International Journal of Astrobiology 16 (1): 28–39 (2017)
doi:10.1017/S147355041500049X

Critical role of spatial information from chiral-asymmetric peptides in the earliest occurrence of life

Hugo I. Cruz-Rosas[1,2], Francisco Riquelme[3], Mariel Maldonado[4] and Germinal Cocho[2]

[1]*Posgrado en Ciencias Biológicas, Universidad Nacional Autónoma de México, Ciudad Universitaria, CP. 04510, D. F., Mexico e-mail: hcruz@fisica.unam.mx*
[2]*Instituto de Física, Universidad Nacional Autónoma de México, Ciudad Universitaria, CP. 04510, D. F., Mexico e-mail: cocho@fisica.unam.mx*
[3]*Paleobiología, Escuela de Estudios Superiores del Jicarero, Universidad Autónoma del Estado de Morelos, Jicarero CP. 62909, Morelos, Mexico*
[4]*Facultad de Ciencias, Universidad Nacional Autónoma de México, Ciudad Universitaria, CP. 04510, D.F., Mexico*

Abstract: The earliest functional living system on Earth should have been able to reproduce an ordered configuration and a self-organization dynamics. It was capable of resisting a random variability in time and space to keep the functionality. Amino acids (AAs) and nucleobases generated from abiotic reactions as seen in laboratory-based experiments have demonstrated that molecular elements for life can be obtained by predictable physicochemical processes. However, a functional, self-organized living system needs complex molecular interactions to endure. In this paper, we address the transference of spatial information on highly enantiopure polymers as a critical condition to support the dynamics in a self-organized biogenic system. Previous scenarios have considered almost exclusively the information encoded in sequences as the suitable source of prebiotic information. But the spatial information transference has been poorly understood thus far. We provide the supporting statements which predict that the ordered configuration in a biogenic system should be significantly influenced by spatial information, instead of being exclusively generated by sequences of polymers. This theoretical approach takes into consideration that the properties of mutation and inheritance did not develop before definition of the structures that allow the management of information. Rather, we postulate that the molecular structures to store and transfer information must exist at first, in order to retain particular functional 'meaning', and subsequently, such information can be 'inherited' and eventually modified. Thus, the present contribution follows the theory that life was originated from an unstable prebiotic environment that involves the early spatial information transference based on large chiral asymmetry.

Received 2 September 2015, accepted 27 October 2015, first published online 19 January 2016

Key words: biochirality, biogenic system, origin of life, self-organization, spatial information.

Introduction

Interactions between chiral organic compounds (including those with axial chirality) are deeply investigated in multiple contributions. Some examples are the recognition of D-glucose by cellular transporters (Yang *et al.* 2001; Tyagi *et al.* 2007), DNA, RNA and protein supramolecular interactions (Pablo & Sauer 1984; Williamson 2000; Simonneaux *et al.* 2014), and other recognition processes involving chiral molecules and macromolecular surfaces (Peczuh & Hamilton 2000; Berthod 2006; Tamura 2011; Yin *et al.* 2015). Accordingly, the living systems are organized on chiral asymmetry to optimize its inner space. This reduces the amount of interacting elements both in molecular reactions and in spatial recognition between macromolecules. In this sense, the (bio-) homochirality is expressed as the exclusive use of D-ribose and D-deoxyribose in the synthesis of nucleic acids (RNA/DNA) and the use of L-amino acids (L-AAs) for protein formation (Kauffman 2011). Because of the use of only one version of handedness, it is clear that the homochirality in biological systems supports the decreasing of uncertainty in molecular and supramolecular interactions and keeps an internal enantiomeric bias (a chiral order). Opposed to, when the number of interacting elements increases by the use of heterochiral components, it shows that this introduces ambiguity in the system. Thus, the heterochirality in living systems not only introduces uncertainty on molecular interactions, but also causes a failure in the information content in polymers with chiral elements (Carroll 2009).

Another distinctive feature that any living system must have as a fundamental condition is the use of information to self-sustain (Trifonov 2011). It has been largely considered the importance of the information transference by coding sequences (Eigen 1993; Radu 2004; and others). However, the information contained in the conformation (the geometry) from

molecular structures (spatial information) must be distinguished from the information encoded in sequences in order to understand the system functionality.

Previously, it has been addressed both theoretically and experimentally the key role of enantiopure peptides in the first occurrence of life (Brack & Orgel 1975; Brack 1977; Spach & Brack 1979; and others). However, these authors have proposed scenarios that mainly address the information encoded in sequences as the suitable source – almost exclusively – of prebiotic information. Here, the adopted geometry is a secondary contingency by which the molecular structure becomes endurable and the chiral-asymmetry is retained, but mostly, the order in the peptide chain is the only desirable information that must be transmitted. Although some authors (e.g. Ogayar & Sánchez-Pérez 1998; Maury 2009; Woolf 2015) have situated the origin of life in a scenario where the information source is the molecular geometry, to our knowledge, no previous published works have traced a whole approach wherein the spatial information transference may result in a biogenic system.

In the present contribution, we consider that the conformational meaning is the message conveyed by nascent-informational enantiopure-peptides. We note that one of the most general and simple function of a polymer is the endurance under environmental disturbances. Thus, we claim that the spatial information in living systems supplied by the handedness in molecules from a polymer is just as important as the information encoded by the sequenced elements. Furthermore, life may be defined as a system that self-sustains an inner homochirality (Carroll 2009). In accordance, here we assume that both homochirality and life conceivability *have the same origin*. This implies that an asymmetric requirement was present in prebiotic conditions.

Evidences for natural-occurring chiral asymmetry apart from those provided in the biosphere are given under interstellar (IS) conditions: The birefringence measurements in the Murchison meteorite have demonstrated chiral asymmetry on mineral surface samples (Arteaga *et al.* 2010). Also, a water-insoluble kerogen-like compound is present in the Allende, Murray, and Murchison meteorites and shows an R-enantiomeric bias (Kawasaki *et al.* 2006). Additionally, meteoritic α-AAs are favouring the L-enantiomer in water-soluble organic material from several carbonaceous chondrites (CCs) (Cronin & Pizzarello 1997; Pizzarello & Cronin 2000; Pizzarello *et al.* 2003; Meierhenrich 2008).

Chiral asymmetry in carbonaceous meteorites is currently addressed and well documented as natural-occurring handedness-imbalance outside the biosphere (Pizzarello & Groy 2011). This suggests that asymmetric chiral systems are also formed in the IS medium and the L-enantiomeric excess (L-EE) in α-AAs is not restricted to terrestrial conditions only. It is a general assumption that molecular asymmetry found in meteorites was able to 'twist' the prebiotic chemistry, by means of delivered components on the Earth (e.g. Shapiro 2000; Brack 2007; Pizzarello 2007; Ehrenfreund & Cami 2010). However, we note that this assumption not necessarily states that meteoritic L-AAs were sufficient to attain significant amounts of these enantiomers in prebiotic Earth. Our assumption is a bit more general: the asymmetry from CCs was the source (the *seed*) of chiral imbalance for non-symmetric native-dynamics.

A possible dynamic is one of enantioselective amplification. Here, meteoritic asymmetry in the water-insoluble kerogen-like compound or in the mineral matrix may be a substrate with chiral domains, having the same handedness, capable of promoting the L-enantiomer preponderance for AAs.

In this context, we take the L-EE in α-AAs as the initial condition in the prebiotic milieu. Here the molecular asymmetric-interactions promote chiral-ordered events. As a consequence, the self-organization processes based on homochiral oligomerizations seem a valid pathway to give rise to enantiopure peptides. The chiral-asymmetric chains can establish supramolecular interactions determined by the distribution of its α-AAs. In accordance with this model, in the present contribution, we postulate that these spatial references are supporting a truly kind of information in the context of supramolecular interactions. This spatial information allows for considering the phenomena of the emergence of chiral-ordered prebiotic-systems as the base to give rise to a functional biogenic system. The present proposal examines the viability of such scenario in the onset of life.

