Quantum Indistinguishability in Chemical Reactions

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Quantum indistinguishability plays a crucial role in many low-energy physical phenomena, from quantum fluids to molecular spectroscopy. It is, however, typically ignored in most high temperature processes, particularly for ionic coordinates, implicitly assumed to be distinguishable, incoherent and thus well-approximated classically. We explore chemical reactions involving small symmetric molecules, and argue that in many situations a full quantum treatment of collective nuclear degrees of freedom is essential. Supported by several physical arguments, we conjecture a "Quantum Dynamical Selection" (QDS) rule for small symmetric molecules that precludes chemical processes that involve direct transitions from orbitally non-symmetric molecular states. As we propose and discuss, the implications of the Quantum Dynamical Selection rule include: (i) a differential chemical reactivity of para- and ortho-hydrogen, (ii) a mechanism for inducing inter-molecular quantum entanglement of nuclear spins, (iii) a new isotope fractionation mechanism, (iv) a novel explanation of the enhanced chemical activity of "Reactive Oxygen Species", (v) illuminating the importance of ortho-water molecules in modulating the quantum dynamics of liquid water, (vi) providing the critical quantum-to-biochemical linkage in the nuclear spin model of the (putative) quantum brain, among others.

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I. INTRODUCTION

A. Motivation

The far reaching impact of quantum indistinguishability in few-particle collisions, in molecular spectroscopy[1] and in the low temperature behavior of macroscopic many-body systems (e.g., superfluidity) is well appreciated and extensively studied.[2] However, the role of indistinguishability for the dynamics of macroscopic systems at high temperature remains virtually unexplored, typically neglected due to the presumed absence of necessary quantum coherence. For cohesion of both solids and molecules, while electrons are treated quantum-mechanically, the much heavier ions are treated as distinguishable and classical. Moreover, in chemical reactions of molecules in solution, nuclear spins are generally believed to play little role, despite their macroscopic quantum coherence times (especially for spin-1/2 nuclei[3,4]). However, for small symmetric molecules the Pauli principle can inextricably entangle the coherent nuclear spin dynamics with the molecular rotational properties. The latter must modulate chemical reaction rates, even if weakly, thereby coupling nuclear spin dynamics to quantum chemistry.

Molecular hydrogen offers the simplest setting for discussing the interplay of indistinguishability and chemical reactivity. While the two electrons are tightly bound in a symmetric molecular orbital, the proton nuclear spins are weakly coupled, so that molecular hydrogen comes in two isomers, para-hydrogen (nuclear spin singlet) and ortho-hydrogen (nuclear spin triplet). Treating the motion of the nuclei quantum-mechanically, the Pauli principle dictates that molecular para- and ortho-hydrogen rotate with even and odd angular momentum, respectively.

A natural question, that to the best of our knowledge has not been asked, is whether the para- and ortho-spin-isomers of molecular hydrogen exhibit different chemical reaction rates in solvent. If yes, as might be expected from the different rotational properties of the two spin-isomers, what is the magnitude and "sign" of the effect? Intuitively, one might expect such effects to be small, especially at temperatures well above the rotational constant.

B. "Quantum Dynamical Selection"

In this paper we explore this and related questions in a number of systems, focusing on enzymatic reactions with the substrate consisting of a small symmetric molecule, characterized by a "quasi-angular-momentum", L_{quasi} (to be defined in Section II). As we elaborate and motivate in the next section, and in contrast to the aforementioned "conventional-wisdom", such bond-breaking chemical reactions can be very sensitive to nuclear spin states, via Pauli transduction through the allowed molecular rotations. Our central conjecture is that symmetric molecules can only have a direct bond-breaking chemical reaction from a state with an orbitally symmetric wavefunction, i.e., with zero 'quasi-angular-momentum" $L_{\text{quasi}} = 0$, (e.g., the symmetric para-hydrogen). On the other hand,

a molecule constrained by Fermi/Bose indistinguishability to have a nonzero odd orbital angular momentum is precluded from breaking its bond by a "Quantum Dynamical Selection" (QDS) rule, a "closed bottleneck" in Hilbert space. Physically, this closed bottleneck is due to a destructive interference between the multiple possible bond-breaking processes – one for each of the symmetry related molecular orbital configurations. We emphasize that *QDS is not of energetic origin*, operational even if the molecule's rotational constant is much smaller than the temperature.

C.   Quantum coherence

Before exploring the role of quantum indistinguishability on chemical processes, we briefly comment on the important issue of quantum decoherence, the common prejudice being that rapid decoherence in a wet solution will render *all* quantum phenomena inoperative. Indeed, elevated temperatures will generally move a system towards classical behavior. For example, when a physical process oscillating with a characteristic frequency, ω, is immersed in a thermal environment, quantum effects will typically wash out for T$\geq \hbar\omega/k_B$. At body/room temperature it is thus only phenomena oscillating at very high frequencies (10^{13}Hz, say, such as molecular vibrational modes) where quantum mechanics can modify the dynamics. But this argument implicitly presumes thermal equilibrium.

Nuclei with spin-1/2 in molecules or ions tumbling in water are so weakly coupled to the solvent that macroscopic coherence times of seconds or minutes are possible and regularly measured in liquid state NMR.[7] But weak coupling is a two-way street; if the solvent disturbs only weakly the nuclear spins, the nuclear spin dynamics will only weakly disturb the dynamics of the molecule and the surrounding solvent. However, small *symmetric* molecules, where quantum indistinguishability can entangle nuclear spin states with molecular rotations, provide an exception.

As we detail in the next section, the symmetry of the nuclear spin wavefunction in such symmetric molecules will dictate a characteristic "quasi-angular-momentum", L_{quasi} – equal to a small integer in units of $\hbar$ – that is symmetry protected even in the non-rotationally invariant solvent environment. And, provided the molecule's thermal angular momentum is much larger than $\hbar$ the environment can not readily measure L_{quasi}, so that the different nuclear-spin symmetry sectors will remain coherent with one another for exponentially long times. Remarkably, even though the solvent is ineffective at measuring L_{quasi}, we will argue that enzymes (which catalyze irreversible bond-breaking chemical reactions) can, in effect, measure L_{quasi} – implementing a projective measurements onto $L_{\text{quasi}} = 0$.

D.   Outline

The rest of the paper is organized as follows. In Section II, focusing on small symmetric molecules with C$_n$ symmetry, we formulate the general problem and then for concreteness specialize to the case of $n = 2$ and $n = 3$. With this formulation, in Sec.III we then state our Quantum Dynamical Selection conjecture, discussing both physical and mathematical plausibility arguments for it in Sec.IV. We conclude in Sec.V with experimental implications of the QDS rule, proposing a number of experiments to test the conjecture.

II.   THEORETICAL FRAMEWORK

A.   Beyond Born-Oppenheimer approximation

In this section we present the basic framework for our subsequent discussion of the role of symmetry and quantum indistinguishability in chemical processes involving catalytically-assisted bond-breaking in symmetric molecules. In molecular processes the electrons, as fast degrees of freedom, are appropriately treated as fully quantum-mechanical indistinguishable fermions. In contrast, the constraints of quantum indistinguishability on the nuclear orbital degrees of freedom when treated within the Born-Oppenheimer approximation are invariably neglected, especially in solution chemistry (although not always in molecular spectroscopy[1]). The molecular dynamics and chemical reactions are thus assumed to be fully controlled by classical motion of the molecular collective coordinates on the Born-Oppenheimer adiabatic energy surface. While this may be adequate for some systems, we argue that it can be wholly insufficient for chemical reactions in small symmetric molecules. As we will discuss, in such systems, the nuclear and electron spin degrees of freedom can induce Berry phases that constrain the molecular orbital dynamics on the adiabatic energy surface, which must then be treated quantum mechanically since these Berry phases do not enter the classical equations of motion. As we shall argue, the presence of Berry phases can have strong, and previously unappreciated order-one effects in chemical bond-breaking processes.

