

Posner qubits: spin dynamics of entangled $\text{Ca}_9(\text{PO}_4)_6$ molecules and their role in neural processing

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Abstract

It has been suggested that ^{31}P nuclear spins in $\text{Ca}_9(\text{PO}_4)_6$ molecules could form the basis of a quantum mechanism for neural processing in the brain. A fundamental requirement of this proposal is that spins in different $\text{Ca}_9(\text{PO}_4)_6$ molecules can become entangled and remain so for periods (estimated at many hours) that hugely exceed typical ^{31}P spin relaxation times. Here, we consider the coherent and incoherent spin dynamics of $\text{Ca}_9(\text{PO}_4)_6$ arising from dipolar and scalar spin-spin interactions and derive an upper bound of 37 min on the entanglement lifetime under idealized physiological conditions. We argue that the spin relaxation in $\text{Ca}_9(\text{PO}_4)_6$ is likely to be much faster than this estimate.

Keywords: Entanglement, cognition, spin dynamics, singlet relaxation.

1 Introduction

In a recent article entitled “Quantum Cognition”, Matthew Fisher suggested that nuclear spins might act as qubits in neural processing [1]. He proposed that ^{31}P nuclei could be quantum mechanically entangled in networks of ‘Posner molecules’, $\text{Ca}_9(\text{PO}_4)_6$, formed by the enzymatic hydrolysis of pyrophosphate ($\text{P}_2\text{O}_7^{4-}$), and that pairs of Posner molecules might remain entangled for a day “or possibly much longer” [2]. It was argued that such abnormally long-lived spin coherence could “modulate quantum correlations between the pairwise binding of multiple Posner molecules, even when the pairs are well separated” in spatially distant neurons, apparently allowing long-range quantum-correlated discharge of Ca^{2+} ions as part of a “quantum-to-biochemical transduction” mechanism [3].

Long-lived nuclear spin states are well known in NMR spectroscopy [4–11]. Normally involving just two spin- $\frac{1}{2}$ nuclei in the same molecule (but see Refs [12, 13]), nuclear singlet states have been created that persist for many multiples of

the spin-lattice relaxation time T_1 . In one case, a relaxation time in excess of an hour ($\sim 50T_1$) was measured for a pair of ^{13}C spins in a bespoke organic compound [14]. Such states owe their longevity not just to their immunity from dominant spin relaxation pathways but also to careful experimental control of the coherent spin dynamics arising from chemical shifts and J -couplings, using field shuttling, spin-locking, and spin-decoupling [4]. Fisher’s proposal, by contrast, concerns a molecule whose spin relaxation is claimed to be extremely slow for *all* nuclear spin states, without the requirement to manipulate the coherent part of the spin Hamiltonian [1, 15].

‘Posner’s cluster’ was originally identified by Betts and Posner as a structural unit in hydroxyapatite [16], the main inorganic constituent of bone tissue. It is now thought to be an early intermediate in the nucleation of amorphous calcium phosphate, the precursor of hydroxyapatite [17–20]. *Ab initio* structure calculations suggest that, *in vacuo*, an isolated Posner’s cluster, $\text{Ca}_9(\text{PO}_4)_6$ —henceforth referred to as a Posner molecule [15]—has eight calcium ions at the vertices, and a ninth in the centre, of a distorted cube, with a phosphate ion near the middle of each cubic face [21]. The phosphorus atoms, positioned at the vertices of an octahedron stretched along one of its three-fold rotation axes, have S_6 symmetry with a nearest neighbour separation of $\sim 0.5\text{ nm}$ [21]. Figure 1 shows a representation of the arrangement of the phosphorus atoms in this structure.

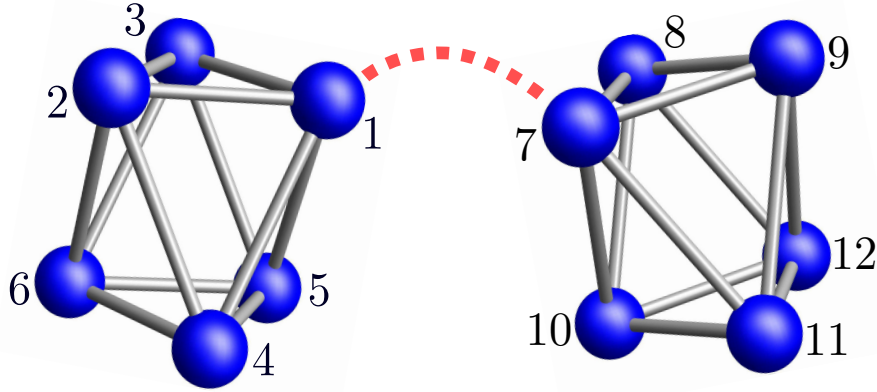


Figure 1: Arrangement of phosphorus atoms in a pair of model Posner molecules $\text{Ca}_9(\text{PO}_4)_6$. The dotted line indicates the two entangled spins in the singlet state $\hat{P}_{1,7}^S$ (see section 2). The S_6 geometry has been emphasized in this representation by exaggeratedly stretching an O_h structure along a three-fold rotation axis. Coupling constants [15]: nearest neighbours (e.g. 1 and 2), $J_A = +0.178\text{ Hz}$; next nearest neighbours (e.g. 1 and 4), $J_B = +0.145\text{ Hz}$; third nearest neighbours (e.g. 1 and 6), $J_C = -0.003\text{ Hz}$. Atoms in the second Posner molecule are numbered 7–12 in the same order as the first.

Several features of $\text{Ca}_9(\text{PO}_4)_6$ suggest slow ^{31}P spin relaxation in aqueous

solution. (a) ^{31}P , the only stable isotope of phosphorus, has spin- $\frac{1}{2}$ and therefore no electric quadrupole moment that would be relaxed by locally fluctuating electric field gradients. (b) Of the five stable isotopes of calcium, only ^{43}Ca , with a natural abundance of 0.135%, has non-zero spin. Unlike phosphate ions (HPO_4^{2-} and H_2PO_4^-), Posner’s molecule contains no other magnetic nuclei (e.g. ^1H) that would lead to efficient dipolar relaxation. (c) Although ^{31}P relaxation in strong magnetic fields is often dominated by chemical shift anisotropy (CSA), this mechanism will be negligibly slow in the Earth’s magnetic field. (d) As a small ($\sim 0.9\text{ nm}$ diameter), approximately spherical molecule [18], the relatively rapid rotational diffusion of $\text{Ca}_9(\text{PO}_4)_6$ would tend to reduce the influence of intermolecular spin-spin interactions. Taken together, these properties conjure up a molecule whose nuclear spins are magnetically isolated from one another and from their surroundings. It was from such considerations that Fisher obtained his original estimate of a 1-day ^{31}P relaxation time [1, 2], subsequently revised to $1.8 \times 10^6\text{ s} \simeq 21\text{ days}$ or “may be even longer” [15]. ^{31}P relaxation times of small molecules in mobile liquids are normally a few seconds at most [22].

Struck by the many orders of magnitude difference between these numbers, we were prompted to look more closely at the spin dynamics of $\text{Ca}_9(\text{PO}_4)_6$ to derive an upper bound on the lifetime of the quantum entanglement of a pair of Posner molecules. In particular, we consider here intramolecular ^{31}P – ^{31}P dipolar and scalar coupling and the Zeeman interaction of the ^{31}P spins with the Earth’s magnetic field. Interesting, but beyond the scope of this report, are other aspects of Fisher’s proposal, such as the enzymatic reaction that creates the pairs of phosphate ions from which the entangled Posner molecules are assembled, and the chemical/physical nature of the read-out process in which Ca^{2+} ions are simultaneously released from entangled molecules that have been transported into remote neurons [1–3, 23].

2 Methods

We treat $\text{Ca}_9(\text{PO}_4)_6$ as a rigid molecule, in which the phosphorus atoms have the distorted octahedral (S_6) arrangement shown in figure 1. We consider the simplest case of intermolecular entanglement—a pair of identical Posner molecules constructed such that two ^{31}P spins, one in each molecule, are initially in the maximally entangled nuclear singlet state, $\hat{P}_{1,7}^{\text{S}} = |\text{S}_{1,7}\rangle\langle\text{S}_{1,7}|$, where $|\text{S}_{1,7}\rangle = [|\alpha_1\beta_7\rangle - |\beta_1\alpha_7\rangle]/\sqrt{2}$. The other ten spins (labelled 2–6 in one molecule and 8–12 in the other, figure 1) are assigned maximally mixed initial states. The spin Hamiltonian of this 12-spin system, $\hat{H}(t) = \hat{H}_0 + \hat{H}_1(t)$, has a time-independent part,

$$\hat{H}_0 = \omega_0 \sum_k \hat{S}_{kz} + \sum_{j < k} \sum_k 2\pi J_{jk} \hat{\mathbf{S}}_j \cdot \hat{\mathbf{S}}_k, \quad (2.1)$$

in which $\hat{\mathbf{S}}_k$ and \hat{S}_{kz} are, respectively, the spin angular momentum operator, and its z -component, for nucleus k . The first term in equation (2.1) accounts

for the Zeeman interaction with the Earth’s magnetic field, taken to have flux density $B_0 = 50 \mu\text{T}$. The ^{31}P Larmor frequency is $|\omega_0/2\pi| = \gamma_{\text{P}} B_0/2\pi = 863 \text{ Hz}$, where $\gamma_{\text{P}} = 10.84 \times 10^7 \text{ T}^{-1} \text{ s}^{-1}$ is the magnetogyric ratio of ^{31}P . The six ^{31}P spins in each molecule (figure 1) are magnetically equivalent, with identical chemical shifts. The second term in equation (2.1) represents the intramolecular J -couplings: values of the three distinct coupling constants, taken from [15], are given in figure 1. We ignore the tiny natural abundance of ^{43}Ca and all intermolecular spin interactions.