Statements and discussion

There is not a single approach to the concept of information, several theories and systems have been comprehensively proposed (Shannon 1948; Israel & Perry 1990; Lenski 2010; Kohlas & Schmid 2014; Kofler 2014; and others). However, a general overview from the information's approaches shows recognizable traits. Thereby, it can be assumed with confidence that information is an inherent property of the so-called information systems that should present the following conditions:

1. It can be deduced from a process, physical object or representations of something, i.e. information may be understood or interpreted.
2. It is representing processes or components in a system, thus information always is about something which has a meaning.
3. It is reducing the uncertainty in a system, so information allows the discrimination between components.
4. It is a kind of pattern which influences the formation or transformation of other patterns (the patterns can be processes, objects or symbols/tokens): information is transmitted and stored.
5. It is affecting the state of a dynamic system. The information makes possible the 'controlled' changing or definition of the system development.

Considering these five criteria that help to characterize the information, we distinguish at least two sources of information in biological systems. First, the information obtained from the order of monomers in a string, the so-called sequence-coded information; and second, the recognition of a molecular-shape addressed by the orientation of a single or grouped atoms in a molecule, the so-called spatial information.

https://doi.org/10.1017/S147355041500049X Published online by Cambridge University Press

The sequence-coded information

The sequence-coded information is cryptic, in the sense that a message is hidden in ordered molecular-strings, making use of specific sequences to employ information at several times after it is acquired. The sequence-coded information shows an ability to be regulated at the same time that it is used for regulating the system itself. This type of information is also symbolic, because the monomers (or groups of them, such as codons) play this function like tokens (Radu 2004). As symbolic information, a transducer deciphers the sequence-coded information; therefore, this supports the differential expression of information by means of the use of discrete units. In current living systems, this kind of information is the leading content in nucleic acids.

The most likely scenarios of the origin of life are typically focused on the occurrence of a self-replicating polymer, such as the RNA, which emphasizes the emergence of a basic dynamic from sequence-coded information (Jheeta 2015). However, the surrounding physicochemical conditions have an effect in the three-dimensional (3D) arrangement on a polymer. Consequently, the spatial conformation in a macromolecule is another source of information closely related to environmental context. In this regard, the spatial references from a macromolecule can be considered as a source of prebiotic information. Definitely, sequences in a polymer affect its physicochemical behaviour, so spatial references are not rejecting the references in the string. Here, we claim that spatial information is, at least, just as important as sequence-coded information in a theoretical scenario for the origin of life.

The spatial information

Several authors have demonstrated that molecular recognition is implicated in diverse essential processes in biological systems, accomplished by the selective-binding through the spatial data from the geometry of the interacting components (Lo Conte *et al.* 1999; Nooren & Thornton 2003; and others). These spatial references are indeed a source of information. In this regard, the interacting molecules are representing the processes and context that have originated and shaped them (i.e. they have a meaning). They trigger other processes as a result of the interaction (i.e. information is transmitted and interpreted). Therefore, they are reducing the uncertainty in the interactions. In accordance with this, the spatial data are affecting and directing the state of the living systems. Regarding the processes accomplished by transmembrane and nuclear receptors, substrate recognition, enzymatic catalysis and interactions between chiral-compounds, all are supported by the spatial information at the (supra) molecular level (Lehn 1990, 2007).

The spatial information is a case of explicit information. In this regard, it can be received or copied without a transducer. An illustrative example is in biological systems, where the receptor–ligand complex triggers cellular processes by direct 'understanding' of the message by the spatial recognition of the ligand. Explicit information also is of the fact that DNA/RNA cannot produce a whole cell by itself from a complete set of its molecular components, thus the information about the 3D architecture and spatial order is inherited by explicit information from a pre-existing cell (Radu 2004). At the same time, the spatial information is able to convey contextual information as a 'reflex' of surrounding conditions operating on a molecular structure (e.g. the protein folding).

Because the 3D distribution of atoms in a molecule can be described by means of a coordinate system (Carroll 2009), the biological components can be considered as different if its geometric descriptions are not coincident in all their coordinates. In accordance with this, the spatial information is referred here as all data contained in the geometry of a structure which allows the discrimination among the forms *A* and *B*, within a context of supramolecular recognition.

The spatial information is observed in the distribution of single or grouped atoms in the molecules, as well as in the entire form of a structure (recognition of the whole or local molecular shape, spatial complementarity, molecular conformations and structural motifs). As a consequence, the high chiral-order in proteins and nucleic acids has spatial information. The above is shown in the results as presented by Carroll (2009), here binary bits of information in peptides represent the chirality from the AAs. Therefore, proteins are informational entities capable of storing, transmitting and recognizing spatial information in living systems. In accordance with this, subsequently we argue for the spatial information as the type of information that is able to be carried by prebiotic systems, using predominantly the L-enantiopure peptides.

The chiral-ordered interactions and the emergence of enantiopure peptides

The L-EE on AAs in prebiotic Earth is assumed as the initial condition for the present scenario. This assumption is validated by the input of meteoritic chiral-asymmetry, which is the most plausible non-symmetric source influencing the terrestrial chemistry (Bonner *et al.* 1999; Ehrenfreund & Charnley 2000; Cronin & Reisse 2005; Pizzarello 2006, 2007). The increased frequency on molecular interactions related to the L-AAs can lead to highly non-racemic peptides. Polymerization of AAs under aqueous media in prebiotic conditions is possible due to its ability 'to jump' the energy barrier to form chains at high temperatures (above to 100°C), so these organics are one of the most probable molecules for self-assembling to form 3D systems, also with the hydrocarbons and lipids (Kompanichenko 2012a). At the same time, the so called salt-induced peptide formation reaction, also in aqueous milieu, is considered as the simplest and most plausible explanation for the formation of peptides under prebiotic conditions (Brack 2007; Fitz *et al.* 2007).

Such particular interactions leading to the peptide formation are under environmental influences and thermodynamic control, so the racemic condition is stable under symmetric environments. Accordingly, high enantiopure peptides may occur only as a consequence of chiral-ordered events. In our asymmetric scenario, the all-homochiral and the racemic polymerizations are the opposite trends and they are infrequent events due to the significant L-EE assumed. The interactions are

https://doi.org/10.1017/S147355041500049X Published online by Cambridge University Press

dominated by non-racemic but heterochiral assemblages with diverse enantiopurities. Here, low EE is preserved by the enantiomeric environmental bias.

Notably, in this proposal we highlight the environmental non-symmetric chiral-influences (i.e. those given by the L-AAs) from other physicochemical conditions that affect the molecular interactions, such as temperature, pH and salinity, among others. Thus, when these physicochemical conditions are balanced, the polymerization trend adopts regular patterns that result in very similar conformations, which hardly suffer drastic changes after its formation. Particularly, this is the case of numerous hypotheses about the origin of life that assume a hypothetical highly stable environment. However, an unbalanced milieu in the prebiotic Earth lets a constant disturbance on molecular networks and over its products. This makes the polymerization patterns become stable or unstable in turn. Similarly, their conformations are subjected to drastic perturbations which more likely cause its spatial rearrangement, and also the polymer 'disassemble'. Unbalanced physicochemical conditions permit considering a major diversity in conformations and settled molecular-networks, as well as the exchange on them. Chiral imbalance does not cause disturbances on interactions by itself, but the L-EE is only making possible the highly chiral-ordered events on molecular networks while assembly and disassembly of polymers is taking place.

