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New Directions for an Experimental Approach to the Chemistry of the Origin of Life

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► **To cite this version:**

Grégoire Danger, L. Le Sergeant D'hendecourt, V. Vinogradoff, R. Pascal. New Directions for an Experimental Approach to the Chemistry of the Origin of Life. Michele Fiore. Prebiotic Chemistry and Life's Origin, Royal Society of Chemistry, pp.424-455, 2022, Chemical Biology, 978-1-78801-749-7. 10.1039/9781839164798-00424 . hal-03858230

HAL Id: hal-03858230

<https://hal.science/hal-03858230>

Submitted on 8 Dec 2022

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3 **X New Directions for an Experimental Approach to the Chemistry of the Origin**
4 **of Life**

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17

18 ABSTRACT

19 Organic matter is formed in molecular clouds from which planetary systems arise as

20 well as in planetary environments. Most of these locations are not likely to harbour

21 life, questioning the genuine prebiotic character of the corresponding chemistry and

22 its relevance to the origin of life. The formation of organic matter does therefore not
23 necessarily constitute a systemic trend towards life in our Universe. However, its
24 sluggish reactivity at low temperatures is likely to have allowed the delivery of volatile
25 elements essential for life at the surface of planets like the Earth. Kinetic selection
26 may also have played a role for sorting specific active species or complex catalytic
27 processes during the self-organization preceding life owing to the kinetic barriers
28 hindering the reactions of covalent bonds and holding the system in a far-from-
29 equilibrium state. As a result of both processes, early environments on telluric
30 planets that exhibit other essential factors, namely, liquid water and light as an
31 energy source, may then become favourable to the origin of life. In both processes,
32 reactivity matters as much, if not more, than structures. Next to focusing on the
33 synthesis of building blocks, emphasis must be made on reactivity for identifying
34 networks involving autocatalysis, replication, or positive feedback.

35 X. 1. Introduction

36 The topic of this book – Prebiotic Chemistry and Life’s Origin – is connected with the
37 hypothesis, expressed almost one century ago, that life could have emerged from
38 abiotically formed organic matter^{1,2}. This hypothesis is reminiscent of the fact that the
39 designation of organic matter itself derives from its intimate association with life. The
40 report of the famous Miller experiment³, carried out a few decades later, apparently
41 provided support to this hypothesis. It suggested that the issue of the origin of life
42 could have been solved soon after it was demonstrated that biochemical “building
43 blocks of life” are abiotically formed under somehow arbitrary conditions judged at
44 that time compatible with the presumed environment of the early Earth. In spite of
45 the fact that vitalist beliefs had been refuted with the synthesis of urea from abiotic
46 and inorganic chemical compounds since the beginning of the 19th century⁴, the
47 enthusiasm raised by the Miller’s experiment can still be considered as a remain of
48 the belief that organic matter and life on Earth and by extension elsewhere, are
49 intimately connected. Moreover, more than 50 years later, at a workshop organized
50 by Pier Luigi Luisi and Kepa Ruiz-Mirazo, the following question was set forth⁵:
51 *“Would you agree with the statement, that from the conceptual point of view the field*
52 *has not progressed much since the early experiments of Stanley Miller? And why do*
53 *you think/not think so?”* The fact that the relationship between abiotically formed
54 organic matter and the origin of life still seems questionable put under scrutiny the
55 relationship between these two topics. In other words, no definite evidence has been
56 provided by the scientific community in support of a more or less deterministic
57 development of chemistry, which could have yielded systems capable of evolving in
58 a way similar to living organisms. We therefore have a limited understanding of the
59 pathways through which such a hypothetical deterministic process could have

60 happened. No comprehensive answer has been given to the question of how could
61 the chemical evolution of matter have been converted into the process of natural
62 selection. This question can be reformulated more precisely as how chemical
63 changes, driven by chemical affinities, can give rise to a process in which occasional
64 replication errors can be selected as a source of self-organization and subsequent
65 evolution. Any change towards a more organized state associated with a decrease in
66 entropy contradicts the directives of the Second Law of thermodynamics. Proposing
67 that some unknown chemical determinism played a role at the early stages of the
68 self-organization of life requires that the process acted as a driving force to
69 overcome the constraints of the Second Law. It also implies that this process
70 disappeared without leaving any easily recognizable remnant after natural selection
71 became prevailing.

72 Alternatively, contingency cannot be excluded as a factor responsible for the self-
73 organization of life, even though estimates of the probability of a single transition for
74 the emergence of an organism from scratch imply that this event is virtually
75 impossible^{6,7,8}. Any transition process based on a highly improbable event
76 constitutes a violation of the Second Law of thermodynamics. In spite of this
77 drawback, it has been suggested that low-probability events may have been
78 responsible for the transition, such as the emergence of specific sequences having
79 the ability of catalysing their own replication in a population of ribonucleic acid
80 (RNA), polymers playing a role of information carriers⁹. However, this appealing
81 proposal constituting the 'RNA world' hypothesis, in which replication results from the
82 activity of ribozymes, is highly improbable. The evolution of the 'RNA World' would
83 indeed have required the occurrence of a process able of sustaining an environment

84 rich in a full set of activated RNA monomers, which constitutes a “prebiotic chemist’s
85 nightmare”¹⁰.