$\hat{H}_1(t)$, the incoherent part of the spin Hamiltonian, contains the 15 pairwise dipolar interactions in each molecule, which are time-dependent as a result of rotational diffusion:

$$\hat{H}_1(t) = -\sqrt{6}\hbar\gamma_{\text{P}}^2 \left(\frac{\mu_0}{4\pi}\right) \hat{R}_{\text{mol}}(t) \sum_{j < k} \sum_k \hat{R}_{\text{pos}}^{(jk)} \hat{T}_{2,0}^{(jk)} / r_{jk}^3. \quad (2.2)$$

In equation (2.2), μ_0 is the vacuum permeability, r_{jk} is the distance between spins j and k , and $\hat{T}_{2,0}^{(jk)}$ is one of the five second rank irreducible spherical tensor operators for spins j and k . $\hat{R}_{\text{pos}}^{(jk)}$ and $\hat{R}_{\text{mol}}(t)$ are rotations that define, respectively, the fixed direction of the j - k dipolar axis in the molecular frame and the time-dependent orientation of the molecule in the laboratory frame. The atomic coordinates needed to calculate r_{jk} and $\hat{R}_{\text{pos}}^{(jk)}$ were obtained using density functional theory (see electronic supplementary material).

The coherent spin dynamics driven by \hat{H}_0 , and the spin relaxation induced by $\hat{H}_1(t)$, together determine the time-dependence of the density operator $\hat{\rho}(t)$ of the 12-spin system:

$$\frac{d\hat{\rho}(t)}{dt} = -i\hat{L}\hat{\rho}(t) \implies \hat{\rho}(t) = \exp\left(-i\hat{L}t\right) \hat{\rho}(0) \quad (2.3)$$

where the Liouvillian, $\hat{L} = \hat{H}_0 + i\hat{\Gamma}$, contains the commutator superoperator corresponding to \hat{H}_0 and the relaxation superoperator $\hat{\Gamma}$ (discussed below).

3 Results

3.1 Coherent spin dynamics

The initial density operator, $\hat{\rho}(0) = \hat{P}_{1,7}^{\text{S}}/2^{10}$, commutes with the Zeeman interaction but not with the J -coupling term in equation (2.1). As a consequence, the singlet order, $p_{1,7}^{\text{S}}(t) = \text{Tr}[\hat{\rho}(t)\hat{P}_{1,7}^{\text{S}}]$, of the initially entangled pair of spins oscillates at a variety of frequencies determined by the three coupling constants. Ignoring spin relaxation for the moment, $p_{1,7}^{\text{S}}(t)$ has the complex time-dependence shown in figure 2a. Within a second, $p_{1,7}^{\text{S}}(t)$ drops to 0.25, the value expected for a pair of spins in a maximally mixed state, and only occasionally rises above 0.5 as the various oscillations come partially back into phase. Simultaneously, coherence is transferred to the other ten spins via the J -couplings. Although

all intermolecular pairs of spins have non-zero singlet order at some point (i.e. $p_{j,k}^S(t) > 0.25$), only $p_{6,12}^S(t)$ rises above 0.5 (figure 2b) during the first 400 s (spins 6 and 12 are related to 1 and 7, respectively, by the inversion symmetry, figure 1).

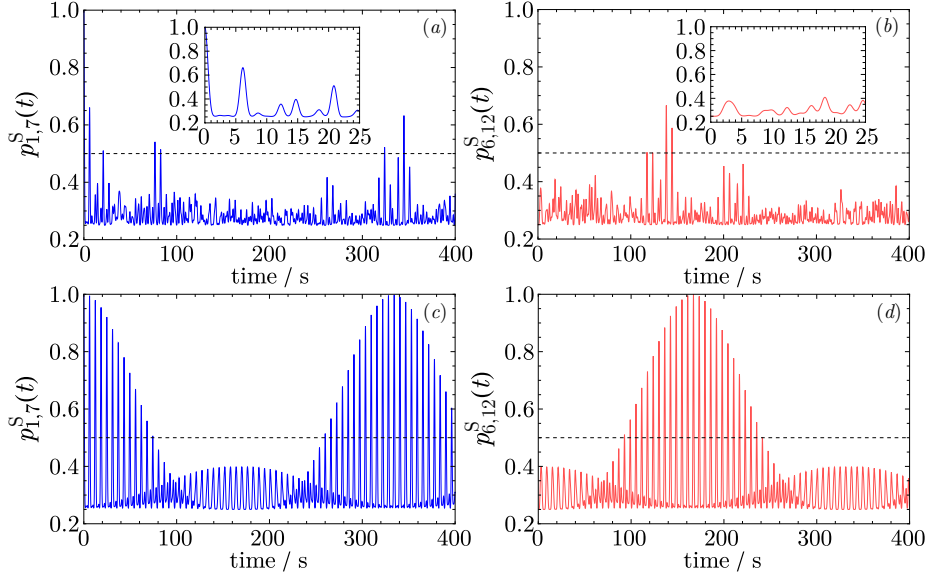


Figure 2: The singlet order $p_{j,k}^S(t)$ of spins 1 and 7, (a) and (c), and spins 6 and 12, (b) and (d), as a function of time after the formation of a pair of entangled Posner molecules in the initial state $\hat{P}_{1,7}^S$. (a) and (b) are calculated assuming S_6 symmetry, (c) and (d) with O_h symmetry. The dashed horizontal lines indicate $p_{j,k}^S = 0.5$. The insets in (a) and (b) show expanded views of the main plots.

Figures 2c and 2d show $p_{1,7}^S(t)$ and $p_{6,12}^S(t)$ for a simplified coupling pattern in which the two largest coupling constants have been set equal to their mean, $J_{AB} = \frac{1}{2}(J_A + J_B)$. This situation would arise if the four degenerate S_6 conformations of the molecule were to interconvert under conditions of fast exchange, i.e. on a timescale rapid compared to $|J_A - J_B|^{-1} \simeq 30$ s. As expected, with only two distinct couplings, the time-dependence of the singlet order is somewhat simpler than in figures 2a and 2b.

Figure 2 suggests that the coherent spin dynamics may distribute the initial entanglement around the two molecules. The degree of entanglement of spins j and k was quantified by taking the partial trace of the density matrix over the other ten spins and then calculating $C_{j,k}(t)$, the two-qubit concurrence [24]. Taking $\hat{\rho}(0) = \hat{P}_{1,7}^S/2^{10}$, $C_{j,k}(t)$ was determined for all pairs of spins, for both the full set of couplings $\{J_A, J_B, J_C\}$, figure 3a, and the simplified coupling pattern $\{J_{AB}, J_{AB}, J_C\}$, figure 3b. In both cases, $C_{j,k}(t) = 0$ (i.e. no entanglement) for all pairs of spins (j, k) except (1,7) and (6,12) and those pairs are only entangled (i.e. $C_{j,k}(t) > 0$) when the corresponding singlet order $p_{j,k}^S(t)$ (figure 2) rises

above 0.5. This is the threshold for entanglement of a two-qubit density matrix describing a mixture of $|S\rangle\langle S|$ and $(\hat{1} - |S\rangle\langle S|)/3$ [25]. Although for most of the time in figure 3a there is no two-spin entanglement at all, it is possible that intermolecular entanglement involving more than two spins may exist at all times.

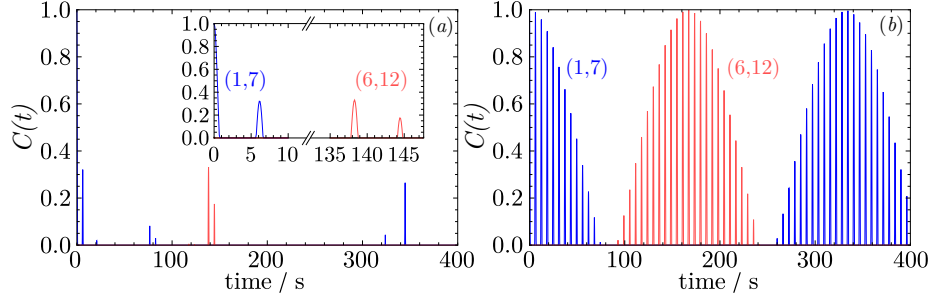


Figure 3: The two-qubit concurrence $C_{j,k}(t)$ of spins 1 and 7 (blue) and spins 6 and 12 (red) as a function of time after the formation of a pair of entangled Posner molecules in the initial state $\hat{P}_{1,7}^S$. (a) and (b) were calculated assuming S_6 and O_h symmetry respectively. The inset in (a) shows an expanded view of the main plot.

3.2 Spin relaxation

There are some states (the eigenstates of \hat{H}_0) that do not evolve coherently. However, with one exception (section 3.3), all spin states of a pair of Posner molecules are relaxed by $\hat{H}_1(t)$, the incoherent part of the spin Hamiltonian (equation (2.2)). The most important relaxation pathways for spin- $\frac{1}{2}$ nuclei normally arise from rotational modulation of intramolecular dipolar interactions and chemical shift anisotropy. As the latter will be negligibly slow in an Earth-strength magnetic field, we focus on dipolar relaxation, using Redfield theory to obtain $\hat{\Gamma}$ [26–28]. The validity of this approach is justified in the electronic supplementary material. The two $\text{Ca}_9(\text{PO}_4)_6$ molecules are assumed to undergo uncorrelated isotropic Brownian rotational diffusion with a correlation time τ_c estimated from the Stokes–Einstein relation, $\tau_c = 4\pi\eta a^3/3k_B T$, for a spherical object of radius a in a medium with viscosity η at temperature T . Taking $a = 0.44$ nm [18] and $T = 37^\circ\text{C}$ (approximate physiological temperature), we obtain $\tau_c \simeq 58$ ps for a Posner molecule in pure water ($\eta = 6.9 \times 10^{-4}$ kg m $^{-1}$ s $^{-1}$ [29]). Given that τ_c^{-1} (~ 17 GHz) hugely exceeds the difference between the largest and smallest eigenvalues of \hat{H}_0 ($\sim 6|\omega_0| \simeq 33$ kHz), the extreme narrowing limit can be used to obtain $\hat{\Gamma} = -\langle \hat{H}_1(t)\hat{H}_1(t) \rangle \tau_c$, where $\hat{H}_1(t)$ is the commutator superoperator corresponding to $\hat{H}_1(t)$ and the angled brackets indicate the ensemble average necessary to obtain $g(t)$, the correlation

function of $\hat{H}_1(t)$ (see electronic supplementary material for details). As is customary in such calculations, we assume $g(t)$ decays exponentially: $\exp(-t/\tau_c)$.