Fluctuations caused by geological variables have been previously considered by Kompanichenko (2009). This author suggests that physicochemical fluctuations have generated a periodic diversity in the prebiotic microsystems (Kompanichenko 2009). When environment displays balanced fluctuations, the disturbance on molecular microsystems is also balanced, thus the network is shifted to nearby thermodynamic states and its chiral-order is maintained with no significant changes. Therefore, polymers and other macromolecular structures are formed with similar extents of enantiopurity. While the environment is becoming unbalanced by energy released during tectonic activity, volcano eruptions, hydrothermal systems or any geochemical changes, and such fluctuations become too sudden, the thermodynamic states by which a molecular network is stable are moving away from each other, destabilizing its interactions. In this context, a new molecular network is defined and a novel enantiopurity degree may be acquired due to the preferential L-AAs incorporation into the microsystem. Gradual input of the meteoritic EE causes a progressive increase in enantiopurity fluctuations from these networks under unbalanced milieu. According to the above explanation, the environmental fluctuations encourage a diversity of molecular interactions in prebiotic microsystems. This notably contrasts with those scenarios that only consider a single type of molecular interaction during polymerization in a hypothetically stable environment.

The sharp environmental oscillations cause a fast destabilization of molecular networks that involves the AAs, thus also a rapid exchange on their chiral-order levels. These interactions are ranging abruptly between near-racemic and near-homochiral peptides caused by the delivered meteoritic L-EE. In this context, prebiotic microsystems constituted by molecular networks joined by a general dynamic, show a degree of chiral-order defined by their asymmetric interactions. Since microsystem configurations are supported by the molecular networks, there are many degrees of chiral asymmetry capable of maintaining a same general configuration. Analogously, there are many stable configurations for one given system depending on the stage of the environmental oscillations. As a result, equivalently enantiopure systems possibly support different configurations at each time, and must coexist with other systems with diverse degree of chiral order.

Because 'accidental' variations have taken place at times of abrupt rearrangement; the interaction networks are exactly neither alike among them at the same stage, nor equal to themselves along the environmental cycle, even though they show an internal periodicity. Therefore, we noted that each of the system configurations is in fact, representative of equally stable microsystems. Among them, we focus on those with equivalent level of chiral-order, which constitute a class of stable microsystems with similar enantiopurity.

Peptides adopt spatial conformations that are stable under the dominant surrounding conditions. Considering the unbalanced milieu, these structures cannot be maintained through a single conformation, but spatial modifications occur over the same enantiopurity of the polymer. Under abrupt fluctuations, these structures are disassembled at minimum and maximum points from the unbalanced cycle of physicochemical variables, so novel polymers are assembled. Consequently, an exchange of chiral-order on peptides is enabled as a result of these 'rebuilding'.

The sharp environmental oscillations provoke a rapid exchange on molecular networks, which may get different extents of chiral asymmetry ranging from quasi-racemic until quasi-homochiral. Therefore, the microsystems are becoming able to acquire particular chiral-order state between these opposite endings. A rapid alternation between the opposite states is tautening the networks, until the microsystem assumes a dual nature. Both prebiotic conditions of the high L-EE and the unbalanced physicochemical fluctuations are causing that the microsystem cannot hold the ends of chiral-order in its configuration, so a bifurcation is routed.

Additionally, the branching in the dynamic arises under a period of greater rearrangement on interactions. The bifurcation zone supports a far from chiral-equilibrium dynamic wherein polymerizations may occur with high chiral-order and retain the asymmetry in remnants of peptides. The above induces a subsequent development by which the resulting interactions will be defined with a new extent of chiral-order. The phenomenon of bifurcation does not depend exclusively on external factors, but also on the ability of the microsystem to establish a 'thrust' over the constant exchange of interactions. Once that bifurcation is done, both ends of chiral-order may give way to peptides with the ability to adopt enduring stable conformations under persistent sharp unbalanced fluctuations from the milieu. The new developed path of the microsystem goes back to balanced oscillations over its interactions, but with a novel degree of chiral-order defined by the bifurcation, as seen in Fig. 1.

https://doi.org/10.1017/S147355041500049X Published online by Cambridge University Press

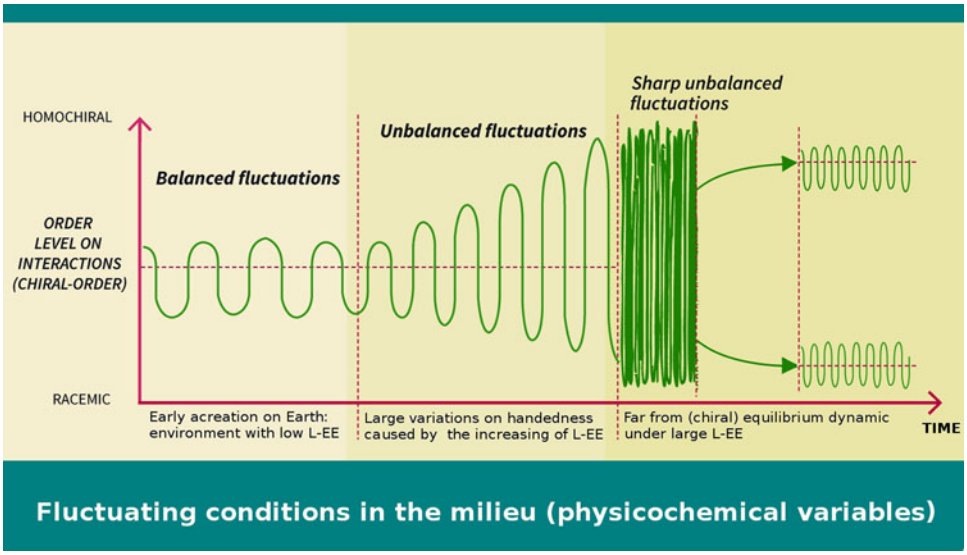

Fig. 1. Schematic diagram illustrating a model for bifurcation of chiral-order in molecular interactions where unstable prebiotic conditions prevail.

Figure 1 shows that under non-equilibrated environment, there are three general stages that influence the amplitude of the chiral-order interactions by which enantiopure peptides presumably arise:

1. The milieu with significant low EE keeps preferential homochiral interactions with L-AAs. The assembling and disassembling of peptides is done between neighbouring degrees of enantiopurity. This is defining balanced oscillations in the chiral-order of interactions. Peptides with low-enantiopurity dominate the microsystem configurations.
2. During the Earth accretion phase, the progressive input of chiral-asymmetry provokes an increasing in the amplitude of enantiopurity variations, while interactions are setting and unsetting. In this context, with sharp unbalanced oscillations, there is an assembling and disassembling of structures giving rise to the distal ends of near-racemic and near-homochiral peptides. The polymerizations will be switched abruptly between these ends of symmetric and asymmetric interactions.
3. The large L-EE content and external sharp perturbations cause an almost simultaneous occurrence of both chiral-ordered ends. The bifurcation in the chiral-order induces the new way for development of interactions between the opposite extents of chiral-asymmetry. The microsystem configurations adopt its novel enantiopurity level.

After its passage through the critical zone, the molecular networks define a further development by the following four possible general branches: (A) an equivalent chiral-condition to the initial one; (B) a complete thermodynamic stability by networks based on fully racemic interactions, (C) a develop of low chiral-order whereby thermodynamic stability increases but is not reached (i.e. racemic interactions are predominant over the homochiral ones), and (D) a high chiral-order by which the network is able to move further away from its equilibrium. Only the last two branches are depicted in Fig. 1.

In this context, it is possible the emergence of conformations that are able to support a broad range of external variations by the molecular structures. Resistant conformations on peptides retain their L-EE and the enantiopurity of the system. Presumptively, this is the base for extending the acquired chiral-order in the configuration. Enantiopure peptides may influence molecular interactions that promote the homochiral encounters and also support the emergence of chiral-ordered supramolecular pairing, such as the matching interactions. The β-sheet architectures on polypeptides give rise to amyloid conformations, which are broadly resistant structures and have been proposed as relevant entities for the origin of life in the Amyloid World hypothesis (Maury 2009). This resistant conformation is supporting the permanence of a prebiotic system. As a result, enantiopure amyloid peptides are structures that may keep the chiral-order and work as templates for subsequent nucleation or polymerization events. Thus, the chiral-order can be amplified in the microsystem.