86 From the dilemma between a “*piece of statistical luck*” or “*an evolutionary process*”⁸
87 many scientists chose the latter^{7,11,12}. No sharp transition marked by a highly
88 improbable event is required in such an evolutionary process that may proceed
89 through stages separated by less improbable transitions. The onset of fully effective
90 natural selection may on the contrary constitute the conclusion in a fuzzy transition
91 towards life^{13,14}. The living world grew as a result of a driving force associated with
92 the occurrence of reproduction with modifications and natural selection, as
93 developed by the theory of evolution¹⁵. This evolutionary force is therefore mainly
94 related to kinetics. Its kinetic nature suggests that rudimentary selection based on
95 chemical kinetics, could have preceded its full implementation as the prevailing
96 evolutionary driving force. It could have led the system towards higher degrees of
97 organisation before natural selection is considered established and therefore
98 provides grounds for a continuous process for the self-organization of life. This
99 process may be already considered as reminiscent of natural selection even before
100 actual biological life.

101 The whole process also involves a transition into a state presenting an alternative
102 form of stability, namely Dynamic Kinetic Stability (DKS), able to replace
103 thermodynamic stability as a source of persistence^{16–22}. The direction of evolution is
104 not constrained by the Second Law since DKS can only be observed from open
105 systems maintained out of equilibrium. This is consistent with the thermodynamic
106 analysis of the development of self-organization and the conclusion that living
107 organisms must behave as open thermodynamic systems to avoid a violation of the
108 Second law²³. Kinetic selection requires the system to be held in a far from

109 equilibrium situation. It must therefore be fed with energy and open to the
110 environment. All this body of evidence suggests that chemical evolution preceding
111 the transition should have been driven towards higher degrees of functional
112 organization by a factor orientating its direction of evolution that is of kinetic nature.
113 But kinetic selection may have also played a more general role, diverging from
114 natural selection, for instance in the segregation of a diversity of chemical
115 environments that allowed only some of them to become favourable to the origin of
116 life.

117 This chapter is aimed at demonstrating that life is governed by physical principles
118 and that these principles are sufficient to account for the main features of life and,
119 most importantly, of its origin. It is built on the basis of previous work that
120 emphasized on the importance of kinetics in the process^{16,24,25}. One of our main
121 tenets is based on the role of kinetic selection during the whole process. There is
122 indeed no reason to consider that this kind of selection was only present just before
123 the onset of natural selection and that of the living world. Kinetic selection could also
124 play a role as early as in the differentiation of cosmic materials in astrochemistry and
125 continued over the whole process of self-organization based on the multiplication
126 and selection of material entities that led to biological life. Kinetic selection should
127 indeed be considered as a tool available for sorting essential building blocks from the
128 huge chemical diversity generally found in abiotic organic materials and most
129 prebiotic synthesis experiments^{26,27,28} before it reached its utter role in the
130 evolutionary biology of living organisms. Experimental studies in the origin of life
131 research should take these considerations into account and focus on processes by
132 which kinetic selection associated with the multiplication of chemical entities might
133 allow change to occur in the direction of increased functional organization¹⁶.

134 **X. 2. What Makes Organic Matter so Specific?**

135 **X. 2. 1. The Historical Status of Organic Matter as Regards the Origins of Life**

136 To which extent is organic matter necessary and sufficient to the emergence of life?

137 The answer to this question is intimately associated with the process that has driven
138 the self-organization of matter to life. According to the vitalist belief, prevailing before
139 the nineteenth century, organic matter was only associated with living organisms.

140 Though devoid of scientific grounds, this description was considered to account for
141 its difference from mineral matter. Remains of this belief are so deeply anchored in
142 our culture that inorganic and organic chemistries are still considered as different
143 fields of science in spite of the fact that their interface has become larger. A similar
144 comment could apply to the identification of organic matter in a space science
145 context that is often directly associated with the occurrence of life in popular science
146 media. A recent example was the glycine detection in the comet 67P/Churyumov–
147 Gerasimenko²⁹, targeted by the Rosetta mission. The implicit idea that is suggested
148 by this description^{30,31} is that, as soon as ingredients are present and delivered in a
149 favourable environment, then life is bound to emerge. Hence, the sole detection of
150 organic matter in extraterrestrial environments would constitute a first indication for
151 the possibility of the presence of life in any favourable environment. However, these
152 favourable environments are quite far from being clearly defined at the present time.

153 Similar misconceptions with respect to the status of organic matter have also
154 hindered the development of science as regards its detection and characterization in
155 meteorites during the nineteenth century and persisted all over the first half of the next
156 one³². This chapter is aimed at describing the factors that could explain why organic
157 chemistry is associated with life as we know it and that it is not the precise nature of
158 organic matter that is the most important but its reactivity. Our aim is not to suggest

159 that life can emerge in the absence of organic matter, as one of our conclusions is
160 indeed that organic chemistry is necessary but not sufficient for the origin of life
161 when considering liquid aqueous environments. *The issues of the abiotic formation*
162 *of organic matter and that of the origin of life most probably constitute two different*
163 *processes* even though the latter may not be considered independently of the
164 former.

