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On the Stability Analysis of Chiral Networks and the Emergence of Homochirality

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Abstract

We study a particular set of chemical reaction networks related to the emergence of homochirality. Each element of this set is a chemical reaction mechanism intended to produce homochirality. Those mechanisms contains a pair of enantiomers, the central subject of this study, which are involved in a series of reactions that produce and consume them. The other species concentrations are considered constant. The reactions of each mechanism are arranged into six categories, that we have called synthesis, first order decomposition, autocatalytic, second order decomposition, non-enantioselective and inhibition reactions. The reaction networks must satisfy a symmetry constraint that is related to the kinetic and thermodynamic indiscernibility of the isomers. We investigate the emergence of homochirality phenomena in those networks. To this end, we introduce a mathematical notion of homochiral states that we call Frank states, and which seems to be deeply related to the occurrence of homochiral dynamics. We find sufficient and necessary conditions for the existence of Frank states, and we use those results to develop an algorithmic tool. This tool can be used to recognize networks admitting homochiral states, and in given case, it can also be used to construct Frank states of the input-network. We test the mathematical machinery, and the aforementioned algorithm, analyzing the well-established models of Frank and Kondepudi-Nelson. We were able to show that those two networks admit homochiral dynamics. We use our tools to analyze three further network models derived from the Kondepudi-Nelson model and which were adapted to the Strecker synthesis of amino acids.

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1 Introduction

Life is a mysterious thing, full of complex mechanisms and phenomena, and one of them is homochirality. This particular characteristic of life corresponds to the fact that some special molecules have identical chemical composition but they are the specular image of each other, exactly as our left and right hands. The most peculiar thing about homochirality is that when we synthesize this kind of molecules, most of the time the products are *racemic*. However, in living things, the involved chiral molecules are homochiral as D-sugars in DNA and L-amino acids in proteins [1]. It is known that homochirality is critical for molecular recognition and replication processes, and would thus seem to be a prerequisite for the origin of life [2]. Nevertheless, the homochirality of biological molecules is a phenomenon that is not completely understood [3].

The two forms of a chiral molecule, called *enantiomers* [4], have similar physical and chemical properties, and therefore both enantiomers should form in equal amounts (a racemic mixture), if the synthesis is made in isotropic phase and in the absence of any chiral object which could favor an asymmetric synthesis. It is important to mention that asymmetric synthesis has become a very active field of research, and we know how to synthesize a lot of homochiral compounds [5], especially if asymmetric catalysis is used [6]. However, in this work, we restrict ourselves to the usual laboratory conditions that are not suitable for asymmetric synthesis. Then, we are considering only the simple isotropic conditions for which asymmetric synthesis becomes unlikely. It seems that under isotropic conditions the homochirality of living molecules is non-consistent with the basic models of chemical kinetics [7, 8]. We would like to show that this is not the case, we would like to show that chemical reaction networks containing a single pair of enantiomers are likely to evolve towards homochiral states.

Now, given a chemical network involving a pair of enantiomers, we say that it exhibits homochiral behavior, if and only if, there exists a *racemic steady state*, which after being perturbed gives place to *homochiral dynamics*. This type of dynamics corresponds to those dynamics along which the concentration of one of the two enantiomers vanishes while the concentration of the other grows. We are interested in the homochirality phenomenon observed in nature: Homochiral dynamics seem to be frequent [9].

There are many different theories that want to explain the homochirality phenomenon [1, 7, 9]. We, in turn, do not want to explain this phenomenon, we just want to show that it is consistent with the theoretical models of chemical kinetics. We would like to show that given a chemical network involving a pair of enantiomers (isomers), and according with

the mathematical models of chemical kinetics, it is very likely that, after being perturbed, the network is driven towards a *homochiral dynamics*.

This work is organized into nine sections including the introduction. The first one is this introduction. In section 2 we present the basic concepts of chemical networks and network dynamics. In section 3 we introduce the necessary concepts of stability analysis. In section 4 we introduce *Chiral Networks* which are the chemical networks that we want to analyze. Moreover, we introduce a classification of chemical reactions that becomes important in the stability analysis of chiral networks. In section 5 we begin the stability analysis of chiral networks. We find a mathematical criterion that seems to be related to the emergence of homochirality. We use the well known Frank Model [10] to test our criteria. In section 6 we introduce the notion of *Frank States*, and we argue that these are the states that are related to the emergence of Homochirality. In this section, we find sufficient and necessary conditions for the existence of Frank States. In section 7 we develop an algorithm for the computation of Frank States. A computer program implementing the algorithm, and written in Python, was developed to analyze different chemical models and to obtain the ranges where the kinetic rate constants give place to Frank states. In section 8 we study the Kondepudi-Nelson Model (KN, for short) [11] as well as three further models that are derived from KN and adapted to the Strecker synthesis of amino acids [12]. In the first one, the $L\text{-X} + D\text{-X} \longrightarrow \text{Product}$ reaction of the KN Model is replaced by two reactions that produce the L and D amino acids; we call this model KNS-AP. In the second mechanism, we add to the KNS-AP model two non-enantioselective autocatalytic reactions [13], also called limited enantioselective reactions [14], and we call this model KNS-AP-LES. The last network is the KN model plus a set of non-enantioselective autocatalytic reactions, and it is called the KNS-LES model. The theoretical analysis indicates that KN, KNS-AP-LES and KNS-LES networks are unstable and give place to homochiral dynamics. The theoretical analysis also indicates that the KNS-AP network is stable and that all their stationary states are racemic. Numerical simulations[§] of each one of those models were executed, and none of them contradicted with the theoretical analysis [15]. The simulations indicate that, beginning with a Frank state and a racemic concentration, the dynamics of the unstable networks tend to evolve towards homochiral concentrations. If the simulations are initialized at states that are not Frank states, then the dynamics evolve towards racemic concentrations. On the other hand, the computer experiments indicate that for KNS-AP all the dynamics evolve towards racemic concentrations, even if

[§]All simulations were executed using software developed for this purpose. The software is available at <https://gitlab.com/homochirality/chemulator>.

those dynamics are initialized at non-racemic concentrations. The reported experimental results are positive, and they suggest that our notion of Frank state is appropriate and effectively related to the emergence of homochirality. We finish in section 9 with some concluding remarks.

The present work is related to all those previous works that are devoted to the stability analysis of chemical reactions networks (see for instance [16–18], and references therein). Our work is also related to all those previous works devoted to the mathematical and chemical analysis of homochirality (see for instance [11, 19, 20], and references therein).

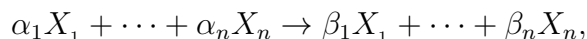
The main contributions of this work are the following: We identify a mathematical condition that is related to the emergence of homochirality; the steady states satisfying the condition are called Frank states. We find a set of linear inequalities (that we call *Frank inequalities*) characterizing the set of Frank states. We get two important results from the analysis of Frank inequalities:

1. We design an elementary and efficient algorithm that can be used to compute Frank states of any chiral network given as input.
2. We prove a formal version of a claim that is first indebted to Frank, namely: *Autocatalysis is a necessary condition for the emergence of homochirality*.

And, last but not least, we can conclude that homochirality is a likely phenomenon, and that any network admitting homochiral dynamics is likely to evolve towards homochiral states.

2 Basic concepts of chemical networks

A *chemical reaction* over the *chemical species* X_1, \dots, X_n is an expression of the form

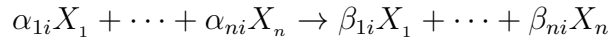


where $\alpha_1, \dots, \alpha_n$ and β_1, \dots, β_n are small positive integers (some of which could be equal to zero).

The above expression indicates that the mixture of α_1 units of X_1, \dots , and α_n units of X_n gives place to β_1 units of X_1, \dots , and β_n units of X_n .

Definition 1. A *chemical network* over the species $\{X_1, \dots, X_n\}$ is a set of chemical reactions, say $\{R_1, \dots, R_r\}$, over this set of species.

Given a chemical network $\Omega = \{(X_1, \dots, X_n), (R_1, \dots, R_r)\}$ we use the expression



to denote the reaction R_i .

Notation. Let $\Omega = \{(X_1, \dots, X_n), (R_1, \dots, R_r)\}$ be a chemical network, we use variables x_1, \dots, x_n to denote the concentrations of the n chemical species at a given instant.

Chemical reactions occur at different rates. Let (k_1, \dots, k_r) be a vector of rate constants related to the reactions R_1, \dots, R_r . We know that the dynamics of network Ω is determined by the *law of mass action* [21]. Thus, the dynamics of Ω is captured by the polynomial system of differential equations:

$$\begin{aligned} \frac{dx_1}{dt} &= \sum_{j=1}^r (\nu_{1j}) \cdot k_j \cdot x_1^{\alpha_{1j}} \cdot \dots \cdot x_n^{\alpha_{nj}} \\ &\vdots \\ \frac{dx_n}{dt} &= \sum_{j=1}^r (\nu_{nj}) \cdot k_j \cdot x_1^{\alpha_{nj}} \cdot \dots \cdot x_n^{\alpha_{nj}}, \end{aligned}$$

where ν_{ij} denote the quantity $\beta_{ij} - \alpha_{ij}$ for all $i \leq n$ and for all $j \leq r$. This is the kind of polynomial systems that we analyse in this work. We say that those systems are *autonomous systems of polynomial differential equations* (polynomial systems, for short). Recall that the variables x_1, \dots, x_n represent the concentrations of the species X_1, \dots, X_n and hence the solutions of the above system are supposed to describe the temporal evolution of those concentrations. It happens that most *rate constants* should be considered as variable parameters ranging over an (small) positive interval of the real numbers. On the other hand, most of those polynomial systems cannot be solved by analytical means, and for this reason we have to consider a qualitative analysis.