B.   Planar symmetric molecules

For simplicity of presentation we focus primarily on molecules which possess only a single n-fold symmetry axis that under a $2\pi/n$ planar rigid-body rotation (implemented by the operator $\hat{C}_n$) cyclically permutes n indistinguishable fermionic nuclei. A water molecule provides a familiar example for $n = 2$ and ammonia for $n = 3$, wherein the protons are cyclically permuted.

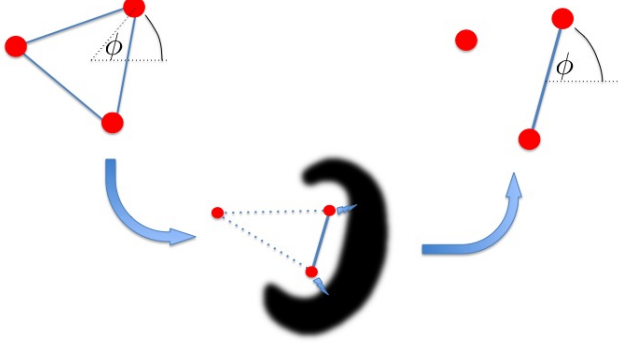For such molecules the nuclear spin states can be con-

FIG. 1: Schematic of a bond-breaking chemical reaction: (a) Initial state of a C_3 symmetric molecule with two molecular electrons (blue) bonding the three nuclei (red) together. (b) An intermediate state where the reaction is catalyzed by an enzyme that "grabs" two of the nuclei, weakening their bonds to the third by depletion of electronic charge. (c) Final product state composed of a molecular dimer and an isolated atom.

veniently chosen to be eigenstates of $\hat{C}_n$, acquiring a phase factor (eigenvalue) $\omega_n^{-\tau}$ with $\omega_n = e^{i2\pi/n}$ and the "pseudospin", τ taking on values $\tau = 0, 1, 2, ..., n-1$. Due to Fermi statistics when the molecule is physically rotated by $2\pi/n$ radians around the C_n symmetry axis, the total molecular wavefunction – which consists of a product of nuclear rotations, nuclear spins and electronic molecular states – must acquire a sign $(-1)^{n-1}$ due to a cyclic permutation of fermionic nuclei. Provided the electron wavefunctions transform trivially under the C_n rotation, this constraint from Fermi statistics of the nuclei, $e^{i(-2\pi\tau/n+2\pi L/n-\pi(n-1))} = 1$, implies that the collective orbital angular momentum of the molecule is constrained by τ, taking on values $L = L_{\text{quasi}} + n\mathbb{Z}$ with the "quasi-angular-momentum" given by

$$L_{\text{quasi}} = \begin{cases} \tau, & n \text{ odd}, \\ \tau + n/2, & n \text{ even}. \end{cases} \quad (1)$$

1. Molecular trimer of identical fermionic nuclei

For illustrative clarity we first formulate the problem for the case of $n = 3$, specializing to three identical fermionic nuclei with nuclear spin $1/2$ and electrical charge $+1$. We focus on a singly ionized trimer molecule T$\equiv$A$_3^+$ undergoing a chemical reaction,

$$A_3^+ \rightarrow A_2 + A^+, \quad (2)$$

into a singly ionized atom, A^+, and a neutral dimer molecule, D$\equiv$A$_2$. The process is schematically displayed

in Fig.1, where the molecular trimer is composed of the three fermionic nuclei with creation operators, $\hat{F}_\alpha^\dagger$, in spin state $\alpha = \uparrow, \downarrow$, that form a C$_3$ symmetric molecular configuration characterized by a collective coordinate ϕ. The nuclei part of such a molecular state is created by the three-nuclei operator,

$$\hat{T}_\tau^\dagger(\phi) = \sum_{\alpha\beta\gamma} \chi_{\alpha\beta\gamma}^\tau \hat{F}_\alpha^\dagger(\phi) \hat{F}_\beta^\dagger(\phi + 2\pi/3) \hat{F}_\gamma^\dagger(\phi + 4\pi/3). \quad (3)$$

The three-nuclei spin wavefunction $\chi_{\alpha\beta\gamma}^\tau$ is chosen as a τ representation of cyclic permutations, an eigenstate of $\hat{C}_3$,

$$\hat{C}_3 \chi_{\alpha\beta\gamma}^\tau = \chi_{\gamma\alpha\beta}^\tau = \omega_3^\tau \chi_{\alpha\beta\gamma}^\tau, \quad (4)$$

with $\omega_3 = e^{i2\pi/3}$, required by $(\hat{C}_3)^3 = 1$. Thus, for this trimer molecule, τ takes on one of three values, $\tau = 0, 1, 2$ (or equivalently, $\tau = 0, \pm 1$). By construction $\hat{T}_\tau(\phi)$ then also forms an irreducible representation of $\hat{C}_3$ satisfying,

$$\hat{T}_\tau(\phi + 2\pi/3) = \omega_3^\tau \hat{T}_\tau(\phi). \quad (5)$$

We will at times refer to τ as a "pseudospin", that encodes both the nuclear spin and the orbital qubits, entangled through the Pauli principle of identical nuclei.

Because a discrete $2\pi/3$ rotation executes a fermionic cyclic interchange, the τ representation of the nuclear spin wavefunction imprints a nontrivial Berry phase ω^τ onto the orbital degree of freedom, ϕ, which we discuss below. For simplicity we have suppressed the position coordinate describing the center of mass of the trimer molecule as well as the orientation of the normal to this planar trimer molecule.

In addition to the nuclei, a correct description of a molecule must also consist of bonding electrons that, within the Born-Oppenheimer approximation, occupy the molecular orbitals. For concreteness we consider a (singly ionized) molecule with only two electrons that form a spin-singlet in the ground-state molecular orbital $\psi_T(\mathbf{r}; \phi)$, where the subscript denotes the trimer nuclear configuration. This wavefunction transforms symmetrically under $\hat{C}_3$, satisfying $\psi_T(\mathbf{r}; \phi + 2\pi/3) = \psi_T(\mathbf{r}; \phi)$. We denote the electron creation operator in this orbital as,

$$\hat{c}_\sigma^\dagger(\phi) = \int_{\mathbf{r}} \psi_T(\mathbf{r}; \phi) \hat{c}_\sigma^\dagger(\mathbf{r}). \quad (6)$$

The trimer molecular state we thus consider can be written as,

$$|T\rangle = \sum_\tau \int_\phi \Psi_\tau(\phi) \hat{c}_\uparrow^\dagger(\phi) \hat{c}_\downarrow^\dagger(\phi) \hat{T}_\tau^\dagger(\phi) |\text{vac}\rangle \otimes |\mathcal{E}\rangle_\phi, \quad (7)$$

characterized by an orbital wavefunction in the τ representation,

$$\Psi_\tau(\phi + 2\pi/3) = \omega_3^\tau \Psi_\tau(\phi). \quad (8)$$

Were the general orbital wavefunction $\Psi_\tau(\phi)$ expanded in angular momentum eigenstates, $e^{iL\phi}$, with $L \in \mathbb{Z}$, this constraint implies that $L = L_{\text{quasi}} + 3\mathbb{Z}$ with a "quasi-angular-momentum" $L_{\text{quasi}} = \tau$, consistent with Eq.(1) for $n = 3$.

