

The Biological Qubit: Calcium Phosphate Dimers, Not Trimers

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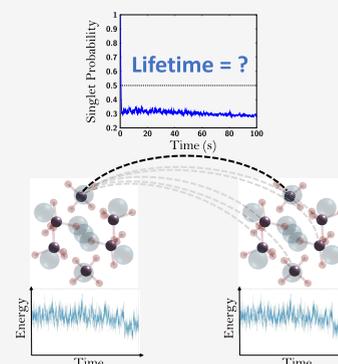
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ABSTRACT: The Posner molecule (calcium phosphate trimer, $\text{Ca}_9(\text{PO}_4)_6$) has been hypothesized to function as a biological quantum information processor due to its supposedly long-lived entangled ^{31}P nuclear spin states. This hypothesis was challenged by our recent finding that the molecule lacks a well-defined rotational axis of symmetry—an essential assumption in the proposal for Posner-mediated neural processing—and exists as an asymmetric dynamical ensemble. Following up, we investigate here the spin dynamics of the molecule's entangled ^{31}P nuclear spins within the asymmetric ensemble. Our simulations show that entanglement between two nuclear spins prepared in a Bell state in separate Posner molecules decays on a subsecond time scale—much faster than previously hypothesized, and not long enough for supercellular neuronal processing. Calcium phosphate dimers ($\text{Ca}_6(\text{PO}_4)_4$) however, are found to be surprisingly resilient to decoherence and are able to preserve entangled nuclear spins for hundreds of seconds, suggesting that neural processing might occur through them instead.



The Posner molecule (calcium phosphate trimer, $\text{Ca}_9(\text{PO}_4)_6$), was first hypothesized to exist in the bone mineral hydroxyapatite,¹ and has since been identified as the structural unit of amorphous calcium phosphate.² Its aggregation is thought to underpin bone growth.^{3–6} Although the Posner molecule is yet to be unambiguously experimentally observed in an isolated form, its biochemical relevance has long been recognized. In recent years, Fisher and co-workers have suggested that pairs of isolated Posner molecules could act as “neural qubits” by harboring long-lived entangled spin states among the 12 ^{31}P nuclei.^{7–9} This has been hypothesized to facilitate the long-range quantum-correlated release of Ca^{2+} ions in presynaptic neurons and thus to potentially give rise to correlated postsynaptic neuron firing.⁷

Central to the above-mentioned proposal is the supposed S_6 -symmetric arrangement of the molecule, wherein a rotational axis of symmetry allows the binding and unbinding of Posner molecules to act as a “pseudospin” entangler for the nuclear spin states.^{7,8} However, through an extensive series of first-principles simulations, we demonstrated recently¹⁰ that the Posner molecule does not exhibit the required symmetry and instead exists as a dynamical ensemble of predominantly low-symmetry clusters. Given that all prior works,^{8,11} until now, have considered the S_6 -symmetric structure of the Posner molecule to make theoretical predictions on the entanglement times of the nuclear spin states and for examining the viability of the molecule as a potential biomolecular qubit, here, we explore if, and for how long, ^{31}P nuclear spin coherences can be maintained for the multiple asymmetric configurations found in our work.

Keeping Fisher's original proposal in mind,^{7,8} and closely following the work by Player et al.,¹¹ one of the simplest measures to assess the pertinent spin coherences is the

temporal evolution of the (maximally entangled) singlet state for a pair of ^{31}P nuclei in identical, spatially separated Posner molecules, with the remaining ten uncorrelated nuclear spins serving as background (see Figure 1). In this arrangement, the evolution of the singlet probability over time serves as a measure of the conservation of quantum correlation among the Posner molecules and can be calculated for a variety of structural configurations of the molecule. Eventually, for the

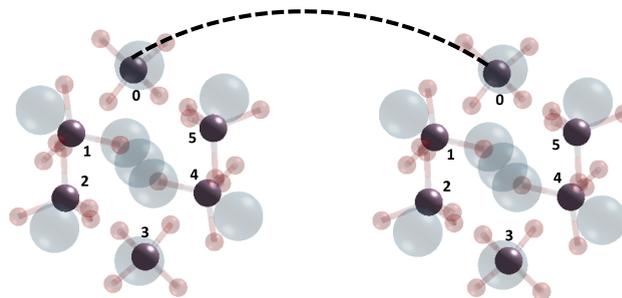


Figure 1. A pair of ^{31}P nuclei, namely the pair labeled (0, 0), entangled and initialized in the singlet state in two separate but identical Posner molecules. The separation between the molecules, although arbitrary, is large enough for intermolecular interactions between the ^{31}P nuclear spins to be negligible. The entanglement between the nuclear spins has been depicted by a dotted line.

