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Research Article

Probing the Discriminatory role of Non-Equilibrium effects in the Emergence of Biological Homochirality by Considering Quantum Constraints

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ABSTRACT

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The emergence of biological homochirality is an everlasting mystery in the history of interdisciplinary research. This work discusses the discriminatory role of non-equilibrium effects in the emergence of chiral configurations of biological conformers. Based on the theory of open quantum system, a Born-Markov master equation is derived for the analysis of chiral weights when the chiral molecule interacts with two environments at different temperatures, simultaneously. It is shown that the interaction of a chiral molecule with non-equilibrium environments, results in discrimination of specific handedness for both possible configuration that depends on the characteristics of the environments. Real chiral chromophores for which experimental results are available, have been examined under the proposed theoretical framework.

KEYWORD

Homochirality, Non-equilibrium effects, theory of open quantum systems, chiral discrimination, Racemic mixtures.

I. INTRODUCTION

The emergence of Homochirality is among the most well-known dilemma in the history of biology and chemistry [1-5]. Chirality refers to the non-superimposable property of some category of molecules on their mirror images. A chiral molecule and its mirror image, are known as an enantiomer. Enantiomers have identical physio-chemical properties. The only difference is their ability to rotate the polarized light in opposite directions. The isomer that deviates polarized light to the left, is known as left-handed and its counterpart as right-handed isomer. The biological importance of chirality is that “Life” is chiral. All building blocks of life, like amino acids, sugars, and nucleic bases are chiral molecules. The other important issue is that they also have definite chirality. All sugars have right and all of the amino acids have left chirality. Left sugars and right amino acids have never been found in nature. The exclusive appearance of fundamental molecules of life is one specific configuration in known Homochirality [6-9]. Biophysical grounds for the emergence of homochirality have not been cleared yet. However, it has been confirmed that

Homochirality should be a hallmark of the evolution process. Changes in the chirality of amino acids hindered the folding of proteins in the right way [10-12]. Sugars with the wrong chirality cannot be consumed in cyclic processes which results in energy providing for different organs [13-15]. DNA molecule with wrong-handedness of nucleic bases does not incorporate correctly in the replication process [16-17]. It is an interesting phenomenon that whenever one tries to prepare chiral molecules in the lab, a mixture containing equal weights of right and left configurations is obtained. Such a mixture known as a racemic mixture, is not optically active. In other words, the same rotation in the direction of polarized light to the right compensates for the corresponding rotation to the left. Then, the mixture is optically inactive. Neat treatment at the level of chemistry synthesis should be done for making unequal chiral weights of one enantiomer [18-20]. As a consequence, it seems that nature is equipped with fascinating abilities which allow for an exclusive generation of one-handedness against the other. For having a thorough examination of the emergence of homochirality referring to the theories that probe the molecular interactions and light-matter interactions is inevitable.

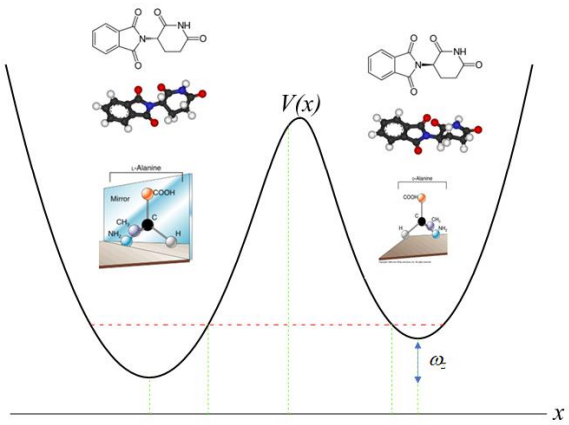

Fig. **1** The effective quantum model of chirality can be given by a double-well potential. Localization of the molecule in the left or right well is in correspondence with the emergence of left or right-handed configuration. Homochirlaity manifests itself in the exclusive handedness of building block molecules of life. Thalidomide (up) should be entirely prepared in its right configuration. The other left isomer may cause serious damage in children when it is prescribed as a drug. All amino acids used in the proteins are entirely in their left configuration and all the sugars are naturally selected in their right configuration.