*The thermodynamic trend inversion (*sensu *Kompanichenko 2008)*

The thermodynamic trend in living systems is to increase the internal free energy and concentrate information, which overcomes entropy that they produce. If we want to link both prebiotic chemistry and living systems, then, the distance between life and non-life entities seems to be abysmal. There is a hypothetical scenario, developed particularly by Kompanichenko (*sensu* 2008), referred to as the thermodynamic trend inversion. This suggests a reduction on this gap among life and non-life entities as a consequence of spontaneous, self-organized, highly ordered events (Kompanichenko 2009, 2012a, b, 2014).

This scenario assumes the unstable prebiotic environment wherein highly ordered, uncommon-spontaneous events occur in microsystems. Here, the non-living ratio of entropy/free-energy presumably can be reversed at times, favouring the storage of free energy and order in structures of low

https://doi.org/10.1017/S147355041500049X Published online by Cambridge University Press

entropy. Correspondingly, in the present contribution we follow the chiral-ordered interactions as a particular way for the thermodynamic trend inversion. In this context, transference of spatial information between endurable–enantiopure peptides can be the property leading to the occurrence of biogenic systems on Earth.

The present hypothesis supports the critical role of the spatial information transference, which retains the configuration of prebiotic microsystems. Most likely, this critical role of the spatial information transference may be achieved by supramolecular-interactions between enantiopure structures with the ability to transfer stable conformations. The above may lead to a system stable-configuration. The resulting stabilized configuration can be the basis for the subsequent development of self-catalytic polymers, such as those proposed in the RNA and RNA–Protein World hypothesis (Kaddour & Sahai 2014). In addition, the hypothesis as presented here can be linked to the origin of a collectively autocatalytic set as proposed by Kauffman (1986, 1993; Hordijk *et al.* 2010).

Also, the prion-like matching mechanism that induces the 3D rearrangement has been suggested as a key property in prebiotic systems. Thus, information provided by conformations is the source of references by which a spatially ordered structure presumably is spread in a molecular network. Peptides which are able to induce a conformation change in prebiotic systems have been called 'conformers' (Ogayar & Sánchez-Pérez 1998). In accordance with the Amyloid World hypothesis, highly enantiopure enduring conformers probably transfer these kinds of resistant conformations by means of matching with equivalent enantiopure peptides. Therefore, they contribute to keep the chiral-order and also provide structural stability to the configuration. So we consider that the dynamic (the kinetic pathway) based on preferential polymerization of the L-EEs is favoured over the thermodynamic pathway when these enduring conformers arise in microsystems.

As noted, the initial data mentioned above suggest that our theoretical scenario is placing at an earlier time to the moments considered in the RNA-World hypothesis. Although nitrogenous bases, several sugars and other chemical precursors for nucleobases have been identified in the CCs (Sephton 2002; among others), neither nucleotides as such nor chiral bias are observed thus far. Terrestrial chiral influences that produce the EEs have been ruled out due to their inability to represent a real asymmetric source (Bonner 1995). As a consequence, if the RNA-World was not preceded by specific previous steps, it is quite possible that the RNA started racemic and the asymmetry requirements were meeting after the establishment of a well-defined biogenic dynamic. With racemic RNA, the first incorporated peptides/proteins were racemic too (or poorly asymmetric) because the chiral-order was not a restriction for the dynamic. In such scenario, the homochirality is an exclusive consequence of the occurrence of life, which is related with the meteoritic handedness by the opportunist character of living systems (i.e. the use of the most abundant sources). Although the latter cannot be rejected, the spontaneous polymerization on nucleobases is difficult to assume due to the fact that they cannot easily 'jump' the energy barrier for self-assembles in aqueous milieu, mainly because ribose is unstable under temperatures greater than 100°C (Larralde *et al.* 1995), temperature upon RNA monomers can be spontaneously self-assembled. The early prebiotic managing of spatial information by means of endurable-enantiopure conformers likely contribute to reach the conditions of stability in a system to allow the emergence of the RNA as the polymer driving the self-replicating systems. In the following section, a *theoretical* scenario is described, by which the biogenic systems may occur with the property of carrying spatial information by endurable (like-amyloid) highly enantiopure peptides.

Tracking the mechanism in the onset of biogenic systems

Different stable configurations at the same time can be supported by states with equivalent level of order, such as symmetry, lattice periodicity frame or internal regionalization. Thus, several microsystems can be originated with similar extent of chiral asymmetry, which is the class of equivalently enantiopure microsystems. Additionally, a same microsystem can take more than one level of chiral order by going through the abrupt oscillations of the milieu. The influence from environmental variations promotes the stabilization or destabilization of configurations based on chiral extent, which restricts or allows inner interactions and continuity of molecular structures. In consequence abrupt exchange between configurations with lower and higher chiral-order by sharp environmental oscillations causes the microsystem to endure two opposite chiral-states in rapid alternations. As a result, chiral-asymmetric systems meet the four general properties earlier defined by Kompanichenko (2009) for bistate-microsystems: (i) they present a latent dual structure (racemic/homochiral trends in our case), (ii) have a dichotomy at the end of the normal cycle of its existence as bistate systems (the definition of a novel chiral extent in their configuration), (iii) show an oscillatory character of their existence (recurrence on the degree of enantiopurity for interactions involving the AAs) and (iv) they present a deployment of mutability and inheritance not yet in the biological context: modifications/rearrangements on molecular and supramolecular chiral-asymmetric interactions and the presence of enantiopure peptides that lie beyond a particular system configuration.

On account of this last property, we propose herein that the ability to store and to transfer information is an active feature in the system, only if the structures that support such dynamics are present. This is due to the fact that the conditions that allow the store and transfer information must exist before the information can be inherited and modified. In regard to the spatial information, the trait to manage (the information) is a consequence of the supramolecular dynamics in the prebiotic system.

The properties in any microsystem are observable traits caused not only by their inner dynamics but also due to the relationships between the system and the environment. The elements that build up putative informational structure presumably are already present but not interacting specifically among them. Both (quasi-) racemic and (quasi-) homochiral peptides can constitute conformers, as well as those with intermediate extents of enantiopurity. However, probably this

https://doi.org/10.1017/S147355041500049X Published online by Cambridge University Press

incipient structure cannot actively manifest its traits of storing and transferring spatial information at the beginning. The matching between homochiral conformers require fewer 3D tuning to fit than those between the racemic ones, because the pairing is due to the steric, hydrophobic, other non-covalent and spatial restrictions on supramolecular interactions (Janin 1996; Gabb *et al.* 1997; Chakrabarti & Janin 2002). Accordingly, the inductions of conformational changes between peptides occur at high rates while the enantiopurity in the polymer is increased. Therefore, sharp perturbations on microsystems more possibly is 'buffered' by the fast spreading of resistant peptide conformations via the matching between highly enantiopure conformers.

In addition to the high rate for spreading of resistant conformations among largely enantiopure conformers, it is not difficult to see that a low-asymmetric microsystem has a highly diverse of polymers than other high-asymmetric system. If we had a microsystem with N monomers of the same chemical specie that will build up a polymer (e.g. AAs to form peptides), and M of them are chiral ($0 < M \leq N$). So, how many N-mers from those monomers can we get? Case 1: if the set of monomers is homochiral, then all the M components have the same handedness and they will alternate with the N–M achiral monomers to occupy every position. Therefore, the M and the N–M monomers need to be ordered to constitute each N-mer, so we have the ordering with no replacement of the N elements chosen from samples of N length (i.e. their permutations). Thus, the homochiral set can give rise to $N! = N \times (N–1) \times (N–2) \times \cdots \times 2 \times 1$ different polymers. Case 2: if the set of monomers is racemic, then each of the M chiral components has its antipode, as a result, the microsystem has $N + M$ monomers to build up the N-mer (there are $2M$ chiral components plus the N–M achiral ones). The $2M$ chiral monomers are alternating with the achiral elements to form the N-mer. Hence, ordering without replacement of the $N + M$ elements is $(N + M) \times ((N + M)–1) \times ((N + M)–2) \times \cdots \times (M + 2) \times (M + 1)$, this is the amount of the different polymers of N length, from a racemic set of monomers. We observe that the diversity on polymers of a given N-length is greater in a racemic microsystem than in a homochiral one: because of the first term in the ordering expressions, we have $N < N + M$ (more diversity in the racemic case), thus in the second term $N - 1 < (N + M) - 1$, and so on until we get the Nth term, where $1 < M + 1$. The different cases of intermediate enantiopurity are between these ends.