3 Stability analysis of polynomial systems

Consider a polynomial system

$$\frac{dx_i}{dt} = f_i(x_1, \dots, x_n, k_1, \dots, k_r); \quad i = 1, \dots, n.$$

We say that $(\mathbf{a}_0, \mathbf{b}_0) \in \mathbb{R}^n \times \mathbb{R}^r$ is a *steady state*, if and only if, the equalities

$$0 = f_i(a_1, \dots, a_n, b_1, \dots, b_r); \quad i = 1, \dots, n$$

hold.

If the system is driven to the state $x_1 = a_1, \dots, x_n = a_n$, under the well controlled conditions represented by b_1, \dots, b_r , then nothing occurs, the system is stuck at a fixed point of its dynamic.

In real life, steady states are quickly reached because of friction, dissipation, entropy growth, etc. However, we see dynamics all the time. This happens because physical systems are continuously perturbed by external noise. Thus, it can be argued that most of the dynamics that we see every day correspond to dynamics that occur when steady states are perturbed. According to the later point of view it makes sense to study the dynamics that occur when one exerts a small perturbation on the steady states of the system under study.

The *qualitative analysis* of nonlinear systems studies the dynamics that occur near the steady states. Steady states can be either *stable* or *unstable*. The rough idea is that all the interesting dynamics occur in the vicinities of unstable states. Then, it becomes important to develop mathematical and algorithmic tools for the detection of the later type of states. The later problem can be reduced to matrix analysis.

Let $(\mathbf{a}_0, \mathbf{b}_0)$ be a steady state of the system, the *jacobian matrix* at state $(\mathbf{a}_0, \mathbf{b}_0)$ is the matrix

$$J_{\mathbf{a}_0, \mathbf{b}_0} = \left[\frac{\partial f_i}{\partial x_j}(\mathbf{a}_0, \mathbf{b}_0) \right]_{i,j=1, \dots, n}.$$

We say that $(\mathbf{a}_0, \mathbf{b}_0)$ is a *hyperbolic steady state*, if and only if, the real part of any λ eigenvalue of $J_{\mathbf{a}_0, \mathbf{b}_0}$ is non-null. The Theorem of Grobman-Hartman [22] tells us that the stability (instability) properties of any hyperbolic state $(\mathbf{a}_0, \mathbf{b}_0)$ can be deduced from the eigen-structure of $J_{\mathbf{a}_0, \mathbf{b}_0}$.

Definition 2. Let $(\mathbf{a}_0, \mathbf{b}_0)$ be a hyperbolic steady state, and let $\lambda_1, \dots, \lambda_n$ be the eigenvalues of $J_{\mathbf{a}_0, \mathbf{b}_0}$. We say that $(\mathbf{a}_0, \mathbf{b}_0)$ is λ -stable, if and only if, for all $i \leq n$ the inequality $\text{Re}(\lambda_i) < 0$ holds. On the other hand, we say that $(\mathbf{a}_0, \mathbf{b}_0)$ is λ -unstable, if and only if, there exists i such that $\text{Re}(\lambda_i) > 0$.

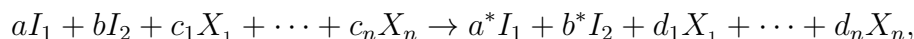
We observe that the λ -unstable states are the hyperbolic states that can produce homochiral dynamics. Thus, our work is to characterize the λ -unstable states that are related to the occurrence of homochiral dynamics, and to develop algorithmic tools that

allow one to check if a given network admits the existence of the later type of steady states.

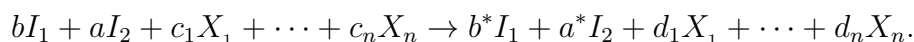
4 Chiral networks

Suppose that $\Omega = \{(I_1, I_2, X_1, \dots, X_n), (R_1, \dots, R_r)\}$ is a chemical network and suppose that I_1 and I_2 represent a pair of enantiomers. Recall that any pair of enantiomers is indiscernible from the point of view of chemical kinetics. Thus, if the network Ω is a realistic model of a chemical reaction network it must satisfy a symmetry constraint related to the pair of enantiomers. The symmetry constraint is the following one:

Given R_i equal to

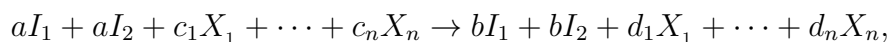


there must exist $j \leq r$ such that R_j is equal to



We say, in the later case, that reactions R_i and R_j are *dual reactions*.

Remark. If the reaction R_j has the form



we say that it is a self-dual reaction since it is equal to its dual reaction.

Remark. We have that if R_i and R_j are dual reactions, then their reactions rates constants are the same. The later fact allows us to talk about the *reaction rate of the pair* (R_i, R_j) .

If the network Ω violates the above symmetry constraint, the designer of this theoretical model has introduced an asymmetry that could explain the occurrence of homochiral dynamics in Ω , and these cases will not be considered here since the striking character of the homochirality phenomenon is based on the following fact: Isomers are supposed to be indiscernible from the point of view of chemical kinetics, and it means that the homochirality phenomenon corresponds to a *spontaneous symmetry breaking* [23,24]. Observe that the supposed indiscernibility of isomers is captured by the symmetry constraint discussed

above. If a network Ω satisfies that constraint, we say that Ω is a *symmetric network*. From now on, we focus on symmetric networks.

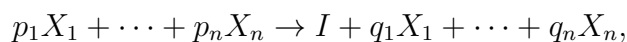
Let $\Omega = \{(I_1, I_2, X_1, \dots, X_n), (R_1, \dots, R_r)\}$ be a symmetric network. We are interested in the temporal evolution of the variables i_1 and i_2 that describe the concentrations of the enantiomers I_1 and I_2 . One can observe that different types of chemical reactions play different roles in the evolution of those two variables. Let $j \in \{i_1, i_2\}$, we have that

$$\frac{dj}{dt} = \sum_{l \leq r} j_l,$$

where for all $l \leq r$ the symbol j_l denotes the *contribution of reaction R_l* . We have that for all $l \leq r$, the contribution j_l is a monomial in the variables $x_1, \dots, x_n, i_1, i_2, k_1, \dots, k_r$.

The specific role played by reaction R_l is completely determined by the monomials $(i_1)_l$ and $(i_2)_l$. Then, it is a good idea to begin with a classification of reactions that is based on the different types of monomials contributed by each reaction. We consider six different types of reactions, there are important heuristic reasons to focus on those six different types of reactions (see below).

1. We say that the reaction R_l is an *enantiomeric synthesis reaction* if it has the form



where $I \in \{I_1, I_2\}$. Example: The Strecker reaction [25]



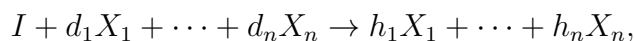
Let us suppose that $I = I_1$, in this case we have

$$(i_1)_l = k_l \cdot x_1^{p_1} \dots x_n^{p_n} \text{ and } (i_2)_l = 0.$$

Notice also that

$$\frac{\partial (i_1)_l}{\partial i_1} = \frac{\partial (i_1)_l}{\partial i_2} = \frac{\partial (i_2)_l}{\partial i_1} = \frac{\partial (i_2)_l}{\partial i_2} = 0.$$

2. We say that the reaction R_l is an *enantiomeric first order decomposition reaction*, abbreviated fo-decomposition, if it has the form



where $I \in \{I_1, I_2\}$. Example: In the Kondepudi-Nelson model [19], we have the following two fo-decomposition reactions



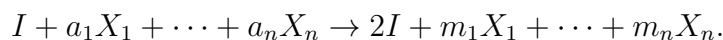
Let us suppose that $I = I_1$, we have that

$$(i_1)_l = -k_l \cdot i_1 \cdot x_1^{d_1} \cdots x_n^{d_n} \text{ and } (i_2)_l = 0.$$

Moreover, we have

$$\begin{aligned} \frac{\partial (i_1)_l}{\partial i_1} &= -k_l \cdot x_1^{d_1} \cdots x_n^{d_n}, \\ \frac{\partial (i_1)_l}{\partial i_2} &= \frac{\partial (i_2)_l}{\partial i_1} = \frac{\partial (i_2)_l}{\partial i_2} = 0. \end{aligned}$$

3. We say that the reaction R_l is an *enantiomeric autocatalytic reaction* if it has the form



.

Example: The Soai reaction [26]:



Let us suppose $I = I_1$, we have that

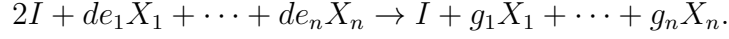
$$(i_1)_l = k_l \cdot i_1 \cdot x_1^{a_1} \cdots x_n^{a_n} \text{ and } (i_2)_l = 0.$$

Then, we have that

$$\begin{aligned} \frac{\partial (i_2)_l}{\partial i_1} &= \frac{\partial (i_2)_l}{\partial i_2} = \frac{\partial (i_1)_l}{\partial i_2} = 0, \\ \frac{\partial (i_1)_l}{\partial i_1} &= \frac{\partial (k_l \cdot i_1 \cdot x_1^{a_1} \cdots x_n^{a_n})_l}{\partial i_1} = k_l \cdot x_1^{a_1} \cdots x_n^{a_n}. \end{aligned}$$

.

4. We say that the reaction R_l is a *enantiomeric second order decomposition* reaction, so-decomposition for short, if it has the form



Example: In the Kondepudi-Nelson model [19], we have the following two so-decomposition reactions



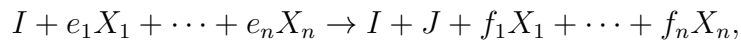
If we suppose $I = I_1$, we have

$$(i_1)_l = -k_l \cdot (i_1)^2 \cdot x_1^{de_1} \cdots x_n^{de_n} \text{ and } (i_2)_l = 0.$$

Moreover, we have

$$\begin{aligned} \frac{\partial (i_2)_l}{\partial i_1} &= \frac{\partial (i_2)_l}{\partial i_2} = \frac{\partial (i_1)_l}{\partial i_2} = 0, \\ \frac{\partial (i_1)_l}{\partial i_1} &= \frac{\partial (-k_l \cdot (i_1)^2 \cdot x_1^{de_1} \cdots x_n^{de_n})}{\partial i_1} = -2k_l \cdot i_1 \cdot x_1^{de_1} \cdots x_n^{de_n}. \end{aligned}$$

5. We say that the reaction R_l is a *non-enantioselective autocatalytic reaction*, abbreviated no-enantioselective, if it has the form



where I, J are the pair of enantiomers.