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thermalized spin system, the singlet probability will settle down to $1/4$, the value expected for a maximally mixed state. A value of the singlet probability greater than $1/2$ indicates that entanglement is maintained (i.e., a mixed state of singlets and unpolarized triplet states in which more than 50% of the spins are in a singlet state is called entangled).¹¹ Additionally, the two-qubit concurrence^{11,12} between the ^{31}P nuclear spin pairs serves as a direct measure of entanglement. A value of one indicates a maximally entangled state; a value of zero indicates total loss of entanglement. A priori, we expect that the absence of symmetry in the Posner molecule will increase the number of unique scalar spin–spin couplings (J -couplings) in the coupling network^{13,14} which, as we explain later, dominate the coherent spin dynamics for this system. A large number of unique coupling constants implies a large number of unique frequencies that characterize the coherent evolution of the singlet probability. In turn, this is expected to accelerate the decay of the singlet probability through destructive interference in our model.^{11,15,16} Here, we address if this accelerated decay of spin correlation is realized for all structures of the ensemble, and if this is detrimental to the Fisher's proposal of calcium phosphate-mediated quantum information processing in neurons. Note that our detailed discussion on the link between the symmetry of the Posner molecule and the longevity of the singlet state is motivated by the importance given to the former as a key ingredient for the theory of Posner-mediated neural processing.^{7,8} However, as we show later, our calculations on the tricalcium biphosphate dimers and subsequent analysis shown in the [Supporting Information \(SI\)](#) suggest that while the symmetry of the molecule and its coupling constant values are certainly relevant, the longevity of the singlet state is primarily dictated by the number of coupled nuclear spins, i.e., the number of ^{31}P atoms.

Using an S_6 molecular point group symmetry for the Posner molecule, which renders the six ^{31}P nuclei magnetically equivalent, a singlet relaxation time of 37 min has been calculated previously by Player et al.¹¹ The authors of that work, while refining the original estimate of 21 days for the entanglement lifetime of nuclear spin states,^{7,8} acknowledge that the singlet state may relax even faster due to various interactions present in realistic scenarios. Here, we calculate the singlet probability for a pair of ^{31}P nuclear spins due to their coherent evolution in the presence of dominant relaxation mechanisms. Our approach closely follows the above reference,¹¹ but is extended to explicitly include spin relaxation in the calculation. Unlike the above work, however, which analyzed only a couple of symmetric structures, while using coupling constants from ref 8 (calculated for a *different* S_6 -symmetric structure), we aim to explore the full ensemble of symmetric and asymmetric structures. To this end, and because the J -coupling constants are expected to be different for each structural configuration of the molecule, we estimate the coupling constants for all investigated structures through first-principles calculations. We contend that our calculations and findings are more directly relevant to investigations of the viability of Fisher's proposal than those of earlier studies. Details of our Density Functional Theory (DFT) approach used can be found in the [SI](#).

Lastly, given that the structures of the calcium phosphate monomer, $\text{Ca}_3(\text{PO}_4)_2$, and the dimer, $\text{Ca}_6(\text{PO}_4)_4$, are more conclusively known,^{10,17} we also performed similar calculations on these structures and found extremely long-lived singlet states, irrespective of the symmetry of the molecule, for the

case of the dimer. Their presence *in vivo* has not yet been considered, but is something that invites thorough future investigation. Further details about the monomer and dimer results can be found in the [SI](#).

We consider the coherent evolution of the six ^{31}P nuclear spins in each Posner molecule subject to the spin Hamiltonian \hat{H}_0 , where

$$\hat{H}_0 = \omega_0 \sum_k \hat{I}_{k,z} + 2\pi \sum_{j < k} \sum_k J_{jk} \hat{I}_j \cdot \hat{I}_k \quad (1)$$

Here, $\omega_0 = -\gamma_k(1 - \sigma)B$ is the Larmor frequency of the ^{31}P nucleus; σ is the isotropic chemical shielding constant; \hat{I}_k is the spin angular momentum operator for nucleus k ; $\hat{I}_{k,z}$ is the z -component of the spin angular momentum operator; and J_{jk} is the scalar coupling constant between nuclear spins indexed j and k . The first term accounts for the Zeeman interactions, whereby differences in the chemical shielding will be assumed to be negligible in the low magnetic field considered. The second term corresponds to the intramolecular scalar spin–spin coupling interactions, characterized by the coupling constants J_{jk} . Since the evolution of the singlet probability and entanglement of pairs of spins are strongly dependent on the scalar coupling constants, it is critical to obtain accurate values of J_{jk} . Moreover, the coupling constants differ for each molecular structure. Here, the J_{jk} values have been derived from DFT calculations for every molecular geometry using the pcJ-n basis set,¹⁸ built specifically for the calculation of these interaction constants, for P and O atoms. The pcseg-n basis¹⁹ set, optimized for the calculation of nuclear magnetic shielding, was used for the Ca atoms. Further details can be found in the [SI](#). We remark that the values obtained by us are appreciably different from those reported, and used, in earlier studies.^{8,11} Our use of an optimized method and of a more accurate and specialized basis set for each atom gives us confidence in the preciseness of constants employed for the calculations reported here.