The relaxation rate constant of the intermolecular two-spin singlet, $\hat{P}_{1,7}^S/2^{10}$, is obtained as

$$\Gamma_S = \text{Tr} \left[\hat{P}_{1,7}^S \hat{\Gamma} \hat{P}_{1,7}^S \right] / \text{Tr} \left[\hat{P}_{1,7}^S \hat{P}_{1,7}^S \right] \quad (3.1)$$

(see electronic supplementary material and Ref. [30] for details of the calculation). Equation (3.1) gives $\Gamma_S/s^{-1} = 7.86 \times 10^{-6} \tau_c/\text{ps}$ and a relaxation time (Γ_S^{-1}) of ~ 37 min for Posner molecules dissolved in pure water ($\tau_c = 58$ ps) at 37°C . Given that the two Posner molecules tumble independently, we would expect the entanglement to be lost on the same timescale as the relaxation of the individual molecules. A simple order-of-magnitude check may therefore be obtained as follows. The dipolar spin-lattice and spin-spin relaxation rates for a pair of ^{31}P spins with separation r in the extreme narrowing limit are $T_1^{-1} = T_2^{-1} = \frac{3}{2} (\hbar\gamma_P^2 r^{-3} \mu_0 / 4\pi)^2 \tau_c$ [31]. Taking $r \simeq 0.5$ nm and multiplying this relaxation rate by 10, because each of the entangled spins is relaxed by its five neighbours, we get $\sim 1.5 \times 10^{-5} \tau_c/\text{ps}$, which is within a factor of two of equation (3.1).

Relaxation is a little slower if, instead of just one intermolecular singlet, the initial state is a linear combination of up to six shared singlets. We find relaxation times that increase with each additional singlet pair by up to a factor of around two for six shared singlets. It seems unlikely that a pair of Posner molecules with more than one or two shared singlets could arise biochemically.

For comparison, we have also used equation (3.1) to calculate self-relaxation rates for intramolecular singlets. With the atoms numbered as in figure 1, the three distinct two-spin singlet states, (1,2), (1,4), and (1,6), have self-relaxation times of 51, 43, and 25 min respectively.

3.3 Long-lived singlet states

Nuclear singlet states are not relaxed by local magnetic fields whose fluctuations are correlated at the sites of the participating nuclei [4]. In practice this means that the geometrical arrangement of the spins should have a centre of inversion [13]. While this is certainly the case for a single Posner molecule, it is clearly not for a pair of Posner molecules undergoing independent rotational diffusion (as shown in figure 1). We can anticipate therefore that, although there may be one or more long-lived intramolecular singlet states, there is no possibility that singlets comprising spins in more than one molecule could be immune to dipolar (or indeed any other type of) relaxation. The only intramolecular eigenstate of the dipolar relaxation superoperator $\hat{\Gamma}$ that has a zero eigenvalue (apart from the identity operator $\hat{\mathbb{I}}$) is

$$\left(\frac{1}{2} \hat{\mathbb{I}} - \hat{P}_{1,6}^S \right) \left(\frac{1}{2} \hat{\mathbb{I}} - \hat{P}_{2,5}^S \right) \left(\frac{1}{2} \hat{\mathbb{I}} - \hat{P}_{3,4}^S \right). \quad (3.2)$$

All six phosphorus nuclei are involved in this state in inversion-related, locally singlet pairs. It seems unlikely that this state could arise from the enzymatic

hydrolysis of pyrophosphate, which would create singlet pairs of ^{31}P spins without the correlation amongst the pairs inherent in equation (3.2). And, being intramolecular, it could not fulfil the proposed quantum cognition function [1].

Of the remaining 4094 eigenstates of the intramolecular dipolar relaxation superoperator, $\hat{\Gamma}$, 553 have self-relaxation times longer than 37 min, the longest being only three times longer. Even if any of these states could be formed biochemically in both molecules simultaneously and would correspond to intermolecular singlet entanglement—both of which seem highly unlikely—they would not persist for much longer than 37 min. All of the additional factors (see section 4) that could relax the $\hat{P}_{1,7}^S$ state in seconds would also apply to these more slowly relaxing states. It is therefore impossible in our view to imagine entangled states of pairs of Posner molecules that have the extraordinarily long lifetimes required by Fisher’s proposal.

4 Discussion

The relaxation time calculated here (37 min) is much smaller than Fisher’s most conservative estimate (1 day), obtained by assuming that intermolecular ^{31}P dipolar interactions with the protons in rapidly tumbling water molecules would be the dominant relaxation pathway. It is clear from the considerations presented here that intramolecular ^{31}P – ^{31}P dipolar relaxation is much more efficient. However, 37 min is still a great deal slower than would normally be expected for ^{31}P . Given the model employed here, in which relatively weak dipolar interactions are modulated by relatively rapid tumbling, 37 min is not surprising. However, there are several reasons why Posner molecules could relax much more rapidly than this.

(a) The two-spin singlet relaxation rate Γ_S is proportional to τ_c , so anything that hinders the rotation of the molecule will accelerate its ^{31}P relaxation. For example: (i) environments more viscous than water; (ii) dimerization (suggested by Fisher to be essential for the read-out of the quantum entanglement [1]); (iii) formation of larger oligomeric complexes (such as those formed during the nucleation of amorphous calcium phosphate [16]); and (iv) transient binding to large, slowly moving objects (e.g. proteins and membranes).

(b) Other magnetic interactions are unlikely to be negligible. (i) Paramagnetic species such as metal ions and in particular molecular oxygen O_2 are effective as relaxation agents by virtue of their large electronic magnetic moments [10]. (ii) Using *ab initio* calculations with implicit solvation models, Lin and Chiu report two structures of $\text{Ca}_9(\text{PO}_4)_6$ that are more stable than the S_6 form and possess enormous dipole moments (10 D and 31 D) [32]. Such structures would be strongly solvated in aqueous solution, giving rise to significant ^{31}P – ^1H dipolar relaxation. (iii) Spin-rotation relaxation (due to the interaction between nuclear spins and the fluctuating magnetic field generated by rapid molecular rotations) may well be significant given the weak dipolar interactions and the absence of CSA relaxation [5].

(c) Lin and Chiu’s study suggests that $\text{Ca}_9(\text{PO}_4)_6$ may have multiple struc-

tures of similar energy [32]. If any of them are able to interconvert, our assumption of a rigid, stable molecular framework is unlikely to be valid. (i) Intramolecular rearrangements would modulate both scalar and dipolar ^{31}P - ^{31}P couplings and so open new relaxation pathways. For instance, degenerate interconversion of S_6 conformations (see above) occurring in the intermediate exchange regime could destroy the singlet order within seconds. (ii) Intermolecular exchange of phosphate groups, for example:



(where $*$ denotes the incoming phosphate), would swap an entangled spin for one with a random spin state and so attenuate the intermolecular spin correlation. Given that ^{31}P in free phosphate (HPO_4^{2-} or H_2PO_4^- , depending on the pH) relaxes in seconds [22], exchange reactions of this sort could dramatically accelerate the ^{31}P relaxation of $\text{Ca}_9(\text{PO}_4)_6$. (iii) A molecular dynamics study by Mancardi *et al.* found Posner-type clusters with low Ca:P ratios that contained protonated phosphate groups, clusters that shared phosphate groups, and clusters in which Na^+ is partially substituted for Ca^{2+} [20]. Formation and interconversion of such structures could also contribute to spin relaxation.

All of these factors would also reduce the coherence lifetimes of other states, such as those with multiple singlets (mentioned in section 3.2) and the “long-lived” intramolecular state in equation (3.2).

Finally, Fisher has recently proposed “quantum dynamical selection” rules based on the indistinguishability of symmetry-related nuclei in small molecules [33]. Two consequences are that homolytic bond-breaking of ortho- H_2 should be symmetry-forbidden and that entanglements of nuclear spin states with molecular rotations (e.g. in Posner’s molecule) could persist “for exponentially long times”. Such arguments seem to overlook the inevitability of intramolecular nuclear spin relaxation processes and the interconversion of nuclear spin isomers. Wigner showed in 1933 that ortho- and para- H_2 are interconverted when the hydrogen nuclei experience different local magnetic fields [34]. Subsequently Curl *et al.* established that dipolar and spin-rotation interactions can rapidly equilibrate nuclear spin isomers in larger molecules [35]. These interactions couple states of different nuclear and rotational symmetry because they have components that are antisymmetric with respect to exchange of both the positions and the spins of symmetry-related nuclei [36, 37]. The C_3 symmetry of a Posner molecule gives rise to states with a “pseudospin” quantum number, $\tau = 0, 1, 2$, which Fisher predicts will be exceedingly long-lived [1, 33]. We believe that the relaxation processes described here would invalidate any selection rules associated with τ .