In Eq.(7) the ket $|\mathcal{E}\rangle_\phi$ denotes the initial quantum state of the environment – i.e., the solvent and enzyme – that is entangled with the molecular rotations through the angle ϕ, as generically the environment can "measure" the molecular orientation. Note that we have implicitly assumed that the initial state of the environment does not depend on τ, so that $|\mathcal{E}\rangle_{\phi+2\pi/3} = |\mathcal{E}\rangle_\phi$. For a molecule with thermal angular momentum, L_T (defined through $\hbar^2 L_T^2/\mathcal{I} = k_B T$, with moment of inertia $\mathcal{I}$) that is much greater than one, $L_T \gg 1$, the solvent is ineffective in "measuring" the molecular quasi-angular-momentum, which is a small fraction of L_T. Indeed, the quasi-angular-momentum decoherence time should be exponentially long for large thermal angular momentum, varying as $t_{\text{coh}}^\tau \sim t_0 \exp(cL_T^2)$ with an order one constant c and t_0 a microscopic time of order a picosecond.

2. Molecular dimer and atom products state

As illustrated in Fig.1, the bond-breaking reaction proceeds through an intermediate enzymatic stage, that is challenging to describe microscopically. Through its interaction with the electronic orbital degrees of freedom the enzyme temporarily binds and "holds" two of the nuclei, separating them from the third nucleus. This causes molecular rotations to cease and also weakens the molecular bonds. We assume that the final product state consists of a neutral molecular dimer, $D \equiv A_2$, held together by the two electrons and a singly ionized atom A^+. The orientation of the dimer is characterized by a single angle coordinate, which we again denote as ϕ (see Figure 1).

This final product state $|P\rangle$ can then be expressed as,

$$|P\rangle = \sum_\tau a_\tau \int_\phi \sum_{\mu,\alpha\beta\gamma} \Psi_\mu(\phi)\chi_{\alpha\beta\gamma}^\tau |A_\alpha\rangle |D_{\beta\gamma},\phi\rangle \otimes |\mathcal{E}^*\rangle_\phi,$$
(9)

where $|\mathcal{E}^*\rangle_\phi$ describes the state of the environment (solvent plus enzyme) after the chemical reaction, $|A_\alpha\rangle = \hat{F}_{\mathbf{r}_A,\alpha}^\dagger|\text{vac}\rangle$ denotes the state of the atom (located at position $\mathbf{r}_A$), and the state of the dimer molecule (located at position $\mathbf{r}_D$) is given by,

$$|D_{\beta\gamma},\phi\rangle = \hat{F}_{\mathbf{r}_D,\beta}^\dagger(\phi)\hat{F}_{\mathbf{r}_D,\gamma}^\dagger(\phi+\pi)\hat{c}_\uparrow^\dagger(\phi)\hat{c}_\downarrow^\dagger(\phi)|\text{vac}\rangle. \quad (10)$$

The electron creation operators on the dimer molecule are given by,

$$\hat{c}_\sigma^\dagger(\phi) = \int_{\mathbf{r}} \psi_D(\mathbf{r};\phi)\hat{c}_\sigma^\dagger(\mathbf{r}), \qquad (11)$$

with the ground state molecular orbital for the dimer molecule (when oriented at angle ϕ) $\psi_D(\mathbf{r};\phi)$, assumed to transform symmetrically under the C_2 symmetry of

the dimer molecule, $\psi_D(\mathbf{r};\phi+\pi) = \psi_D(\mathbf{r};\phi)$. The dimer orbital wavefunction $\Psi_\mu(\phi)$ transforms as $\Psi_\mu(\phi+\pi) = e^{i\mu\pi}\Psi_\mu(\phi)$ with $\mu = 0,1$.

Because we do not expect the nuclear spins state in each τ-sector to change through the chemical reaction, the atomic and dimer states remain entangled through the nuclear spin wavefunction, $\chi_{\alpha\beta\gamma}^\tau$. We have introduced an overall amplitude, a_τ which we shall discuss further below.

Since an enzymatic chemical reaction will typically be strongly exothermic (releasing, for example, a fraction of eV in energy) the quantum state of the environment after the reaction, $|\mathcal{E}^*\rangle_\phi$ will be very different than before the chemical reaction, $|\mathcal{E}\rangle_\phi$ – that is $_\phi\langle\mathcal{E}^*|\mathcal{E}\rangle_\phi = 0$.

3. Generalization to arbitrary n-mer

Here we briefly generalize from $n = 3$ to a planar molecule with n-fold symmetry consisting of n fermionic spin-1/2 nuclei. The nuclear spin wavefunction $\chi_{\alpha_1\alpha_2...\alpha_n}^\tau$ can be chosen as an eigenstate of the cyclic permutation symmetry, $\hat{C}_n$,

$$\hat{C}_n\chi_{\alpha_1\alpha_2...\alpha_n}^\tau = \chi_{\alpha_n\alpha_1\alpha_2...\alpha_{n-1}}^\tau = \omega_n^\tau\chi_{\alpha_1\alpha_2...\alpha_n}^\tau, \quad (12)$$

with $\omega_n = e^{i2\pi/n}$ required by $(\hat{C}_n)^n = 1$. The pseudospin now takes on one of n values, $\tau = 0,1,2,...n-1$. Due to Fermi statistics of the nuclei the total molecular wavefunction must acquire a factor of $(-1)^{n-1}$ under a molecular rotation by $2\pi/n$. Assuming that the bonding electrons transform trivially under C_n, the molecular orbital wavefunction (as in Eq.(8)) must satisfy, $\Psi_\tau(\phi+2\pi/n) = (-1)^{(n-1)}\omega_n^\tau\Psi_\tau(\phi)$. Equivalently, the allowed orbital angular momenta are given by $L = L_{\text{quasi}} + n\mathbb{Z}$ with the quasi-angular-momentum L_{quasi} given in Eq.(1).

III. QUANTUM DYNAMICAL SELECTION RULE

We can now state our conjecture, which we refer to as a "Quantum Dynamical Selection" (QDS) rule:

A bond-breaking enzymatic chemical reaction on a symmetric planar molecule implements a projective measurement onto zero quasi-angular momentum, $L_{\text{quasi}} = 0$.

More generally, including for molecules with three-dimensional rotational symmetries such as H_2 and CH_4, our Quantum Dynamical Selection rule implies that:

Enzymatic chemical reactions that (directly) break the bonds of a symmetric molecule are strictly forbidden from orbitally non-symmetric molecular states.

Here, "direct" implies that the transition proceeds without the molecule first undergoing a nuclear spin flip. For example, the ortho-state of molecular hydrogen (which has odd angular momentum) cannot undergo a direct bond-breaking transition without passing through the para-state. For the $n = 3$ planar molecule described

in Section II B our QDS rule implies that the amplitude in Eq.(9) vanishes unless $\tau = 0$, that is $a_\tau = \delta_{\tau 0}$. In the following Section we present an argument that offers support for the Quantum Dynamical Selection rule.

IV. ARGUMENTS FOR QDS CONJECTURE

For conceptual reasons it is helpful to divide the enzyme mediated chemical reaction into three stages, each a distinct quantum state of the molecule and enzyme: (a) a state ψ_a, in which the molecule is free to rotate and dynamical processes that exchange the atoms are allowed, (b) a state ψ_b, in which the molecule's rotations are stopped by the enzyme and dynamical processes that exchange the atoms are forbidden, and (c) a state ψ_c, in which the chemical bond is broken and the molecule is fragmented into its constituents. For each of these three quantum states a careful discussion of the properties of the accessible Hilbert space will be necessary, and is taken up in the first three subsections below.

The full enzymatic chemical reaction corresponds to a dynamical process that takes the system from state ψ_a to ψ_b and then to ψ_c. In subsection D, below, we explore the tunneling amplitude between these quantum states. Since these transitions are either microscopically or macroscopically irreversible the full enzymatic reaction should be viewed as implementing "projective measurements" on the molecule. As we will demonstrate, the tunneling amplitude vanishes unless $L_{\text{quasi}} = 0$, which offers an argument for the validity of the conjectured Quantum Dynamical Selection rule.