165 **X. 2. 2. From Prebiotic Chemistry to the Origin of Life**

166 The first conceptual approaches to the origin of life made by Oparin, assumed that
167 life could evolve from abiotically formed organic matter (the so-called heterotrophic
168 hypothesis)¹. Actually, the main originality of the Oparin's hypothesis¹ relied on the
169 fact that he indeed considered *the formation of organic matter and the origin of life*
170 *as constituting two separate processes*. The Oparin hypothesis found experimental
171 support through the result of the Miller experiment³. This experiment, proving the
172 formation of α -amino acids from simple inorganic precursors, constituted a milestone
173 in the origin of life studies. It testified that, as soon as dioxygen is absent from the
174 environment, the chemistry of carbon at a reduced state of oxidation becomes
175 ubiquitous. The lack of knowledge on the precise conditions prevailing on the early
176 Earth, and especially on the composition and reduced state of the atmosphere
177 during the early Archean and Hadean periods (ca. 3.5–4.5 Gy before present), led
178 many scientists to consider that organic matter was not abundant on the Earth's
179 surface before the origin of life. The chemo-autotrophic hypothesis, stating that life
180 emerged in connexion with a carbon metabolism built from inorganic sources of
181 carbon and mineral reducing agents, was then proposed as a solution to circumvent
182 a presumed limited availability of abiotic organic matter^{33,34}. In line with the above-
183 developed ideas, the autotrophic hypothesis might be considered as step backwards

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184 to a conceptual stage in which the origin of life and the formation of organic matter
185 were not considered as separate processes. This assertion is worth mentioning in
186 spite of the popularity of a chemo-autotrophic origin of life in the scientific
187 community. The main tenets of this approach have been debated on the grounds
188 that the process clearly lacks experimental support³⁵. Other criticism stated that
189 biochemistry can hardly recapitulate prebiotic processes because the emergence of
190 metabolic pathways is unlikely in prebiotic chemistry³⁶. Additionally, a surface
191 metabolism would require multiple catalytic steps to work at the same time and an
192 appropriate arrangement of catalysts that seems even more unlikely³⁷. Among these
193 issues, the last one is probably the most crucial. The hypothesis of an autotrophic
194 origin of life indeed presumes that carbon fixation was not independent from the
195 origin of life process. Organics should therefore be both synthesized from inorganic
196 sources of carbon (CO₂ for instance) and used as food by the first living organisms.
197 One of its most achieved versions involves a catalytic contribution of inorganic
198 surfaces on which reactants could be adsorbed. However, the existence of a
199 metabolism requires that several chemical steps are efficiently proceeding at the
200 same time. Therefore, a collection of different catalysts must have been present and
201 the intermediates must have been able to move between the different surfaces
202 playing a catalytic role. This motion requires metabolites to be desorbed from the
203 surface and to be released in solution. This hypothesis is therefore highly unlikely
204 unless both the catalysts and the metabolites are sequestered within a single
205 compartment. Otherwise the formation of organic matter and its metabolic use
206 should be considered as two distinct processes and the corresponding entities as
207 heterotrophs. We are thus conducted to the need of compartments possessing a
208 collection of catalytic surfaces between which metabolites could be able to migrate

209 without being released in the environment. This hypothesis implies that
210 compartments having a wide range of catalytic sites are available, which makes
211 them improbable unless they can be multiplied into numerous copies. The issue of
212 the reproduction of entities based on organic matter would therefore be changed into
213 that of compartments containing a full set of homogeneous or heterogeneous
214 catalysts acting on the metabolism. These observations do not mean that studies on
215 prebiotic reaction networks that could predate metabolism are useless^{38–42}. On the
216 contrary such studies may help understanding why, at a given (but not necessarily
217 early) stage, these processes could have been harvested by systems able to
218 reproduce themselves and evolve on the pathway from non-life to the living state⁴³
219 (Figure X.1).

220 [Insert Figure X.1 here]

221 In addition to the above-mentioned drawbacks of hypotheses involving contributions
222 of mineral surfaces, it is worth noting that they put the emphasis on the role of
223 catalysis that is generally understood as a mean to avoid kinetic barriers. This
224 emphasis appears to be in contradiction with the role independently assumed for
225 kinetic barriers needed to hold the system in a far from equilibrium state as a
226 prerequisite for self-organization^{44–47}. Otherwise, the system would rapidly reach the
227 equilibrium state, which prevents any possibility of self-organization associated with
228 disequilibrium. The equilibrium state indeed corresponds to the statistically more
229 probable one. In other words, most components of a system capable of self-
230 organizing far from equilibrium should preferably show sluggish reactivity rather than
231 rapidly undergoing relaxation towards equilibrium. Any catalysis should only be
232 expressed on very specific chemical steps rather than on a wide range of processes.

233 In this way, fuelling the systems with energy would favour specifically the chemical
234 steps associated with the development of self-organization.

235 **X. 2. 3. Extraterrestrial Chemistry**

236 Extraterrestrial chemistry pertains to the chemistry, elements and molecules, that
237 can be observed in various extraterrestrial environments, evolving in a repeating
238 cycle that includes stars, the diffuse interstellar medium (ISM), molecular clouds,
239 planetary systems down to comets and asteroids and finally to meteorites recovered
240 on the Earth's surface. All these environments are prone to a rich chemistry where,
241 in most of them, organic chemistry is at work. There, very diverse organic molecules
242 form and evolve. They are observed in the gas phase as well as in numerous solid
243 phases. The complex interplay between these different sites and processes are often
244 discussed in the astrochemistry community, which addresses the global chemical
245 evolution of the Galaxy⁴⁸.