5 Conclusions

There are three main conclusions. (a) The J -couplings of the ^{31}P spins in a non-interacting pair of $\text{Ca}_9(\text{PO}_4)_6$ molecules drive coherent spin dynamics in which the initial two-spin order is spread around the 12 spins and varies from one

second to the next. Whether this is consistent with Fisher’s quantum cognition mechanism will probably depend critically on the details of the chemical process that ‘reads out’ the information carried by the spins in the two distant molecules. (b) There are no long-lived intermolecular singlets that are immune to either the coherent or incoherent parts of the spin Hamiltonian. (c) A strict upper limit of 37 min has been obtained for the lifetime of a singlet state shared between two Posner molecules. Various factors have the potential to accelerate this relaxation; we suspect a lifetime of a few seconds for any intermolecular singlet state is more likely than half an hour. Indeed, the only way we can envisage a molecule with ^{31}P relaxation as slow as 1 min under physiological conditions would be a two-spin *intramolecular* nuclear singlet (which would be useless as a source of “spooky action at a distance” [38]).

Data accessibility. This article has no additional data.

Author’s contributions. P.J.H. conceived the study. T.C.P. performed the study. Both authors discussed the results and wrote the manuscript.

Competing interests. We declare we have no competing interests.

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References

- [1] Fisher MPA. Quantum cognition: The possibility of processing with nuclear spins in the brain. *Ann Phys.* 2015 Nov;362:593–602. Available from: <http://www.sciencedirect.com/science/article/pii/S0003491615003243>.
- [2] Weingarten CP, Doraiswamy PM, Fisher MPA. A New Spin on Neural Processing: Quantum Cognition. *Front Hum Neurosci.* 2016;10:541. Available from: <https://www.frontiersin.org/articles/10.3389/fnhum.2016.00541/full>.
- [3] Fisher MPA. Are we quantum computers, or merely clever robots? *Int J Mod Phys B.* 2017 Mar;31(07):1743001. Available from: <https://www.worldscientific.com/doi/abs/10.1142/S0217979217430019>.
- [4] Levitt MH. Singlet Nuclear Magnetic Resonance. *Annu Rev Phys Chem.* 2012;63(1):89–105. Available from: <http://dx.doi.org/10.1146/annurev-physchem-032511-143724>.
- [5] Pileio G. Relaxation theory of nuclear singlet states in two spin-1/2 systems. *Prog Nucl Magn Reson Spectrosc.* 2010 Apr;56(3):217–231.

Available from: <http://www.sciencedirect.com/science/article/pii/S0079656509000958>.

- [6] Carravetta M, Johannessen OG, Levitt MH. Beyond the $\{T\}_1$ Limit: Singlet Nuclear Spin States in Low Magnetic Fields. *Phys Rev Lett*. 2004 Apr;92(15):153003. Available from: <https://link.aps.org/doi/10.1103/PhysRevLett.92.153003>.
- [7] Pileio G, Carravetta M, Hughes E, Levitt MH. The Long-Lived Nuclear Singlet State of ^{15}N -Nitrous Oxide in Solution. *J Am Chem Soc*. 2008 Sep;130(38):12582–12583. Available from: <https://doi.org/10.1021/ja803601d>.
- [8] Vasos PR, Comment A, Sarkar R, Ahuja P, Jannin S, Ansermet JP, et al. Long-lived states to sustain hyperpolarized magnetization. *Proc Natl Acad Sci USA*. 2009 Nov;106(44):18469–18473. Available from: <http://www.pnas.org/content/106/44/18469>.
- [9] Pileio G, Carravetta M, Levitt MH. Storage of nuclear magnetization as long-lived singlet order in low magnetic field. *Proc Natl Acad Sci USA*. 2010 Oct;107(40):17135–17139. Available from: <http://www.pnas.org/content/107/40/17135>.
- [10] Tayler MCD, Levitt MH. Singlet nuclear magnetic resonance of nearly-equivalent spins. *Phys Chem Chem Phys*. 2011 Mar;13(13):5556–5560. Available from: <http://pubs.rsc.org/en/content/articlelanding/2011/cp/c0cp02293d>.
- [11] Feng Y, Davis RM, Warren WS. Accessing long-lived nuclear singlet states between chemically equivalent spins without breaking symmetry. *Nat Phys*. 2012 Nov;8(11):831–837. Available from: <http://www.nature.com/nphys/journal/v8/n11/full/nphys2425.html>.
- [12] Stevanato G, Roy SS, Hill-Cousins J, Kuprov I, Brown LJ, Brown RCD, et al. Long-lived nuclear spin states far from magnetic equivalence. *Phys Chem Chem Phys*. 2015 Feb;17(8):5913–5922. Available from: <http://pubs.rsc.org/en/content/articlelanding/2015/cp/c4cp05704j>.
- [13] Hogben HJ, Hore PJ, Kuprov I. Multiple decoherence-free states in multi-spin systems. *J Magn Reson*. 2011 Aug;211(2):217–220. Available from: <http://www.sciencedirect.com/science/article/pii/S1090780711001881>.
- [14] Stevanato G, Hill-Cousins JT, Hakansson P, Roy SS, Brown LJ, Brown RCD, et al. A Nuclear Singlet Lifetime of More than One Hour in Room-Temperature Solution. *Angew Chem Int Ed*. 2015 Mar;54(12):3740–3743. Available from: <http://onlinelibrary.wiley.com/doi/10.1002/anie.201411978/abstract>.

- [15] Swift MW, Van de Walle CG, Fisher MPA. Posner molecules: from atomic structure to nuclear spins. *Phys Chem Chem Phys*. 2018;20(18):12373–12380. Available from: <http://pubs.rsc.org/en/Content/ArticleLanding/2018/CP/C7CP07720C>.
- [16] Posner AS, Betts F. Synthetic amorphous calcium phosphate and its relation to bone mineral structure. *Acc Chem Res*. 1975 Aug;8(8):273–281. Available from: <http://dx.doi.org/10.1021/ar50092a003>.
- [17] Yin X, Stott MJ. Biological calcium phosphates and Posner’s cluster. *J Chem Phys*. 2003 Feb;118(8):3717–3723. Available from: <http://scitation.aip.org/content/aip/journal/jcp/118/8/10.1063/1.1539093>.
- [18] Dey A, Bomans PHH, Muller FA, Will J, Frederik PM, de With G, et al. The role of prenucleation clusters in surface-induced calcium phosphate crystallization. *Nat Mater*. 2010 Dec;9(12):1010–1014. Available from: <http://www.nature.com/nmat/journal/v9/n12/full/nmat2900.html>.
- [19] Wang L, Li S, Ruiz-Agudo E, Putnis CV, Putnis A. Posner’s cluster revisited: direct imaging of nucleation and growth of nanoscale calcium phosphate clusters at the calcite-water interface. *CrystEngComm*. 2012 Aug;14(19):6252–6256. Available from: <http://pubs.rsc.org/en/content/articlelanding/2012/ce/c2ce25669j>.
- [20] Mancardi G, Tamargo CEH, Di Tommaso D, de Leeuw NH. Detection of Posner’s clusters during calcium phosphate nucleation: a molecular dynamics study. *J Mater Chem B*. 2017 Sep;5(35):7274–7284. Available from: <http://pubs.rsc.org/en/content/articlelanding/2017/tb/c7tb01199g>.
- [21] Treboux G, Layrolle P, Kanzaki N, Onuma K, Ito A. Existence of Posner’s Cluster in Vacuum. *J Phys Chem A*. 2000 Jun;104(21):5111–5114. Available from: <http://dx.doi.org/10.1021/jp994399t>.
- [22] Gorenstein DG. *Phosphorus-31 NMR*. Orlando: Academic Press; 1984. Available from: <http://linkinghub.elsevier.com/retrieve/pii/C20090029869>.
- [23] Halpern NY, Crosson E. Quantum information in quantum cognition. *arXiv:171104801*. 2017 Nov; Available from: <http://arxiv.org/abs/1711.04801>.
- [24] Wootters WK. Entanglement of Formation of an Arbitrary State of Two Qubits. *Phys Rev Lett*. 1998 Mar;80(10):2245–2248. Available from: <https://link.aps.org/doi/10.1103/PhysRevLett.80.2245>.
- [25] Hogben HJ, Biskup T, Hore PJ. Entanglement and Sources of Magnetic Anisotropy in Radical Pair-Based Avian Magnetoreceptors. *Phys Rev Lett*.

