Å apart and just outside the protein surface, either 10 Å from W\textsubscript{C} (near Lys344), or 11 Å away from W\textsubscript{C} (near Leu349). The covalently-bridged tunneling model predicted MFEs > 30\% for more-distant scavengers located about 7 Å from the protein surface, approximately equidistant from the protruding residues Glu332 and Lys344.

Simulations of the FAD\textsuperscript{*−} / ( W\textsubscript{D}\textsuperscript{−} / S\textsuperscript{*} ) models in \textit{DmCry} predicted maxima in the MFEs > 20\% for all four tunneling parameters considered. The two “vacuum-like” tunneling models predicted sharp maxima with MFEs of 30\% (\( \beta = 4.0 \, \text{Å}^{-1} \)) and 36\% (\( \beta = 2.8 \, \text{Å}^{-1} \)), both within 7 Å of W\textsubscript{D} and 1.2 Å apart from one another, co-located in between residues Met506 and Met509 just inside the protein surface. Through-protein simulations predicted maxima just outside the protein surface, with maximum MFEs of 24\% (for \( \beta = 1.4 \, \text{Å}^{-1} \)) adjacent to Met506, and 44\% (for \( \beta = 0.9 \, \text{Å}^{-1} \)) above the protein surface between Arg513 and the segment connecting Arg430, Glu429, and Phe428 (near the protein C-terminus).

Scavenging of FAD\textsuperscript{*−} by Radical S\textsuperscript{*}

For the ( S\textsuperscript{*} / FAD\textsuperscript{*−} ) / W\textsubscript{C}\textsuperscript{−} system in \textit{DmCry} the three weakest tunneling models consistently predicted maximum MFEs of 7\% or 8\%. Weakly-coupled models predicted optimal scavenger locations inside the protein fold, in direct contact with the FAD itself.
Models of scavenging via tunneling through typical protein were optimized for scavengers located either in contact with Leu405, or in direct proximity to an FAD phosphate (between Gln311 and His378). The covalently-bridged models predicted maximum MFEs of 23% for scavengers positioned across a broad arc of locations extending 18 Å from Ile308 to Phe272.

For the (S• / FAD•−) / W•+ reactions in DmCry the vacuum-like models predicted maximum MFEs of 10% at optimal locations within 6 Å of the FAD flavin. The typical protein model predicted a bimodal optima of 8% for scavengers 11 Å away from the FAD flavin, but 15 Å apart from each other, in contact with either Leu405 or Thr389. In comparison, covalently-bridged models predicted maximum MFEs of 23% for many possible scavenger positions along a broad arc of possible locations extending 26 Å from His13 to His307.

The FAD-scavenged model of ClCry4 also produced distinctive maximum MFEs, where a [FAD•− / W•+] primary radical pair was assumed. The (S• / FAD•−) / W•+ model, in particular, predicted Γ > 9% for a scavenger located in contact with WA for β = 1.4 Å−1 (roughly equidistant between FAD and WD), or likewise for a scavenger nestled between FAD and Asn391 (or Z•−near) for β = 4.0 Å−1. On the other hand, the (S• / FAD•−) / W•+ model predicted Γ > 7% for scavengers within close contact of Gln287 or Gln380 for β = 1.4 Å−1, or likewise for those nestled inside the FAD U-turn for β = 2.8 Å−1.

Scavenging of Z•− by Radical S•

The FADH• / (Z•−near / S•) simulations all predicted MFEs > 25% for scavengers optimally located inside the DmCry protein surface, in contact with either Asp412 (Γ = 38%, β = 4.0 Å−1), Leu408 (Γ = 29%, β = 2.8 Å−1), Trp 375 (Γ = 29%, β = 1.4 Å−1), or Glu373 (Γ = 36%, β = 0.9 Å−1). For the two weakly-coupled tunneling models, optimal scavenger locations were both within 6 Å of Z•−near, whereas the protein-coupled models predicted more distant scavenger locations positioned 10 Å and 15 Å away from Z•−near, respectively.