Quantum theory in this respect is a relevant framework that tries to shed new light on the physical grounds behind the emergence of handedness in biology according to microscopic constraints [21-25]. On the other side, non-equilibrium media are necessary for living systems [26-30]. Such systems should be equipped with aptitudes to enable them to work far from equilibrium since equilibrium coincides with the death of living beings.

In this work, we analyze the dynamics of the emergence of homochirality in biological systems according to the theory of open quantum systems where the chiral molecule is in interaction with non-equilibrium environments. In section II, the quantum model is extended. Section III summarizes the relationship between the parameters of the model and real biological systems for which experimental data are available. In sections IV and V, the results and concluding remarks are addressed.

II. MATHEMATICS

The dynamics of a chiral molecule can be effectively modeled by a double-well potential where the localization of the chiral configuration corresponds to the left-handed chirality [31-32]. The same is true for right-handed configuration. Considering ω_x and ω_z as tunneling and asymmetric frequency, the Hamiltonian of a chiral molecule can be given by:

$$\hat{\mathbf{H}}_0 = -\frac{\omega_x}{2}\hat{\boldsymbol{\sigma}}_x - \frac{\omega_z}{2}\hat{\boldsymbol{\sigma}}_z \qquad (1)$$

Where $\hat{\boldsymbol{\sigma}}_{x(z)}$ are Pauli's operators in $x-z$ direction, respectively, and $\hbar \equiv 1$. The environment consists of bosonic modes, a collection of harmonic oscillators, which can be given as:

$$\hat{\mathbf{H}}_{\varepsilon}=\sum_{i}\omega_i\hat{\mathbf{b}}_i^{\dagger}\hat{\mathbf{b}}_i \tag{2}$$

ω_i is the frequency of the ith mode and $\hat{\mathbf{b}}_i^{\dagger}\left(\hat{\mathbf{b}}_i\right)$ is the creation (annihilation) operator. To consider the non-equilibrium character of the dynamics, one can assume that the chiral molecule may be coupled to two baths in different temperatures. The other way of introducing non-qulibrium effects is to consider environment with different frequency distribution. Supposing that chiral molecule interacts in its left state by harmonic bath characterized by $\hat{\mathbf{b}}_i^{\dagger}\left(\hat{\mathbf{b}}_i\right)$ and right state by $\hat{\mathbf{c}}_i^{\dagger}\left(\hat{\mathbf{c}}_i\right)$, the interaction Hamiltonian will read as:

$$\begin{aligned}\hat{\mathbf{H}}_{\text{int}}&=-\frac{1}{2}\sum_i c_{i,L}\left|\mathbf{L}\right\rangle\left\langle\mathbf{L}\right|\otimes\left(\hat{\mathbf{b}}_i+\hat{\mathbf{b}}_i\right)\\&-\frac{1}{2}\sum_i c_{i,R}\left|\mathbf{R}\right\rangle\left\langle\mathbf{R}\right|\otimes\left(\hat{\mathbf{c}}_i^{\dagger}+\hat{\mathbf{c}}_i\right)\end{aligned} \tag{3}$$

Where c_i determines the coupling constant of chiral molecule with its environment. Using the following unitary operator [33-34],

$$\hat{\mathbf{U}}=e^{-i\frac{\boldsymbol{\sigma}_z}{2}\sum_i\frac{c_{i,L}}{\omega_i}\left(\mathbf{b}_i^{\dagger}-\mathbf{b}_i\right)\otimes\sum_j\frac{c_{i,R}}{\omega_j}\left(\mathbf{c}_i^{\dagger}-\mathbf{c}_i\right)} \tag{4}$$