- 2012 Nov;109(22):220501. Available from: <https://link.aps.org/doi/10.1103/PhysRevLett.109.220501>.
- [26] Goldman M. Formal Theory of Spin-Lattice Relaxation. *J Magn Reson.* 2001 Apr;149(2):160–187. Available from: <http://www.sciencedirect.com/science/article/pii/S1090780700922390>.
 - [27] Redfield AG. The Theory of Relaxation Processes. *Adv Magn Reson.* 1965 Jan;1:1–32. Available from: <http://www.sciencedirect.com/science/article/pii/B9781483231143500076>.
 - [28] Slichter CP. *Principles of Magnetic Resonance.* Berlin: Springer-Verlag; 1978.
 - [29] Korson L, Drost-Hansen W, Millero FJ. Viscosity of water at various temperatures. *J Phys Chem.* 1969 Jan;73(1):34–39. Available from: <https://doi.org/10.1021/j100721a006>.
 - [30] Kuprov I, Wagner-Rundell N, Hore PJ. Bloch-Redfield-Wangsness theory engine implementation using symbolic processing software. *J Magn Reson.* 2007 Feb;184(2):196–206. Available from: <http://www.sciencedirect.com/science/article/pii/S1090780706003259>.
 - [31] Harris RK. *Nuclear Magnetic Resonance Spectroscopy: A Physicochemical View.* London: Pitman; 1983.
 - [32] Lin TJ, Chiu CC. Structures and infrared spectra of calcium phosphate clusters by ab initio methods with implicit solvation models. *Phys Chem Chem Phys.* 2017 Dec;20(1):345–356. Available from: <http://pubs.rsc.org/en/content/articlelanding/2018/cp/c7cp05975b>.
 - [33] Fisher MPA, Radzihovsky L. Quantum indistinguishability in chemical reactions. *Proc Natl Acad Sci USA.* 2018 Apr;115(20):E4551–E4558. Available from: <http://www.pnas.org/content/115/20/E4551>.
 - [34] Wigner EP. Über die paramagnetische Umwandlung von Para-Orthowasserstoff. III. *Z Phys Chem B.* 1933;23:28–32.
 - [35] Curl RF, Kasper JVV, Pitzer KS. Nuclear Spin State Equilibration through Nonmagnetic Collisions. *J Chem Phys.* 1967 Apr;46(8):3220–3228. Available from: <https://aip.scitation.org/doi/abs/10.1063/1.1841193>.
 - [36] Petzinger KG, Scalapino DJ. Para- to Ortho-Hydrogen Conversion on Magnetic Surfaces. *Phys Rev B.* 1973 Jul;8(1):266–279. Available from: <https://link.aps.org/doi/10.1103/PhysRevB.8.266>.
 - [37] Steiner UE, Ulrich T. Magnetic field effects in chemical kinetics and related phenomena. *Chem Rev.* 1989 Jan;89(1):51–147. Available from: <https://pubs.acs.org/doi/abs/10.1021/cr00091a003>.

- [38] Einstein A, Podolsky B, Rosen N. Can Quantum-Mechanical Description of Physical Reality Be Considered Complete? *Phys Rev.* 1935 May;47(10):777–780. Available from: <https://link.aps.org/doi/10.1103/PhysRev.47.777>.

Supporting Information

Posner qubits: spin dynamics of entangled $\text{Ca}_9(\text{PO}_4)_6$ molecules and their role in neural processing

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1 Spin Hamiltonian

For a pair of Posner molecules, the total spin Hamiltonian can be written as

$$\hat{H}(t) = \hat{H}_0 + \hat{H}_1(t), \quad (1.1)$$

where \hat{H}_0 describes coherent interactions, and $\hat{H}_1(t)$ describes time-dependent interactions that are responsible for relaxation of spin states. This can equivalently be written as a sum of smaller Hamiltonians for the individual molecules (which will be intermolecularly singlet entangled in Fisher’s theory), labelled a and b :

$$\hat{H}(t) = \hat{H}^a(t) \oplus \hat{H}^b(t) \quad (1.2)$$

where \oplus denotes the Kronecker sum $\hat{A} \oplus \hat{B} = \hat{A} \otimes \hat{\mathbb{1}}_B + \hat{\mathbb{1}}_A \otimes \hat{B}$.

2 Coherent spin dynamics

The time-dependent singlet probability $p_{j,k}^S(t)$, given an initial intermolecular singlet state $\hat{\rho}(0) = \hat{P}_{a,b}^S / (Z_a Z_b)$ where Z_i is a normalization constant to account for the other nuclear spin states in molecule i , is

$$\begin{aligned} p_{j,k}^S(t) &= \text{Tr} \left[\hat{\rho}(t) \hat{P}_{a,b}^S \right] \\ &= \frac{1}{4} - \sum_{\beta=x,y,z} \text{Tr} \left[\hat{\rho}(t) \hat{S}_{j\beta} \hat{S}_{k\beta} \right], \end{aligned} \quad (2.1)$$

where $\hat{\rho}(t) = e^{-i\hat{H}_0 t} \hat{\rho}(0) e^{+i\hat{H}_0 t}$ and $\hat{P}_{j,k}^S = \frac{1}{4} \hat{\mathbb{1}} - \hat{\mathbf{S}}_j \cdot \hat{\mathbf{S}}_k$. This is time consuming to calculate in the full Hilbert space of two Posner molecules, and so we used a method for calculating time-dependent singlet probabilities of radical pairs in a smaller Hilbert space, described in [1, 2].

The second term in Eq. (2.1) can be rewritten using Eq. (1.2) and the fact that $\hat{H}^a(t)$ and $\hat{H}^b(t)$ commute as

$$-\frac{1}{Z_a Z_b} \sum_{\beta=x,y,z} \text{Tr} \left[e^{-i\hat{H}_0 t} \left(\frac{1}{4} \hat{\mathbb{1}} - \sum_{\alpha=x,y,z} \hat{S}_{a\alpha} \hat{S}_{b\alpha} \right) e^{+i\hat{H}_0 t} \hat{S}_{j\beta} \hat{S}_{k\beta} \right] = \sum_{\alpha,\beta} R_{\alpha\beta}^{a,j}(t) R_{\alpha\beta}^{b,k}(t), \quad (2.2)$$

where

$$R_{\alpha\beta}^{a,j}(t) = \frac{1}{Z_a} \text{Tr} \left[\hat{S}_{a\alpha} e^{+i\hat{H}_0^a t} \hat{S}_{j\beta} e^{-i\hat{H}_0^a t} \right] = \frac{1}{Z_a} \text{Tr} \left[\hat{S}_{a\alpha}(0) \hat{S}_{j\beta}(t) \right] \quad (2.3)$$

is an element of the spin correlation tensor for the chosen nucleus in molecule a , and we have used cyclic permutation under the trace.

Using Eqs (2.1) and (2.2), we can therefore calculate the time-dependent singlet probability in the smaller Hilbert space of each individual molecule as

$$p_{j,k}^S(t) = \frac{1}{4} + \sum_{\alpha,\beta} R_{\alpha\beta}^{a,j}(t) R_{\alpha\beta}^{b,k}(t). \quad (2.4)$$

3 Concurrence

The concurrence between two spins was calculated by first tracing out the other ten spins in the two-molecule system from the density matrix to give $\rho(t) = \text{Tr}_{i \neq \{j,k\}} [\hat{\rho}(t)]$ ¹. The concurrence was then calculated as in [4]:

$$C_{j,k}(t) = \max\{0, \lambda_1 - \lambda_2 - \lambda_3 - \lambda_4\}, \quad (3.1)$$

where λ_i are the eigenvalues, in decreasing order, of the matrix $\rho(t) (\sigma_y \otimes \sigma_y) \rho(t) (\sigma_y \otimes \sigma_y)$ and σ_y is the second Pauli matrix. This concurrence, which has range 0 (not entangled) to 1 (fully entangled), can then be used directly as a measure of bipartite entanglement.

4 Validity of the Redfield approach

The dominant relaxation pathway for many molecules containing non-quadrupolar nuclei is dipolar relaxation via the interaction of nuclear magnetic moments in the molecule. Note that this is intramolecular dipolar coupling, as opposed to the intermolecular dipolar coupling considered by Fisher and colleagues [5, 6]. Brownian rotational diffusion of the molecule then modulates these dipolar couplings and leads to relaxation. We use Redfield theory to model this kind of spin relaxation. The validity of the Redfield approach used can be established from the following estimates.

(1) For the Redfield approach to be valid, we require $|b|\tau_c \ll 1$ [7, 8]. In this expression b is the dipolar coupling constant of two ^{31}P spins separated by a distance r , defined as $b = -(4\pi r^3)^{-1} \mu_0 \gamma_P^2 \hbar$, where γ_P is the magnetogyric ratio of ^{31}P and μ_0 is the vacuum permeability. Taking $r = 0.5 \text{ nm}$ as a rough figure for the average separation of the ^{31}P nuclei, we obtain $b \simeq 990 \text{ Hz}$. The correlation time for Brownian rotation diffusion of a spherical molecule of radius a in a medium with viscosity η at temperature T can be estimated using the Stokes–Einstein equation as $\tau_c = 4\pi\eta a^3 (3k_B T)^{-1}$. Using $a = 0.44 \text{ nm}$ [9] and $T = 310 \text{ K}$ (physiological temperature), $\tau_c \simeq 58 \text{ ps}$ for water ($\eta = 0.69 \text{ mPas}$). Multiplying by the dipolar coupling constant calculated above, we see that the Redfield approach is clearly valid.

¹The code used for the partial trace can be found online at [3].

(2) To simplify the calculation further we use the extreme narrowing limit, as described in [10], which is valid when all the eigenvalue differences of the time-independent part of the spin Hamiltonian \hat{H}_0 are much smaller than τ_c^{-1} . In the present case, since the J -couplings are small compared to the Earth's magnetic field, this means we require $6|\omega_0|\tau_c \ll 1$, where $\omega_0 = -\gamma_P B_0$ is the ^{31}P nuclear Larmor frequency in the Earth's magnetic field B_0 . Taking $B_0 \simeq 50 \mu\text{T}$, $\omega_0 \simeq 5.4 \text{ kHz}$ and so the extreme narrowing condition is clearly satisfied for the rotational correlation time quoted above. We also note that the six ^{31}P nuclei in a Posner's molecule would have the same chemical shift since they are magnetically equivalent, and so the ^{31}P NMR spectrum would be a singlet.

These two conditions establish that the extreme narrowing Redfield approach to calculating nuclear spin relaxation, as described elsewhere in [7, 10–14] and below, will be valid for Posner's molecules.

5 Dipolar Hamiltonian

The following description of the dipolar Hamiltonian follows that described by Wagner-Rundell [10] and the references therein.