This high diversity provides more significant chances to stabilize the conformation through some conformer. On the other hand, once this has happened (the occurrence of conformers), the induction of the conformational change by matching has also more options to get a successfully 3D induction. Furthermore, the dynamic under sharp variations of physicochemical conditions involves rapid environmental changes that exceed the spreading rate of endurable peptide conformations due to more options to interact. Although the conformers more likely are abundant in racemic systems, also there are too many intermediate interactions to attain a successfully supramolecular fit. As a consequence, more diversity on polymers involves a lot of time to get a supramolecular matching to buffer the external perturbations, which represents not the best option for the system permanence under a sharp fluctuating milieu.

Accordingly, when bifurcation has routed the system to a low-asymmetric path, a dynamic based on resistant lowly enantiopure conformers will be overwhelmed by the acute disturbances. More options on the fit-matching, not all of them successfully, makes the physicochemical disturbances surpass the rate of matching, promoting the consequent disassemble of peptides with similar low extent of chiral asymmetry. As a result, the transference of spatial information (of enduring conformations), based on high-enantiopure peptides, is beginning to be a very outstanding property for the permanence of the systems and decreases the uncertainty on matching.

Thus, the thermodynamic trend inversion may occur supporting a biogenic dynamic trough the chiral-order in peptides, which is a parameter of order. According to this model, the present hypothesis states that the chiral asymmetry was the initial condition that supports the ability of carrying the spatial information as an active property in prebiotic microsystems, when the large EE was present in nascent informational structures.

Figure 2 illustrates the occurrence of abrupt chiral-ordered events, where the presence of highly enantiopure peptides might be assumed. The microsystems from a class of equivalently chiral-ordered systems support a finite amount of configurations and dynamics at each variable stage in physicochemical conditions. This allows a wide range of emergent properties that are not entirely recurrent at all. As a consequence, the happening of a specific property favoured by an environmental stage, does not result from an unlikely or isolated event, but rather from the 'arbitrary' selection or favouring of any from the microsystems belonging to the class. Figure 2 shows two self-organization events: each of them allows the acquiring of chiral-order in particular configuration (not necessarily in the same system). Despite of these highly ordered events, the average chiral order in the configurations is low.

It is worth mentioning that the homochiral aggregation/oligomerization events do not represent unique self-organizing stages. These represent events occurring in the class of systems with equivalent level of chiral-order. Inside of the configurations from a class, it can be found peptides with the same enantiopurity. Consequently, the emergence of a peptide with high chiral asymmetry neither is a unique event nor has the property of managing the information as unavoidable outcome. Enantiopure conformers are a particular kind of peptides.

On the other hand, the class is only making reference to the simultaneous existence of microsystems with equivalent level of chiral-order and does not necessarily represent physical grouping of systems in particular regions from the prebiotic milieu. The number of members in a class decrease during the abrupt-ordered event and it is increased when returns to the initial conditions of low chiral-order. If nascent (spatial-) informational polymers occur in members of a class, resistant conformations might be transferred, also can help the microsystem to buffer the environmental disturbances. Given the above information it can assume that this structure has been

https://doi.org/10.1017/S147355041500049X Published online by Cambridge University Press

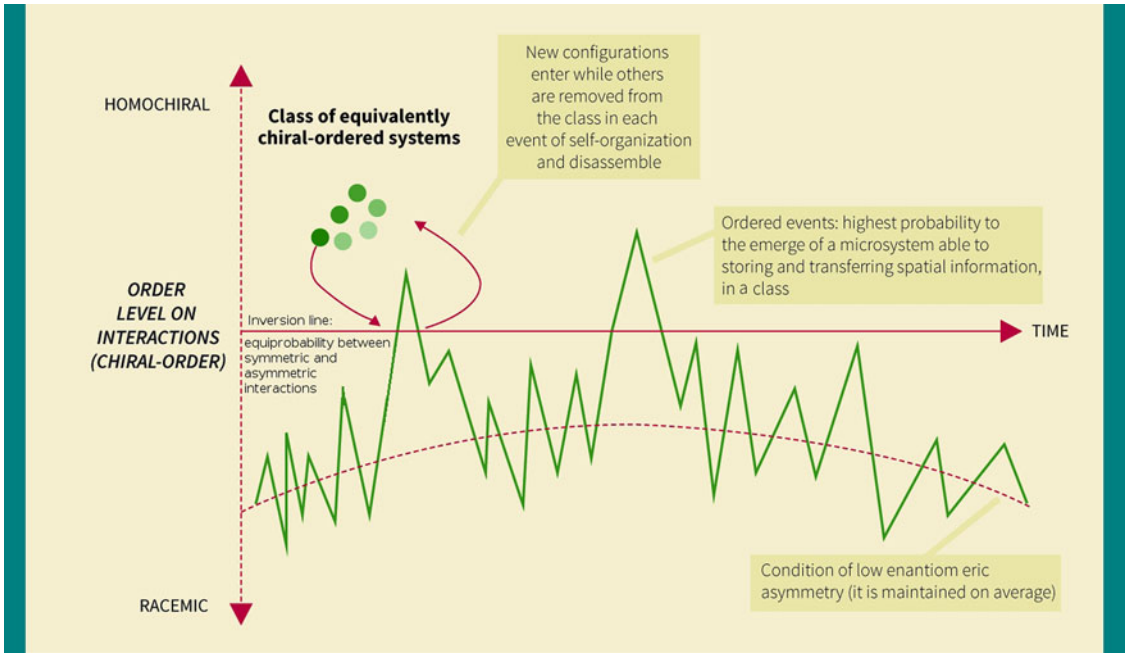

Fig. 2. Hypothetical curve illustrating the spontaneous self-organization events for a highly probable dynamics allowing to store and transfer spatial information in prebiotic systems. Data as presented follow Kompanichenko (sensu 2008).

incorporated into the configuration as an active component. Otherwise, if the polymer does not have behaviour as a conformer or if it is not actively incorporated into the configuration, even if it has a high chiral purity, it will be removed without effects on the chiral-order in the system configuration.

Abrupt events of high chiral-order may give way to self-organization dynamics by highly enantiopure peptides. They increase chiral asymmetry working as templates for enantioselective nucleation or oligomerization, whereas enduring conformers keep the chiral-order in configurations. In this class of equivalently enantiopure microsystems, the free energy might be stored in chiral-ordered polymers and may also exceed the internally produced entropy. As a result, the kinetically preferred pathway dominates at such times, over the thermodynamically preferred pathway. The 'optimal' balance among kinetically- and thermodynamically preferred pathways, going forward over the chiral asymmetry, is a key route to set the stage for the arrival of prebiotic (enantiopure-) self-replicating molecules, in accordance with the property proposed by Scott *et al.* (2014).

Figure 3 indicates two possible trends in chiral-order interactions as a consequence of environmental restrictions over the microsystem configurations. Due to the external perturbation is exerting constraints on interactions, and because the noise associated with the periodicity of the milieu is random, the systems do not take exactly the same configurations despite the environmental periodicity. Thus, we firstly noted that the possible configurations in a microsystem under certain external conditions do not represent all possible configurations that it can admit. We secondly observed a finite set (constrained by the milieu) that are not exactly the same set for equivalent stages in the cycle. In accordance with these observations, unbalanced oscillations allow regularity on the configuration appearance with equivalent level of chiral-order, while it allows the diversity of peptides (and structures) in classes from the enantiopure-prebiotic microsystems. The possible configurations based on an extent of chiral-order are not depleted at all, but novel of them occur in each physicochemical cycle.

