Kinetic Characterization of a Chemical Model System with Chiral Symmetry Breaking

by

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Abstract

Investigations were undertaken which characterized the parameter space of a novel computational chemical model system that demonstrates chiral symmetry breaking under several sets of conditions. The model described is completely symmetrical with no thermodynamic or kinetic advantage in place. The model displays chiral symmetry breaking after a quasi-equilibrium state and quick amplification of the initial break to near homochirality. Using two different computational programs, we performed temperature scans to find an optimal temperature for the model as well as investigated the governing equations and ratios in order to predict whether or not the model would display chiral symmetry breaking. These results were demonstrated in both the stochastic and deterministic programs. Our computational model of chiral symmetry breaking suggests a signature for the evolution of life on Earth and elsewhere. Our better understanding allows us to make connections to other theories of origins life.

Introduction

Many biological molecules display chirality, a property that describes the three-dimensional shape of molecules such that one form is non-superimposable with its mirror image. The two different forms are called enantiomers. For chiral molecules, the molecular formulas are the same, however the structures and therefore the shapes are different, which can lead to the chiral molecules having different biological properties (chemical and physical properties of enantiomers are identical). Chirality is denoted in several different ways: one notation relates to optical activity and another relates to the absolute 3-D structure. The notation, R or S, is used to designate handedness (3-D structure) of enantiomers while $_D$ and $_L$ denote the optical activity of the enantiomer. In ordinary chemical reactions, both chiral forms – left and right hand or R and S structures – are made in equal amounts, a racemic mixture (1,2). However, certain biological molecules, such as amino acids and sugars, exist in only one chiral form – or are said to be homochiral – which presents an outstanding question in prebiotic chemistry: How did these molecules evolve to exhibit homochirality?

Despite the conundrum presented by the existence of homochirality of certain molecules in nature, it would seem that homochirality is crucial for functional macromolecules. Amino acids and sugars, which are monomers for proteins and nucleic acids, must be predominantly one chiral form, because without homochirality in these building blocks, the folding and shape of some biological macromolecules, like proteins, RNA, and DNA, would not permit proper function. Thus, homochirality is a critical early hurdle for life to evolve on Earth and elsewhere and for it to exist efficiently. There are several theories as to how homochirality may have evolved. Of particular interest is the idea that one monomer, such as a simple amino acid, became homochiral and then served as a template for all other monomers of that type (2).

Investigations into the origins of biological homochirality have been the subject of many research projects, both in models and experimental systems. The models of origins of homochirality began with Frank. Many of the existing models demonstrate similar characteristics, such as autocatalysis (X going to 2X) and feed-back inhibition mechanisms, among other traits (1). In recent years, experimental systems have also been the subject of investigations. Progress has been made in understanding the use of chiral surfaces and chiral catalysts to produce a product with a predominant R or S form, or an enantiomeric excess (1,3,4). These experimental systems were inspired by theoretical models and in some cases took decades to come around, but most often lend credence to the models that inspired the experiment.

While currently available models and experiments are remarkable, the model we have developed is unlike any of the existing models. It lacks certain common characteristics, such as autocatalysis and feed-back inhibition. The model was also tested on two computer programs, each with a different approach to the chemistry of the model.

Methods

Our model was investigated using two powerful chemical kinetics computer programs, Kintecus and Chemical Kinetics Simulator. Kintecus, version 4.5, is based on deterministic methods, specifically the Arrhenius equations, and uses Microsoft Office Excel as an interface (5). To verify the output from Kintecus, we will numerically analyze the governing equations that describe the reaction kinetics of the chemical systems. Often, equations are complex and not solvable; solutions can be estimated by numerical methods. Chemical Kinetics Simulator, or CKS, a stochastic program developed by IBM will also be used to investigate the model (6). This program simulates the collisions of molecules. Both of these programs have been used in previous research (7-9).