If we define the the dipole-dipole axis as the principal axis frame (P) z -axis, then the Hamiltonian for dipolar coupling in a molecule between nuclei j and k is given by

$$\hat{H}_D^{jk(\text{P})} = \sqrt{6}b_{jk}\hat{T}_{2,0}^{jk}, \quad (5.1)$$

where $b_{jk} = -\frac{1}{4\pi}\mu_0\gamma_j\gamma_k\hbar r_{jk}^{-3}$ is the dipole-dipole coupling constant, μ_0 is the vacuum permeability, r_{jk} is the internuclear distance, and $\hat{T}_{2,0}^{jk}$ is one of the second-order spherical tensors:

$$\begin{aligned} \hat{T}_{2,\pm 2}^{jk} &= \frac{1}{2}\hat{S}_{j\pm}\hat{S}_{k\pm} \quad , \quad \hat{T}_{2,\pm 1}^{jk} = \mp \frac{1}{2}\left(\hat{S}_{jz}\hat{S}_{k\pm} + \hat{S}_{j\pm}\hat{S}_{kz}\right), \\ \hat{T}_{2,0}^{jk} &= \sqrt{\frac{2}{3}}\left(-\frac{1}{2}\hat{S}_{jx}\hat{S}_{kx} - \frac{1}{2}\hat{S}_{jy}\hat{S}_{ky} + \hat{S}_{jz}\hat{S}_{kz}\right). \end{aligned} \quad (5.2)$$

Any spherical tensor is transformed under a rotation operator \hat{R} as

$$\hat{R}(\alpha, \beta, \gamma)\hat{T}_{l,m}^{jk} = \sum_{m'=-l}^l \hat{T}_{l,m'}^{jk}\mathfrak{D}_{m',m}^{(l)}(\alpha, \beta, \gamma), \quad (5.3)$$

where $\mathfrak{D}_{m',m}^{(l)}(\alpha, \beta, \gamma)$ are elements of the l^{th} rank Wigner D-matrix for a rotation through Euler angles (α, β, γ) .²

This leads to the following expression for the dipolar Hamiltonian in the laboratory frame (L), where it has been rotated from the principal axis frame to the molecular frame through Euler angles

²The convention used here is the z - y' - z'' convention. The first rotation is of an angle α about the rotating object's z axis, then β about the new y' axis, and finally γ about the new z'' axis. This can also be written as $\hat{R}(\alpha, \beta, \gamma) = \hat{R}_{z''}(\gamma)\hat{R}_{y'}(\beta)\hat{R}_z(\alpha)$, in terms of the three separate rotations. This is equivalent to performing all three rotations in a different order about the original axes: $\hat{R}(\alpha, \beta, \gamma) = \hat{R}_z(\alpha)\hat{R}_y(\beta)\hat{R}_z(\gamma)$.

(α, β, γ) , and then into the lab frame through time-dependent Euler angles $(\Omega(t))$:

$$\begin{aligned}\hat{H}_D^{jk(L)} &= \hat{R}_{\text{mol}}(\Omega(t)) \hat{R}_{\text{pos}}^{j,k}(\alpha, \beta, \gamma) \hat{H}_D^{jk(P)} \\ &= \hat{R}_{\text{mol}}(\Omega(t)) \hat{R}_{\text{pos}}^{j,k}(\alpha, \beta, \gamma) \sqrt{6} b_{jk} \hat{T}_{2,0}^{jk} \\ &= -\sqrt{6} \hbar \gamma_P^2 \left(\frac{\mu_0}{4\pi} \right) \hat{R}_{\text{mol}}(\Omega(t)) \hat{R}_{\text{pos}}^{j,k}(\alpha, \beta, \gamma) \hat{T}_{2,0}^{jk} / r_{jk}^3.\end{aligned}\tag{5.4}$$

The time-dependent Hamiltonian is then given by summing over all pairs of nuclei in the molecule (Eq. (2.2) in the main text):

$$\hat{H}_1(t) = -\sqrt{6} \hbar \gamma_P^2 \left(\frac{\mu_0}{4\pi} \right) \hat{R}_{\text{mol}}(\Omega(t)) \sum_{j < k} \sum_k \hat{R}_{\text{pos}}^{j,k}(\alpha, \beta, \gamma) \hat{T}_{2,0}^{jk} / r_{jk}^3.\tag{5.5}$$

We can evaluate the effect of the rotation operators on the spherical tensors using Eq. (5.3), and by defining a positioning parameter $\Phi_m^{jk} = \sqrt{6} b_{jk} \mathfrak{D}_{m,0}^{(2)}(\alpha, \beta, \gamma)$ for each pair of nuclei in the molecule can write the time-dependent Hamiltonian as

$$\hat{H}_1(t) = \sum_{j < k} \sum_k \sum_{m, m'=-2}^2 \Phi_m^{jk} \hat{T}_{2,m'}^{jk} \mathfrak{D}_{m',m}^{(2)}(\Omega(t)).\tag{5.6}$$

This can be made notationally more compact by defining a parameter, $\phi_{m'}^{jk}(t)$, containing all time-dependent positional information about a pair of nuclei:

$$\phi_{m'}^{jk}(t) = \sum_{m=-2}^2 \Phi_m^{jk} \mathfrak{D}_{m',m}^{(2)}(\Omega(t)),\tag{5.7}$$

such that the time-dependent Hamiltonian can be written as

$$\hat{H}_1(t) = \sum_{j < k} \sum_k \sum_{m'=-2}^2 \phi_{m'}^{jk}(t) \hat{T}_{2,m'}^{jk},\tag{5.8}$$

in a form that facilitates fast calculations.

6 Relaxation Theory

Relaxation due to $\hat{H}_1(t)$ can be described using a well-established theory often called Redfield, or Bloch-Redfield-Wangsness, relaxation theory.

The Liouville-von Neumann equation is used to determine the effect of the spin Hamiltonian on the system:

$$\frac{d\hat{\rho}(t)}{dt} = -i \left[\hat{H}_0 + \hat{H}_1(t), \hat{\rho}(t) \right].\tag{6.1}$$

It is shown in [10] and [7] that, using second order perturbation theory and several valid assumptions, that this can be rewritten in the interaction representation. This is indicated by a double dagger (\ddagger), whereby all operators in the laboratory frame are transformed according to

$$\hat{Q}^\ddagger(t) = e^{i\hat{H}_0 t} \hat{Q} e^{-i\hat{H}_0 t}.\tag{6.2}$$

In this representation, the time-evolution of the density matrix is given by

$$\frac{d\hat{\rho}^\dagger(t)}{dt} = - \int_0^\infty \left\langle \left[\hat{H}_1^\dagger(t), \left[\hat{H}_1^\dagger(t-\tau), \hat{\rho}^\dagger(t) \right] \right] \right\rangle d\tau, \quad (6.3)$$

where the ensemble average is over the Hamiltonians. This expression is transformed back out of the interaction representation and into the laboratory frame using Eq. (6.2):

$$\frac{d\hat{\rho}(t)}{dt} = -i \left[\hat{H}_0, \hat{\rho}(t) \right] - \int_0^\infty \left\langle \left[\hat{H}_1(t), \left[e^{-i\hat{H}_0\tau} \hat{H}_1(t-\tau) e^{i\hat{H}_0\tau}, \hat{\rho}(t) \right] \right] \right\rangle d\tau. \quad (6.4)$$

This is clearly a sum of two terms: the first governs the coherent dynamics of the system, which have already been discussed, and the second is the relaxation term. This is known as a “master equation”.

7 Extreme Narrowing

This master equation is not analytically soluble in general, and so an approximation is outlined here, as in [10]. When the random processes (i.e. molecular rotations) take place on a timescale much shorter than all of the eigenvalue differences for the static Hamiltonian (i.e. the transition frequencies), then the conditions for extreme narrowing are met:

$$\omega_{nm}^2 \tau_c^2 \ll 1 \quad \forall \quad n, m, \quad (7.1)$$

where τ_c is the molecular rotational correlation time, i.e. the average time for a molecule to tumble through an angle of one radian, and $\omega_{nm} = \omega_n - \omega_m$ where $\{\omega_n\}$ are the eigenvalues of \hat{H}_0 .

By converting into the eigenbasis of \hat{H}_0 , the relaxation term in Eq. (6.4) can be written

$$- \left(\int_0^\infty \left\langle \left[\hat{H}_1^{(0)}(t), \left[\hat{F}(t, \tau), \hat{\rho}^{(0)}(t) \right] \right] \right\rangle d\tau \right), \quad (7.2)$$

where $\hat{F}(t, \tau) = e^{-i\hat{H}_0\tau} \hat{H}_1^{(0)}(t-\tau) e^{i\hat{H}_0\tau}$, and the (0) superscript indicates quantities transformed into the new basis.