Molecular motion modulates the spin Hamiltonian, which induces spin relaxation (details in the [SI](#)). Here, we discuss possible relaxation pathways such as intra- and intermolecular dipole–dipole interactions, chemical shielding anisotropy (CSA), dipolar coupling with the solvent, and spin-rotation relaxation. The first of these (i.e., intramolecular dipole–dipole interactions) is expected to be the dominant relaxation pathway for rapidly and independently rotating dilute Posner molecules in the geomagnetic field ($\sim 50 \mu\text{T}$). Based on a simple estimate of spin–lattice relaxation times due to the modulation of the dipolar coupling by translational and rotational diffusion, the (concentration-dependent) intermolecular dipolar relaxation is expected to be slower than the intramolecular relaxation for concentrations of up to 7 mol/L (!). The CSA contribution is generally relevant in strong magnetic fields and can be considered negligible in the geomagnetic field, as is the case here (our estimates suggest a marked influence of CSA relaxation only for fields larger than 1 T). Any dipolar coupling with the solvent is expected to average out to zero in the presence of rapid, independent tumbling motion of the molecule. Finally, spin-rotation relaxation, which is thought to be the dominant relaxation mechanism for pyrophosphates,^{20,21} is neglected here under the assumption that the standard deviation in the angular velocity is expected to be much smaller for the larger Posner molecule. Of all these pathways then, the intermolecular contribution is clearly negligible at reasonable concentrations,

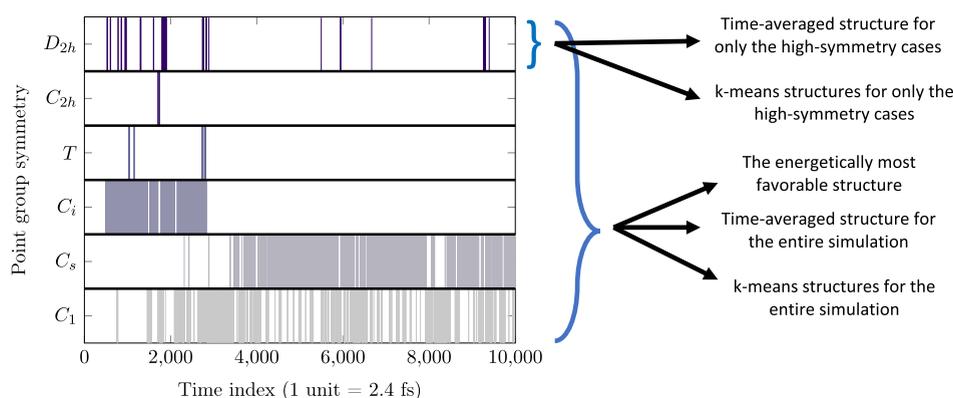


Figure 2. Illustration of the methodology for obtaining different configurations for spin dynamics calculations, starting from the AIMD structures presented in ref 10. Here, we only show the type of structures obtained from one AIMD simulation (out of the eight that were performed). Overall, our approach gave us 102 unique structures. The graph on the left shows the evolution of the molecular point-group symmetry during a dynamic simulation of a transition-state structure of the Posner molecule.