A. A rotating symmetric molecule

We begin with a precise definition of the initial quantum mechanical state of the rotating symmetric molecule, offering three representations of the accessible Hilbert space. For the case of a diatomic ($n = 2$) molecule, these are illustrated in Fig.2.

1. Mapping to quantum bead on a ring

To proceed requires a careful discussion of the Hilbert space for the "angle" kets, that are eigenkets of the angle operator, $\hat{\phi}|\phi\rangle = \phi|\phi\rangle$. They are defined (for $n = 3$) as $|\phi\rangle = \hat{T}_\tau(\phi)|\text{vac}\rangle$, where $\hat{T}_\tau(\phi)$ was introduced in Eq.(3), with a natural generalization for all n. For the n-fold planar molecule we have,

$$|\phi + 2\pi/n\rangle = e^{i\Phi_0}|\phi\rangle, \tag{13}$$

with

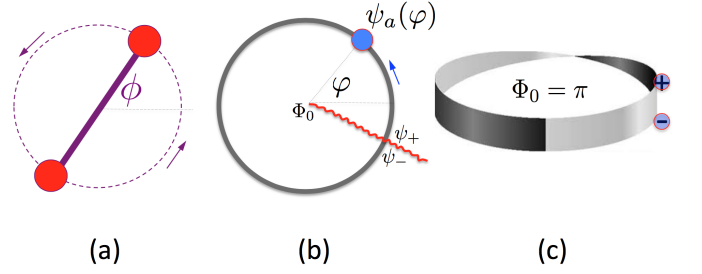$$\frac{\Phi_0}{2\pi} = \frac{L_{\text{quasi}}}{n}, \tag{14}$$

FIG. 2: Three representations of a rotating diatomic molecule composed of identical nuclei: (a) An explicit physical representation. (b) An effective model for the dynamics of the angular coordinate, $\varphi = 2\phi \in [0, 2\pi)$, for a molecule with C_2 symmetry, represented as a quantum bead on a ring with Berry flux, Φ_0 determined by the nuclear spin wavefunction. The bead wavefunction, $\psi_a(\varphi)$, is discontinuous across an n-th root branch cut (red squiggly line), $\psi_+ = e^{i\Phi_0}\psi_-$. (c) Placing the bead on an n-fold cover of the ring with $\varphi \in [0, 2\pi n)$ – a Mobius strip for the $n = 2$ double-cover – resolves any ambiguity in the placement of the branch cut.

so that the angle kets are redundant on the full interval $[0, 2\pi)$. As such, it is convenient to restrict the angle $\phi \in [0, 2\pi/n)$. Then, we can define a new angle operator $\hat{\varphi} \in [0, 2\pi)$ and its canonically conjugate angular-momentum operator $\hat{\ell} \in \mathbb{Z}$ with $[\hat{\varphi}, \hat{\ell}] = i$ via,

$$\hat{\phi} = \hat{\varphi}/n; \quad \hat{L} = n\hat{\ell} + L_{\text{quasi}}. \tag{15}$$

Consider the simplest Hamiltonian for a rotating molecule,

$$\hat{H}_n = \frac{\hat{L}^2}{2\mathcal{I}_n} + V_n(\hat{\phi}), \tag{16}$$

with $V_n(\phi + 2\pi/n) = V_n(\phi)$ an environmental potential (e.g., the enzyme, solution, etc.), with its periodicity encoding the C_n symmetry of the molecule. Re-expressing this Hamiltonian in terms of the "reduced" variables, $\hat{H}_n \to \hat{\mathcal{H}}$ gives,

$$\hat{\mathcal{H}} = \frac{(\hat{\ell} + \Phi_0/2\pi)^2}{2\mathcal{I}} + U(\hat{\varphi}), \tag{17}$$

with a 2π-periodic potential, $U(\varphi + 2\pi) = U(\varphi) \equiv V_n(\varphi/n)$ and a rescaled moment of inertia, $\mathcal{I} = n^2\mathcal{I}_n$. This Hamiltonian can be viewed as describing a "fictitious" quantum bead on a ring, with a "fictitious" magnetic flux, Φ_0, piercing the ring, as shown in Fig.2.

To expose the physics of this flux it is useful to consider the Lagrangian of the quantum bead on the ring:

$$\mathcal{L} = \frac{1}{2}\mathcal{I}(\partial_t\varphi)^2 - U(\varphi) + \mathcal{L}_B, \tag{18}$$

with Berry phase term, $\mathcal{L}_B = (\Phi_0/2\pi)(\partial_t\varphi)$. In a real (or imaginary) time path integral this Berry phase term contributes an overall multiplicative phase factor,

$$e^{iS_B} = e^{i\Phi_0 W}, \tag{19}$$

with $W \in \mathbb{Z}$ a winding number defined via $2\pi W = \varphi(t_f) - \varphi(t_i)$, where t_i, t_f are the initial and final times, respectively.

It must be emphasized that the wavefunction for the bead on the ring, which we denote as $\psi_a(\varphi)$, is not single valued for $L_{\text{quasi}} \neq 0$, since $\psi_a(\varphi + 2\pi) = e^{i\Phi_0}\psi_a(\varphi)$, so that a branch-cut is required. For the planar molecule with C_n symmetry this will be an nth-root of unity branch cut, while for the ortho-dimer molecule it is a square-root cut. In either case, the wavefunction across the branch cut is discontinuous, with the value on either side of the branch cut, denoted ψ_+, ψ_-, being related by a phase factor, $\psi_+ = e^{i\Phi_0}\psi_-$ (see Fig.2(b)). For an isolated molecule this branch cut can be placed anywhere (gauge invariance) but during the enzymatic bond breaking process a natural gauge invariant formulation is not readily apparent.

2. Mobius strip and Umbilic Torus

In order to resolve any ambiguity in the placement of the branch cut with bond breaking present, it is helpful to view the bead as living on an *n-fold cover of the ring*. Mathematically, we simply extend the range of φ to lie in the interval, $\varphi \in [0, 2\pi n)$, so that the wavefunction is periodic in this enlarged domain, $\psi_a(\varphi + 2\pi n) = \psi_a(\varphi)$. For $n = 2$ with $L_{\text{quasi}} = 1$ this corresponds to a quantum bead living on the (single) "edge" of a Mobius strip, as depicted in Fig.2(c). At a given angle on the Mobius strip the wavefunction on the opposite edges of the strip must have a sign change, since in this case $\psi_a(\varphi + 2\pi) = -\psi_a(\varphi)$. For $n = 3$ with $L_{\text{quasi}} = \pm 1$ the quantum bead lives on a (3-sided) umbilic torus, which must be circumnavigated three times before returning to the same "edge".

B. A "not-rotating" molecule

A first step in the bond-breaking process requires stopping of the molecule's rotation as it binds to the enzyme. What does it mean for a small symmetric molecule to be "not-rotating"? Perhaps having zero angular velocity? For 1d translational motion the linear (group) velocity of a quantum particle is $v_g = \partial E_p/\partial p$, suggesting that angular (group) velocity should be likewise defined, $\Omega = \partial E_L/\partial L$. But angular momentum is quantized in units of $\hbar$, so this definition is problematic.