Results and Discussion

We designed a novel chemical system which demonstrated chiral symmetry breaking and amplification of one of the chiral forms. Our chemical system was inputted as a set of chemical reactions into both Kintecus and CKS. The same parameters that were used for Kintecus were used for CKS, with the only difference being that a numerical value for the number of molecules in the simulation had to be chosen in CKS. In our CKS model, we used 100,000 molecules for the simulation. See Figures 1 and 2 for the model scheme and the input parameters for Kintecus and CKS.

Our model is initially completely symmetrical with a racemic mixture of R and S which evolves to break chiral symmetry and amplify one of the chiral forms. From our former research, we knew there was an upper temperature at which the model would not demonstrate breaking. However, we wanted to discover the optimal temperature for chiral symmetry breaking. In this case, optimal means the temperature at which the model is driven the closest to homochirality or the temperature at which the models demonstrates the highest enantiomeric excess. Using a function of Kintecus, we scanned a range of temperatures and discovered the optimal temperature.

We also defined the upper temperature at which our model became stable and no longer demonstrated chiral symmetry breaking. Figure 4 shows the temperature scan output from Kintecus. Above a temperature of about 351 Kelvin, both R and S forms plateau at a concentration of 0.5 M. Below the upper threshold temperature of about 351 Kelvin, the initially racemic mixture of R and S quickly evolved to a quasi-equilibrium state representing an unstable fixed point. In Kintecus, the quasi-equilibrium state lasted significantly longer than it did in CKS due to the different styles of numerical analysis (deterministic versus stochastic) but in both computational programs the smallest perturbation triggered a breaking of chiral symmetry which pushed the system toward a homochiral steady state in which one of the two forms – R or S – significantly predominated. See Figure 4 for a standard Kintecus output. When the models were run using the stochastic program CKS, a similar outcome resulted (not shown).

As discovered in previous research, the numerical perturbation is most likely a mechanical round off error (10) in Kintecus, while the exact mechanism of CKS is not known. These round off errors have been observed in the Soai Reaction (10-12), where they have been credited as playing the role of natural fluctuations, although the observed instability (quasi-equilibrium state in our model) is a dynamic property of the model which is independent of the method used to investigate it. Yet, the numerical perturbations probably reflect random fluctuations in nature. The stochastic and deterministic programs suggested a different mechanism but both demonstrated chiral symmetry breaking and amplification of the initial break to near homochirality.

Previous stability analysis of the quasi-equilibrium state verified the results from Kintecus and revealed a governing ratio which elucidated the upper temperature threshold numerically (the optimized model underwent stability analysis and revealed the ratio had the same property). Further numerical solution of the governing differential equations of our optimized model revealed an additional governing ratio. The additional governing ratio relating the rate constants, k's, revealed was the ratio of k_2/k_3. If $k_2/k_3 = 0.236$ the system is stable and does not exhibit chiral symmetry breaking. If $k_2/k_3 < 0.236$ the system bifurcates. The degree of symmetry breaking depends on the k_2/k_3 ratio, the smaller the ratio, the greater the breaking.

Conclusions

There are various approaches to researching the origin of life; however, most of the investigations involve prebiotic chemistry. We are approaching the problem of how homochirality arose in certain biological precursors very differently than the majority of other research. Gaining a better understating of our novel model has helped us further explain the outputs from the computational program. It remains that the notable bifurcation and then amplification of one enantiomer is a critical early

Model Description		
Reaction #	Reaction Steps	Rate Constants
1	$X + C \Longrightarrow X_C$	k_0
2	$X_C \Longrightarrow R_C$	k_1
3	$X_C \Longrightarrow S_C$	k_1
4	$R_C + R \Longrightarrow R_C + X$	k_2
5	$S_C + S \Longrightarrow S_C + X$	k_2
6	$R_C + S \Longrightarrow S_C + X$	k_3
7	$S_C + R \Longrightarrow R_C + X$	k_3
8	$S_C \Longrightarrow S + C$	k_4
9	$R_C \Longrightarrow R + C$	k_4

Figure 1: Symmetrical model scheme for computational programs; X is a prochiral precursor to R or S, C is an interactive surface to which X, R, or S can bind and k's are rate constants.