Expanding the commutators, remembering that the ensemble average is taken only over the time-dependent Hamiltonian, means that terms similar to \hat{K} arise:

$$\hat{K} = \int_0^\infty \left\langle \hat{H}_1^{(0)}(t) \hat{F}(t, \tau) \right\rangle \hat{\rho}^{(0)}(t) d\tau. \quad (7.3)$$

A single matrix element of \hat{K} can be written as

$$\begin{aligned} \hat{K}_{nm} &= \sum_{p,q} \int_0^\infty \left\langle \left[\hat{H}_1^{(0)}(t) \right]_{np} \left[\hat{F}(t, \tau) \right]_{pq} \right\rangle \left[\hat{\rho}^{(0)}(t) \right]_{qm} d\tau \\ &= \sum_{p,q} \int_0^\infty \left\langle \left[\hat{H}_1^{(0)}(t) \right]_{np} \left[\hat{H}_1^{(0)}(t-\tau) \right]_{pq} \right\rangle \left[\hat{\rho}^{(0)}(t) \right]_{qm} e^{-i\omega_{pq}\tau} d\tau. \end{aligned} \quad (7.4)$$

Using the correlation function

$$\left\langle \hat{H}_1(t) \hat{H}_1(t-\tau) \right\rangle = \left\langle \hat{H}_1(t) \hat{H}_1(t) \right\rangle e^{-\frac{|\tau|}{\tau_c}}, \quad (7.5)$$

where the angle brackets indicate an ensemble average, gives:

$$\hat{K}_{nm} = \sum_{p,q} \int_0^\infty \left\langle \left[\hat{H}_1^{(0)}(t) \right]_{np} \left[\hat{H}_1^{(0)}(t) \right]_{pq} \right\rangle \left[\hat{\rho}^{(0)}(t) \right]_{qm} e^{(-i\omega_{pq} - \frac{1}{\tau_c})\tau} d\tau. \quad (7.6)$$

This integral is simple to compute, and gives:

$$\hat{K}_{nm} = \sum_{p,q} \left\langle \left[\hat{H}_1^{(0)}(t) \right]_{np} \left[\hat{H}_1^{(0)}(t) \right]_{pq} \right\rangle \left[\hat{\rho}^{(0)}(t) \right]_{qm} \left(\frac{\tau_c}{1 + \tau_c^2 \omega_{pq}^2} - i \frac{\omega_{pq} \tau_c^2}{1 + \tau_c^2 \omega_{pq}^2} \right), \quad (7.7)$$

the imaginary component of which is known as the dynamic frequency shift. It corresponds to a shift in energy which is usually small and difficult to measure, and so we ignore it here [8].

Since we are in the extreme narrowing limit, $\tau_c/(1 + \tau_c^2 \omega_{pq}^2) \simeq \tau_c$, and so:

$$\hat{K}_{nm} \simeq \tau_c \sum_{p,q} \left\langle \left[\hat{H}_1^{(0)}(t) \right]_{np} \left[\hat{H}_1^{(0)}(t) \right]_{pq} \right\rangle \left[\hat{\rho}^{(0)}(t) \right]_{qm}. \quad (7.8)$$

Using a similar argument for all terms in Eq. (7.2) means we obtain the relaxation term in the extreme narrowing limit:

$$-\tau_c \left\langle \left[\hat{H}_1^{(0)}(t), \left[\hat{H}_1^{(0)}(t), \hat{\rho}^{(0)}(t) \right] \right] \right\rangle. \quad (7.9)$$

So, by transforming back out of the eigenbasis of \hat{H}_0 , we obtain the master equation in the extreme narrowing limit:

$$\frac{d\hat{\rho}(t)}{dt} = -i \left[\hat{H}_0, \hat{\rho}(t) \right] - \tau_c \left\langle \left[\hat{H}_1(t), \left[\hat{H}_1(t), \hat{\rho}(t) \right] \right] \right\rangle. \quad (7.10)$$

8 Relaxation Superoperator

The time-dependence of the density matrix can also be written using in Liouville space ³ as

$$\frac{d|\hat{\rho}(t)\rangle}{dt} = \left(-i\hat{H}_0 + \hat{\Gamma} \right) |\hat{\rho}(t)\rangle, \quad (8.1)$$

where \hat{H}_0 is the commutation superoperator that corresponds to \hat{H}_0 , and $\hat{\Gamma}$ is the relaxation superoperator:

$$\hat{\Gamma} = - \left\langle \hat{H}_1(t) \hat{H}_1(t) \right\rangle \tau_c. \quad (8.2)$$

Using Eq. (5.5), the relaxation superoperator may be written:

$$\hat{\Gamma} = -\tau_c \left\langle \sum_{j < k} \sum_k \sum_{r < s} \sum_s \sum_{m', n' = -2}^2 \phi_{m'}^{jk}(t) \phi_{n'}^{rs}(t) \hat{T}_{2,m'}^{jk} \hat{T}_{2,n'}^{rs} \right\rangle. \quad (8.3)$$

Since the time-dependence comes from the positioning $\phi(t)$ functions, it is sufficient to consider products of the form:

$$\left\langle \phi_{m'}^{jk}(t) \phi_{n'}^{rs}(t) \right\rangle. \quad (8.4)$$

³This is where density matrices are row-wise flattened into Liouville space state “vectors” that are acted upon by matrix representations of superoperators of the dimension of the Hilbert space squared.

Using Eq. (5.7) and the properties of Wigner functions ⁴, products of this type can be expressed as:

$$\begin{aligned} \left\langle \phi_{m'}^{jk}(t) \phi_{n'}^{rs}(t) \right\rangle &= \sum_{m,n=-2}^2 \Phi_m^{jk} \Phi_n^{rs} \left\langle \mathfrak{D}_{m',m}^{(2)}(\Omega(t)) \mathfrak{D}_{n',n}^{(2)}(\Omega(t)) \right\rangle \\ &= \sum_{m,n=-2}^2 \Phi_m^{jk} \Phi_n^{rs} \left\langle \mathfrak{D}_{m',m}^{(2)}(\Omega(t)) \mathfrak{D}_{-n',-n}^{*(2)}(\Omega(t)) \right\rangle (-1)^{m'-m}. \end{aligned} \quad (8.5)$$

From [10]:

$$\begin{aligned} \left\langle \phi_{m'}^{jk}(t) \phi_{n'}^{rs}(t) \right\rangle &= \frac{1}{5} \sum_{m,n=-2}^2 \Phi_m^{jk} \Phi_n^{rs} \delta_{m',-n'} \delta_{m,-n} (-1)^{m'-m} \\ &= \frac{1}{5} \sum_{m=-2}^2 \Phi_m^{jk} \Phi_{-m}^{rs} \delta_{m',-n'} (-1)^{m'-m}. \end{aligned} \quad (8.6)$$

The relaxation superoperator in the extreme narrowing limit can therefore be calculated directly as:

$$\hat{\Gamma} = -\frac{\tau_c}{5} \sum_{j < k} \sum_k \sum_{r < s} \sum_s \sum_{n,m=-2}^2 (-1)^{n+m} \Phi_m^{jk} \Phi_{-m}^{rs} \hat{T}_{2,-n}^{jk} \hat{T}_{2,n}^{rs}. \quad (8.7)$$

We now consider the effect of $\hat{\Gamma}$ on intermolecular singlet states. The self-relaxation rate constant Γ_S for a state \hat{Q} is given as in [13] and the main text by

$$\Gamma_S = \frac{\text{Tr} \left[\left(\hat{\Gamma} |\hat{Q}\rangle \right) \hat{Q}^\dagger \right]}{\text{Tr} \left[\hat{Q} \hat{Q}^\dagger \right]} = \text{Tr} \left[\hat{Q} \hat{\Gamma} \hat{Q}^\dagger \right] / \text{Tr} \left[\hat{Q} \hat{Q}^\dagger \right], \quad (8.8)$$

where

$$\hat{Q} = \sum_{\{a,b\} \in \mathbb{S}} \hat{P}_{a,b}^S \quad (8.9)$$

is a linear combination of singlet operators, \mathbb{S} is the set of singlet pairs, and a and b are the two entangled spins in the singlet state.

⁴Specifically, $\mathfrak{D}_{m',m}^{(j)}(\alpha, \beta, \gamma) = (-1)^{m'-m} \mathfrak{D}_{-m',-m}^{*(j)}(\alpha, \beta, \gamma)$.

9 Relaxation of an Intermolecular Singlet

Using Eq.s (7.10) and (8.2), the definition and Hermiticity of $\hat{P}_{a,b}^S$, the unnormalized initial singlet relaxation rate constant Γ'_S can be written (in units of $-\tau_c$) as:

$$\begin{aligned}
\Gamma'_S &= \sum_{\{a,b\},\{c,d\} \in \mathbb{S}} \text{Tr} \left[\left\langle \left[\hat{H}_1(t), \left[\hat{H}_1(t), \hat{P}_{a,b}^S \right] \right] \right\rangle \hat{P}_{c,d}^S \right] \\
&= \sum_{\{a,b\},\{c,d\} \in \mathbb{S}} \text{Tr} \left[\left\langle \left[\hat{H}_1(t), \left[\hat{H}_1(t), \frac{1}{4} \hat{\mathbb{1}} - \sum_{\alpha} \hat{S}_{a\alpha} \otimes \hat{S}_{b\alpha} \right] \right] \right\rangle \frac{1}{4} \hat{\mathbb{1}} - \sum_{\beta} \hat{S}_{c\beta} \otimes \hat{S}_{d\beta} \right] \\
&= \sum_{\{a,b\},\{c,d\} \in \mathbb{S}} \sum_{\alpha, \beta=x,y,z} \text{Tr} \left[\left\langle \left[\hat{H}_1(t), \left[\hat{H}_1(t), \hat{S}_{a\alpha} \otimes \hat{S}_{b\alpha} \right] \right] \right\rangle \hat{S}_{c\beta} \otimes \hat{S}_{d\beta} \right] \quad (9.1) \\
&= \sum_{\{a,b\},\{c,d\} \in \mathbb{S}} \sum_{\alpha, \beta=x,y,z} \text{Tr} \left[\left\langle \left[\hat{H}_1(t), \left[\hat{H}_1(t), \hat{S}_{a\alpha} \otimes \hat{S}_{b\alpha} \right] \right] \right\rangle \hat{S}_{c\beta} \otimes \hat{S}_{d\beta} \right] \\
&= \sum_{\{a,b\},\{c,d\} \in \mathbb{S}} \sum_{\alpha, \beta=x,y,z} \text{Tr} \left[\langle A \rangle \hat{S}_{c\beta} \otimes \hat{S}_{d\beta} \right].
\end{aligned}$$