246 **X. 2. 3. 1. Cosmic abundances, depletions and their significance for carbon-** 247 **based life**

248 Cosmic abundances constitute a given characteristic of our "local" neighbourhood. It
249 is important to realize that these abundances, measured for example in the Sun's
250 photosphere but also in CI chondrites⁴⁹ are expected to be the same in the
251 interstellar medium from which the stars continually form. Therefore, the resulting
252 ISM gas chemistry and its subsequent solid phase chemistry are highly influenced by
253 the abundances of the elements, relative to H, initially present in the photospheres of
254 the stars.

255 Three groups of elements, decreasing in abundances, may be considered. The first
256 one consists in non-condensable elements such as H and He (~90% and ~9% by

257 numbers respectively) by far the most abundant ones. Then next to it, the group of
258 “volatiles” mainly consists of O, C, N, and S (and the less abundant P) whose total
259 abundances relative to H amounts to $\sim 10^{-3}$. The third and quite substantial group,
260 as far as telluric planets are concerned, forms the rock-forming elements (Mg, Si, Fe,
261 Al, Ca, Ni, Ti) whose total cosmic abundances barely get up to $\sim 10^{-4}$ that of H, an
262 order of magnitude less than the volatiles. Rock-forming elements are then almost
263 totally absent as atoms in the gas of the ISM, since they form the mineral
264 composition of the dust grains and thus reflect the refractory nature of the minerals,
265 kinetically frozen in the ejected and cooling atmospheres of asymptotic giant branch
266 (AGB) stars^{50,51}.

267 One of the salient points of all living systems, mainly the elemental composition of key
268 molecules of biochemistry (such as amino acids, proteins and the ATP molecule)
269 including the carriers of genetic information (nucleic acids), is that these molecules
270 appear to be *strictly* restricted only to very few elements, the so-called CHNOPS, a
271 terminology much in use in the astrobiology community. The availability of the
272 CHNOPS, for the initial astrochemical and subsequently astrobiological processes,
273 relates to the general astrophysical considerations discussed here. These
274 CHNO(P)S elements (with the notable exception of P that may be evidence for a
275 planetary process) are not only the most abundant ones at the cosmic level but their
276 volatility makes them natural partners for reacting together and with H and the
277 abundant C, which afterwards generates a rich organic chemistry in various
278 environments such as the surface of interstellar grains. The CHNOPS are poorly
279 depleted because, being more abundant than all the others, they cannot be locked
280 into mineral grains whose elements are already fully condensed at higher
281 temperatures.

282 Thus, the general view of the evolution of matter in the Galaxy (see Ref. 52 for a
283 comprehensive description of this evolution) from nucleosynthesis in stars to the
284 formation of refractory solids from AGB stars, the main sources of interstellar grains,
285 provides a factual explanation for the abundance of the CHNOPS. Interstellar abiotic
286 organics may therefore be considered as the result of a *generic* trend at work at a
287 much larger scale than that of the solar system. Furthermore, at a more elementary
288 level, it also explains why the observed extraterrestrial chemistry in the gas phase is
289 largely dominated by volatile species (H₂O, CO...), which also holds true in the solid
290 phase, for interstellar ices for instance and their subsequent evolution into organic
291 matter. Heavier elements, the rock-forming ones, are trapped in non-reactive grains.
292 In the gas phase, CHNOPS do react between themselves (and in particular with H)
293 because they cannot react with already depleted and much less abundant elements.
294 This dichotomy, imposed by the kinetics of solid formation in the mass loss of the
295 outer envelopes of stars, in the elemental distribution between volatiles (ice-forming)
296 and refractory (rock-forming) elements crucially contributes to the rise of the organic
297 chemical world observed in extraterrestrial environments in addition to chemical
298 reactivity.

299 **X. 2. 3. 2. Molecular astrochemistry**

300 Molecular astrochemistry starts in the gas phase of the ISM with the elemental
301 abundances described above. Up to 200 molecules, mostly organics, including
302 radicals and ions, have been identified in the gas phase by radio astronomy. A non-
303 exhaustive list of detected molecules in the gas phase in different settings (molecular
304 clouds, protoplanetary disks and stars' envelopes) is given in Table X. 1. In this
305 table, molecules (and radicals) are arranged by number of atoms in the species.

306 Organic molecules, built from the CHNOPS elements, discernably dominate this list.
307 Note that rare molecules containing heavier atoms (Si, Al, Fe) are observed in
308 circumstellar shells, indeed prior to their condensation in solids. The molecular
309 complexity in the gas phase appears rather limited. Molecular abundances decrease
310 roughly by a factor around 3 for each additional atom in the detected species. This
311 reflects a basic fact of interstellar chemistry: reactions are always two-body ones due
312 to the rather low density of the ISM. As a result, destruction routes prevail in the gas
313 on the contrary to what happens on grains surfaces that offer both a high local
314 density for further reactions and a protection able to mitigate the damaging effect of
315 energetic processes on molecular assemblies of increasing size and complexity.

316 [Insert Table X.1 here]

317 Interestingly, the initially larger abundances and availability of the CHNOPS in the
318 gas phase will determine the initial chemistry in dense molecular clouds and lead to
319 the abundant simple ices widely observed in regions of star formation. As
320 conjectured by Oort and Van de Hulst as far back as 1947⁵⁴, these atoms passing
321 from diffuse to denser clouds, in the presence of cold surfaces (10–30 K) and in such
322 a reducing H rich environment will stick onto the grains and easily react to form
323 hydrides like H₂O, CH₄ and NH₃. H₂ is formed, thanks to the grain surfaces,
324 throughout this accretion phase, during which specific molecules such as CO, HCO,
325 HCO⁺ also form via ion-molecule reactions in the gas phase, then also stick onto the
326 same grains where they join the ices as CO, CO₂, H₂CO, and finally the abundant
327 CH₃OH resulting from the hydrogenation of CO.