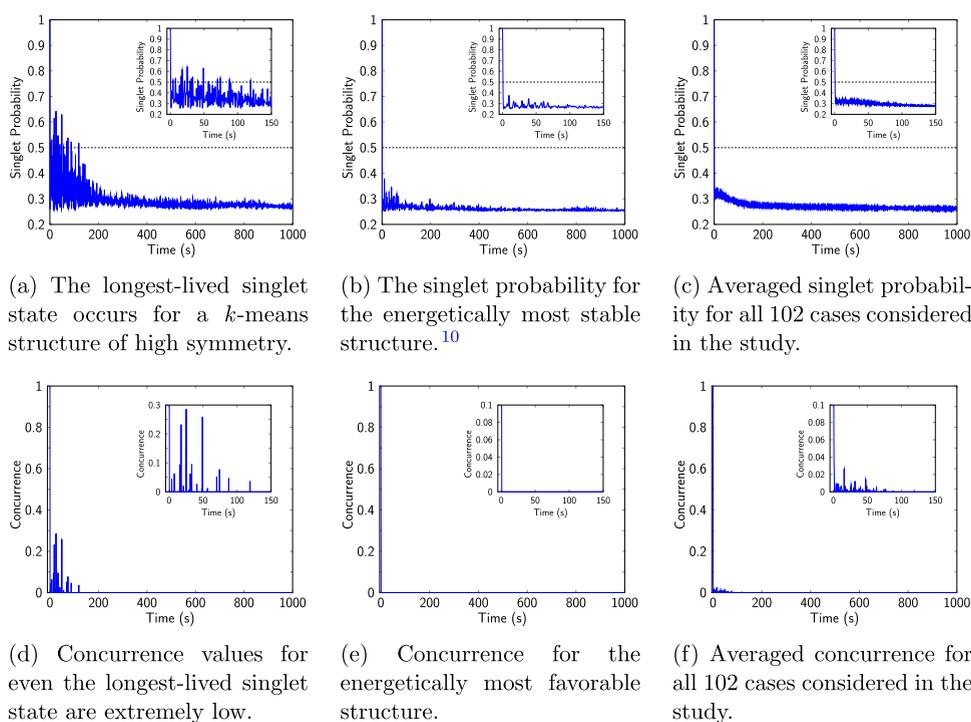


Figure 3. Short-lived nature of the singlet probability and concurrence for the Posner molecule, shown for three representative structures. Insets show zoomed in regions of the plots. (a) and (d) correspond to the structure with the longest-lived singlet state—a k -means structure with D_{2h} symmetry; (b) and (e) correspond to the energetically most stable structure with no symmetry in our dynamical study;¹⁰ (c) and (f) are the average singlet probability and concurrence for all 102 structures considered. Contrary to previous studies,^{7,8,11} the plots above suggest that the system is not suitable for quantum information processing at biologically relevant time scales.

and the dominant relaxation is induced by the 15 pairwise intramolecular dipolar nuclear spin couplings, the detailed form of which can be found in the SI.

We calculate and evolve the singlet state as follows. Indexing the ^{31}P nuclear spins in two separate Posner molecules, A and B , from $0_{(A,B)}$ through $5_{(A,B)}$, we assume that, without loss of generality, the system is initialized in a state with spins 0_A and 0_B in the maximally entangled singlet state, while the ten other spins are uncorrelated. We represent this singlet state as

$$|S_{0_A,0_B}\rangle = \frac{1}{\sqrt{2}}(|\alpha_{0_A}\beta_{0_B}\rangle - |\beta_{0_A}\alpha_{0_B}\rangle)$$

where $|\alpha\rangle$ is the spin-up state, and $|\beta\rangle$ is the spin-down state. Thus, the initial state density operator is proportional to the singlet projection operator, given as

$$\hat{P}_{0_A,0_B} = \sum_{\gamma \neq (0_A,0_B)} |S_{0_A,0_B}; \gamma\rangle \langle S_{0_A,0_B}; \gamma| = |S_{0_A,0_B}\rangle \langle S_{0_A,0_B}| \otimes \mathbb{I} \quad (2)$$

Here $|S_{0_A,0_B}; \gamma\rangle = \frac{1}{\sqrt{2}}(|\alpha_{0_A}\beta_{0_B}\rangle - |\beta_{0_A}\alpha_{0_B}\rangle) \otimes |\gamma\rangle$, and $|\gamma\rangle$ is any of a set of states such that $\sum_{\gamma \neq (0_A,0_B)} |\gamma\rangle \langle \gamma| = \mathbb{I}$; i.e., it assembles the maximally mixed spin state of the other 10 nuclear spins. The singlet probability $p_{0_A,0_B}(t)$ is given by $\text{Tr}[\hat{\rho}(t)\hat{P}_{0_A,0_B}]$ with $\hat{\rho}(0) = \hat{P}_{0_A,0_B}/\text{Tr}(\hat{P}_{0_A,0_B})$. To obtain the

evolution of $p_{0_A,0_B}(t)$ through time, we solve the Liouville-von Neumann equation:²²

$$\frac{d\hat{\rho}(t)}{dt} = -i\hat{L}\hat{\rho}(t) \quad (3)$$

where the Liouvillian superoperator \hat{L} is given by $\hat{H}_0 + i\hat{\Gamma}$, with the relaxation superoperator $\hat{\Gamma}$ given, in the extreme narrowing limit applicable to fast rotational motion, by $-\langle\hat{H}_1(t)\hat{H}_1(t)\rangle\tau_c$.¹¹ Here, double hats denote the commutator superoperator of the operators in question, and τ_c is the rotational correlation constant of the molecule.

To validate the form of the relaxation superoperator, we have calculated the rotational correlation constant of the molecule from molecular dynamics (MD) simulations. Closely following the work by Demichelis et al.,²³ we simulated the Posner molecule in a box of water molecules and followed its trajectory over 34 ns (i.e., at the simulation limits of computational resources available), using LAMMPS.²⁴ Further details about the simulation can be found in the SI. A value of $\tau_c \sim 177$ ps was obtained by analyzing the rotational correlation function in 3 dimensions. Thus, we find a slower rotational dynamics (by roughly a factor of 3) compared to the previous estimate by Player et al.,¹¹ which uses the approximate Stokes–Einstein–Debye relation. The value derived here is still well within the extreme narrowing limit, thus justifying the form of $\hat{\Gamma}$. Details about the calculation of the two-qubit concurrence, ^{11,12} $C_{0_A,0_B}$ can be found in the SI.