As $\hat{\mathbf{U}}^{\dagger}\left(\hat{\mathbf{H}}\right)\hat{\mathbf{U}}$ transforms the total Hamiltonian ($\hat{\mathbf{H}}=\hat{\mathbf{H}}_{\varepsilon}+\hat{\mathbf{H}}_{\text{int}}+\hat{\mathbf{H}}_0$) to a diagonal part and non-diagonal part which represents the interaction Hamiltonian in its polaron form:

$$\hat{\mathbf{H}}_{0,P}=-\frac{\omega_z}{2}\hat{\boldsymbol{\sigma}}_z+\sum_i\omega_i\hat{\mathbf{b}}_i^{\dagger}\hat{\mathbf{b}}_i+\sum_i\omega_i\hat{\mathbf{c}}_i^{\dagger}\hat{\mathbf{c}}_i \tag{5}$$

and

$$\hat{\mathbf{H}}_{\text{int}-P}=-\frac{\omega_x}{2}\left(e^{+i\omega_z t}\left|\mathbf{L}\right\rangle\left\langle\mathbf{R}\right|D(+,\alpha)D(-,\beta)\right)+h.c \tag{6}$$

Where $D(\pm,\alpha)$ is the displacement operator of harmonic baths defined by:

$$D(\pm,\alpha)=e^{\pm\sum_i\frac{c_i}{\omega_i}\left(e^{i\omega_i t}\hat{\mathbf{d}}_k^{\dagger}+e^{-i\omega_i t}\hat{\mathbf{d}}_k\right)} \tag{7}$$

According to (6) and (7) one can obtain $\hat{\mathbf{H}}_{\text{int}-P}(t)$ to calculate the dynamics of the density matrix of the system in the interaction picture $\boldsymbol{\rho}_S^{(I)}(t)$ due to the:

$$\begin{aligned}\frac{d}{dt}\boldsymbol{\rho}_S^I(t)&=-\frac{\omega_x^2}{4}\int_0^t dt' Tr_{\varepsilon}\\&\left[\hat{\mathbf{H}}_{\text{int}-P}(t),\left[\hat{\mathbf{H}}_{\text{int}-P}(t'),\boldsymbol{\rho}_S^I(t')\otimes\boldsymbol{\rho}_{\varepsilon,L}\otimes\boldsymbol{\rho}_{\varepsilon,R}\right]\right]\end{aligned} \tag{8}$$

Where $\boldsymbol{\rho}_{\varepsilon,L(R)}$ stands for density matrix of the left and right environments and Tr_{ε} shows the trace over the environment degrees of freedom. Trace over the bath mode, summarizes the effects of the environments into correlation functions of the form:

$$\mu_k^{\pm}=\left\langle D(+)D(-)\right\rangle_{\boldsymbol{\rho}_{\varepsilon}}.$$

It is conventional to average over the bosonic modes of baths since the Hilbert space of the environment is huge in comparison to the system and it is not possible to probe the dynamics of every of the countless modes of the environment. Accordingly, a smooth function of frequency distribution is supposed in the theory of open quantum systems. It is defined by $J(\omega)$, known as spectral density, which has the following form:

$$J(\omega)=\sum_i c_i^2\delta(\omega-\omega_i) \tag{9}$$

Then, the correlation function of the environment integrates as:

$$\begin{aligned}\mu^{\pm}=\exp\Bigg(&\int_0^{\infty}\frac{J(\omega)}{\omega^2}\\&\Big[\left(1-\cos\omega(t-t')\right)\text{Coth}\frac{\omega}{2k_BT}\\&\pm i\sin\omega(t-t')\Big]\Bigg)\end{aligned} \tag{10}$$

When k_B, T are Boltzmann constant and temperature in Kelvin, respectively. In deriving (10) it is assumed that the two

environments are in thermal equilibrium. However, since their temperatures are different or their frequency distribution may have various types, the interaction of the chiral molecule with both of the environments occurs at non-equilibrium conditions.