328 The main interstellar ice molecules include by order of decreasing abundance H₂O,
329 CH₃OH, CO, CO₂, NH₃, CH₄ and H₂CO^{55, 56}.

330 Energetic processing of interstellar ices from UV photons and cosmic ray particles
331 that are always present to some extent in molecular clouds, has triggered
332 simulations through irradiation experiments on laboratory analogues since the mid
333 80's. Ice analogues can be produced and fully studied in these experimental
334 simulations. Initial ice analogues are irradiated by hard ultraviolet photons or ionizing
335 particles. Molecules break-up and randomly recombine, generating a rich radical
336 chemistry since these atoms and radicals diffuse in the ice, particularly when the
337 temperature of the sample is slowly raised up to room temperature. The goal of
338 these experiments is to simulate the fate of icy materials that originate in molecular
339 clouds, are irradiated by various energetic particles during their journey to
340 protoplanetary disks, then are incorporated into small bodies of the solar system that
341 may finally deliver these on the Earth where some are recovered even nowadays as
342 meteorites.

343 **X. 2. 3. 3. Organics in small bodies of the solar system and their relevance to** 344 **the origin of life**

345 If cold ices in the line of sight to protostellar objects reveal simple molecules and
346 some evidence for energetic and thermal processing of them, observational
347 complications arise from the fact that cold foreground ices mask efficiently warmer
348 regions where sublimation takes place. The expected formation of an organic
349 residue, as routinely achieved in laboratory simulations⁵⁷, is thus not easily
350 observable. The residue characteristics must then rely on these empirical
351 simulations approaches that provide analogues of organics to be compared with the
352 ones present in small bodies of the solar system and further on in carbonaceous
353 meteorites. The recovered residue samples can be studied by diverse and
354 complementary methods of analytical chemistry that involve usually infrared in-situ

355 spectroscopy, mass spectrometry coupled to gas and liquid chromatography⁵⁸ as
356 well as more recent and elaborated methods using ultra-high resolution mass
357 spectrometry from FT-Orbitrap-MS and FT-ICR-MS analytical apparatuses. Infrared
358 in-situ spectroscopies at 300 K of the residues reveal that they contain numerous
359 and highly functionalized organic molecules containing side groups and chemicals
360 functions such as methyl and methylene groups, alcohols, esters, ethers, carboxylic
361 acids, cyanides, amines, amides, aromatics⁵⁹. A very peculiar molecule
362 hexamethylenetetramine (HMT) was identified by infrared spectroscopy in these
363 residues as early as 1995 by Bernstein et al.⁶⁰. More specific and targeted searches
364 for molecules believed to be of prebiotic interest were focused on amino acids,
365 sugars or nucleobases within these organic residues. A high number of racemic
366 amino acids (up to 18) were found by Munoz-Caro et al. in 2002⁶¹ as well as di-
367 amino acids and even some dipeptides⁶². In 2016, Meinert et al.⁶³ evidenced a suite
368 of many sugars up to aldopentoses was recorded in comparable simulations. Ribose
369 was found in the residues, followed just after by the detection of deoxyribose⁶⁴. On
370 the other hand, non-targeted analyses using very high resolution mass spectrometry
371 revealed a very large molecular diversity that is also observed in extracts from
372 chondrites²⁶.

373 An important issue related to this experimental approach is the possible connection
374 between these organic residues with the organic content of natural objects, namely
375 with debris of the solar system formation such as comets or asteroids.

376 All these identified molecules as well as less defined organic materials from
377 laboratory residues have indeed been detected and characterized in carbonaceous
378 meteorites originating from the fragmentation of parent bodies. FT-ICR-MS analyses
379 of Murchison extracts²⁶ revealed the presence of tens of thousands of organic

380 compounds in meteorites, similarly to what is observed in the synthesized organic
381 residues in the laboratory^{27,65}. Targeted analyses on the soluble organic fraction of
382 some meteorites have shown the presence of nucleobases as well as up to 80
383 amino acids. Furthermore, the quite abundant HMT molecule in residues was
384 recently detected in the Murchison meteorite⁶⁶, confirming that the photo- and
385 thermo-chemistry of dense molecular ices⁶⁷ provides a reasonable explanation for
386 the origin of a fraction, at least, of the organic matter of meteorites.

387 An important feature of this extra-terrestrial organic matter lies in its reactivity. It is
388 worth emphasizing the role of the kinetic barriers associated with covalent bonds that
389 are on the one hand involved for the long-term stability of organic matter in solid
390 bodies in space and, on the other hand, have been considered as key parameters in
391 the further self-organization process leading to life^{44–47}. This importance of kinetic
392 barriers with respect to these two unrelated processes, namely the formation of
393 organic solids in space and the self-organization of life, makes an unexpected
394 connection between the chemistry of interstellar media and the habitability of the
395 surface of the Earth. The development of life could have opportunistically taken
396 advantage of the presence of diverse and abundant organic matter delivered from
397 space in conjunction with liquid water though, by itself, it is not the only determining
398 factor triggering the origin of life, as mentioned earlier. Neither the fall of meteorites
399 or comets, or alternative processes for the local production of organic matter (in the
400 atmosphere or in hydrothermal environments), are likely sufficient to induce the self-
401 organization of matter. Dealing with these issues requires a deeper analysis of how
402 self-organization of life could occur.