The maximum MFEs predicted using the FADH• / (Z•−far / S•−) reactions showed a monotonic dependence on the type of tunneling assumed, predicting smaller MFEs for
weak couplings, and larger MFEs for stronger couplings. The hard vacuum-mediated model predicted optimal MFEs of just 5% for scavengers located 6 Å from the $Z_{\text{far}}$ radical, inside the protein cavity (but outside the protein surface) close to Trp536 in $Dm$Cry. The “soft” vacuum-mediated model predicted optimal MFEs of 14% for locations 7 Å away from the $Z_{\text{far}}$ radical, in the protein cavity (but outside the protein surface) in close proximity to residues Arg237 and Met266. The model of typical through-protein tunneling predicted optimal MFEs approaching 37% for locations within 10 Å of $Z_{\text{far}}$ on the edge of the protein surface in close contact with one FAD phosphate. The covalently-bridged model predicted optimal MFEs nearing 53% for scavengers placed 15 Å away from $Z_{\text{far}}$, just inside the $Dm$Cry protein surface, in close proximity to residues Gln369 and Glu373.

**Scavenging of FADH$^\bullet$ by Radical S$^\bullet$**

Next, we consider (S$^\bullet$− / FADH$^\bullet$) / Z$^\bullet$near reactions schemes, where the weakly-coupled models predicted immense MFEs exceeding 65% for optimally-placed scavengers at two locations within 6 Å of the FAD flavin, near both Asn419 and Arg381 in $Dm$Cry. The protein-coupled models predicted optimal MFEs of about 25% for scavengers located in the vicinity of either Phe318 (for $\beta = 1.4$ Å$^{-1}$) or Gln389 (for $\beta = 0.9$ Å$^{-1}$). Finally, we consider the (S$^\bullet$− / FADH$^\bullet$) / Z$^\bullet$far reaction schemes, for which vacuum tunneling-mediated ET models predict optimal MFEs near 30% for scavengers in close proximity to the FAD flavin. The model of electron tunneling through typical protein predicted MFEs approaching 23% for scavengers placed in coordination with Tyr317, Phe318, and Trp314 in $Dm$Cry. The covalently-bridged model of ET again predicted MFEs approaching 30% for scavengers placed next to Thr386.

**Summary:** Of particular interest were predictions of MFEs of about 20% for a scavenger at the protein surface (in the vicinity of Met506) reacting with $W_D$ to form a stable (closed-shell) product. Curiously, through-vacuum tunneling models predicted that a scavenger in the vicinity of Met343 and Trp394 ($W_D$) could act as a scavenger of $W_C$ producing MFEs in the range of 8% to 10% (assuming activationless ET via “soft” vacuum $\beta = 2.8$ Å$^{-1}$).
RF magnetic field effects

Figure S13: Sensitivity of the magnetic field effect on the reaction yield of the signalling state for the \([\text{FAD}^{\bullet-} / \text{W}^{\bullet+}_D]\) radical pair in ClCry4 (blue, left axis) and its cation-scavenged successor in the form of \([\text{FAD}^{\bullet-} / (\text{W}^{\bullet+}_D / \text{S}^{\bullet})]\) (red, right axis). For both systems, \(k_f^{-1} = 3 \mu s\). For the RPM-model \(k_b^{-1} = 3 \mu s\) while the corresponding rate was neglected in the triad model, as we have discussed in the main manuscript. The scavenger radical \(S^{\bullet}\) has been assumed at the location of maximal sensitivity at a distance \(R = 9.9 \text{ Å}\) from the \(\text{W}^{\bullet+}_D\) for which \(\Gamma = 24.1\%\) is realized in the absence of RF fields. The RPM model only provides \(\Gamma = 0.13\%\).

The RF perturbation was assumed to have amplitude \(5 \mu T\) and be oriented parallel to the molecular \(x\)-axis. The MFE is here assessed in terms of \(2(Y_{\text{max}} - Y_{\text{min}})/(Y_{\text{max}} + Y_{\text{min}})\), where \(Y_{\text{max,min}}\) is the yield evaluated for the static magnetic field direction of maximal/minimal reaction yield in the absence of the RF perturbation, \(i.e.\) in terms of the relative change of the yield at these two selected orientations of the geomagnetic field. To elicit a RF magnetic field sensitivity like that observed in behaviour experiments, a significantly longer lifetime or amplified RF field amplitude needed to be assumed for both the RPM-model and the model suggested here. Horizontal dashed lines indicate the MFE at zero RF frequency.
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