It is worth noting that in writing a dynamical map in (8), we have considered the system-bath interaction as weak. As a result, the density matrix of the system and the environment can be written in a tensor product for all the time regions. It is known as Born approximation which is widely used in tackling open quantum systems problems [35-36]. Imposing Markov approximation transforms equation (8) into a time local differential equation that can be solved analytically. Due to Markov approximation, the memory effects in the environment are negligible because of the large dimension of its Hilbert state [37-38]. Then, the correlation function of the environment decays in time intervals which is absolutely shorter than time intervals in which the quantum system itself proceeds. Markovian approximation allows us to redefine $\tau = t - t'$ as the time parameter of the time evolution of the reduced state of the system. Moreover, we can extend the upper limits of integral on the r.h.s of (8) to infinity.

Although the Born approximation is necessary for surveying the dynamics of open systems analytically, the Markov approximation can be neglected when the temperature of the environment is sufficiently low. Moreover, when the interaction between the system and the environment is strong, usually, both mentioned approximations are useless and numerical simulations should be hired. By the way, the hot and wet nature of the biological medium allows imposing both approximations without losing the generality.

The shape of the distribution of frequencies in the environments, also, may be the source of non-equilibrium effects. $J(\omega)$ in its general form can be given by:

$$J(\omega) = \frac{\pi\lambda}{\omega_c \Gamma(s)} \frac{\omega^s}{\omega_c^{s-1}} e^{-\frac{\omega}{\omega_c}} \tag{11}$$

where λ is reorganization energy and $\omega_c, \Gamma(s)$ are cut-off frequency and Gamma functions, respectively. For $s = 1, s > 1, 0 < s < 1$, Ohmic, super-Ohmic, and sub-Ohmic spectral densities result respectively. For many biological models, it is verified that Ohmic environments properly reproduce the experimental results obtained by spectroscopic data. Defining the density matrix of the environment as:

$$\boldsymbol{\rho}_s^I(t) = \begin{pmatrix} \boldsymbol{\rho}_{LL}(t) & \boldsymbol{\rho}_{LR}(t) \\ \boldsymbol{\rho}_{RL}(t) & \boldsymbol{\rho}_{RR}(t) \end{pmatrix} \tag{12}$$

and replacing it in the master equation (8), multiplying both sides of (8) from left and right by $\langle \mathbf{R}|...|\mathbf{R}\rangle, \langle \mathbf{L}|...|\mathbf{L}\rangle$, and respecting the Born-Markov approximation lead to the following system of differential equations that can be hired to determine the final chiral weights under non-equilibrium conditions

:

$$\begin{aligned} \frac{d}{dt}\boldsymbol{\rho}_{LL}(t) &= \chi_1 \boldsymbol{\rho}_{LL}(t) - \chi_2 \boldsymbol{\rho}_{RR}(t) \\ \frac{d}{dt}\boldsymbol{\rho}_{RR}(t) &= -\chi_1 \boldsymbol{\rho}_{LL}(t) + \chi_2 \boldsymbol{\rho}_{RR}(t) \end{aligned} \tag{13}$$

Where;

$$\begin{aligned} \chi_1 &= \frac{\omega_x^2}{4}\left(\int_0^\infty e^{+i\omega_z \tau} \mu_L^+ \mu_R^+ d\tau + \int_0^\infty e^{-i\omega_z \tau} \mu_L^- \mu_R^- d\tau \right) \\ \chi_2 &= \frac{\omega_x^2}{4}\left(\int_0^\infty e^{-i\omega_z \tau} \mu_L^+ \mu_R^+ d\tau + \int_0^\infty e^{+i\omega_z \tau} \mu_L^- \mu_R^- d\tau \right) \end{aligned} \tag{14}$$

Based on the type of spectral densities and the temperature difference between the environments, the emergence of one specific configuration can be analyzed according to the results of equation (13) for left and right populations.