403 In summary, since stars and planetary systems originate from the formation and
404 subsequent evolution of molecular clouds, the organic matter found in minor bodies

405 resulting from the described process constitutes, at least partially, a remnant of the
406 one present before the accretion of the interstellar grains to form, in a sequence,
407 interplanetary dust disks, then planetesimals in the protoplanetary disk that will
408 transform into planets but leaving various debris, the so-called minor bodies. The
409 whole process eventually leads to the meteorites analysed after they reached the
410 Earth's surface. For telluric planets in the inner solar system like the Earth, volatile
411 elements have most probably been lost⁶⁸. The delivery of water and organic matter
412 through the fall of these small bodies after the accretion process might turn out to be
413 a decisive parameter of their future ability to sustain the processes leading to life.

414 **X. 3. The Self-organization of Life**

415 **X. 3. 1. Diversity, Complexity and Organization**

416 In the extant world, actually nothing can be considered at equilibrium. Even the
417 elemental composition of nebulae and other objects in the Universe does not
418 correspond to equilibrium mixtures. The strong barriers that inhibit reactions between
419 nuclei actually thwarted the evolution of mixtures of gas that were initially mainly
420 constituted by hydrogen and helium. Interestingly in the context of the study of self-
421 organization and as already pointed out by Eigen and Schuster²⁵, some of the
422 processes that rule the evolution of elements in hot stars actually correspond to
423 catalytic cycles as the Bethe and von Weizäcker cycle. Kinetic features are likely to
424 play a role in the self-organization of organic matter as well. Analyses of abiotic
425 organic matter found in meteorites²⁶ or formed under simulated conditions^{27,65}
426 demonstrate a wide molecular diversity exceeding the one observed in living
427 systems^{69,70}. For instance, its diversity in terms of isomer compositions should
428 correspond to the maximal degree allowed by stochastic mechanisms of formation

429 (including regio- and stereo-isomerism or chirality) rather than the more reduced set
430 driven by cellular activities. Biochemical systems have to be considered as complex
431 in term of functional organization, while abiotic organic matter is complex in term of
432 molecular diversity. Therefore, the transition from abiotic to living corresponds to
433 processes that drove the chemistry to *a higher degree of organizational complexity*
434 *and a reduction of structural diversity*. It has been suggested that high molecular
435 diversity in complex mixtures might be the source of functional properties⁷¹.
436 However, the processes through which such features of self-organization might be
437 brought about remain unknown. By contrast, the high degree of diversity in abiotic
438 organic matter suggests that any pathway for self-organization must involve
439 selection. This requirement for selection is in agreement with our above-made
440 observation that the mere presence of the elements necessary for life at the surface
441 of the Earth may be considered as a result of their ability to be involved in the
442 formation of solid organic matter and thus to overcome the volatility of their lower
443 mass combinations. The late delivery of these elements as meteorite components
444 may constitute a way to overcome the loss of CHNOPS components, which are
445 essential for life, during the accretion process. Selection processes may actually
446 have played a much broader part in astrochemistry. It has been for instance
447 demonstrated that chiral imbalance can be observed under the influence of circularly
448 polarized light in simulated interstellar ices⁷². The observation of enantiomeric
449 excesses exceeding the outcome of these processes⁷³ also suggests that, in their
450 parent bodies, the organic matter of meteorites should have endured chemical
451 transformations leading to chiral amplification. Such processes, initially suggested
452 from the study of mathematical models^{74,75} and supported by experiments in the
453 laboratory (though not in a context compatible with life as we know it) by Soai et al.⁷⁶;

454 can obviously be classified as kinetic selection acting by driving the composition of
455 organic matter away from the statistical distribution expected from equilibrium
456 thermodynamics.

457 **X. 3. 2. On the Possible Occurrence of Chemical Determinism as a Driving** 458 **Force for Evolution**

459 The development of living organisms, as that of embryos or the growth of
460 populations of cells, corresponds to processes in which the system increases its
461 overall degree of organization, in contradiction with the direction of evolution signified
462 by the Second Law. These processes must then be coupled to the dissipation of
463 energy so that the overall entropy does not decrease. The systems must therefore
464 be open to exchanges of matter and energy and receive low-entropy forms of
465 energy²³. Understanding the processes through which the system achieves self-
466 organization in a way coupled to energy dissipation is therefore essential to identify
467 the pathways through which life could have emerged. In evolutionary biology, this
468 process has been identified as an improved ability to give rise to a numerous
469 offspring in population of variants submitted to natural selection¹⁵. A logical
470 consequence would be to consider that natural selection was present and effective
471 at very early stages in the process. However as suggested by Pross¹⁶, there is a
472 logical issue in using concepts defined at a higher hierarchical level of complexity
473 (within the context of biology for instance) to explain phenomena occurring at a lower
474 hierarchical level of integration of science (in chemistry for instance). Any circular
475 reasoning of this kind should be avoided when trying to explain how life proceeds.
476 However, it remains that the occurrence of more or less efficient kinetic selection
477 processes might be a first clue for the identification of self-organization processes.