One plausible definition of a molecule to be "not-rotating" is for its orbital motion to be described by a real wavefunciton. For odd n this is equivalent to requiring zero quasi-angular-momentum, $L_{\text{quasi}} = 0$, while for n-even it is not since for $L_{\text{quasi}} = n/2 \neq 0$ a real wavefunction can still be constructed. But in either case, once we allow for quantum entanglement between the molecule and the solvent/enzyme the notion of the "molecule's wavefunction" becomes problematic.
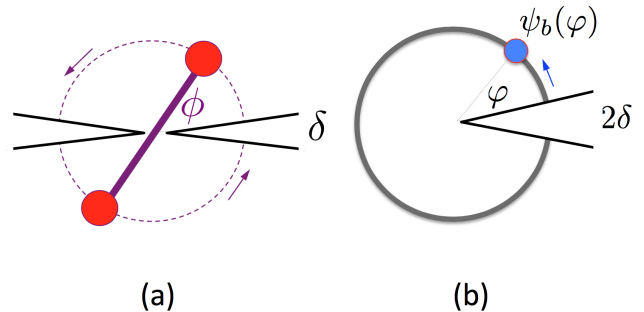

FIG. 3: Two representations of a *non-rotating* diatomic molecule composed of identical nuclei: (a) An explicit physical representation with impenetrable potential wedges inserted around $\phi = 0$ and π, that restrict the molecular rotation angle and constrain one nuclei to the upper-half plane, and the other to the lower half-plane. These wedges strictly forbid all rotational motions that dynamically exchange the two nuclei. The *identical* nuclei thus become effectively *distinguishable*. (b) An effective quantum bead model, where the "ring", now restricted to the angular range, $\varphi \in [\delta, 2\pi - \delta)$, has been "cut-open" - and the bead is constrained to move on a line-segment.

We believe the best way to impose a "not-rotating" restriction of the molecule, is to impose a constraint that disallows a dynamical rotation which implements an exchange of the constituent atoms. This can be achieved by inserting impenetrable potential wedges at angles centered around $\phi = 0$ and $\phi = \pi$, as illustrated in Fig. 3(a) for the diatomic molecule. These wedges restrict the molecular rotation angle so that one of the nuclei is restricted to the upper-half plane, $\delta/2 < \phi \leq \pi - \delta/2$, while the other resides in the lower half-plane, $\pi + \delta/2 < \phi < 2\pi - \delta/2$. Rotations that exchange the nuclei are thereby strictly forbidden. And the two nuclei, while still *identical*, have effectively become "*distinguishable*" - even if their spins are aligned.

Upon mapping to the effective coordinate, $\phi \to \varphi/n$, the wavefunction of the bead on the ring in this "not-rotating" configuration, which we denote as $\psi_b(\varphi)$, is restricted to the *line segment* $\varphi \in (\delta, 2\pi - \delta)$. As illustrated in Fig.3(b), the "ring" has in effect been "cut-open". As such, there is no meaning to be ascribed to the effective flux through the ring, present in Fig.2 for the rotating molecule. In contrast to the n-fold cover of the rotating wavefunction, $\psi_a(\varphi + 2\pi n) = \psi_a(\varphi)$, the non-rotating wavefunction, $\psi_b(\varphi)$ is defined on a single cover of the cut-open ring with $\varphi \in (\delta, 2\pi - \delta)$.

C. A bond-broken molecule

Once the molecule is "not-rotating" and the identical fermions are effectively "distinguishable", a breaking of the chemical bond is greatly simplified. As illustrated in Fig.4(a), with the impenetrable barriers present the molecular bond can break and the constituent atoms are free to move off into the upper and lower half-planes, re-
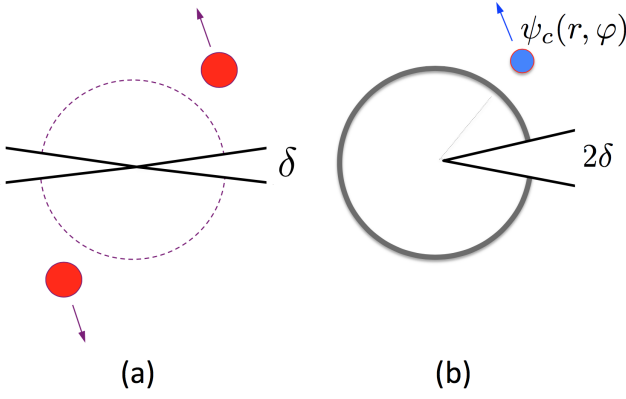
FIG. 4: Two representations of a bond-broken diatomic molecule composed of identical but *distinguishable* nuclei: (a) An explicit physical representation with impenetrable potential wedges inserted at $\phi = 0$ and π, allowing for bond-breaking process to the distinguishable-nuclei state. (b) An effective quantum bead on a ring model, restricted to the angular coordinate range, $\varphi \in [\delta, 2\pi - \delta)$, with bond-breaking modeled by tunneling the bead off the ring.

spectively. Once the atoms are physically well separated, their "distinguishability" no longer rests on the presence of the impenetrable barriers.

In the quantum-bead representation, illustrated in Fig.4(b), the bond-breaking process corresponds to the bead tunneling off the line-segment. As such, the location of the bead must now be specified by both the angle φ and a radial coordinate, r, the bead wavefunction taking the form $\psi_c(r, \varphi)$.

Since this bond-breaking process will typically be macroscopically irreversible we assume that once the bead tunnels off the line segment it will not return. The tunneling rate for this process can be then expressed in terms of a Fermi's Golden rule, $\Gamma_{b \to c} \sim |\mathcal{A}_{b \to c}|^2$, with tunneling amplitude,

$$\mathcal{A}_{b \to c} = \int_{\delta}^{2\pi - \delta} d\varphi \; H_{bc}(\varphi) \psi_c^*(R, \varphi) \psi_b(\varphi), \quad (20)$$

with H_{bc} a tunneling Hamiltonian and R the radius of the molecule.

D. Indistinguishable-to-Distinguishable Projective Measurement

We now turn to the more subtle process where the "rotating" molecule transitions into the "not-rotating" state, which occurs when the enzyme "catches" the molecule. When the molecule is rotating, in state ψ_a, dynamical processes that interchange the identical fermions are allowed and will generally be present. As such, these identical fermions are truly "indistinguishable" in the rotating state. But when the enzyme catches and holds the molecule in place, in the state ψ_b, a projective measurement of the atomic positions has been implemented (the

enzyme is the "observer") and the identical fermions are now "distinguished".

The transition rate for this process, $\Gamma_{a \to b}$, can be expressed as a product of a microscopic attempt frequency, ω_{ab} and a Born measurement probability, P_{ab}, that is $\Gamma_{a \to b} = \omega_{ab} P_{ab}$. The Born probability can in turn be expressed as the squared overlap of the projection of the "distinguishable" state, ψ_b, onto the "indistinguishable" state, ψ_a, that is $P_{ab} = |\langle \psi_b | \psi_a \rangle|^2$.

Since the rotating molecule wavefunction, $\psi_a(\varphi)$, is defined on the n-fold cover of the ring (Mobius strip for n=2) with $\varphi \in (0, 2\pi n)$, while the not-rotating wavefunction, $\psi_b(\varphi)$ lives on a single cover of the line segment, $\varphi \in (\delta, 2\pi - \delta)$, the two states are seemingly defined in a different Hilbert space. This ambiguity can be resolved by noting that tunneling from the Mobius strip onto the open line segment can occur from any of the n "edges" of the Mobius strip, and that these n processes must be summed over,

$$\langle \psi_b | \psi_a \rangle = \sum_{m=0}^{n-1} \int_{\delta}^{2\pi - \delta} d\varphi \; \psi_b^*(\varphi) \psi_a(\varphi + 2\pi m). \quad (21)$$

Upon using the 2π periodicity condition for the Mobius strip wavefunction, $\psi_a(\varphi + 2\pi m) = e^{im\Phi_0} \psi_a(\varphi)$ with $\Phi_0 = 2\pi L_{\text{quasi}}/n$, this can be re-expressed as,

$$\langle \psi_b | \psi_a \rangle = \mathcal{C}_n \int_{\delta}^{2\pi - \delta} d\varphi \; \psi_b^*(\varphi) \psi_a(\varphi), \quad (22)$$

with the amplitude,

$$\mathcal{C}_n = \sum_{m=0}^{n-1} e^{im\Phi_0} = \sum_{m=0}^{n-1} e^{i2\pi m L_{\text{quasi}}/n} = n \delta_{L_{\text{quasi}}, 0}. \quad (23)$$

The Born probability $P_{ab} = |\langle \psi_b | \psi_a \rangle|^2$ thus vanishes unless $L_{\text{quasi}} = 0$, as does the rate, $\Gamma_{a \to b}$, that the enzyme grabs and holds the molecule in a non-rotating "distinguishable" configuration.