As shown in Fig. 3, the upper line indicates the evolutionary trend from the abrupt self-organization events. This may support a dynamic that is able to keep an acquired order and endure despite of external forces. Thus, the external influences act on the system when the configuration is dominated by interactions of high chiral-order. Subsequent development in configurations keeps chiral asymmetry in structures and environmental factors, that restrict certain dynamics while are enabling the active play for another ones, are the trigger. Bottom line illustrates the branch by which the external influences constrain a particular dynamics in any configuration, causing destabilization of the system when the maximum value of chiral-order in the self-organization event has been left behind. Therefore, it is not able to neutralize the external influences. Thus, it is oriented to disorder and eventually disappears as a unity.

Internal constraints have similar results that allow diversity in molecular configurations. However, these inner restrictions are randomly originated by incorporation of new molecular components or by random modifications in its architecture as observed in polymers. Thus, the favouring of a specific representative from a class of equivalently enantiopure systems also means the favouring of properties supported by the configuration and macromolecular structures belonging to that microsystem. Thus, the onset of biogenic systems is the result of the occurrence of informational structures involved in their configuration. Furthermore, potentially biogenic dynamics

https://doi.org/10.1017/S147355041500049X Published online by Cambridge University Press

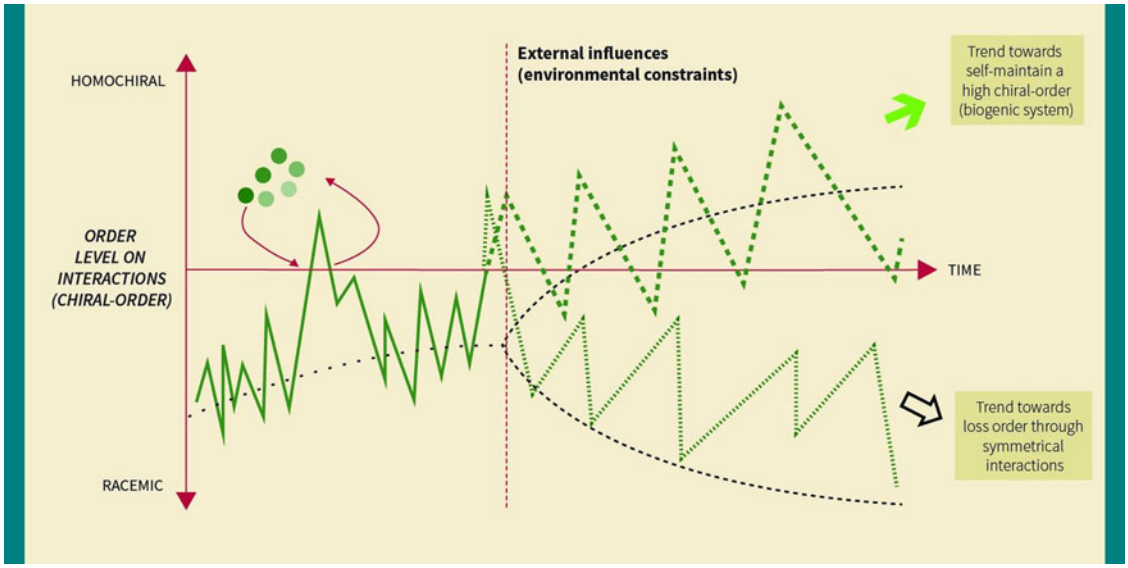

Fig. 3. Hypothetical curves illustrating two possible trends in chiral-order interactions caused by disturbance from the milieu, which induce bifurcation in chiral interactions and separation among prebiotic microsystems with low or high chiral-order. Data as presented follow Kompanichenko (sensu 2008).

from the spread of enantiopure-endurable-conformations may lead to a particular way of the thermodynamic trend inversion and reduce the distance between living and non-living systems.

Additionally, the microsystems can be oriented to keep a high chiral-order due to their interactions with the milieu as seen in the upper trend in Fig. 3, if this happens, the presence of enduring peptides coming from homochiral interactions might be assumed. The system composed in this manner may be favoured ('selected'), if it is able to store and transfer those enantiopure conformations. Due to drastic variations in the surroundings, enantiopure peptides which are resistant at a particular time, they are not at another moment, suffering spatial rearrangement or, even, they are disassembled. This allows the occurrence of new conformations in the microsystem, where they do not destabilize the configuration with their replacement and also support the integrity of the system. These enduring enantiopure conformers are emerging and consequently, the microsystem will remain with opportunities to maintain its highly chiral-ordered configuration and the flow of (supramolecular) spatial information. Following the trend that retains a high chiral-order, the homochiral dominate over the heterochiral interactions. So, if the environmental constraints are influencing the microsystem when chiral-asymmetric interactions promote the formation of enantiopure structures, then, the preferential polymerization of L-AAs makes most plausible both the emergence of resistant conformers, and the maintenance of a configuration by buffering/counteraction of the external influences. As a consequence, an immediately adjacent event of self-organization is highly probable to occur.

In contrast, as seen at the bottom from Fig. 3, the trend towards loss of chiral-order in the system is defined when the chiral-asymmetric dynamics of self-organization has left behind its maximum value and goes into the stage of disassemble of enantiopure structures. Here, the heterochiral interactions have a greater influence in the molecular configuration. As a consequence, the resistant low-enantiopure conformers cannot counteract the sharp disturbances from the milieu. In these cases, the spatial matching needs to spend many events of pairing to let a specific peptide that can support the induction of conformational changes. Thus, the general trend in this scenario is to lose both chiral-order and system unity.

Several examples of self-organization have been considered to explain the formation of organized structures or patterns in the prebiotic Earth, closely linked to the onset of life (Eigen 1971; Oparin & Gladilin 1980; Cornish-Bowden & Cárdenas 2008; Cleaves 2013). These kinds of processes give rise to spontaneous events with high order and dynamism, such as those reported by Leduc (1912). As was the process in the plasmogeny theory reported by Herrera (1924, 1942). In this regard, although the goal of synthesizing a living system in the laboratory was not reached by the later authors, their experiments have demonstrated that it is possible to abruptly generate ordered structures (with spatial and dynamical analogy to the biological forms) by the influence of physicochemical forces only. Additionally, the patterns in the Belousov–Zhabotinsky reaction are also examples from abiotic systems that can support the emergence of a heterogeneous dynamics, which are able to keep ordered patterns by themselves. Most likely, self-organization is a closely model for the formation of enantiopure peptides, whose stochastic self-assemble was the trigger for carrying of spatial information as an emergent property in the microsystem.

Once achieved the occurrence of chiral-asymmetric conformers in the configuration, the appearance of an autopoietic network can be supported (Varela *et al.* 1974). As a consequence, this putative enantiopure–autopoietic microsystem was able to maintain cohesion by itself, and it was also able

https://doi.org/10.1017/S147355041500049X Published online by Cambridge University Press

to support its subsequent development towards the ability to reproduce its (entire) configuration. So it evolved as a spatial and temporal unity, and the homochiral condition in the informational polymers (proteins and nucleic acids) is an accomplished consequence of this. Following the outcome of the biogenic system as an autopoietic network based on conformers with high L-enantiomeric purity, the properties that are commonly considered distinctive for life, such as to evolve, reproduce, to handle and differentially express information in nucleic acids (Trifonov 2011), it can support and deploy them in subsequent stages.

In addition, the influence of cooperative events during the structure formation may be considered. For example, the formation of asymmetric aggregates with high enantioselectivity has been introduced into discussions about the origin of the bio-homochirality (Micali *et al.* 2012). Also Gleiser *et al.* (2012) show these cooperative effects using mathematical modelling in chiral-selective polymerization from open network reactions. In this sense, Ribó *et al.* (2001) have reached asymmetric nucleation by stirring with achiral molecules, where an initial seed of nucleation with axial chirality is considered the inset for the cooperative process. However, the results and data as presented in these previous experiments are symmetric unless there is an asymmetric influence (see Palmans & Meijer 2007 for an overview about amplification of chirality). The non-symmetric influence which is considered in the present proposal is the chiral imbalance due to the input of the meteoritic EE.