478 The question of the driving force that could have preceded natural selection, before
479 life was established, has not received a definitive answer, yet. In order to answer this
480 question, the kind of evolutionary force, which can direct the systems in a direction
481 opposite to the imperative of the Second Law has to be identified. Since the variety
482 of biomolecules found in living organisms is limited compared to that produced by
483 abiotic synthesis, it is very likely that self-organization processes leading to life
484 involved selection of a kinetic kind, to avoid the combinatorial explosion leading to
485 the wide diversity that abiotic molecular chemistry can statistically produce. This
486 possibility is fully consistent with a principle of evolutionary continuity since by
487 essence natural selection is based on kinetics¹⁶. This observation suggests that the
488 driving force for the self-organization of life would rather be revealed by focusing on
489 the kinetics according to which change is produced in the corresponding system,
490 rather than by searching for any other chemical properties of biomolecules. This
491 emphasis made on kinetics constitutes the most important point that will be
492 developed in our approach. The search for deviations to statistical distributions
493 between or within families of organics should therefore constitute a criterion for the
494 identification of these processes.

495 Nevertheless, other possibilities of driving forces have been considered in order to fill
496 the gap between usual chemical systems in which evolution is ruled by the second
497 law and biological ones in which natural selection is responsible for organization. No
498 clear evidence in favour of a possibility of an independent driving force can be found
499 in the historical record of the biological world. For instance, it can be suggested that
500 an evolutionary process towards the equilibrium state might have led self-
501 organization at early stages. Hypotheses corresponding to that possibility have been
502 proposed. One of them argues that some selectivity may be induced by the presence

503 of minerals in a given environment. This is the case for instance for the formation of
504 ribose, a low yield product of the formose reaction while it constitutes an unstable
505 intermediate in the formation of valuable nucleic acid building-blocks⁷⁷. Borates have
506 been proposed to solve this issue through the formation of covalent adducts⁷⁸.
507 However, though not impossible, the eventuality that the adduct corresponds to a
508 state in which a compound like ribose can be both protected from breakdown and
509 reactive in selected pathways is improbable. The occurrence of similar processes at
510 the same time and in a same place for different components of a protometabolism
511 actually corresponds to an almost zero probability.

512 Another hypothesis involves self-organization processes reminiscent to
513 crystallization in which the entropy loss associated with an increase in organization is
514 compensated by the formation of numerous weak but favourable interactions. For
515 instance, the replication of layers in clays⁷⁹ has been considered as a way of
516 reproducing information. How the arrangements formed in this way could have
517 evolved further into a system based on the polymerization of chemical building
518 blocks remains, however, merely speculative. We therefore have a limited
519 understanding of the pathways through which a deterministic process of evolution of
520 matter driven by chemical affinities could have been converted into the process of
521 natural selection, in which occasional replication errors can be selected as a source
522 of self-organization.

523 Other proposals consider that systems in a far from equilibrium state may undergo
524 evolution towards self-organization as a result of processes like dissipative
525 adaptation or of a tendency to maximize energy dissipation or entropy production^{80–}
526 ⁸⁶. These hypotheses are consistent with the observation that life is associated with
527 processes occurring in far from equilibrium situations. Living organisms must

528 therefore behave as open systems fed with low entropy forms of energy to avoid a
529 violation of the second law²³. Energy dissipation is therefore associated with these
530 processes. Living organisms indeed correspond to the definition of dissipative
531 structures and their presence induces an increase in dissipation as they exchange
532 energy and matter within an environment characterized by a strong disequilibrium.
533 Much work has been carried out to identify a principle of maximization of energy
534 dissipation as a driving force for the self-organization of living organisms as well as
535 that of the whole biosphere^{82–86}. These theoretical approaches point towards a
536 maximization of the amount of heat or entropy released by the system, which
537 characterizes changes in macroscopic state functions. They are in contradiction with
538 the view developed subsequently that understanding the process requires analysing
539 what takes place at the microscopic scale. The important parameter would therefore
540 rather lie in the potential of the source of energy able to drive the system than in the
541 scalar amount of heat dissipated^{87,88}. This property is just related to the fact that
542 energy is quantified when considering events occurring at the scale of particles,
543 atoms or molecules. Even if macroscopic thermodynamic state functions can be
544 helpful in predicting the evolution of systems near equilibrium, the role of kinetics
545 becomes essential at a larger distance from equilibrium⁸⁹. It must be emphasized
546 that there is no relationship between the thermodynamics and the kinetics of
547 chemical processes involving species bound by covalent bonds. In other words, the
548 kinetic barriers between reactants and products are not related to the relative
549 energies of the initial and final state of a reaction. Therefore, macroscopic
550 thermodynamic state functions could hardly govern the evolution of a far from
551 equilibrium system towards self-organization⁹⁰.

552 Independently of this issue, laws effective at the macroscopic scale could hardly be
553 helpful in understanding processes occurring at the microscopic scale like variation
554 in the structure of metabolites and catalysts as well as that of polymers that gain a
555 property of information carriers. Apart from determinism, the conditions present on
556 the surface of a planet are likely to be mostly the result of contingent events. These
557 events may lead to specific arrangements of matter or specific conditions (e.g. the
558 presence of both liquid water and organic matter at the surface of a telluric planet).
559 As mentioned in the preceding sections, these specific arrangements may be the
560 result of phenomena occurring at different stages (like the interstellar formation of ice
561 grains and their further accretion into larger bodies). Though the relationship
562 between the two processes can have an explanatory power to account for these
563 contingencies, considering the two processes as a linear progress of a deterministic
564 kind corresponds to teleological views that must be firmly avoided in modern
565 science, the very essence of the Copernican revolution¹⁶.