Kinetic Parameters		
Rate Constants	Arrhenius Constant (A)	Energy of Activation (Ea)
k_o	1.00E+01	17
k_1	1.00E+01	17
k_2	4.00E+02	16
k_3	1.00E+01	1
k_4	1.10E+02	10

Figure 2: Input parameters for computational programs.

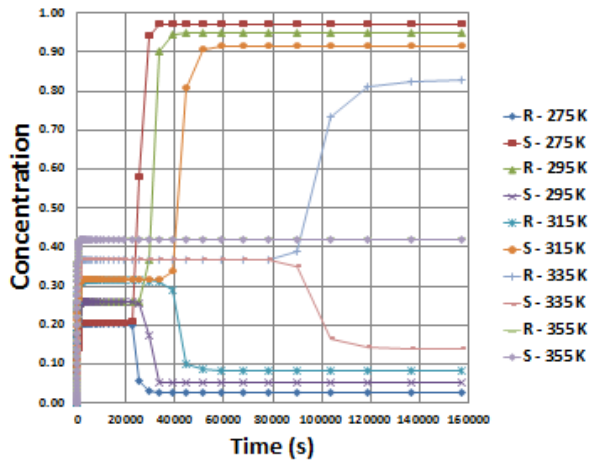

Figure 3: The temperature boundaries for the model were investigated for several sets of different initial conditions. The output of the temperature boundary analysis for the conditions R = S = 0M, X = 1M C = 1 M (held constant) and all intermediates are 0M are shown in Figure 3.

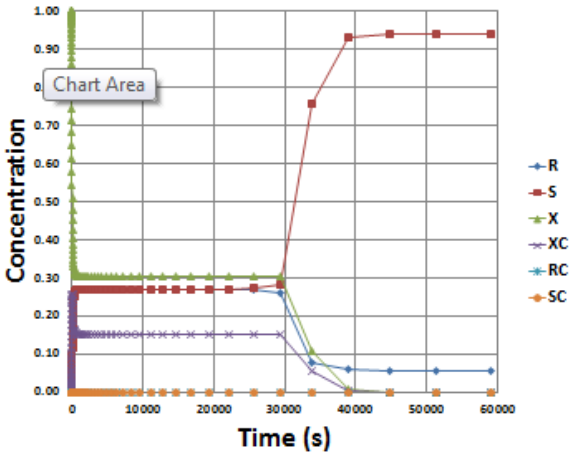

Figure 4: A typical output from Kintecus for the model under the conditions R = S = 0M, X = 1M C = 1 M (held constant) and all intermediates are 0M is shown.

hurdle for the evolution of life and is possibly the signature for life.

We previously concluded that a perfectly symmetrical model can exhibit chiral symmetry breaking and predicts chiral symmetry breaking and amplification of homochirality with no preference for the chiral form that predominates and that both stochastic and deterministic models show that there is an upper limit of constant temperature where symmetry no longer breaks. We have further optimized our model and these conclusions hold true.

There are several opposing theories concerning the evolution of L-amino acids and D-sugars on Earth. Our model supports the hypothesis that chirality of a key molecule evolved randomly and then served as a template for the chirality of other molecules. Chiefly, our model supports a theory proposed by R.G. Cooks and colleagues who showed that serine forms stable octamers that can "transmit" chirality to other amino acids and sugars by acting as a template (13). Our optimized model system adds to this theory by showing how a symmetrical model can generate one particular conformation of a critical amino acid which could then act as a template for the chirality of other important molecular precursors on the early Earth. Our model also supports the idea that the evolution of a homochirality in a key molecule was random, with no preference for one enantiomer over the other initially.

We hope that this more complete understanding of our chemical model will encourage experimental systems that will provide clues to the prebiotic chemistry resulting in breaking chiral symmetry on the early Earth.

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