Physically, for $L_{\text{quasi}} \neq 0$, there is a destructive interference between the n-parallel paths, each tunneling from an "edge" of the Mobius strip/torus, onto the line segment. For the diatomic molecule this is illustrated in Fig.5, where the two tunneling paths with opposite signs will destructively interfere. The rate for this process which stops the molecule's rotation, $\Gamma_{a \to b}$, will vanish unless $L_{\text{quasi}} = 0$ - the molecule simply can not get caught by the enzyme for non-zero L_{quasi},

Since the enzymatic reaction requires both stopping the molecules rotation, with rate $\Gamma_{a \to b}$, and subsequently breaking the chemical bond, with rate $\Gamma_{b \to c} \neq 0$, the full chemical reaction rate is,

$$\Gamma_{a \to c} = \frac{\Gamma_{a \to b} \Gamma_{b \to c}}{\Gamma_{a \to b} + \Gamma_{b \to c}} \sim \delta_{L_{\text{quasi}}, 0}, \quad (24)$$

and vanishes unless $L_{\text{quasi}} = 0$. Mathematically, the chemical bond breaking process is "blocked" by the presence of the Berry's phase, operative whenever the orbital molecular state is non-symmetric.
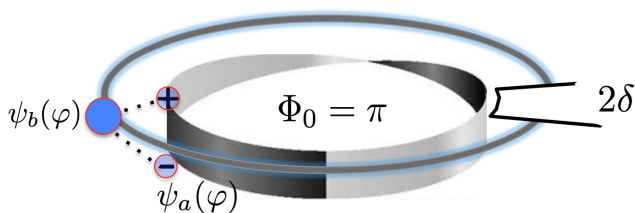
FIG. 5: The enzymatic projective measurement that induces a transition from a "rotating" to a "not-rotating" molecular state can be described as a projective overlap between the rotating state with the quantum bead on the Mobius strip, ψ_a, and a not-rotating state where the bead is on the "cut-open" outer ring, ψ_b. This projective measurement implements a transition between an initial state in which the identical atoms are "indistinguishable: to a final "distinguishable" state - the enzyme acting as an "observer".

More physically, this blocking is due to the destructive interference between the n-possible bond-breaking processes - one for each of the symmetry related molecular orbital configurations. These considerations thus provide support for our conjectured Quantum Dynamical Selection rule that states the impossibility of (directly) breaking a chemical bond of a symmetric molecule rotating non-symmetrically.

V. CONCEPTUAL AND EXPERIMENTAL IMPLICATIONS

There are numerous experimental implications of the QDS rule. Since this rule should indeed be viewed as a conjecture, it will have to be validated or falsified by comparison of theoretical predictions with experiments. Below, we discuss some implications of QDS.

A. Differential reactivity of para/ortho-hydrogen

Hydrogen provides the most familiar example of molecular spin-isomers, para-hydrogen with singlet entangled proton spins and rotating with even angular momentum, and ortho-hydrogen with triplet spin entanglement and odd rotational angular momentum. Since the allowed rotational angular momentum of such homonuclear dimer molecules with S=1/2 fermionic ions (protons) are given by $L = L_{\text{quasi}} + 2\mathbb{Z}$, the quasi-angular-momentum, while zero for para-hydrogen, is equal to one for ortho-hydrogen. The presence of the Berry phase in the rotation of ortho-hydrogen will suppress the bond-breaking chemical reactivity.

Many microbes in biology[5] use H_2 as a metabolite, and the enzyme hydrogenase catalyzes the bond-breaking chemical reaction, $H_2 \rightarrow 2H^+ + 2e^-$. Based on the Quantum Dynamical Selection rule we would expect a differential reactivity between para- and ortho-hydrogen, with

the reaction rate suppressed for ortho-hydrogen. Indeed, if this reaction were to proceed "directly" - without an ionized intermediary or a flipping of nuclear spin - QDS would predict a complete blocking of ortho-hydrogen reacting. At body temperature in a thermal distribution the ortho:para ratio approaches 3:1 (set by triplet degeneracy), while it is possible to prepare purified para-hydrogen where this ratio is strongly inverted (say 1:10). One might then hope to observe different enzymatic activity for hydrogenase catalysis in these two situations, with purified para-hydrogen being significantly more reactive.

Possible differential combustion of para- and ortho-hydrogen with, say oxygen, might also be interesting to explore, even though this reaction is not enzymatic.

B. Intermolecular entanglement of nuclear spins

The ability to prepare purified para-hydrogen molecules in solvent and drive a bond-breaking chemical reaction enables the preparation of two protons with nuclear spins entangled in a singlet. If/when these two protons bind onto a large molecule with different chemical environments, it is sometimes possible to perform a π rotation on one of the two nuclei to create alignment of the two spins, termed hyperpolarization. These hyperpolarized proton spins can then be used to transfer spin polarization to the nuclei of atoms on the molecules to which they are bonded.

There is, of course, a long precedent for liquid state NMR, exploiting the fact of very long decoherence times in the rapidly fluctuating liquid environment.[3] Indeed, soon after Peter Shor developed his prime factoring quantum algorithm, liquid state NMR quantum computing efforts were the first out of the block.[8] In NMR quantum computing one employs a solvent hosting a concentration of identical molecules with multiple nuclear spins (say protons). Ideally, the chemical environment of the different nuclei are different, so that they each have a different NMR chemical-shift, and can thereby be addressed independently by varying the radio frequency. In principle it is then possible to perform qubit operations on these spins. However, there are two major drawbacks to NMR quantum computing – the difficulty in scalability and the challenge of preparing sufficiently entangled initial states. As we now suggest, it is possible that both of these can be circumvented by employing small symmetric molecules which are the substrate for bond-breaking enzymes.

By way of illustration, we consider the symmetric biochemical ion pyrophosphate, $P_2O_7^{4-}$ (usually abbreviated as PPi), which is important in metabolic activity. Pyrophosphate is a phosphate dimer, which consists of two phosphate ions, PO_4^{3-}, that share a central oxygen. (The inorganic-phosphate ion, abbreviated as Pi, consists of a phosphorus atom tetrahedrally bonded to 4 oxygens.) Since the phosphorus nuclei is a S= 1/2 fermion and the

oxygens are $S = 0$ bosons, the two-fold symmetry of PPi, which interchanges the two ^{31}P nuclei and the three end oxygens, will, like molecular hydrogen, have two isomers, para-PPi and ortho-PPi. Moreover, para- and ortho-PPi will rotate with even and odd angular momentum, respectively. Thus ortho-PPi, with $L_{quasi} = 1$, rotates with a non-trivial Berry phase.

In biochemistry there is an enzyme (called pyrophosphatase) which catalyzes the bond-breaking reaction, PPi $\rightarrow$ Pi + Pi. Due to the Berry phase term in ortho-PPi, we expect that this reaction will be strongly suppressed, if not blocked entirely. Then, provided only para-PPi reacts, the two liberated Pi ions will have nuclear spins which are entangled in a singlet. Such intermolecular entanglement of nuclear spins could, in principle, jump start liquid state NMR quantum computing efforts, allowing for both scalability and highly entangled initial state preparation.