Example: The authors of reference [13], study a model that include the following pair of no-enantioselective reactions



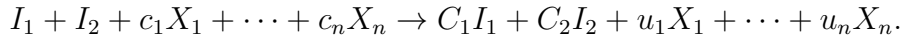
Let us suppose that $I = I_1$. We have that

$$(i_2)_l = k_l \cdot i_1 \cdot x_1^{e_1} \cdots x_n^{e_n} \text{ and } (i_1)_l = 0.$$

Moreover, we have

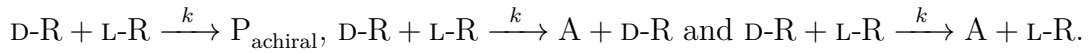
$$\begin{aligned}\frac{\partial (i_1)_l}{\partial i_1} &= \frac{\partial (i_1)_l}{\partial i_2} = \frac{\partial (i_2)_l}{\partial i_2} = 0, \\ \frac{\partial (i_2)_l}{\partial i_1} &= \frac{\partial (k_l \cdot i_1 \cdot x_1^{e_1} \cdots x_n^{e_n})}{\partial i_1} = k_l \cdot x_1^{e_1} \cdots x_n^{e_n}.\end{aligned}$$

6. We say that the reaction R_l is an *enantiomeric inhibition reaction* if it has the form



where C_1 and C_2 are small positive integers.

Example: The following set of reactions presented in reference [27]



We have that

$$\begin{aligned}(i_1)_l &= (C_1 - 1) \cdot k_l \cdot i_1 \cdot i_2 \cdot x_1^{c_1} \cdots x_n^{c_n}, \\ (i_2)_l &= (C_2 - 1) \cdot k_l \cdot i_1 \cdot i_2 \cdot x_1^{c_1} \cdots x_n^{c_n}.\end{aligned}$$

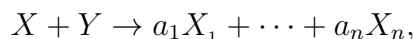
Then, we have

$$\begin{aligned}\frac{\partial (i_1)_l}{\partial i_1} &= (C_1 - 1) \cdot k_l \cdot i_2 \cdot x_1^{c_1} \cdots x_n^{c_n}, \\ \frac{\partial (i_1)_l}{\partial i_2} &= (C_1 - 1) \cdot k_l \cdot i_1 \cdot x_1^{c_1} \cdots x_n^{c_n}, \\ \frac{\partial (i_2)_l}{\partial i_1} &= (C_2 - 1) \cdot k_l \cdot i_2 \cdot x_1^{c_1} \cdots x_n^{c_n}, \\ \frac{\partial (i_2)_l}{\partial i_2} &= (C_2 - 1) \cdot k_l \cdot i_1 \cdot x_1^{c_1} \cdots x_n^{c_n}.\end{aligned}$$

Notice that R_l is self-dual, if and only if, $C_1 = C_2$. Also, it is important to remark that the class of inhibition reactions is constituted by two different types of reactions: Cross inhibition reactions and purely destructive inhibitions. Cross inhibitions are the reactions for which $C_1 + C_2 > 0$, while purely destructive inhibitions are the inhibitions for which $C_1 = C_2 = 0$.

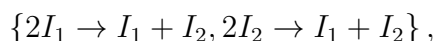
The above classification into six categories is not a full classification of chemical reactions. However, it works well for the practical purposes of this work. Moreover, we have:

- Molecular chemistry tells us that most chemical reactions have the form



that is: Most chemical reactions involve just two reactants. We say that those reactions are *binary reactions*. Ternary reactions are scarce but could occur, while reactions of higher orders are very unlikely [28, 29].

- Chemical reactions are reversible. Notice that this fact, together with the previous one, implies that most elemental chemical reactions are constituted by no more than three reactants and no more than three products.
- Recall that given a chemical reaction, it must be possible to decompose it as a sequence of elementary steps, and elementary steps are usually binary [29]. Thus, it makes sense to restrict the attention to binary reactions. There is only one type of binary chemical reactions that is not included, in our six members classification. The seventh category is constituted by the pair of binary reactions



called “racemization” or “chiral inversion”. We will not consider this type of reactions because they do not occur in the models that we want to analyze. It is worth to remark that those reactions cannot favor the emergence of Homochirality. However, the analytic machinery can be extended to include this additional type of reactions, but that work will not be done here.

Let us introduce a signature for *chiral networks*, which are the symmetric networks that we want to study.

Definition 3. A chiral network is an 8-tuple $(\mathcal{X}, \mathcal{R}, \mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4, \mathcal{R}_5, \mathcal{R}_6)$, where:

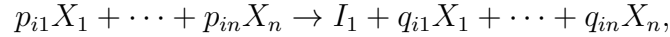
1. $\mathcal{X} = \{I_1, I_2, X_1, \dots, X_n\}$ is a set constituted by $n + 2$ chemical species, and species I_1 and I_2 represent the pair of enantiomers.

2. \mathcal{R} is the set of reactions, and

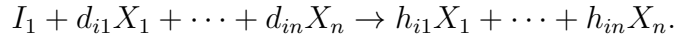
$$\mathcal{R} = \mathcal{R}_1 \sqcup \mathcal{R}_2 \sqcup \mathcal{R}_3 \sqcup \mathcal{R}_4 \sqcup \mathcal{R}_5 \sqcup \mathcal{R}_6.$$

That is: The set \mathcal{R} is equal to the disjoint union of $\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4, \mathcal{R}_5$ and \mathcal{R}_6 .

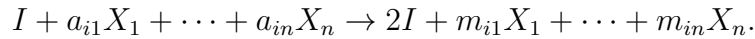
3. The set \mathcal{R}_1 is equal to $\{P_1, P_1^*, P_2, P_2^*, \dots, P_t, P_t^*\}$, where for all $i \leq t$ the pair P_i, P_i^* is a pair of dual reactions, and for all i the reaction P_i is a synthesis reaction of the form



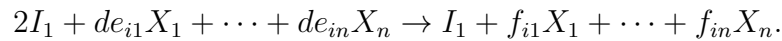
4. The set \mathcal{R}_2 is equal to $\{D_1, D_1^*, D_2, D_2^*, \dots, D_l, D_l^*\}$, where for all $i \leq l$ the pair D_i, D_i^* is a pair of dual reactions, and for all i the reaction D_i is a fo-decomposition reaction of the form



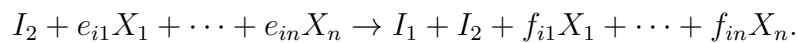
5. The set \mathcal{R}_3 is equal to $\{A_1, A_1^*, A_2, A_2^*, \dots, A_r, A_r^*\}$, where for all $i \leq r$ the pair A_i, A_i^* is a pair of dual reactions, and for all i the reaction A_i is an autocatalytic reaction of the form



6. The set \mathcal{R}_4 is equal to $\{Q_1, Q_1^*, Q_2, Q_2^*, \dots, Q_w, Q_w^*\}$, where for all $i \leq w$ the pair Q_i, Q_i^* is a pair of dual reactions, and for all i the reaction Q_i is a so-decomposition reaction of the form

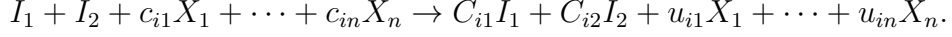


7. The set \mathcal{R}_5 is equal to $\{E_1, E_1^*, E_2, E_2^*, \dots, E_p, E_p^*\}$, where for all $i \leq p$ the pair E_i, E_i^* is a pair of dual reactions, and for all i the reaction E_i is a no-enantioselective reaction of the form



8. The set \mathcal{R}_6 is equal to $\{C_1, C_1^*, C_2, C_2^*, \dots, C_s, C_s^*\}$, where for all $i \leq s$ the pair C_i, C_i^*

is a pair of dual reactions, and for all i the reaction C_i is an inhibition reaction of the form



We say that $C_{i1} + C_{i2} - 2$ is the stoichiometric coefficient of the pair (C_i, C_i^*) and we use the symbol S_i^c to denote it. If C_i is self-dual, we work with the pair (C_i, C_i) . We say that $C_{i1} - 1$ is the stoichiometric coefficient of the (self-dual) pair (C_i, C_i) , and we use the symbol S_i^c to denote it.

5 Stability analysis of chiral networks

Given a chiral network $\Omega = \{\mathcal{X}, \mathcal{R}, \mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4, \mathcal{R}_5, \mathcal{R}_6\}$, we are interested in describing the dynamics of the concentration variables i_1 and i_2 . Then, we have to analyze the system

$$\begin{aligned} \frac{d(i_1)}{dt} &= \sum_{j \leq t} k_j^p \cdot x_1^{p_{j1}} \cdots x_n^{p_{jn}} - \sum_{j \leq l} k_j^d \cdot i_1 \cdot x_1^{d_{j1}} \cdots x_n^{d_{jn}} \\ &\quad + \sum_{j \leq r} k_j^a \cdot i_1 \cdot x_1^{a_{j1}} \cdots x_n^{a_{jn}} - \sum_{j \leq w} k_j^{de} \cdot i_1^2 \cdot x_1^{de_{j1}} \cdots x_n^{de_{jn}} \\ &\quad + \sum_{j \leq p} k_j^e \cdot i_2 \cdot x_1^{e_{j1}} \cdots x_n^{e_{jn}} + \sum_{j \leq s} S_j^c \cdot k_j^c \cdot (i_1 \cdot i_2) \cdot x_1^{c_{j1}} \cdots x_n^{c_{jn}} \\ \frac{d(i_2)}{dt} &= \sum_{j \leq t} k_j^p \cdot x_1^{p_{j1}} \cdots x_n^{p_{jn}} - \sum_{j \leq l} k_j^d \cdot i_2 \cdot x_1^{d_{j1}} \cdots x_n^{d_{jn}} \\ &\quad + \sum_{j \leq r} k_j^a \cdot i_2 \cdot x_1^{a_{j1}} \cdots x_n^{a_{jn}} - \sum_{j \leq w} k_j^{de} \cdot i_2^2 \cdot x_1^{de_{j1}} \cdots x_n^{de_{jn}} \\ &\quad + \sum_{j \leq p} k_j^e \cdot i_1 \cdot x_1^{e_{j1}} \cdots x_n^{e_{jn}} + \sum_{j \leq s} S_j^c \cdot k_j^c \cdot (i_1 \cdot i_2) \cdot x_1^{c_{j1}} \cdots x_n^{c_{jn}} \end{aligned}$$

Let us fix some notation.