III. Biological Spectral Densities

To relate the formalism extended above to relevant biological systems, we consider in this section the parameters of the model which can be referred to biological data and empirically verified. Spectral densities can be directly calculated according to spectroscopic data [39]. Relaxation times are due to different processes and can be extracted with electronic spectra of the chromophore-protein-solvent system.

The inverse of relaxation times is a fair measurement for cut-off frequencies included in spectral densities. The coupling constant $\frac{\lambda}{\omega_c}$ can also be approximated by spectroscopic data.

Chromophores are chiral molecules usually surrounded by a protein and immersed in a solvent. To represent the dynamics of the triad system sketched above, three component spectral densities are hired which contain the dynamics of relaxation in the protein itself, bound water to the protein-Chromophor, and the solvent. A typical form of the spectral density can be represented by the following equation:

$$J(\omega)=\frac{J_{0,1}\omega}{1+(\omega\tau_1)^2}+\frac{J_{0,2}\omega}{1+(\omega\tau_2)^2}+\frac{J_{0,3}\omega}{1+(\omega\tau_3)^2} \quad (15)$$

Where $J_0=\frac{\lambda}{\omega_c}$ is the coupling constant between the system and the environment and τ is the relaxation time.

Table I summarizes some triad systems, and experimental verification of spectral parameters has been done. In what follows, we hire these systems to estimate chiral amplification and discrimination under non-equilibrium conditions. Data are extracted from a reference [40].

Table I. Coupling constants and Relaxation times extracted from experimental data are given for different Chromophore-Protein-Solvent systems.

Chr. Protein Solvent	$J_{0,1},\tau_1(fs)$	$J_{0,2},\tau_2(ps)$	$J_{0,3},\tau_3(ns)$
Eosin Lys. Water	0.165-310	3.72-7	-
Prodan HSA Water	1.018-780	10.00-2.6	54.96-0.032
Acryl. HSA Water	2.057-710	19.11-3.7	258.55-0.057

IV. Results

Fig.2 (Up-Middle) shows that the chiral enrichment is a function of the ratio of $\frac{\chi_1}{\chi_2}$. In Fig.2 (Bottom) it is shown that when the mentioned ratio is equal to one, the chiral discrimination disappears and the initial racemic mixture maintains its value. Moreover, the predominance of all the parameters over the other results in amplification in the weight of one of the isomers. Accordingly, it deserves to analyze to what extent the χ can be changed according to the nature of the environment and the physical parameters in the system.