With this computational framework for spin relaxation calculations in hand, we build upon our previous work,¹⁰ wherein we demonstrated that the Posner molecule exists as an asymmetric dynamic ensemble. *Ab initio* molecular dynamics (AIMD) simulations of eight transition state structures of the molecule formed the core of that previous contribution. Here, we examine the singlet probability and concurrence not only for the above transition state structures, but also for the time-averaged structures of each of the eight AIMD simulations. Additionally, to cover a wider range of possibly relevant structures, we also calculate here the singlet probability for the energetically most favorable structures from each simulation, and the time-averaged configurations for structures associated with high-symmetries, as shown in Figure 2. Lastly, we also use *k*-means clustering to further generate statistically relevant structures—both for the entire simulation and for the high-symmetry cases only—and calculate the singlet probabilities and concurrence for all of them. This thorough examination gives us over 100 unique structures to analyze.

We show the time evolution of the singlet probability and concurrence for two representative cases in Figure 3, namely the longest-lived singlet state (Figure 3a and 3d), and the energetically most stable structure as per our dynamical analysis¹⁰ (Figure 3b and 3e). Given that the Posner molecule is expected to exist as a dynamic ensemble, we also show the singlet probability and the concurrence averaged over all 102 cases described above (Figure 3c and 3f). We immediately observe that, in general, the singlet probabilities decay at a rate much faster than what may be necessary for neural processing,^{7,8} and fall below the $1/2$ entanglement threshold within a second. Correspondingly, the concurrence plots also suggest that the system loses entanglement within a second. Note that the plots presented in this study are for a model

incorporating spin relaxation (in contrast with those presented in Player et al.'s work¹¹), although spin relaxation is a minor contributor to the decay of the singlet probability on the time scales shown. For a majority of the cases, as shown in Figure 4,

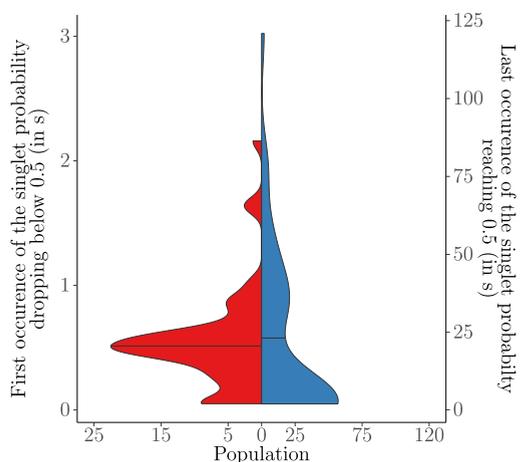
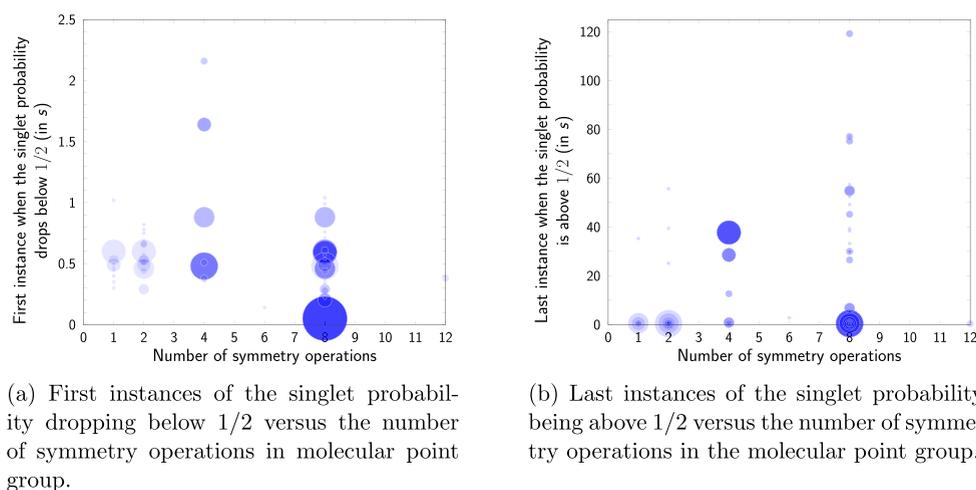


Figure 4. First and last instances of the singlet probability crossing the threshold of $1/2$. The number of structures for each case, with different scales, has been represented on the x-axis. Note that the y-axes have different scales. A total of 102 structures have been considered, obtained from methods depicted in Figure 2. The 50% quantile line has been shown in each case and confirms that a majority of the structures are unable to maintain the singlet state for more than a second.

the trend of Figure 3b is followed. Overall, it is important to emphasize that the singlet probability rapidly decays below the $1/2$ threshold within a second, regardless of the symmetry of the Posner molecule. Moreover, in cases where the singlet state is longer-lived, it is not entangled throughout, i.e., the singlet probability decays quickly and then refocuses sporadically. This has major implications on the viability of the molecule as a quantum information processor, because any information processing will have to be done only at the instances when the system is entangled, i.e., when the singlet probability is greater than $1/2$. In other words, the molecule may only act as a biological qubit for very short periods of time, or only at specific time instances.