- The symbol k_j^p denotes the rate constant of the pair (P_j, P_j^*) .
- The symbol k_j^d denotes the rate constant of the pair (D_j, D_j^*) .
- The symbol k_j^a denotes the rate constant of the pair (A_j, A_j^*) .
- The symbol k_j^{de} denotes the rate constant of the pair (Q_j, Q_j^*) .
- The symbol k_j^e denotes the rate constant of the pair (E_j, E_j^*) .

- The symbol k_j^c denotes the rate constant of the pair (C_j, C_j^*) .

In this work we consider a simplified scenario in which the concentrations of all the secondary species remain constant. We can suppose that the constant concentrations of secondary species are all equal to 1. If we do the later we get that

$$\begin{aligned}\frac{d(i_1)}{dt} &= \sum_{j \leq t} k_j^p - \sum_{j \leq l} k_j^d \cdot i_1 + \sum_{j \leq r} k_j^a \cdot i_1 \\ &\quad - \sum_{j \leq w} k_j^{de} \cdot i_1^2 + \sum_{j \leq p} k_j^e \cdot i_2 + \sum_{j \leq s} S_j^c \cdot k_j^c \cdot (i_1 \cdot i_2), \\ \frac{d(i_2)}{dt} &= \sum_{j \leq t} k_j^p - \sum_{j \leq l} k_j^d \cdot i_2 + \sum_{j \leq r} k_j^a \cdot i_2 \\ &\quad - \sum_{j \leq w} k_j^{de} \cdot i_2^2 + \sum_{j \leq p} k_j^e \cdot i_1 + \sum_{j \leq s} S_j^c \cdot k_j^c \cdot (i_1 \cdot i_2).\end{aligned}$$

Remark. From a mathematical point of view, the scenario considered in this paper is equivalent to the scenario determined by the following constraint: Chiral networks contain only three species, the two enantiomers and only one secondary species.

Notice that, under the later assumption, the steady states can be succinctly described by short tuples. Given a chiral network $\Omega = \{\mathcal{X}, \mathcal{R}, \mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4, \mathcal{R}_5, \mathcal{R}_6\}$, a state of the network can be completely described by a vector

$$(i_1, i_2, \mathbf{k}_0) \in \mathbb{R}_+^{2+t+l+r+w+p+s},$$

where

$$\mathbf{k}_0 = (k_1^p, \dots, k_t^p, k_1^d, \dots, k_l^d, k_1^a, \dots, k_r^a, k_1^{de}, \dots, k_w^{de}, k_1^e, \dots, k_p^e, k_1^c, \dots, k_s^c).$$

Remark. We say that the state (i_1, i_2, \mathbf{k}_0) is racemic, if and only if, $i_1 = i_2$.

Recall that we are interested in the racemic λ -unstable states. Then, we have to compute the jacobian matrix of the system at state (a, a, \mathbf{k}_0) . First, we set

$$b(a, \mathbf{k}_0) = - \sum_{j \leq l} k_j^d + \sum_{j \leq r} k_j^a - 2a \sum_{j \leq w} k_j^{de} + a \sum_{j \leq s} S_j^c \cdot k_j^c,$$

and then we set

$$c(a, \mathbf{k}_0) = \sum_{j \leq p} k_j^e + a \sum_{j \leq s} S_j^c \cdot k_j^c.$$

After some computations we get that

$$J_{a,a,\mathbf{k}_0} = \begin{pmatrix} b(a, \mathbf{k}_0) & c(a, \mathbf{k}_0) \\ c(a, \mathbf{k}_0) & b(a, \mathbf{k}_0) \end{pmatrix},$$

and we get as a corollary the following theorem.

Theorem 1. The jacobian matrix J_{a,a,\mathbf{k}_0} is equal to the symmetric matrix

$$\begin{pmatrix} b(a, \mathbf{k}_0) & c(a, \mathbf{k}_0) \\ c(a, \mathbf{k}_0) & b(a, \mathbf{k}_0) \end{pmatrix},$$

whose eigenvalues are equal to

$$\{b(a, \mathbf{k}_0) - c(a, \mathbf{k}_0), b(a, \mathbf{k}_0) + c(a, \mathbf{k}_0)\}.$$

Proof. It only remains to compute the eigenvalues of J_{a,a,\mathbf{k}_0} . First we compute

$$\det \begin{pmatrix} b(a, \mathbf{k}_0) - \lambda & c(a, \mathbf{k}_0) \\ c(a, \mathbf{k}_0) & b(a, \mathbf{k}_0) - \lambda \end{pmatrix}.$$

We have

$$\begin{aligned} \det (J_{a,a,\mathbf{k}_0}) &= (b(a, \mathbf{k}_0) - \lambda)^2 - c(a, \mathbf{k}_0)^2 \\ &= (b(a, \mathbf{k}_0) - \lambda + c(a, \mathbf{k}_0))(b(a, \mathbf{k}_0) - \lambda - c(a, \mathbf{k}_0)) \\ &= ((b(a, \mathbf{k}_0) + c(a, \mathbf{k}_0)) - \lambda)((b(a, \mathbf{k}_0) - c(a, \mathbf{k}_0)) - \lambda) \end{aligned}$$

and hence we get that the eigenvalues of J_{a,a,\mathbf{k}_0} are equal to

$$b(a, \mathbf{k}_0) \pm c(a, \mathbf{k}_0),$$

and the theorem is proved □

The type of dynamics that occur near a hyperbolic state are determined by the eigenvalues of its jacobian matrix. Recall that we are interested in computing λ -unstable steady states giving place to homochiral dynamics. We conjecture that these states can be fully characterized in terms of their eigen-structure. Let us review a famous model of chemical network exhibiting homochirality. We study this small and well known model because it can give us some clues about which are the λ -unstable states related to homochirality.

5.1 Frank model: A network exhibiting homochirality

In 1953, Charles Frank proposed a model to demonstrate that homochirality is a consequence of autocatalysis [10]. Frank's model corresponds to the abstract network

$$\Omega_F = \{(I_1, I_2, X), (I_1 + X \rightarrow 2I_1, I_2 + X \rightarrow 2I_2, I_1 + I_2 \rightarrow X)\}.$$

Frank model is a very interesting mathematical model of homochirality: All their steady states are unstable, and all those states give place to homochiral dynamics.

We observe that Ω_F is a chiral network that can be represented as the 8-tuple

$$\{\mathcal{X}, \mathcal{R}, \emptyset, \emptyset, (I_1 + X \rightarrow 2I_1, I_2 + X \rightarrow 2I_2), \emptyset, \emptyset, (I_1 + I_2 \rightarrow X, I_1 + I_2 \rightarrow X)\}.$$

Remark. Observe that \mathcal{R}_6 contains the single reaction $I_1 + I_2 \rightarrow X$, and notice that this reaction is self-dual. Therefore, we say that \mathcal{R}_6 is constituted by the pair $(I_1 + I_2 \rightarrow X, I_1 + I_2 \rightarrow X)$

The dynamic of the above chiral network is governed by the equations

$$\begin{aligned} \frac{d(i_1)}{dt} &= k_1^a \cdot i_1 - k_1^c \cdot i_1 \cdot i_2. \\ \frac{d(i_2)}{dt} &= k_1^a \cdot i_2 - k_1^c \cdot i_1 \cdot i_2. \end{aligned}$$

Let (i, i, k_1^a, k_1^c) be a racemic state. We use the symbol (i, i, \mathbf{k}_0) to denote this state, where \mathbf{k}_0 is equal to (k_1^a, k_1^c) . If (i, i, \mathbf{k}_0) is a steady state, the equality

$$k_1^a \cdot i = k_1^c \cdot i^2$$

must hold, and hence $k_1^a = k_1^c \cdot i$. The jacobian matrix, denoted by J_{i,i,\mathbf{k}_0} , is equal to

$$\begin{pmatrix} k_1^a - k_1^c \cdot i & -k_1^c \cdot i \\ -k_1^c \cdot i & k_1^a - k_1^c \cdot i \end{pmatrix}.$$

And the eigenvalues of J_{i,i,\mathbf{k}_0} are equal to $\{k_1^a, -k_1^c \cdot i\}$.

If (i, i, \mathbf{k}_0) is a non-null steady state, then it is hyperbolic and λ -unstable. Moreover, it satisfies the inequalities

$$\begin{aligned} k_1^a &= b(i, \mathbf{k}_0) - c(i, \mathbf{k}_0) > 0, \\ -k_1^c \cdot i &= b(i, \mathbf{k}_0) + c(i, \mathbf{k}_0) < 0. \end{aligned}$$

6 Homochiral states

The analysis of the Frank model shows that the inequalities

$$b(a, \mathbf{k}_0) - c(a, \mathbf{k}_0) > 0 \text{ and } b(a, \mathbf{k}_0) + c(a, \mathbf{k}_0) < 0$$

always hold. On the other hand, the theoretical analysis of the model as well as multiple simulations indicate that all its steady states are unstable and give place to homochiral dynamics. It happens that the above inequalities, which we call *Frank inequalities*, are related to this fact.