C. A new mechanism for isotope fractionation

Isotope fractionation refers to processes that affect the relative abundance of (usually) stable isotopes, often used in isotope geochemistry and biochemistry. There are several known mechanisms. Kinetic isotope fractionation is a mass dependent mechanism in which the diffusion constant of a molecule varies with the mass of the isotope. This process is relevant to oxygen evaporation from water, where an oxygen molecule, which has one (or two) of the heavier oxygen isotopes (^{17}O and ^{18}O) is less likely to evaporate. This leads to a slight depletion in the isotope ratios of ^{17}O/^{16}O and ^{18}O/^{16}O in the vapor relative to that in the liquid water.

Another mass dependent isotope fractionation phenomena occurs in some chemical reactions, where the isotope abundances in the products of the reaction are (very) slightly different than in the reactants. In biochemistry this effect is usually ascribed to an isotopic mass-induced change in the frequency of the molecular quantum zero-point vibrational fluctuations when bonded in the pocket of an enzyme. This modifies slightly the energy of the activation barrier which must be crossed in order for the bond-breaking reaction to proceed.

However, there are known isotopic fractionation processes which are "mass-independent", a classic example being the increased abundance of the heavier oxygen isotopes in the formation of ozone from two oxygen molecules.[9] In ozone isotope fractionation the relative increased abundance of ^{17}O and ^{18}O is largely the same. While there have been theoretical proposals to explain this ozone isotope anomaly, these are not without controversy.[10]

Here, as we briefly describe, our conjectured QDS rule for chemical reactions involving small symmetric molecules leads naturally to the prediction of a *new mechanism for isotope fractionation*, driven by the quantum distinguishability of the two different isotopes. In the presence of isotopes that destroy the molecular rotational symmetry, the QDS rule is no longer operative and one would expect the chemical reaction to proceed more rapidly.

By way of illustration we again consider the enzymatic hydrolysis reaction, PPi $\rightarrow$ Pi + Pi. As we now detail, in this experiment one would predict a large heavy oxygen isotope fractionation effect. Indeed, if one of the six "end" oxygens in PPi is a heavy oxygen isotope the symmetry of PPi under a rotation is broken and the reaction becomes "unblocked" (independent of the nuclear spin state).

If correct, we would then predict a very large mass-independent oxygen isotope fractionation which concentrates the heavy oxygen isotopes in the products (Pi + Pi). For the early stages of this reaction, before the isotopically modified PPi are depleted, one would, in fact, predict a factor of 4 increase in the ratios of ^{17}O/^{16}O and ^{18}O/^{16}O in the enzymatic reaction PPi $\rightarrow$ Pi + Pi.

To be more quantitative we introduce a dimensionless function, $R(f)$, where R denotes the ratio of the heavy isotope of oxygen in the products, relative to the reactants,

$$R(f) = \frac{[^{18}O/^{16}O]_{prod}}{[^{18}O/^{16}O]_{react}}, \qquad (25)$$

and $f \in [0, 1]$ is the "extent" of the reaction. In a conventional isotope fractionation framework, one would expect a very small effect, that is $R(f) \approx 1$. But within our QDS conjecture, if correct, one would have,

$$R(f) = \frac{1 - (1 - f)^\lambda}{f}, \qquad (26)$$

with $\lambda = 4$. Experiments to look for this effect are presently underway.[11]

D. Activity of reactive oxygen species (ROS)

In biochemistry it is well known that during ATP synthesis the oxygen molecule picks up an electron and becomes a negatively charged "superoxide" ion, O_2^-.[12] Having an odd number of electrons (with electron spin-1/2) superoxide is a "free radical". Together with hydrogen peroxide (H_2O_2) and the hydroxyl radical (the electrically neutral form of the hydroxide ion) the superoxide ion is known as a Reactive Oxygen Species (ROS). ROS ions can cause oxidative damage due in part to their reactivity. Indeed, in the free-radical theory, oxidative damage initiated by ROS is a major contributor to aging. In biology there are specific enzymes to break down the ROS to produce benign molecules (e.g. water).[13]

In contrast to the ROS, the stable state of molecular oxygen ("triplet oxygen") is less reactive in biology. As we detail below, we propose that this difference from triplet molecular oxygen can be understood in terms of our conjectured QDS rule.

First we note that standard analysis of electronic molecular states (that we relegate to the appendix) shows that under C_2 rotation the electronic states in the triplet molecular (neutral) oxygen exhibit an overall sign change. Because ^{16}O nuclei are spinless bosons, there is no nuclear contribution to the Berry phase.

Thus the triplet neutral oxygen molecule, O_2 exhibits a purely electronic π Berry phase, despite a spinless bosonic character of the ^{16}O nuclei. It therefore rotates with odd angular momentum, $L = L_{quasi} + 2\mathbf{Z}$, with $L_{quasi} = 1$, identical to ortho-hydrogen. Our QDS conjecture then implies that *a direct bond-breaking chemical reaction of triplet oxygen is strictly forbidden.*

In contrast to triplet oxygen, the superoxide ion, O_2^- is not blocked by the QDS rule and can thus undergo a direct chemical bond-breaking transition. Indeed, as detailed in the appendix, due to the electronic non-zero orbital and spin angular momenta aligned along the body axis, the two ends of the superoxide ion are *distinguishable.* Thus, in contrast to triplet oxygen, superoxide does not have any symmetry under a 180 degree rotation that interchanges the two oxygen nuclei. The superoxide ion can thus rotate with any integer value of the angular momentum, $L = 0, 1, 2, 3, ...$

As a result, the QDS is not operative and thus there is no selection rule precluding a direct bond-breaking chemical reaction of the superoxide ion. We propose that it is this feature of superoxide, relative to triplet oxygen, which accounts, at least in part, for the high reactivity of superoxide and explains why it is a "Reactive Oxygen Species".

E. Ortho-water as a Quantum Disentangled Liquid

Molecular water has a C_2 symmetry axis which exchanges the two protons. Thus, as for molecular hydrogen, water comes in two variants, para-water and ortho-water which rotate with even and odd angular momentum, respectively. QDS then predicts that the ortho-water molecule (with $L_{quasi} = 1$) can not undergo a direct chemical reaction that splinters the molecule into a proton and a hydroxide ion, OH^-.

Since the difference between the rotational kinetic energy of a para-water and an ortho-water molecule is roughly 30K, liquid water consists of 75% ortho-water molecules and 25% para-water molecules. In one remarkable paper[14] it was reported that gaseous water vapor can be substantially enriched in either ortho- or para-water molecules, and then condensed to create ortho- and para-liquid water – although attempts to reproduce this work have been unsuccessful. If QDS is operative, ortho-liquid water would be quite remarkable, having zero concentration of either "free" protons or "free" hydroxide ions, despite these being energetically accessible at finite temperature. Theoretically, ortho-liquid water would then be an example of a "Quantum Disentangled Liquid" in which the protons are enslaved to the oxygen ions and do not

contribute independently to the entropy density.[16]

Experimentally, one would predict that ortho-liquid water would have exactly zero electrical conductivity. Data on "shocked" super-critical water indicates that above a critical pressure the electrical conductivity increases by 9 orders of magnitude[17]. Perhaps this is due to a transition from a quantum-disentangled to a thermal state, where most (if not all) of the ortho-water molecules are broken into a proton and hydroxide ion, leading to a significant electrical conductivity?

The properties of ortho-solid ice might also be quite interesting, provided QDS is operative. While an extensive equilibrium entropy would still be expected (consistent with the ice rules) the quantum dynamics would be quite different. Rather than protons hopping between neighboring oxygen ions, in ortho-ice these processes would actually correspond to collective rotations of the water molecules. The nature of the quantum dynamical quenching of the entropy when ice is cooled to very low temperatures is worthy of future investigation.