The longest time for which a singlet state was sustained in the presence of relaxation was a recurrence at 119 s (Figure 3a), observed in one of the structures obtained using *k*-means clustering of the high-symmetry phase of a dynamic simulation (D_{2h} point group symmetry). Note that this time is defined as the last instance when the singlet probability was above the threshold of $1/2$, and that it does not correspond to the singlet lifetime. A comprehensive overview of the relevant singlet probability parameters for the structures examined in this study is provided in Figure 4. It is clear that, for 95% of the cases, the singlet state loses entanglement in less than a second. While a few structures do show recurrence of entanglement at time scales of tens of seconds, we reiterate that the molecule may act as a biological qubit at only the instances when the probability breaches the $1/2$ threshold, and not throughout. Additionally, we also consider the transfer of entanglement from one pair of ^{31}P nuclear spins to another, owing to their interactions via the *J*-coupling constants. Unsurprisingly, the singlet probabilities for all spin pairs remain low (~ 0.25)



(a) First instances of the singlet probability dropping below $1/2$ versus the number of symmetry operations in molecular point group.

(b) Last instances of the singlet probability being above $1/2$ versus the number of symmetry operations in the molecular point group.

Figure 5. Symmetry of the molecule does not seem to play a major role in maintaining entanglement in the system, and Posner molecules generally have short entanglement lifetimes (<1 s) irrespective of their point-group symmetry. The marker size in each plot is proportional to the number of data points at the location, whereas darker areas represent overlapping of markers.

throughout the considered time duration (further details can be found in the SI).

The above analysis suggests that the Posner molecule might not maintain long-lived singlet states for more than a second. However, Figure 3a suggests that in a hypothetical high symmetry configuration, the molecule may sustain the nuclear singlet state for a longer duration, albeit only at specific instances when the singlet probability refocuses. Thus, to better understand the effect of symmetry on the longevity of the nuclear spin singlet state in the Posner molecule, we plotted the first and last instances when the singlet probability crosses the $1/2$ threshold against the point group symmetry of the molecule or, more specifically, the number of symmetry operations associated with the point group. This has been depicted in Figure 5.

Contrary to the expectation that the entanglement lifetime would be longer for structures that have higher symmetry, we find that the singlet state in the Posner molecule is, on average, short-lived (up to a few seconds at best) irrespective of the symmetry. We would also like to mention in passing that in addition to the 102 structures described above arising out of our AIMD simulations and subsequent analyses, we considered the two specific Posner molecule configurations explored in ref 8 and ref 11. These configurations were not found to be energetically or structurally relevant in our dynamical simulations.¹⁰ However, for these structures too, we found that the singlet probability falls below the $1/2$ threshold within a second, and without any refocusing. On the other hand, if we make use of the J -coupling constants as suggested in ref 8 for one of these structures, our calculation broadly reproduces the results from ref 11, albeit with minor differences due to slightly different values of the chemical shielding tensor and the rotational correlation time. A comparison of the singlet probabilities in the above cases has been depicted in Figure 6. Note that this comparison has only been done for two specific molecular configurations of the Posner molecule, and the results should not be generalized to other structures. Our observation above is consistent with the fact that, on average, symmetric molecules are expected to have a better entanglement yield. However, as we show in the SI, the values of the J -coupling constants matter in the sense that it is possible for a molecular configuration to have a wide range of

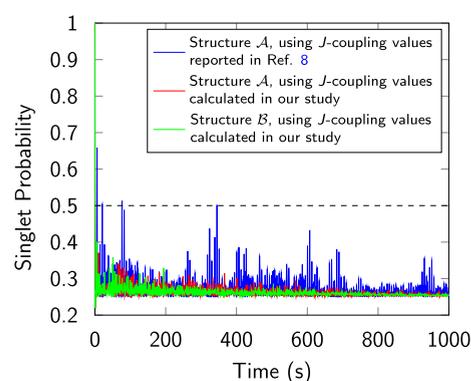
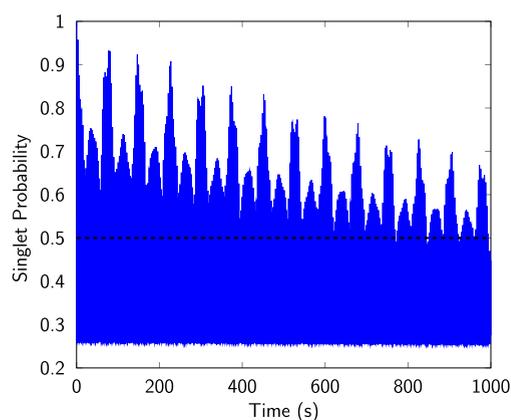