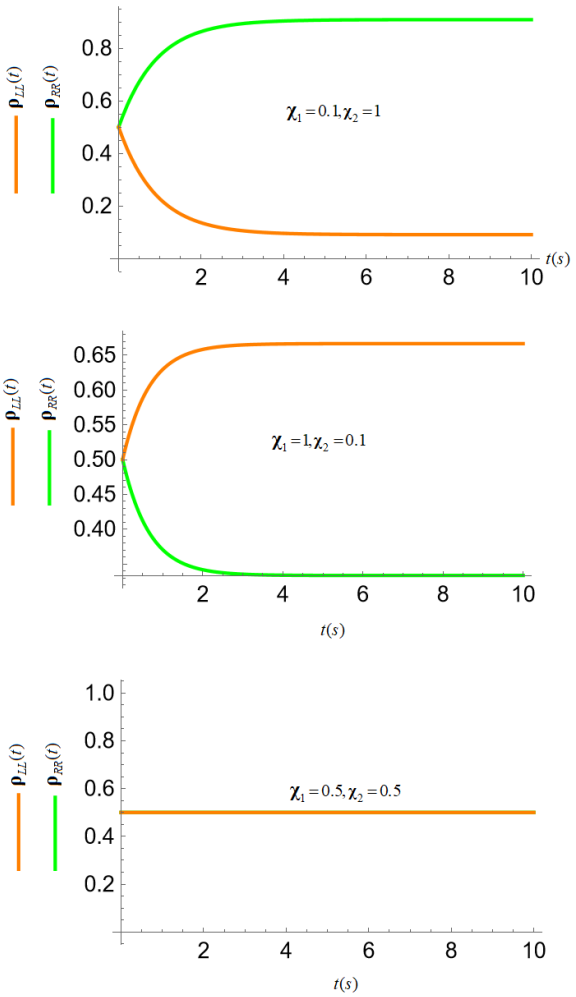

Fig. **2** Amplification in chiral weights is depicted against time for different ratios of χ parameters. Up and Middle: An increase in χ_1 against χ_2 results in an increase in the weight of the left-handed isomers. Bottom: When the value of χ is comparable, chiral discrimination has been lost.

In Fig. 3, one can pursue the change in the $\frac{\chi_1}{\chi_2}$ against ω_z for Prodan-HSA-Water as the chromophore-protein-solvent system. As can be inferred based on the value of $\frac{\hbar}{k_B T \tau}$ both predominance of left and the right configuration would be possible. At very low values of such parameter, which in constant temperature means to have larger values of cut-off frequencies, non-equilibrium effects result in larger $\frac{\chi_1}{\chi_2}$ which is in correspondence with amplification in left-handed chiral weights. A rise into 0.1 (middle) results in large amounts of chiral amplification in the other configuration. Under equilibrium conditions, the same occurs for the left-handed isomers. An increase in $\frac{\hbar}{k_B T \tau}$ (bottom) again, results in large amounts of enrichment in the opposite direction. As a result, competition between equilibrium and non-equilibrium effects may cause a discriminatory agent in the stability of one of the isomers against the other. Fig.4 shows the same analysis when the system of interest is replaced by Eyosin.-Lysosome-Water. The same discriminatory role of non-equilibrium effects can be verified. Furthermore, as can be seen, non-equilibrium effects result in the dominancy of $\frac{\chi_1}{\chi_2}$ in $\frac{\hbar}{k_B T \tau} = 5$ for the left-handed isomer, where the reverse is true for the Prodan-HAS-Water system. It admits that amplification in chiral weights under the non-equilibrium condition is also a characteristic of the chiral system. When the chromophore and the surrounded protein are replaced by Eosin and Lysosome, the change in the value of τ_1 is three times smaller, and at the same choice of temperatures, the discriminatory role of non-equilibrium effect is in favor of stabilization of the right-handed configuration. The same behavior repeats in all amounts of $\frac{\hbar}{k_B T \tau}$.

At last, we should mention that considering the non-equilibrium effects in the emergence of homochirality has been studied in some works. G. Laurent and coworkers have shown that symmetry breaking can result in a non-equilibrium network of chemical reactions [41]. R. Plasson et. al have shown that symmetry breaking in a racemic mixture can be obtained in a far-from-equilibrium reactive system initiated with an initial imbalance [42]. Analyzing the chemistry of the emergence of homochirality under non-equilibrium conditions in relation to macromolecules and biological molecules is also addressed in

different studies [43-45]. However, all approaches in these works are based on classical statistical constraints, and the general treatment of the issue according to quantum implications has not been scrutinized yet.