VI. SUMMARY AND CONCLUSIONS

In this paper we have explored the role of quantum indistinguishability of nuclear degrees of freedom in enzymatic chemical reactions. Focussing on chemical bond-breaking in small symmetric molecules, we argued that the symmetry properties of the nuclear spins, which are entangled with – and dictate – the allowed angular momentum of the molecules orbital dynamics, can have an order one effect on the chemical reaction rate. Our central thesis is a Quantum Dynamical Selection(QDS) rule which posits that *direct* bond-breaking reactions from orbitally asymmetric molecular states are "blocked", and only orbitally symmetric molecular states can undergo a bond-breaking reaction. This selection rule, which is not of energetic origin, is quantum dynamical and for orbitally non-symmetric molecular states involves the "closing of a bottleneck" in the systems' Hilbert space.

The QDS rule is intimately linked to the importance of Fermi/Bose indistinguishability of the nuclei during the enzymatic process which implements a projective measurement onto orbitally symmetric molecular states. Mathematically, a Berry phase term, which encodes the Fermi/Bose indistinguishability leads to an interference between the multiple bond-breaking processes – one for each of the symmetry related molecular orbital configurations. For an orbitally non-symmetric molecular state this interference is destructive, thereby closing off the bond-breaking reaction – offering a mathematical description of the QDS rule.

In much of this paper we focused on simple molecules with a planar C_n rotational symmetry about a particular molecular axis. In this case the Berry phase is determined by a "quasi-angular-momentum", L_{quasi}, set by the symmetry of the nuclear spin wavefunction. For this planar case our QDS rule predicts that an enzymatic

bond-breaking transition implements a projective measurement onto $L_{\text{quasi}} = 0$.

Our QDS rule leads to a number of experimental implications that we explored in Section V, including (i) a differential chemical reactivity of para- and ortho-hydrogen, (ii) a mechanism for inducing inter-molecular quantum entanglement of nuclear spins, (iii) a new, mass-independent isotope fractionation mechanism, (iv) a novel explanation of the enhanced chemical activity of "Reactive Oxygen Species" and (vi) illuminating the importance of ortho-water molecules in modulating the quantum dynamics of liquid water. For each topic we have only scratched the surface, and a more detailed exploration of these, and other experimental implications of QDS, will be left for future work.

Appendix A: Electronic structure of the oxygen molecule and the "superoxide" ion, O_2^-

Here we briefly review the electronic structure of both the stable electrically neutral (triplet) oxygen molecule and of the superoxide ion. In each, we focus on the symmetry transformation properties of the molecular electrons under a π rotation.

First consider a single neutral oxygen atom, which has eight electrons in the atomic orbitals, $1s_2 2s_2 2p_4$. It is convenient to organize the three 2p-orbitals as p_z and $p_\pm = p_x \pm i p_y$, with wavefunctions in spherical coordinates, $\psi_{p_z} = \cos(\theta)$ and $\psi_{p_\pm} = e^{\pm i\phi} \sin(\theta)$.

For two oxygen nuclei located at $\vec{R}_\pm = \pm a\hat{z}$, the electronic molecular orbitals in order of increasing energy are the 1s bonding (σ_{1s}), the 1s anti-bonding (σ_{1s}^*), the 2s bonding orbital (σ_{2s}), the 2s anti-bonding orbital (σ_{2s}^*), the $2p_z$ bonding orbital (σ_z), the two-fold degenerate $2p_\pm$ bonding orbitals ($\Pi_\pm$), the two-fold degenerate $2p_\pm$ antibonding orbitals ($\Pi_\pm^*$) and the $2p_z$ antibonding orbital (σ_z^*). The molecular wavefunctions for the $2p_\pm$ antibonding orbitals $\Pi_\pm^*$ are given by,

$$\Psi_{\Pi_\pm^*}(\mathbf{r}) = e^{\pm i\phi(x,y)} \sum_{s=\pm 1} s \sin(\theta(z - sa)). \qquad (A1)$$

The oxygen molecule has 16 electrons, 14 in spin singlet pairs in the 7 lowest energy molecular orbitals, $(\sigma_{1s}, \sigma_{1s}^*, \sigma_{2s}, \sigma_{2s}^*, \sigma_z, \Pi_\pm)$. We focus on the two electrons in the highest occupied molecular orbitals (HOMO) $\Pi_\pm^*$. Due to a molecular Hund's rule, these two electrons are in a spin-aligned triplet state with wavefunction,

$$\Psi_{\uparrow\uparrow}(\mathbf{r}_1, \mathbf{r}_2) = \frac{1}{\sqrt{2}} [\Psi_{\Pi_+^*}(\mathbf{r}_1)\Psi_{\Pi_-^*}(\mathbf{r}_2) - \Psi_{\Pi_+^*}(\mathbf{r}_2)\Psi_{\Pi_-^*}(\mathbf{r}_1)], \qquad (A2)$$

which has been appropriately antisymmetrized $\Psi_{\uparrow\uparrow}(\mathbf{r}_1, \mathbf{r}_2) = -\Psi_{\uparrow\uparrow}(\mathbf{r}_2, \mathbf{r}_1)$. From Eq.(A1) this wavefunction can be re-expressed as,

$$\Psi_{\uparrow\uparrow}(\mathbf{r}_1, \mathbf{r}_2) = \sin(\phi_1 - \phi_2) \sum_{s_1, s_2 = \pm 1} s_1 s_2 \sin(\theta_1) \sin(\theta_2), \qquad (A3)$$

with $\phi_j \equiv \phi(x_j, y_j)$ and $\theta_j = \theta(z_j - s_j a)$ for $j = 1, 2$.

We now consider performing a body rotation of the oxygen molecule by 180 degrees about an axis in the x-y plane with unit normal $\hat{n} = \cos(\alpha)\hat{x} + \sin(\alpha)\hat{y}$ for some angle α. Under this transformation, $\phi \to 2\alpha - \phi$ and $\theta \to \pi - \theta$ (equivalently $z \to -z$). Thus, one has, $\sin(\phi_1 - \phi_2) \to -\sin(\phi_1 - \phi_2)$ and $\sin(\theta(z - sa)) \to \sin(\theta(z + sa))$, implying that this 180 degree rotation induces a sign change in the wavefunction for the two HOMO electrons,

$$\Psi_{\uparrow\uparrow}(\mathbf{r}_1, \mathbf{r}_2) \to -\Psi_{\uparrow\uparrow}(\mathbf{r}_1, \mathbf{r}_2). \qquad (A4)$$

Since the other molecular orbitals are occupied by two (spin-singlet) electrons each contributes an overall plus sign, either $(+1)^2$ or $(-1)^2$. Thus, under C_2 rotation in triplet molecular oxygen O_2 the electronic states exhibit an overall sign change.

In contrast, for superoxide the two HOMO orbitals are now occupied by three electrons (two in one orbital, say Π_+^*, and the third in Π_-^*). These three electrons carry a net unit of angular momentum aligned along the molecular axis of the oxygen molecule, $J_z = \pm 1$ for the extra electron in the $\Pi_\pm^*$ molecular orbital, respectively. Together with the total electron spin which take on two values, $S_z = \pm 1/2$, the molecule has a 4-fold degeneracy $(J_z, S_z) = (\pm 1, \pm 1/2)$. In the presence of spin-orbit interactions, $H_{\text{s-o}} = -\lambda \vec{J} \cdot \vec{S}$ this degeneracy is broken, and the molecular ground state is a doublet with $(J_z, S_z) = (1, 1/2)$ and $(J_z, S_z) = (-1, -1/2)$, as required by Kramer's theorem.

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