The term labelled A can then be written, using Eq. (1.2) and expanding the commutators, as

$$\begin{aligned}
A &= \left[\hat{H}_1^a(t) \oplus \hat{H}_1^b(t), \left[\hat{H}_1^a(t) \oplus \hat{H}_1^b(t), \hat{S}_{a\alpha} \otimes \hat{S}_{b\alpha} \right] \right] \\
&= \left[\hat{H}_1^a(t), \left[\hat{H}_1^a(t), \hat{S}_{a\alpha} \right] \right] \otimes \hat{S}_{b\alpha} + 2 \left[\hat{H}_1^a(t), \hat{S}_{a\alpha} \right] \otimes \left[\hat{H}_1^b(t), \hat{S}_{b\alpha} \right] \\
&\quad + \hat{S}_{a\alpha} \otimes \left[\hat{H}_1^b(t), \left[\hat{H}_1^b(t), \hat{S}_{b\alpha} \right] \right]. \quad (9.2)
\end{aligned}$$

The second term of the last expression will be zero under an ensemble average since the tumbling of the two molecules is uncorrelated. We note that the commutators in Eq. (9.2) are of the same form as those in Eq. (8.2), and so we define a relaxation superoperator for each separate molecule i ,

$$\hat{\Gamma}^i = - \left\langle \hat{H}_1^i(t) \hat{H}_1^i(t) \right\rangle \tau_c. \quad (9.3)$$

This means that Eq. (9.1) can now be written as

$$\begin{aligned}
\Gamma'_S &= \sum_{\{a,b\},\{c,d\} \in \mathbb{S}} \sum_{\alpha, \beta=x,y,z} \text{Tr} \left[\left(\left(\hat{\Gamma}^a | \hat{S}_{a\alpha} \rangle \right) \otimes \hat{S}_{b\alpha} + \hat{S}_{a\alpha} \otimes \left(\hat{\Gamma}^b | \hat{S}_{b\alpha} \rangle \right) \right) \left(\hat{S}_{c\beta} \otimes \hat{S}_{d\beta} \right) \right] \\
&= \sum_{\{a,b\},\{c,d\} \in \mathbb{S}} \sum_{\alpha, \beta=x,y,z} \text{Tr} \left[\left(\hat{\Gamma}^a | \hat{S}_{a\alpha} \rangle \right) \hat{S}_{c\beta} \otimes \hat{S}_{b\alpha} \hat{S}_{d\beta} + \hat{S}_{a\alpha} \hat{S}_{c\beta} \otimes \left(\hat{\Gamma}^b | \hat{S}_{b\alpha} \rangle \right) \hat{S}_{d\beta} \right] \\
&= \sum_{\{a,b\},\{c,d\} \in \mathbb{S}} \sum_{\alpha, \beta=x,y,z} \text{Tr} \left[\left(\hat{\Gamma}^a | \hat{S}_{a\alpha} \rangle \right) \hat{S}_{c\beta} \right] \text{Tr} \left[\hat{S}_{b\alpha} \hat{S}_{d\beta} \right] + \text{Tr} \left[\hat{S}_{a\alpha} \hat{S}_{c\beta} \right] \text{Tr} \left[\left(\hat{\Gamma}^b | \hat{S}_{b\alpha} \rangle \right) \hat{S}_{d\beta} \right] \\
&= \sum_{\{a,b\} \in \mathbb{S}} \sum_{\alpha=x,y,z} 2^{N_a-2} \text{Tr} \left[\left(\hat{\Gamma}^a | \hat{S}_{a\alpha} \rangle \right) \hat{S}_{a\alpha} \right] + 2^{N_b-2} \text{Tr} \left[\left(\hat{\Gamma}^b | \hat{S}_{b\alpha} \rangle \right) \hat{S}_{b\alpha} \right], \quad (9.4)
\end{aligned}$$

using the fact that $\text{Tr} [\hat{S}_{ip}\hat{S}_{jq}] = 2^{N_i-2}\delta_{ij}\delta_{pq}$, where N_i is the number of spins in a molecule i . Therefore, the normalized singlet relaxation rate constant can be calculated as

$$\Gamma_S = \sum_{\{a,b\} \in \mathbb{S}} \sum_{i=a,b} 2^{N_i-2} \sum_{\alpha=x,y,z} \text{Tr} [\hat{S}_{i\alpha}\hat{\Gamma}^i\hat{S}_{i\alpha}] / \text{Tr} [\hat{Q}\hat{Q}^\dagger], \quad (9.5)$$

with the relaxation superoperators each in the Liouville space of just one molecule, rather than of the whole system. By comparison with Eq. (8.8), it can be seen that this is a sum of the self relaxation rates for each Cartesian component of the singlet states.

In general $\hat{\Gamma}^1 \neq \hat{\Gamma}^2$, since the two molecules in the intermolecular singlet state could be different, but in our case the two molecules are identical and so $\hat{\Gamma}^1 = \hat{\Gamma}^2 = \hat{\Gamma}^*$, further simplifying the calculation:

$$\Gamma_S = \sum_{\{a,b\} \in \mathbb{S}} \sum_{i=a,b} 2^{N_i-2} \sum_{\alpha=x,y,z} \text{Tr} [\hat{S}_{i\alpha}\hat{\Gamma}^*\hat{S}_{i\alpha}] / \text{Tr} [\hat{Q}\hat{Q}^\dagger]. \quad (9.6)$$

10 DFT Results

Table 1 shows the DFT optimized atomic coordinates of an S_6 Posner molecule. These were obtained by optimizing the geometry for a Posner molecule with S_6 symmetry from [15] in Gaussian 09 using density functional theory (DFT). The Ahlrich triple-zeta basis set def2-TZVPP was used in combination with the BP86 functional. The DFT work was performed by Daniel Kattnig (now at the Living Systems Institute, University of Exeter, UK).

References

- [1] K. Schulten and P. G. Wolynes, J. Chem. Phys. **68**, 3292 (1978).
- [2] D. E. Manolopoulos and P. J. Hore, J. Chem. Phys. **139**, 124106 (2013).
- [3] T. Cubitt, “Dr. Qubit,” (2018).
- [4] W. K. Wootters, Phys. Rev. Lett. **80**, 2245 (1998).
- [5] M. P. A. Fisher, Ann. Phys. **362**, 593 (2015).
- [6] M. W. Swift, C. G. Van de Walle, and M. P. A. Fisher, Phys. Chem. Chem. Phys. **20**, 12373 (2018).
- [7] M. Goldman, J. Magn. Reson. **149**, 160 (2001).
- [8] J. H. Freed and G. K. Fraenkel, J. Chem. Phys. **39**, 326 (1963).
- [9] A. Dey, P. H. H. Bomans, F. A. Muller, J. Will, P. M. Frederik, G. de With, and N. A. J. M. Sommerdijk, Nat. Mater. **9**, 1010 (2010).
- [10] N. Wagner-Rundell, *Electron Spin Relaxation Effects on Radical Recombination Reactions in Weak Magnetic Fields*, Ph.D. thesis, University of Oxford (2008).

- [11] A. G. Redfield, Adv. Magn. Reson. **1**, 1 (1965).
- [12] C. P. Slichter, *Principles of Magnetic Resonance* (Springer-Verlag, Berlin, 1978).
- [13] I. Kuprov, N. Wagner-Rundell, and P. J. Hore, J. Magn. Reson. **184**, 196 (2007).
- [14] S. Worster, D. R. Kattnig, and P. Hore, J. Chem. Phys. **145**, 035104 (2016).
- [15] G. Treboux, P. Layrolle, N. Kanzaki, K. Onuma, and A. Ito, J. Phys. Chem. A **104**, 5111 (2000).

Table 1: DFT optimized atomic coordinates, in Å, for Posner’s molecule with S_6 symmetry. Numbering of the phosphorus nuclei is as in Fig. 1, main text.

		x	y	z
1	O	−0.9344	+3.8163	+1.4609
2	Ca	−2.7835	+2.0443	+0.7842
3	O	−1.7198	+2.5381	−1.1499
4	Ca	+0.3786	+3.4328	−0.7842
5	O	−3.7722	+1.0989	−1.4609
6	P(1)	+0.0000	+2.6944	+2.0654
7	P(5)	−2.3334	+1.3472	−2.0654
8	O	−1.9765	+1.4995	−3.5593
9	O	+0.3104	+2.4615	+3.5593
10	O	+1.3382	+2.7585	+1.1499
11	O	−0.8317	+1.3528	+1.6409
12	O	+2.8378	+2.7174	−1.4609
13	O	−3.0580	−0.2203	+1.1499
14	O	+0.7557	+1.3966	−1.6409
15	O	−1.5874	−0.0439	−1.6409
16	P(4)	+2.3334	+1.3472	−2.0654
17	Ca	−3.1622	−1.3885	−0.7842
18	O	−2.2869	−0.9619	+3.5593
19	Ca	+0.0000	+0.0000	−3.4214
20	Ca	+0.0000	+0.0000	+0.0000
21	Ca	+0.0000	+0.0000	+3.4214
22	O	+2.2869	+0.9619	−3.5593
23	Ca	+3.1622	+1.3885	+0.7842
24	P(3)	−2.3334	−1.3472	+2.0654
25	O	+1.5874	+0.0439	+1.6409
26	O	−0.7557	−1.3966	+1.6409
27	O	+3.0580	+0.2203	−1.1499
28	O	−2.8378	−2.7174	+1.4609
29	O	+0.8317	−1.3528	−1.6409
30	O	−1.3382	−2.7585	−1.1499
31	O	−0.3104	−2.4615	−3.5593
32	O	+1.9765	−1.4995	+3.5593
33	P(2)	+2.3334	−1.3472	+2.0654
34	P(6)	+0.0000	−2.6944	−2.0654
35	O	+3.7722	−1.0989	+1.4609
36	Ca	−0.3786	−3.4328	+0.7842
37	O	+1.7198	−2.5381	+1.1499
38	Ca	+2.7835	−2.0443	−0.7842
39	O	+0.9344	−3.8163	−1.4609