As presented, our hypothesis leads to consider the occurrence of biogenic systems as a result of the managing of spatial information in chiral-ordered microsystems. This managing initially means that the prebiotic system was able to spread its endurable (peptide) structures, achieving the buffering or even the counteraction of the external influences. This spreading occurs through highly enantiopure conformers, which grants the possibility to store structural-stabilizing peptides. At the same time, the enantiopure conformers constitute the first informational entities that are capable to store environmental references in the system by stable conformations, as well as disseminate them through its configuration. Therefore, the microsystem becomes able to sustain its unity by itself at different conditions through time.

Conclusions

As we currently know, one of the most outstanding necessary conditions for the onset of a biogenic system is the existence of structures with an active ability to store and transfer spatial information that allows the system to be endurable. It is also requiring a particular conformation on highly enantiopure structures to deploy this property on (supramolecular) interactions. As a consequence, the enantiomeric purity allows the emergence of the informational property as collective trait in prebiotic polymers.

Subsequently, the environmental influences that cause deformations on the system configuration may be 'fixed' or stored in enantiopure peptides with ability to transfer spatial information to other enantiopure polymers or equivalent chiral-asymmetric structures under forming processes. The mechanism for this transference can be similar to those deployed by extant prions, including the matching and the induction of conformational changes.

In addition, with a prebiotic system able to 'make use' of spatial information, the biogenic systems may emerge as a result of the transference of resistant conformations among enantiopure peptides, reducing the distance between living and non-living systems. It can be achieved a scenario of the thermodynamic trend inversion. The enantiopure peptides are very suitable structures for the start-point of the homochirality observed in current biological systems.

Thus, the theoretical proposal herein predicts that the ordered configuration in a biogenic system should be significantly influenced by spatial information, instead of being exclusively generated by sequences of polymers. Furthermore, we conclude that the properties of mutation and inheritance were not developed before definition of the structures that allow the management of (spatial) information. Rather, the molecular structures to store and transfer information must exist at first, in order to retain particular functional 'meaning' and such information can be subsequently 'inherited' and eventually modified. The carrying of spatial information by enantiopure conformers would have been an early bottleneck for the origin of life. Considering the above elements in such scenario, the bio-homochirality and life presumably have had the same origin.

Acknowledgements

For H. I. Cruz-Rosas this paper constitutes a partial fulfillment of the Doctoral granting-program from the Posgrado en Ciencias Biológicas, Universidad Nacional Autónoma de México, financially supported by the CONACyT (233810). G. Cocho wishes to thank the financial support provided by PAPIIT-UNAM project number IN107414. The authors thank Vladimir N. Kompanichenko from the Institute for Complex Analysis of Regional Problems, Russia, for providing literature and useful comments. We also thank Citlaly Andrade, for helping with the graphic design and Bertha Acuña from the University of Florida at Gainesville, for helping with the English review. We thank the Academic Editor and anonymous reviewers, their comments have significantly improved the final version of this paper.

References

Arteaga, O., Canillas, A., Crusats, J., El-Hachemi, Z., Jellison, G.E. Jr., Llorca, J. & Ribó, J.M. (2010). Chiral biases in solids by effect of shear gradients: a speculation on the deterministic origin of biological homochirality. *Orig. Life Evol. Biosph.* **40**, 27–40.

Berthod, A. (2006). Chiral recognition mechanisms. *Anal. Chem.* **78**(7), 2093–2099.

Bonner, W.A. (1995). Chirality and life. *Orig. Life Evol. Biosph.* **25**, 175–190.

Bonner, W.A., Greenberg, J.M. & Rubenstein, E. (1999). The extraterrestrial origin of the homochirality of biomolecules-rebuttal to a critique. *Orig. Life Evol. Biosph.* **29**, 215–219.

https://doi.org/10.1017/S147355041500049X Published online by Cambridge University Press

Brack, A. (1977). β-Structures of alternating polypeptides and their possible role in chemical evolution. *Biosystems* **9**, 99–103.

Brack, A. (2007). From interstellar amino acids to prebiotic catalytic peptides: a review. *Chem. Biodivers.* **4**(4), 665–679.

Brack, A. & Orgel, L.E. (1975). β-Structures of alternating polypeptides and their possible prebiotic significance. *Nature* **256**, 383–387.

Carroll, J.D. (2009). A new definition of life. *Chirality* **21**, 354–358.

Chakrabarti, P. & Janin, J. (2002). Dissecting protein–protein recognition sites. *Proteins* **47**(3), 334–343.

Cleaves, H.J. (2013). Prebiotic chemistry: geochemical context and reaction screening. *Life* **3**(2), 331–345.

Cornish-Bowden, A. & Cárdenas, M.L. (2008). Self-organization at the origin of life. *J. Theor. Biol.* **252**, 411–418.

Cronin, J. & Reisse, J. (2005). Chirality and the origin of homochirality. In *Lectures in Astrobiology*, ed. Gargaud, M., Barbier, B., Martin, H. & Reisse, J., pp. 473–515. Springer, Berlin Heidelberg.

Cronin, J.R. & Pizzarello, S. (1997). Enantiomeric excesses in meteoritic amino acids. *Science* **275**, 951–955.

Ehrenfreund, P. & Cami, J. (2010). Cosmic carbon chemistry: from the interstellar medium to the early Earth. *Cold Spring Harb. Perspect. Biol.* **2**(12), a002097.

Ehrenfreund, P. & Charnley, S. (2000). Organic molecules in the interstellar medium, comets, and meteorites: a voyage from dark clouds to the early earth. *Annu. Rev. Astron. Astrophys.* **38**, 427–483.

Eigen, M. (1971). Selforganization of matter and the evolution of biological macromolecules. *Naturwissenschaften* **58**(10), 465–523.

Eigen, M. (1993). The origin of genetic information: viruses as models. *Gene* **135**(1), 37–47.

Fitz, D., Reiner, H., Plankensteiner, K. & Rode, B.M. (2007). Possible origins of biohomochirality. *Curr. Chem. Biol.* **1**, 41–52.

Gabb, H.A., Jackson, M.R. & Sternberg, J.E. (1997). Modelling protein docking using shape complementarity, electrostatics and biochemical information. *J. Mol. Biol.* **272**, 106–120.

Gleiser, M., Nelson, B.J. & Walker, S.I. (2012). Chiral polymerization in open systems from chiral-selective reaction rates. *Orig. Life Evol. Biosph.* **42**, 333–346.

Herrera, A.L. (1924). *Biología y plasmogenia*. Herrero Hermanos, Mexico.

Herrera, A.L. (1942). A new theory of the origin and nature of life. *Science* **96**(2479), 14–14.

Hordijk, W., Hein, J. & Steel, M. (2010). Autocatalytic sets and the origin of life. *Entropy* **12**, 1733–1742.

Israel, D.J. & Perry, J. (1990). What is Information? In *Information, Language and Cognition*, ed. Hanson, P., pp. 1–19. Vancouver: University of British Columbia Press.

Janin, J. (1996). Protein-protein recognition. *Prog. Biophys. Mol. Biol.* **64**(2–3), 145–166.

Jheeta, S. (2015). The routes of emergence of Life from LUCA during the RNA and Viral World: a conspectus. *Life* **5**(2), 1445–1453.

Kaddour, H. & Sahai, N. (2014). Synergism and mutualism in non-enzymatic RNA polymerization. *Life* **4**(4), 598–620.

Kauffman, S. (1986). Autocatalytic sets of proteins. *J. Theor. Biol.* **119**, 1–24.

Kauffman, S. (1993). *Origins of Order: Self-organization and Selection in Evolution*. Oxford University Press, USA.

Kauffman, S. (2011). Approaches to the origin of life on Earth. *Life* **1**(1), 34–48.

Kawasaki, T., Hatase, K., Fujii, Y., Jo, K., Soai, K. & Pizzarello, S. (2006). The distribution of chiral asymmetry in meteorites: an investigation using asymmetric autocatalytic chiral sensors. *Geochim. Cosmochim. Acta* **70**, 5395–5402.