Given a matrix

$$\begin{pmatrix} b & c \\ c & b \end{pmatrix},$$

the eigenvectors associated to $b - c$ are the vectors in the set $\{(d, -d) : d \in \mathbb{R}\}$, while the eigenvectors associated to $b + c$ are the vectors in the set $\{(d, d) : d \in \mathbb{R}\}$. Consider the linear system

$$\begin{pmatrix} \frac{dx}{dt} \\ \frac{dy}{dt} \end{pmatrix} = \begin{pmatrix} b & c \\ c & b \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix},$$

we have that the general solution of the system is equal to

$$\begin{pmatrix} x \\ y \end{pmatrix} = A \begin{pmatrix} e^{(b-c)t} \\ -e^{(b-c)t} \end{pmatrix} + B \begin{pmatrix} e^{(b+c)t} \\ e^{(b+c)t} \end{pmatrix}.$$

Then, if the inequalities $b - c > 0$ and $b + c < 0$ both hold, any perturbation of the steady state $(0, 0)$ gives place to *homochiral* dynamics: The concentration of one of the two *species* grows, while the concentration of the other one decreases. Now suppose that S is a polynomial system and let s be a hyperbolic steady state of S . We use the symbol J_s to denote the linear system that is given by the jacobian matrix at state s . We have that the *flow* of S near the state s is *topologically conjugated* to the flow of J_s near the steady state $\mathbf{0}$ (see [30]). The later fact suggests that both flows behave in a similar way when time goes to infinity, and it suggests that any racemic state satisfying Frank inequalities gives place to homochiral dynamics. The notion of topological conjugation (The Grobman-Hartman Linearization Theorem [22]) is not strong enough as to imply that homochiral dynamics are implied by Frank inequalities. However, there are further qualitative and geometrical reasons to associate those two inequalities to the (frequent) emergence of the later type of dynamics.

Definition 4. Given the network $\Omega = \{\mathcal{X}, \mathcal{R}, \mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4, \mathcal{R}_5, \mathcal{R}_6\}$, and given the steady state (a, a, \mathbf{k}_0) , we say that it is a Frank state, if and only if, the inequalities

$$\sum_{j \leq r} k_j^a - \left(\sum_{j \leq l} k_j^d + 2a \sum_{j \leq w} k_j^{de} + \sum_{j \leq p} k_j^e \right) > 0,$$

$$\sum_{j \leq r} k_j^a + \sum_{j \leq p} k_j^e + 2a \sum_{j \leq s} S_j^c \cdot k_j^c - \left(\sum_{j \leq l} k_j^d + 2a \sum_{j \leq w} k_j^{de} \right) < 0.$$

both hold.

The notion of Frank state is a mathematical notion that could be unrelated to the emergence of homochiral dynamics. However, we are strongly convinced that the later is not the case. We will provide some evidence concerning this issue (see below the section on the ‘‘Computational analysis of chiral networks: Experimental results’’), but before of this we would like to observe that:

Remark. Let \mathbf{s} be a Frank state

1. State \mathbf{s} is hyperbolic
2. State \mathbf{s} is a saddle point.

The above two facts allow us to claim that the notion of Frank states is a relevant mathematical notion.

Theorem 2. Let $\Omega = \{\mathcal{X}, \mathcal{R}, \mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4, \mathcal{R}_5, \mathcal{R}_6\}$ be a chiral network admitting Frank states, we have that $\mathcal{R}_3, \mathcal{R}_6 \neq \emptyset$.

Proof. First, we prove that *autocatalytic reactions are necessary*. Observe that the inequality

$$\left(\sum_{j \leq l} k_j^d + 2a \sum_{j \leq w} k_j^{de} + \sum_{j \leq p} k_j^e \right) \geq 0$$

holds for any steady state (a, a, \mathbf{k}_0) . Then, if the inequality

$$\sum_{j \leq r} k_j^a - \left(\sum_{j \leq l} k_j^d + 2a \sum_{j \leq w} k_j^{de} + \sum_{j \leq p} k_j^e \right) > 0$$

holds, we have that

$$\sum_{j \leq r} k_j^a > \left(\sum_{j \leq l} k_j^d + 2a \sum_{j \leq w} k_j^{de} + \sum_{j \leq p} k_j^e \right) \geq 0.$$

Then, we have that $\sum_{j \leq r} k_j^a$ must be larger than zero, and it clearly implies that $\mathcal{R}_3 \neq \emptyset$.
Now suppose that

$$\sum_{j \leq r} k_j^a - \left(\sum_{j \leq l} k_j^d + 2a \sum_{j \leq w} k_j^{de} + \sum_{j \leq p} k_j^e \right) > 0$$

Then, if the inequality

$$\sum_{j \leq r} k_j^a + \sum_{j \leq p} k_j^e + 2a \sum_{j \leq s} S_j^c \cdot k_j^c - \left(\sum_{j \leq l} k_j^d + 2a \sum_{j \leq w} k_j^{de} \right) < 0$$

also holds, we have that *there are inhibition reactions, which are more destructive than productive*. The later assertion is true given that the inequality

$$\sum_{j \leq r} k_j^a + \sum_{j \leq p} k_j^e - \left(\sum_{j \leq l} k_j^d + 2a \sum_{j \leq w} k_j^{de} \right) > 0$$

holds, and it implies that the inequality

$$\left(\sum_{j \leq r} k_j^a + \sum_{j \leq p} k_j^e - \left(\sum_{j \leq l} k_j^d + 2a \sum_{j \leq w} k_j^{de} \right) \right) + 2a \sum_{j \leq s} S_j^c \cdot k_j^c < 0$$

can be satisfied only if the condition $\sum_{j \leq s} S_j^c \cdot k_j^c < 0$ is fulfilled. Then we have that $\mathcal{R}_6 \neq \emptyset$ and the theorem is proved. \square

Remark. Notice that we have given a formal proof to an old claim of Frank [10], namely: Autocatalytic reactions ($\mathcal{R}_3 \neq \emptyset$) are necessary for homochirality (for the existence of Frank states).

Definition 5. We say that a chiral network Ω is a λ -homochiral network, if and only if, network Ω admits Frank states.

We want to solve the following two tasks:

1. Recognizing the networks that are λ -homochiral.
2. Given a λ -homochiral network Ω , compute as many as possible Frank states of Ω (sample the set of Frank states of Ω).

Notice that we have partially solved the first problem: Theorem 2 gives us a necessary condition for the existence of Frank states (condition $\mathcal{R}_3, \mathcal{R}_6 \neq \emptyset$).

Definition 6. Given a chiral network $\Omega = \{\mathcal{X}, \mathcal{R}, \mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4, \mathcal{R}_5, \mathcal{R}_6\}$, we say that it is an *autocatalytic network*, if and only if, $\mathcal{R}_3 \neq \emptyset$, and we say that it is an *inhibition network*, if and only if, $\mathcal{R}_6 \neq \emptyset$ and the later set contains a reaction whose stoichiometric coefficient is negative.

From now on we restrict our attention to inhibition networks that are autocatalytic.

Theorem 3. Let $\Omega = \{\mathcal{X}, \mathcal{R}, \mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4, \mathcal{R}_5, \mathcal{R}_6\}$ be a chiral network, we have that Ω admits Frank states, if and only if, Ω is an inhibition network that is autocatalytic.

Proof. We already know that λ -homochiral networks have autocatalytic and include inhibition reactions. We have to prove that the later two conditions are sufficient for the existence of Frank states.

Let Ω be an autocatalytic and inhibition network. Given $I \subseteq \{1, 2, 4, 5\}$, we suppose that Ω is a network such that

$$\mathcal{R}_i \text{ is non-empty, if and only if, } i \in I \cup \{3, 6\},$$

and hence we prove that Ω admits Frank states. We make the work for $I = \{1, 2, 4, 5\}$ and $I = \{2, 4, 5\}$. The remaining fourteen (14) cases are similar and we omit them. First we suppose that $I = \{1, 2, 4, 5\}$. It means that $\mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_4, \mathcal{R}_5 \neq \emptyset$. Consider the system of homogeneous linear inequalities given by

$$\begin{aligned} A - (D + 2DE + E) &> 0 \\ A + E - (D + 2DE + 2C) &< 0 \\ D + DE + C - E - A - P &= 0 \\ P, D, A, DE, E, C &> 0 \end{aligned}$$

We say that this is *The Master System of Inequalities* for this type of Networks. We notice that the above system has positive solutions, for instance

$$P = D = DE = E = 1, A = C = 5$$

is one of those solutions. We show that if we pick a solution of the above system, we can use it to construct Frank states of Ω . Thus, let

$$(P_0, D_0, A_0, DE_0, E_0, C_0)$$

be a solution to the master system. First, we compute $k_1^c, \dots, k_s^c \in \mathbb{R}_+$ such that the equality

$$\sum_{j \leq s} S_j^c \cdot k_j^c = -C_0$$

holds. Notice that this is possible, since there exists $j \leq s$ such that the stoichiometric coefficient S_j^c is negative. Then, we compute positive values for

$$k_1^p, \dots, k_t^p, k_1^d, \dots, k_l^d, k_1^a, \dots, k_r^a, k_1^{de}, \dots, k_w^{de}, k_1^e, \dots, k_p^e$$

such that the equalities

$$\begin{aligned} \sum_{j \leq p} k_j^p &= P_0, \quad \sum_{j \leq l} k_j^d = D_0, \quad \sum_{j \leq t} k_j^a = A_0, \\ \sum_{j \leq w} k_j^{de} &= DE_0, \quad \text{and} \quad \sum_{j \leq p} k_j^e = E_0 \end{aligned}$$

hold. If we set $a = 1$ and

$$\mathbf{k} = (k_1^p, \dots, k_t^p, k_1^d, \dots, k_l^d, k_1^a, \dots, k_r^a, k_1^{de}, \dots, k_w^{de}, k_1^e, \dots, k_p^e, k_1^c, \dots, k_s^c),$$

we get a racemic λ -homochiral state (a, a, \mathbf{k}) which satisfies Frank inequalities. Then, we have that Ω is λ -homochiral. Notice that each one of the six variables occurring in the master system represents the total contribution of a certain type of reactions. Thus, for instance, the variable A represents the contribution of the set of autocatalytic reactions.