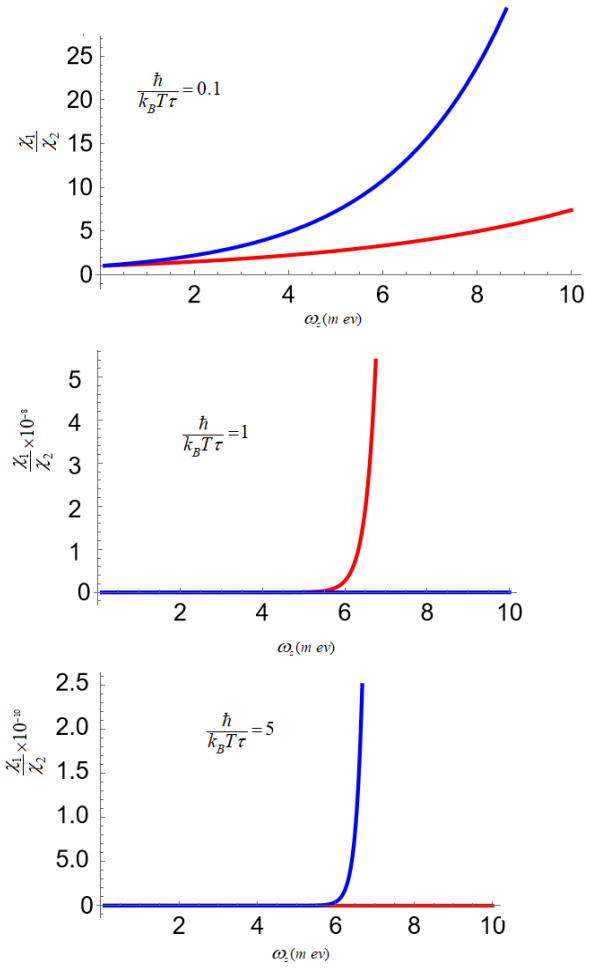

Fig. **3** The ratio of $\frac{\chi_1}{\chi_2}$ is given against asymmetry frequency ω_z for Prodan-HAS-Water system. The blue represents equilibrium and red determines non-equilibrium condition. According to the value of $\frac{\hbar}{k_B T\tau}$ non-equilibrium character of the interaction may result in a predominance of chiral enrichment in the left or the right-handed configuration. $T_C \approx 0.3T_H$ is assumed for computing $\frac{\chi_1}{\chi_2}$.

is assumed elsewhere.

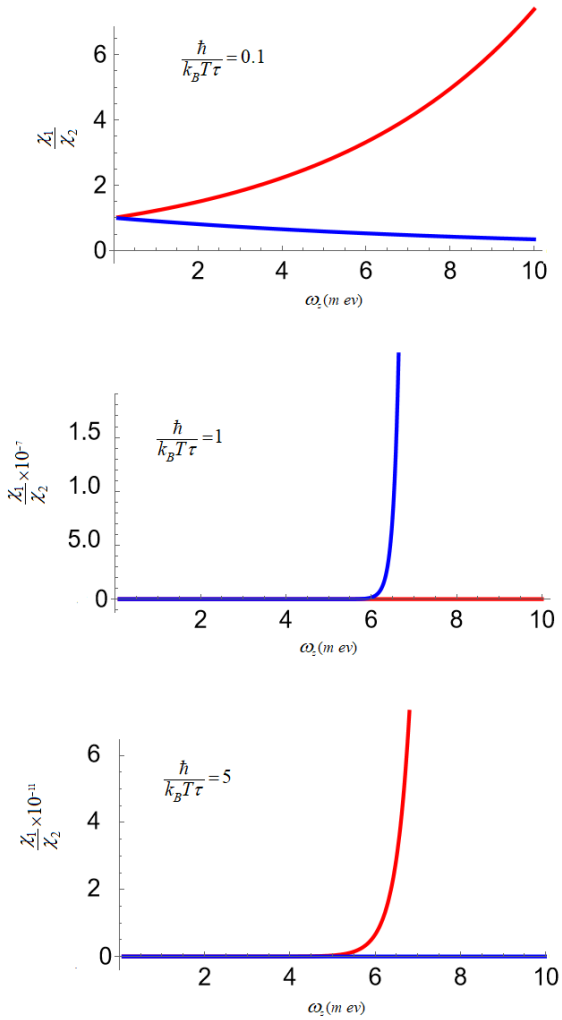

Fig. **4** The ratio of $\frac{\chi_1}{\chi_2}$ is depicted against ω_z for Acryl-HSA-Water system. Non-equilibrium effects, represented by blue, play their discriminatory role in reverse in comparison to the Eosin-Lysosome-Water system. The value of amplification in $\frac{\chi_1}{\chi_2}$ is also different. $T_C \approx 0.3T_H$ is assumed for computing $\frac{\chi_1}{\chi_2}$.