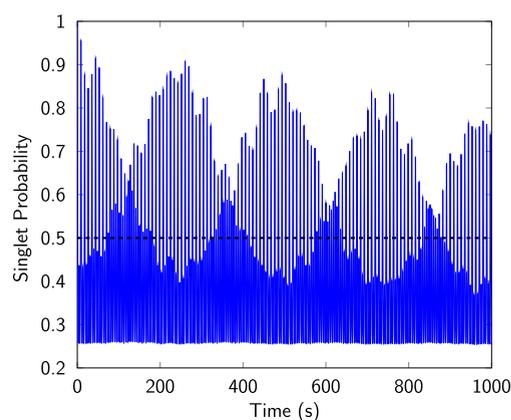
Figure 6. A comparison of the singlet probabilities for two S_6 structures, \mathcal{A} , taken from ref 11, and \mathcal{B} , taken from ref 8, with coupling constants as reported in ref 8 and as calculated in our study.

entanglement yields, depending on the calculated values of those constants. Therefore, it is important to be able to calculate these constants accurately.

Overall, we observe that the singlet state between a pair of ^{31}P nuclear spins in separate Posner molecules generally loses entanglement within a second. Only certain hypothetical or energetically unfavorable configurations of the molecule are found to preserve the state for more than a second. This is significantly shorter than previously suggested.^{7,8,11} Commensurate with these findings, the concurrence values are also observed to drop rapidly within the same period of time. Notably, these findings do not preclude the molecule from being relevant for biological processes taking place at time scales for which the nuclear spin coherences are indeed maintained. However, due to the small diffusion constant of the molecule, it is unable to traverse neuronally relevant length-scales within its short entanglement lifetime, and so it might not be suitable for entanglement mediated neural signal processing, as previously suggested.⁷ Specifically, we estimated the translational diffusion properties of the molecule by analyzing its trajectory in a hydrated environment (details in the SI) and found the diffusion constant to be $\sim 1.01 \times 10^{-9}$ m^2/s . This implies that it would take the Posner molecule approximately 14 h to traverse the length of a neuronal cell



(a) Singlet probability for a dimer structure with a C_2 symmetry indicates a very long-lived coherence.



(b) Singlet probability for a dimer structure with a C_s symmetry also indicated a very long-lived coherence.

Figure 7. Singlet probabilities for two stable dimer structures. Long-lived singlet states are observed irrespective of the symmetry of the dimer, unlike the Posner molecule, potentially making it more suitable for quantum information processing. Similar plots for all dimer structures obtained in our previous study¹⁰ can be found in the SI.

axon (~ 1 cm), much longer than the aforementioned entanglement lifetimes. We also note that the above estimated speeds are markedly slower than the average speed of nerve impulses.²⁵

Surprisingly, exploratory calculations on the tricalcium biphosphate dimer, $\text{Ca}_6(\text{PO}_4)_4$, revealed that the singlet state in the dimer is exceedingly long-lived, irrespective of its structure. As reported in earlier studies,^{10,17} although the dimer also exists in multiple configurations, its energetically favorable structures are known more conclusively. We were able to identify six stable structures for the dimer,¹⁰ although many more may exist. Again, as for the Posner molecules, we initialized a pair of ^{31}P nuclei in two identical, spatially separated dimers in a singlet state, and then evaluated the singlet probability over time. Remarkably, even in the presence of relaxation, the singlet state in tricalcium biphosphate dimers is extremely long-lived (of the order of 10^3 seconds, and with significant refocusing) regardless of the symmetry of the molecule. This has been depicted in Figure 7 for two dimer structures. The plots for the remaining structures, the values of the coupling constants for each structure, as well as a detailed analysis of the transfer of coherence from one ^{31}P nuclear spin pair to another (for one structure), can be found in the SI. Despite these fascinating observations, we remark that the tricalcium biphosphate dimer does not appear to have been observed experimentally.

In general, we expect a spin system with a lesser number of coupled nuclear spins, such as the tricalcium biphosphate dimer, to be more favorable for maintaining long-lived singlet states than a spin system with a larger number of coupled nuclear spins, such as the Posner molecule. Considering systems composed from dimers, with no symmetry (16 distinct energy levels per cluster) and with S_4 symmetry (13 energy levels), and from Posner molecules, with no symmetry (64 energy levels) and with S_6 symmetry (44 energy levels), the number of unique positive frequencies contributing to the coherent evolution of the singlet probability is 7380, 3159, 2035152, and 448877, respectively (details of the calculation have been summarized in the SI). While some of these might be close to degenerate or zero or not significantly contribute to

the singlet probability, these numbers illustrate that destructive interference of coherent contributions will be vastly more likely in larger spin systems, regardless of cluster symmetry. This is in line with our results. We confirm the above argument by evaluating the entanglement yield, in the absence of spin relaxation, for randomly coupled systems with different number of ^{31}P atoms and obtain the same trend (see SI). These calculations corroborate the insight that the preservation or recurrence of entangled states is primarily related to the number of coupled nuclei, and only secondarily influenced by the symmetry of the molecule and the actual J -coupling constants, which impact the evolution through exact and accidental degeneracies of energy levels. Regardless of these observations, we maintain that accurate calculations to determine the J -coupling constants for every molecular configuration are critical to evaluate the longevity of the spin singlet state of molecules in comparison to other structures of the same family, i.e., with the same number of coupled nuclear spins, and to assess effects of spin relaxation.