Now, given $I \subseteq \{1, 2, 4, 5\}$, and knowing the master system for $\{1, 2, 4, 5\}$, we have the corresponding one for any I by simply deleting the variables that are related to empty sets of reactions. Suppose for instance that $I = \{2, 4, 5\}$. The master system for this type of networks is given by

$$\begin{aligned} A - (D + 2DE + E) &> 0 \\ A + E - (D + 2DE + 2C) &< 0 \\ D + DE + C - E - A &= 0 \\ D, A, DE, E, C &> 0 \end{aligned}$$

and this system has solutions, as for example

$$A = 5, \quad D = DE = E = 1, \quad C = 4.$$

Then, we pick a solution of the later system and we use it to construct a Frank state. To accomplish the later task we proceed exactly as we did above with the first type of network. \square

7 An algorithm

We can use the previous results to develop an algorithm that can be used to detect λ -homochiral networks and their Frank states. The algorithm receives as input a quiral network

$$\Omega = \{\mathcal{X}, \mathcal{R}, \mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4, \mathcal{R}_5, \mathcal{R}_6\},$$

where:

1. $\mathcal{X} = \{I_1, I_2, X_1, \dots, X_n\}$.
2. $\mathcal{R}_1 = \{(P_1, P_1^*), \dots, (P_t, P_t^*)\}$.
3. $\mathcal{R}_2 = \{(D_1, D_1^*), \dots, (D_l, D_l^*)\}$.
4. $\mathcal{R}_3 = \{(A_1, A_1^*), \dots, (A_r, A_r^*)\}$.
5. $\mathcal{R}_4 = \{(Q_1, Q_1^*), \dots, (Q_w, Q_w^*)\}$.
6. $\mathcal{R}_5 = \{(E_1, E_1^*), \dots, (E_p, E_p^*)\}$.
7. $\mathcal{R}_6 = \{(C_1, C_1^*), \dots, (C_s, C_s^*)\}$.

Let us suppose that Ω is a network such that $\mathcal{R}_i \neq \emptyset$ for all $i = 1, \dots, 6$. The algorithm works, on the given input, as follows;

1. Check if $\mathcal{R}_3 \neq \emptyset$. If the checking is positive go to step 2, otherwise halt and print: The network does not admit Frank states.
2. Compute the stoichiometric coefficients of the pairs $(C_1, C_1^*), \dots, (C_s, C_s^*)$. If there exists $j \leq s$ such that $S_j^c < 0$ go to step 3, otherwise halt and print: The network does not admit Frank states.
3. Compute positive values for

$$P, D, A, DE, E \text{ and } C$$

such that the system of linear inequalities (and linear equalities)

$$\begin{aligned} 0 &< A - (D + 2DE + E), \\ 0 &> A + E - (D + 2DE + 2C), \\ 0 &= P + A + E - (D + DE + C), \end{aligned}$$

is satisfied.

4. Compute positive values for

$$k_1^p, \dots, k_t^p; k_1^d, \dots, k_l^d; k_1^a, \dots, k_r^a; k_w^{de}, \dots, k_w^{de}; k_1^e, \dots, k_p^e; \text{ and } k_1^c, \dots, k_s^c$$

such that the equations

$$\begin{aligned} P &= \sum_{j \leq t} k_j^p, \quad E = \sum_{j \leq e} k_j^e, \quad D = \sum_{j \leq l} k_j^d, \quad DE = \sum_{j \leq w} k_j^{de}, \\ A &= \sum_{j \leq r} k_j^a \quad \text{and} \quad -C = \sum_{j \leq s} S_j^c \cdot k_j^c \end{aligned}$$

are satisfied.

5. Set

$$s_\Omega = (1, k_1^p, \dots, k_t^p, k_1^d, \dots, k_l^d, k_1^a, \dots, k_r^a, k_1^{de}, \dots, k_w^{de}, k_1^e, \dots, k_p^e, k_1^c, \dots, k_s^c),$$

and print s_Ω .

The theorems in previous section guarantee that the above algorithm is correct.

7.1 Runtime analysis of the algorithm

Given a network

$$\Omega = \{\mathcal{X}, \mathcal{R}, \mathcal{R}_1, \mathcal{R}_2, \mathcal{R}_3, \mathcal{R}_4, \mathcal{R}_5, \mathcal{R}_6\},$$

we say that its size is equal to $|\mathcal{X}| + |\mathcal{R}|$, which is the number of species plus the number of reactions. We would like to observe that the above algorithm can be used to efficiently analyze chiral networks of any size. Notice that the first two steps of the above algorithm run in time $O(s)$, where $s = |\mathcal{R}_6|$. The later means that checking if a network is λ -homochiral can be made in linear time in the number of inhibition reactions. On the

other hand, the whole algorithm runs in time $O(|\mathcal{R}|)$, and it means that it is a linear time algorithm. Moreover, the algorithm is correct and the analysis is conclusive:

- If the algorithm prints that the network does not admit Frank states, then one has for sure that network Ω is not a λ -homochiral network.
- If the algorithm computes a vector $s_\Omega \in \mathbb{R}_+^{n+2+t+l+r+w+p+s}$, then one has for sure that s_Ω encodes a Frank state, which is a saddle point.
- The algorithm can compute any Frank state satisfying the racemic condition

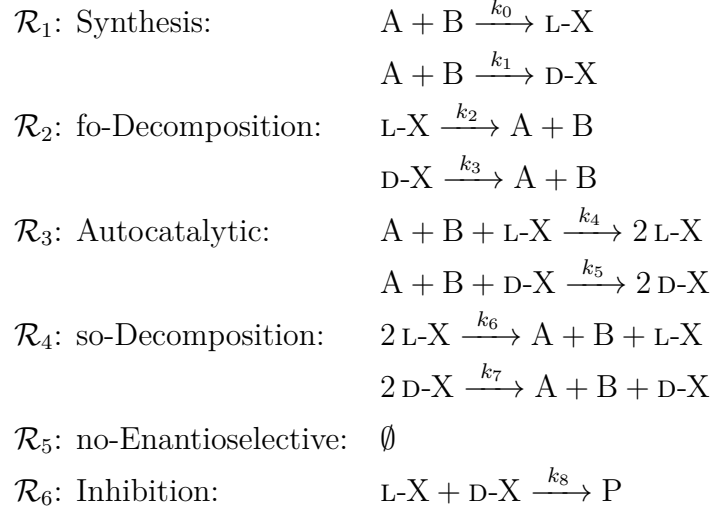
$$i_1 = i_2 = x_1 = \dots = x_n = 1.$$

The above algorithm was implemented as a computer program written in Python. It is available at <https://gitlab.com/homochirality/listanalchem>.

8 Computational analysis of chiral networks: Experimental results.

We want to test our tools. To this end, we analyze four chiral networks. Before of this we have to note that, except for the enantiomeric species, all the reagents are in a constant concentration and the final products do not have any effects on the reactions. Then, the species other than the enantiomers are included only as illustrative information. The later assumption implies that some reactions are redundant, as it will be mentioned in each particular model.

We begin with the Kondepudi-Nelson Network [11], which is given by the abstract reactions:



Notice that in this network we have a single inhibition reaction that is self-dual. The stoichiometric coefficient of this reaction is equal to -1. Moreover, we have that the set \mathcal{R}_3 is not empty. We can conclude that the network is λ -homochiral. We can use our algorithm to compute Frank states. Thus, we look for suitable values of k_0, \dots, k_8 . To begin with, we notice that because of the symmetry constraint related to dual reactions the equalities $k_0 = k_1, k_2 = k_3, k_4 = k_5$ and $k_6 = k_7$ hold. Then, we focus on computing suitable values for k_0, k_2, k_4, k_6 and k_8 , to this end we use our algorithm and computer program. We get the next conditions:

$$\begin{aligned}
k_2 &= k_3 \in (0, \infty) \\
k_4 &= k_5 \in (k_2, \infty) \\
k_6 &= k_7 \in \left(0, -\frac{k_2}{2} + \frac{k_4}{2}\right) \\
k_8 &\in \left(\text{Max}(-k_2 + k_4 - k_6, -\frac{k_2}{2} + \frac{k_4}{2} - k_6), \infty\right) \\
k_0 &= k_1 = k_2 - k_4 + k_6 + k_8
\end{aligned}$$

We can use the above data to sample the set of Frank states. We have for instance that

$$\left(k_2 = 1, k_4 = 2, k_6 = \frac{1}{4}, k_8 = 1, k_0 = \frac{1}{4}\right)$$

is a Frank state. We simulate the dynamics of the network in the vicinity of this state using a computer program based on the DLSODE algorithm [15], and developed in this work for that purpose. The program is available at <https://gitlab.com/homochirality/chemulator>. The experimental results are consigned in figure 1.

It is interesting to remark that the dynamics triggered by perturbations of Frank states give place to homochiral states, while the dynamics triggered by steady states that are non-Frank give place to racemic concentrations, see Figure 1 B-) and C-).