Kofler, W. (2014). 'Information'-from an evolutionary point of view. *Information* **5**(2), 272–284.

Kohlas, J. & Schmid, J. (2014). An algebraic theory of information: an introduction and survey. *Information* **5**(2), 219–254.

Kompanichenko, V.N. (2008). Three stages of the origin-of-life process: bifurcation, stabilization and inversion. *Int. J. Astrobiol.* **7**(1), 27–46.

Kompanichenko, V.N. (2009). Changeable hydrothermal media as a potential cradle of life on a planet. *Planet. Space Sci.* **57**, 468–476.

Kompanichenko, V.N. (2012a). Origin of life by thermodynamic inversion: a universal process. In *Genesis–in the Beginning*, ed. Seckbach, J., pp. 305–320. Springer, Netherlands.

Kompanichenko, V.N. (2012b). Inversion concept of the origin of life. *Orig. Life Evol. Biosph.* **42**, 153–178.

Kompanichenko, V.N. (2014). Emergence of biological organization through thermodynamic inversion. *Front. Biosci.* **6**, 208–224.

Larralde, R., Robertson, M.P. & Miller, S.L. (1995). Rates of decomposition of ribose and other sugars: implications for chemical evolution. *Proc. Natl. Acad. Sci. U.S.A.* **92**(18), 8158–8160.

Leduc, S. (1912). *La Biologie Synthétique*. A. Poinat, France.

Lehn, J.M. (1990). Perspectives in supramolecular chemistry–from molecular recognition towards molecular information processing and self-organization. *Angew. Chem. Int. Ed. Engl.* **29**(11), 1304–1319.

Lehn, J.M. (2007). From supramolecular chemistry towards constitutional dynamic chemistry and adaptive chemistry. *Chem. Soc. Rev.* **36**(2), 151–160.

Lenski, W. (2010). Information: a conceptual investigation. *Information* **1**(2), 74–118.

Lo Conte, L., Chothia, C. & Janin, J. (1999). The atomic structure of protein-protein recognition sites. *J. Mol. Biol.* **285**, 2177–2198.

Maury, C.P.J. (2009). Self-propagating β-sheet polypeptide structures as prebiotic informational molecular entities: the amyloid world. *Orig. Life Evol. Biosph.* **39**, 141–150.

Meierhenrich, U. (2008). A new record for chiral molecules in meteorites. In *Amino Acids and the Asymmetry of Life*, ed. Meierhenrich, U., pp. 145–159. Springer, Berlin Heidelberg.

Micali, M., Engelkamp, H., van Rhee, P.G., Christianen, P.C.M., Monsú Scolaro, L. & Maan, J.C. (2012). Selection of supramolecular chirality by application of rotational and magnetic forces. *Nat. Chem.* **4** (3), 201–207.

Nooren, I.M.A. & Thornton, J.M. (2003). Structural characterisation and functional significance of transient protein–protein interactions. *J. Mol. Biol.* **325**, 991–1018.

Ogayar, A. & Sánchez-Pérez, M. (1998). Prions: an evolutionary perspective. *Int. Microbiol.* **1**, 183–190.

Oparin, A.I. & Gladilin, K.L. (1980). Evolution of self-assembly of probionts. *Biosystems* **12**, 133–145.

Pablo, C.O. & Sauer, R.T. (1984). Protein-DNA recognition. *Annu. Rev. Biochem.* **53**, 293–321.

Palmans, A.R.A. & Meijer, E.W. (2007). Amplification of chirality in dynamic supramolecular aggregates. *Angew. Chem. Int. Ed.* **46**, 8948–8968.

Peczuh, M.W. & Hamilton, A.D. (2000). Peptide and protein recognition by designed molecules. *Chem. Rev.* **100**(7), 2479–2494.

Pizzarello, S. (2006). The chemistry of life's origin: a carbonaceous meteorite perspective. *Acc. Chem. Res.* **39**(4), 231–237.

Pizzarello, S. (2007). The chemistry that preceded life's origin: a study guide from meteorites. *Chem. Biodivers.* **4**, 680–693.

Pizzarello, S. & Cronin, J.R. (2000). Non-racemic amino acids in the Murray and Murchison meteorites. *Geochim. Cosmochim. Acta* **64**(2), 329–338.

Pizzarello, S. & Groy, Th.L. (2011). Molecular asymmetry in extraterrestrial organic chemistry: an analytical perspective. *Geochim. Cosmochim. Acta* **75**, 645–656.

Pizzarello, S., Zolensky, M. & Turk, K.A. (2003). Nonracemic isovaline in the Murchison meteorite: chiral distribution and mineral association. *Geochim. Cosmochim. Acta* **67**(8), 1589–1595.

Radu, P. (2004). The early history of bio-information. In *Between Necessity and Probability: Searching for the Definition and Origin of Life*, ed. Radu, P., pp. 95–120. Springer, Berlin Heidelberg.

Ribó, J.M., Crusats, J., Sagués, F., Claret, J. & Rubires, R. (2001). Chiral sign induction by vortices during the formation of mesophases in stirred solutions. *Science* **292**, 2063–2066.

Scott, W.G., Szöke, A., Blaustein, J., O'Rourke, S.M. & Robertson, M.P. (2014). RNA catalysis, thermodynamics and the origin of life. *Life* **4**(2), 131–141.

Sephton, M.A. (2002). Organic compounds in carbonaceous meteorites. *Nat. Prod. Rep.* **19**, 292–311.

Shannon, C.E. (1948). A mathematical theory of communication. *Bell Syst. Tech. J. 27*, **379–423**, 623–656.

Shapiro, R. (2000). A replicator was not involved in the origin of life. *IUBMB Life* **49**(3), 173–176.

Simonneaux, G., Srour, H., Le Maux, P., Chevance, S. & Carrie, D. (2014). Metalloporphyrin symmetry in chiral recognition and enantioselective catalysis. *Symmetry* **6**, 210–221.

Spach, G. & Brack, A. (1979). β-Structures of polypeptides with L- and D-residues. Part II. –Statistical analysis and enrichment in enantiomer. *J. Mol. Evol*. **13**, 47–56.

Tamura, K. (2011). Molecular basis for chiral selection in RNA aminoacylation. *Int. J. Mol. Sci*. **12**(7), 4745–4757.

Trifonov, E.N. (2011). Vocabulary of definitions of life suggests a definition. *J. Biomol. Struct. Dyn*. **29**(2), 259–266.

Tyagi, N.K., Kumar, A., Goyal, P., Pandey, D., Siess, W. & Kinne, R.K.H. (2007). D-Glucose-recognition and phlorizin-binding sites in human sodium/d-glucose cotransporter 1 (hSGLT1): a tryptophan scanning study. *Biochemistry* **46**, 13616–13628.

Varela, F.J., Maturana, H.R. & Uribe, R. (1974). Autopoiesis: the organization of living systems, its characterization and a model. *Biosystems* **5**, 187–196.

Williamson, J.R. (2000). Induced fit in RNA–protein recognition. *Nat. Struct. Biol*. **7**(10), 834–837.

Woolf, N.J. (2015) A hypothesis about the origin of biology. *Orig. Life Evol. Biosph*. **45**, 257–274.

Yang, W., He, H. & Drueckhammer, D.G. (2001). Computer-guided design in molecular recognition: design and synthesis of a glucopyranose receptor. *Angew. Chem. Int. Ed*. **40**(9), 1714–1718.

Yin, P., Zhang, Z.M., Lv, H., Li, T., Haso, F., Hu, L., Zhang, B., Bacsa, J., Wei, Y., Gao, Y., Hou, Y., Li, Y.G., Hill, C.L., Wang, E.B. & Liu, T. (2015). Chiral recognition and selection during the self-assembly process of protein-mimic macroanions. *Nat. Commun*. **6**: 6475, doi: 10.1038/ncomms7475.