V. Conclusion

In this study, we examined the emergence of homochirality under non-equilibrium conditions. We proposed that when the non-equilibrium condition is considered in the dynamic of an open quantum system, a chiral molecule in our analysis, discrimination between right and left-handed configurations can be obtained. Moreover, our examination

admits that based on the system of interest, enrichment in chiral weights can be reached for both of the isomers. As a consequence, chiral stabilization and chiral discrimination may both find their grounds where the non-equilibrium nature of the dynamics of living system, has been into account in a quantum mechanical picture.

Explaining the emergence of Chirality is a critical matter in understanding the origin of life problems. The other main issue is its role in chiral synthesis in the drug industry. It is a hot and alive field of research that probes making drugs in single enantiomer against their racemic counterparts can be generated more simply in the lab. Most of the drug molecules should be exclusively prepared in a single configuration to be useful for biological applications. Preparing a mixture of imbalanced weights of chiral molecules is the subject of intensive research in organics chemistry. The results of our work may shed new light on the application of non-equilibrium effects in the synthesis of a mixture of molecules with a definite chirality. In experience, non-equilibrium effects may be accessible by using different temperature gradients by applying precise thermometers. However, to have a more detailed picture of the biological traits of the dynamic, computational techniques can be introduced for the simulation of the interaction between the biological medium and the chiral systems that can be the subject of future works.

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SUPPORTING INFORMATION

In doing the math and solving differential equations, the author has used the Mathematica software version 13, 2018.

APPENDIX

Here we try to justify the mathematical functionality of the effective potential introduced by the Hamiltonian given in (1). Using the Born-Oppenheimer approximation electronic states of the molecule can be extracted where the nucleus is supposed to be in a rigid spatial configuration. Then, the Schrodinger equation can be solved for rotation-vibration degrees of freedom. The results are potential energy surfaces that describe the equilibrium structures of the molecule. By using Eckart constraints [46] which mediates the separation of rotation from vibration, the zeroth other of the molecular Hamiltonian contains a rotational term and 3N-6 harmonic oscillators. Non-planner molecules have some modes of vibration with a large domain that facilitates tunneling of the nucleus from a minimum in PES to another. These modes of vibration are called torsional vibrations [47]. The structure of the molecules changes when torsional vibrations happen. The potential of the torsional motion can be defined by $\mathbf{V}(q)$. All non-planner molecules have at least two structures that can be transformed into each other by inversion in the center of mass of the molecule. If the Born-Oppenheimer approximation and Eckart constraints are established, the mentioned inversion conforms with the torsional vibration. An effective picture results where one focuses on the inversion of chiral molecules from left to right configuration, by torsional inversion. As a consequence, a double well potential can be used to describe the transformation of the right molecule to the left one. The mathematical function of $\mathbf{V}(q)$, then, can be defined by:

$$\mathbf{V}(\mathbf{q}) = M\omega_0^2 \frac{\left(\mathbf{q}+\frac{\mathbf{q}_0}{2}\right)^2}{2} + \frac{\omega_z}{2}\mathbf{q} \qquad \text{A-1}$$

Where M is the mass and $\mathbf{q}_0$ determines the position of the minimum of the well.

If ω_0 was the frequency of the vibration in the depth of the well and V_0 the height of the potential well separates the two configurations, at $V_0 >> \omega_0 >> k_B T$ the dynamics of the molecule limited to the first two levels of the electronic state. Accordingly, the potential given in A-1, reduces to the Hamiltonian (1) where we have $\mathbf{a} \to \boldsymbol{\sigma}_-, \mathbf{a}^\dagger \to \boldsymbol{\sigma}_+$.

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