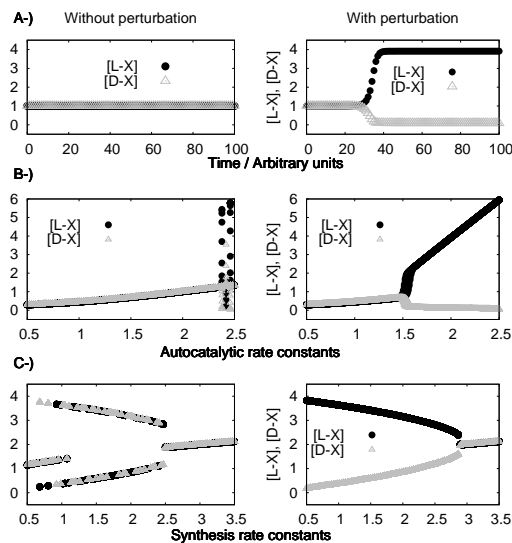
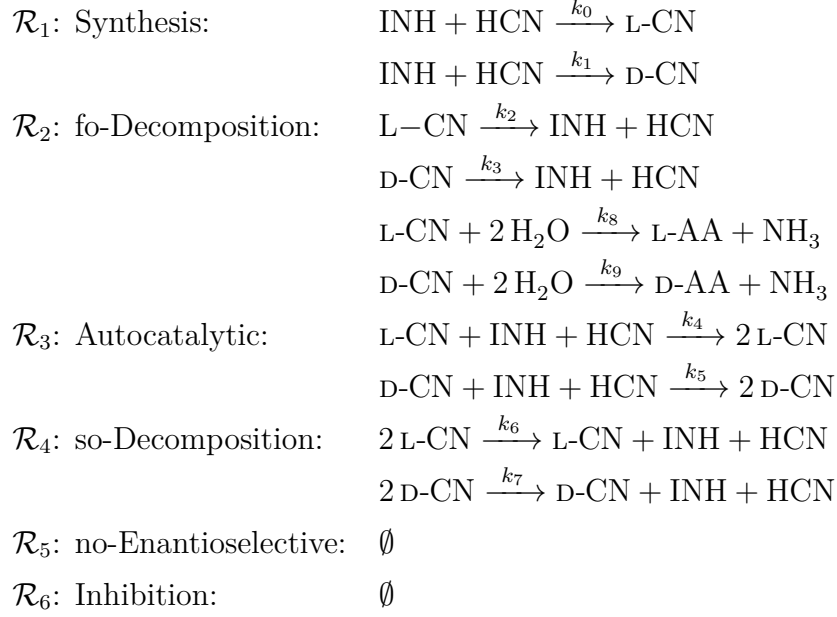


Figure 1. Simulations of the KN Model under the conditions found for instability in this work. A-) Time series for the k_i values proposed in the example, see text, B-) Bifurcation diagrams as a function of the autocatalytic rate constants, and C-) Bifurcation diagrams as a function of the synthesis rate constants. The simulations are presented without (left) and with a perturbation of 1×10^{-7} (right), in the initial concentrations of the isomers which were equal to 1 in all cases. Some unperturbed experiments behave like if they were perturbed, it happens because of the numerical error intrinsic to the computation, as it can be seen in B-) and C-), left side.

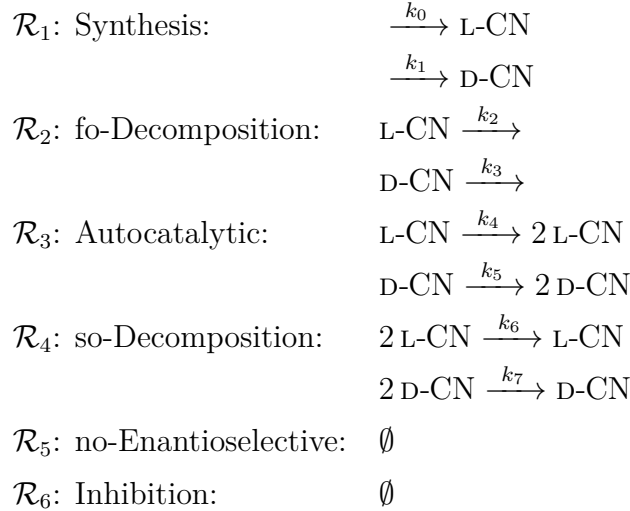
Now, let us study three further networks that are related to the KN Network. Those networks were proposed to study the emergence of homochirality, and they are modifications of the KN model adapted to the Strecker synthesis [12]. The species names involved in the models are the molecules needed in the aforementioned synthesis. These molecules are:

Ammonia:	NH_3
Hydrogen cyanide:	HCN
Imine:	$\text{R}-\text{CH}=\text{NH}$ abbreviated as INH
α -aminonitrile:	$\text{H}_2\text{NCH(R)CN}$ abbreviated as L-CN and D-CN
α -amino acid:	$\text{H}_2\text{NCH(R)COOH}$ abbreviated as L-AA and D-AA
Achiral dimer:	ADCN

We call this first model the Kondepudi-Nelson-Strecker-Amino-acid-Production (KNS-AP) Network, and it is represented in the following way



Observe that this model does not contain inhibition reactions. This implies that, according to our results, the network is not λ -homochiral. Also, note that in the subset of fo-decomposition reactions, only two of the four reactions are necessary because we have two pairs of equivalent reactions. In other words, the KNS-AP model can be represented as:



Simulations of the above mechanism show that all the dynamics triggered by perturbations of steady states evolve toward racemic concentrations, even if the initial conditions are not racemic, see Figure 2.

The second model is the Kondepudi-Nelson-Strecker-Amino-acid-Production-Limited-Enantio-Selectivity (KNS-AP-LES), represented by

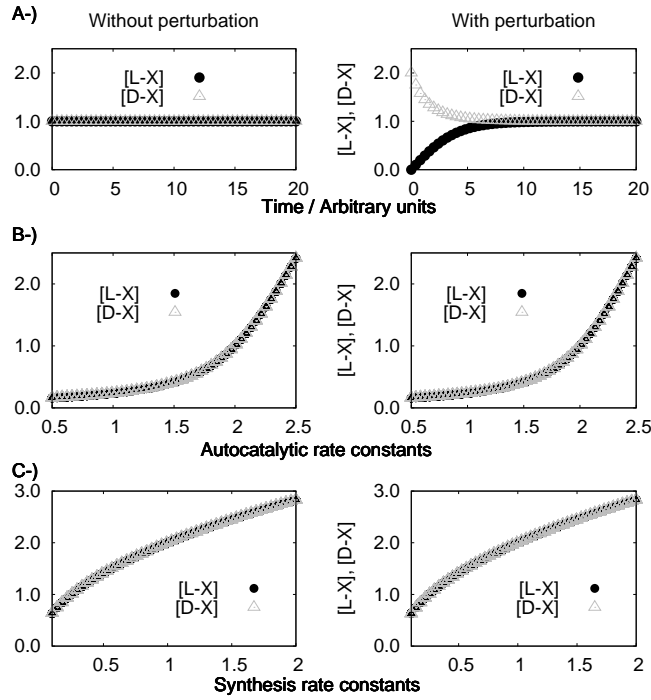
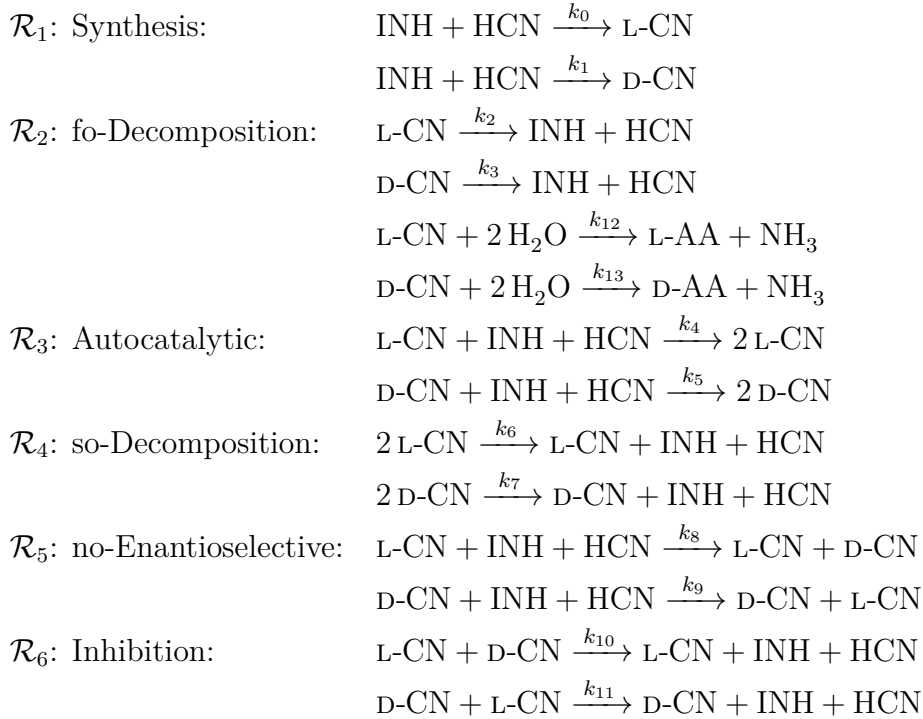


Figure 2. Simulations for the KNS-AP model. A-) Time series, B-) Bifurcation diagram for the autocatalytic rate constants, and C-) Bifurcation diagram for the synthesis rate constants. The initial concentrations of the isomers were 1 for the left side plots (without perturbation), and 0 and 2 for the right side (with perturbation).