In view of the dimers' ability to maintain coherences for exceptionally long times, it is interesting to compare the formation energies per monomer unit of the trimer (Posner molecule) and the dimer. For the dimer configurations studied, the formation energy per monomer unit ranged from -88.700 eV to -89.2007 eV. For the trimer, the value ranges from -88.332 eV to -90.517 eV. In comparison, thermal energy at room temperature is 0.026 eV. Thus, the dimer appears to be roughly as stable as the Posner molecule and is expected to exist as an independent, stable entity without coalescing into Posner molecules. These observations suggest that the nuclear spin entanglement in tricalcium biphosphate dimers could be worth exploring both theoretically and experimentally.

Our comprehensive study on the spin dynamics of the singlet state in pairs of Posner molecules, performed without any assumptions on the structure or the coupling constants of the molecule, shows that the singlet state is short-lived (< 1 s) irrespective of the structural symmetry of the molecule. This also indicates that accurate calculation of the J -coupling constants, instead, is crucial to the study of spin dynamics pertaining to the Posner molecule. Our results suggest that the

Posner molecule might be unsuitable as a biological quantum information processor since entanglement between ^{31}P nuclei in pairs of Posner molecules is not expected to last for more than a second. It may be possible that coherence is transferred from one pair of ^{31}P nuclei to the other, but as shown in earlier studies¹¹ and, to a greater extent, in our SI, this does not increase the singlet probability yield over time in any way. Moreover, recent findings on ^{31}P – ^{31}P singlet lifetimes in common organic phosphorus compounds of interest (e.g., adenosine diphosphate,²⁶ nicotinamide adenine dinucleotide,²⁶ tetrabenzyle pyrophosphate,²⁰ pyrophosphate²¹) show that the singlet lifetime ranges from less than half a second in large diphosphates and pyrophosphates to a few tens of seconds in small, highly symmetric pyrophosphates. Additionally, the latter study suggests that singlet lifetimes may be reduced further in a more realistic biological environment, and identifies spin-rotation relaxation as the dominant relaxation pathway.²¹ While our model neglects spin-rotation relaxation (due to the larger size of the Posner molecule), it will be interesting to see how our results differ after its inclusion. The singlet lifetimes reported in the above studies are of the same order as that of the Posner molecule in the current study and suggest that, without conclusive evidence of the presence of isolated Posner molecules *in vivo*, the longevity of the singlet state reported in this study is comparable to that found in other phosphorus compounds *in vitro*. Additionally, while the current study assumed a weak net external magnetic field, it would be interesting to observe the singlet probability in the presence of stronger magnetic fields, and to see whether that has any effect on increasing the singlet longevity. Finally, we observe long-lived ($\sim 10^2$ – 10^3 seconds) singlet states for the tricalcium biphosphate dimer, regardless of the structural symmetry of the molecule. This fascinating result is explained on the basis of the fact that any system with a smaller number of coupled nuclear spins is expected to better maintain entanglement within the singlet state than a system with a larger number of coupled nuclear spins. This leads us to the conclusion that while the symmetry of the molecule and its coupling constants are critical for evaluating the longevity of the singlet state given a molecule, the behavior of the coherent oscillations is largely dictated by the system size. The fact that the dimers appear to be as energetically stable as the Posner molecule might suggest that the dimer could be a better candidate for a naturally occurring quantum information processor than the Posner molecule. However, confirmation of its presence *in vivo* is necessary.

COMPUTATIONAL METHODS

For the calculation of the scalar coupling constants, we used the pcJ-n basis set¹⁸ built specifically for the calculation of NMR scalar coupling constants. The pseg-n basis set¹⁹ was used for the calcium atoms. We used ORCA²⁷ for calculating the coupling constants, using the B3LYP exchange-correlation functional. The QuTiP library²⁸ was used to extract the spin operators needed for the calculation of the singlet probabilities and concurrences. LAMMPS²⁴ was used for all molecular dynamics simulations, along with the force-fields developed by Demichelis et al.²³ Further details about the above simulations can be found in the SI.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.jpcllett.2c03945>.

Details about our methods and the spin Hamiltonian, complete results of our simulations on monomers and dimers, and plots depicting the transfer of coherence between ^{31}P nuclear spin pairs in representative structures for the Posner molecule and the dimer (PDF)

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Notes

The authors declare no competing financial interest.

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