This model is almost equal to the previous one, except that we added the two non-enantioselective reactions $\text{L-CN} + \text{INH} + \text{HCN} \xrightarrow{k_8} \text{L-CN} + \text{D-CN}$ and $\text{D-CN} + \text{INH} +$

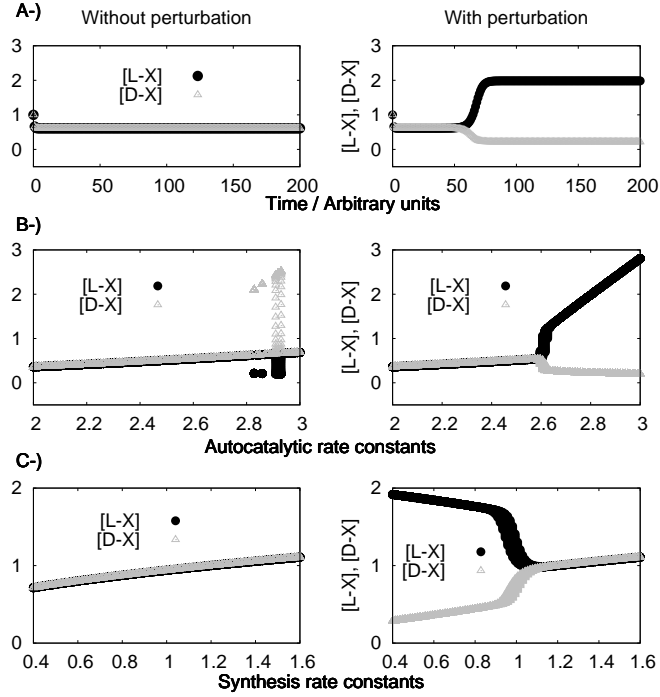


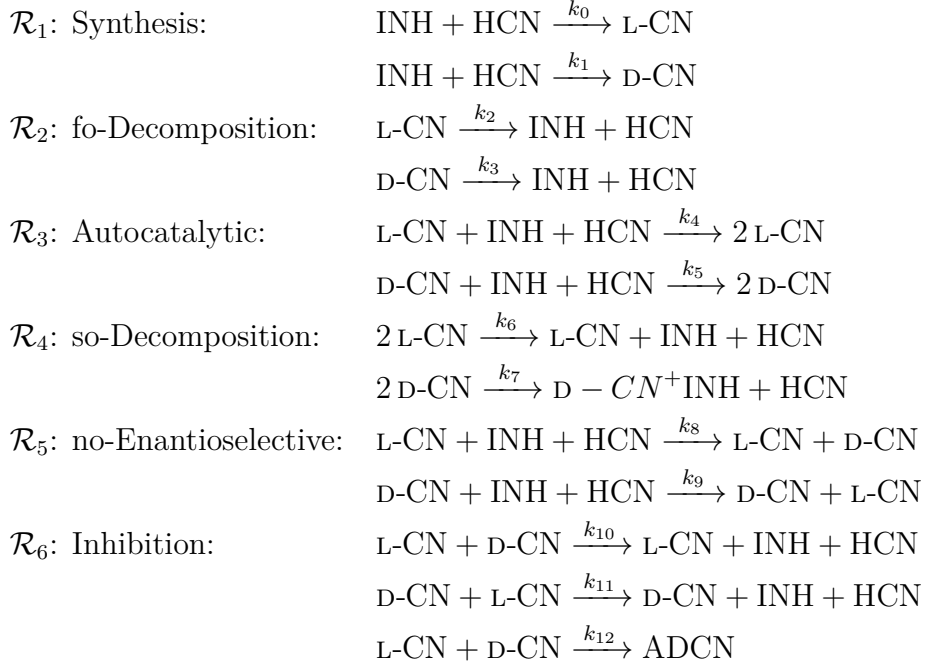
Figure 3. Simulations of the KNS-AP-LES model. A-) Time series, B-) Bifurcation diagram as the autocatalytic rate constants are changed, and C-) Bifurcation diagrams as a function of the synthesis rate constants. The initial concentrations of the isomers were equal to 1. Left side without perturbation, and right side with a perturbation of 1×10^{-7} in one of the isomers. Some unperturbed experiments behave like if they were perturbed because of numerical error intrinsic to the computation as it can be seen in B-), left side.

$\text{HCN} \xrightarrow{k_9} \text{D-CN} + \text{L-CN}$ [14], as well as their reverses which are inhibition reactions. With this modifications, the new model is able to produce λ -homochiral states. Using our algorithm we get the following data:

$$\begin{aligned}
 k_2 &= k_3 \in (0, \infty) \\
 k_4 &= k_5 \in (k_2, \infty) \\
 k_6 &= k_7 \in \left(0, -\frac{k_2}{2} + \frac{k_4}{2}\right) \\
 k_8 &= k_9 \in (0, -k_2 + k_4 - 2k_6) \\
 k_{10} &= k_{11} \in (Max(0, -k_2 + k_4 - k_6 + k_8, -k_2/2 + k_4/2 - k_6 + k_8/2), \infty) \\
 k_0 &= k_1 = k_{10} + k_2 - k_4 + k_6 - k_8
 \end{aligned}$$

We have that the following set of rate constants $k_0 = k_1 = 0.2$, $k_2 = k_3 = 1$, $k_4 = k_5 = 2.8$, $k_6 = k_7 = 0.25$, $k_8 = k_9 = 0.25$, and $k_{10} = k_{11} = 2$ give place to a Frank state. Figure 3 shows the results of our simulations using those values.

The third model is the Kondepudi-Nelson-Strecker-Limited-Enantio-Selectivity (KNS-LES) model given below.



We observe that this network is autocatalytic, and that it contains inhibition reactions whose stoichiometric coefficients are negative. According to our results, this network must be λ -homochiral. We use our algorithm to find a suitable definition of the set of Frank states. We get the following conditions:

$$\begin{aligned}
k_2 &= k_3 \in (0, \infty) \\
k_4 &= k_5 \in (k_2, \infty) \\
k_6 &= k_7 \in \left(0, -\frac{k_2}{2} + \frac{k_4}{2}\right) \\
k_8 &= k_9 \in (0, -k_2 + k_4 - 2k_6) \\
k_{10} &= k_{11} \in (0, \infty) \\
k_{12} &\in (\text{Max}(-k_{10} - k_2 + k_4 - k_6 + k_8, -k_{10} - k_2/2 + k_4/2 - k_6 + k_8/2), \infty) \\
k_0 &= k_1 = k_{10} + k_{12} + k_2 - k_4 + k_6 - k_8
\end{aligned}$$

We can use the above data to sample the set of Frank states. We have for instance that the equalities $k_0 = k_1 = 1$, $k_2 = k_3 = 1$, $k_4 = k_5 = 5$, $k_6 = k_7 = 1$, $k_8 = k_9 = 1$, $k_{10} = k_{11} = 2$ and $k_{12} = 3$ determine a Frank state. We simulate the dynamics that occur in the vicinity of the later state. We have, once again, that perturbations of Frank states give place to homochiral dynamics, while perturbations of non-Frank states give place to dynamics that evolve towards racemic concentrations, see Figure 4.

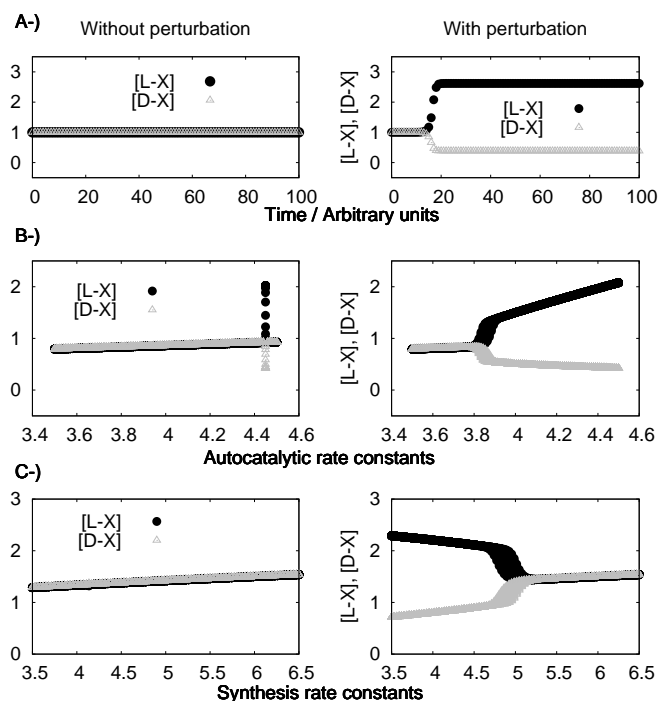


Figure 4. Simulations of the KNS-LES model. A-) Time series, B-) Bifurcation diagram as the autocatalytic rate constants are changed, and C-) Bifurcation diagrams as a function of the synthesis rate constants. The initial concentrations of the isomers were equal to 1. Left side without perturbation, and right side with a perturbation of 1×10^{-7} in one of the isomers. Some unperturbed experiments behave like they were perturbed because of numerical error intrinsic to the computation as it can be seen in B-), left side.

The reported experiments seem to indicate that the tools developed in this work are appropriate for the analysis of chiral networks: Networks that are classified as non-homochiral cannot give place to homochiral dynamics, while Frank states of homochiral networks give place to homochiral dynamics.

9 Concluding remarks: On the probability of being homochiral

We have found a mathematical condition that seems to be related to the homochirality observed in a particular set of chemical networks (chemical mechanisms or models). It is easy to fulfill the aforementioned condition which seems to be related to homochirality: It is enough to count with autocatalytic and inhibition reactions. Moreover, if Ω is an autocatalytic and inhibition network, the probability of being a Frank state of Ω becomes

non-negligible. The later probability can be defined as the quotient

$$\frac{\text{Vol}(\mathcal{F}_\Omega)}{\text{Vol}(\mathcal{S}_\Omega)}.$$

Here, we use the symbol \mathcal{F}_Ω to denote the set of Frank states whose ℓ_1 -norm is equal to 1, and we use the symbol \mathcal{S}_Ω to denote the set of steady states whose ℓ_1 -norm is equal to 1. The volumes of \mathcal{F}_Ω and \mathcal{S}_Ω can be effectively computed using polyhedral computation, and it can be said in advance that all those quotients (probabilities) are non-negligible. Thus, chiral networks are likely to be λ -homochiral (the conditions are not demanding), and steady states of chiral networks are likely to be Frank states. We argue that from a mathematical point of view homochirality is a likely phenomenon.

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Supplementary material. The following files are available free of charge.

- listanalchem.zip: An algorithm for the analysis of the capability of a chemical network (chemical mechanism) to produce homochirality.
- chemulator.zip: A friendly software that can be used to simulate the dynamics of chemical networks and which is based on the DLSODE code. This algorithm can be used to test the homochirality conditions found with the previous software, and it includes the possibility of obtaining bifurcation plots.

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