566 **X. 3. 3. Identifying the Actual Drivers for Self-organization**

567 Finding a proper definition of life is a difficult issue and much work has been devoted
568 to this end⁹¹. Moreover, such a goal does not necessarily rests on well-defined
569 physical grounds and any definition would rather be considered as arbitrary than
570 objective. It is very likely that the long process starting from simple self-reproducing
571 chemical systems and leading to a fully equipped cell involved many intermediary
572 stages. Selecting a given step in that process, as corresponding to the emergence of
573 the first living organism, may certainly not be straightforward and would most
574 probably lead to a lengthy debate. It seems therefore not mandatory to address this
575 issue in an experimental origin of life perspective. Focusing on the driving forces that

576 rule the process would most likely be more important than on the specific nature of
577 the molecular or supramolecular structures through which the process ensued.

578 By contrast, when considering evolutionary biology, the driving force is clearly
579 identified as natural selection operating within populations of variants. Natural
580 selection is of essentially kinetic essence. It would be conform to the continuity
581 principle that the emergence of natural selection was the outcome of an earlier
582 process of selection based on kinetics. The wide diversity of abiotic organic matter
583 makes most of its components useless for the self-organization of life. The
584 occurrence of kinetically favourable processes, orientating synthesis towards that of
585 selected useful species rather than to that of a wide diversity (as a result of catalysis
586 for instance), should be highly favourable to its development. Kinetic features,
587 including catalysis, can indeed be efficiently selected just because they take place
588 rapidly (Figure X.2).

589 [Insert Figure X.2 here]

590 The idea that natural selection evolved from an earlier selection process of kinetic
591 nature was one of the main bases of the proposal of Dynamic Kinetic Stability (DKS)
592 in replicating systems by Addy Pross^{16,92}. This essential feature of systems able to
593 reproduce themselves, whatever their nature – chemical replicators or autocatalytic
594 networks of reactions – lead the most efficient of them to be selected among variants
595 just because they produce more of themselves. The idea that systems able to
596 multiply themselves express a specific kind of stability has been developed by Pross
597 since 2003^{16–19}. The essential property of these systems is that, provided that
598 conditions remain favourable to their survival, they can only evolve in the direction of
599 an increased kinetic stability. The concept of DKS in replicating system was

600 additionally proposed to account for the emergence of functions in the living world as
601 well as its teleonomic character through which changes leading to an improvement
602 of these functions appear as goal-directed^{93,94}, even though it is only the result of
603 chance and selection. It must however be expressed clearly that nothing in the
604 above description is in contradiction with the Second Law since a condition for the
605 expression of DKS is the presence of a disequilibrium such that reproduction can
606 take place according to an exponential law. Within a specific set of conditions
607 involving mainly a far from equilibrium situation, the evolution of systems able to
608 reproduce themselves do not follow a path leading to thermodynamic equilibrium
609 characterized by an increased probability²⁰. On the contrary, provided that they are
610 fuelled to maintain the far from equilibrium situation, they can lead to the kinetic
611 selection of most efficient replicators than can be considered as the most kinetically
612 stable²⁰. This behaviour is closely associated with a general notion of stability,
613 different from its more specific thermodynamic meaning in physical sciences, which
614 can be understood as time stability or persistence²⁰. Tautologically, this definition of
615 stability implies that spontaneous processes can only lead the system to evolve in
616 one direction, that of more stable (more persistent) states, until they reach a situation
617 where they can no longer evolve.

618 The important consequence for the origin of life is that DKS in replicating systems
619 constitutes the fundamental driving force for their evolution. It can lead reproducible
620 systems to evolve in the direction of an improved ability to make more of themselves,
621 provided that possibilities of variations are present in the systems. The intimate
622 nature of the system is not important when considering this kinetic feature.
623 Autocatalytic reaction networks or template replicators are likely to behave similarly.
624 The only condition is that their growth takes place through an exponential law^{25,95}.

625 Deviations to exponential growth have indeed been identified as limitations to this
626 behaviour as in the template replication of polymers^{96–98}.

627 The requirement for exponential growth is also an essential feature of living
628 organisms. This is for instance observed in the irreversible character of reproduction,
629 meaning that the reproduction cycle cannot unfold in the reverse direction (Figure
630 X.3)⁸⁸. Transitions in the cell cycle or in the development of living organisms indeed
631 correspond to irreversible processes without any possibility of reversion into earlier
632 stages. This feature constitutes a drastic difference with the usual approaches,
633 through which physics describe changes in material systems that are commonly
634 simplified to ideal reversible processes before any analysis⁸⁸. For instance, the
635 motion of particles is governed by the principle of microscopic reversibility meaning
636 that it should unfold in the reverse direction upon time reversal. Irreversibility in
637 physics is usually missing at the microscopic scale but classically associated with the
638 statistical description of macroscopic systems as a consequence of Boltzmann's
639 analyses²⁰. Making a process irreversible at the microscopic scale requires
640 additional features to be present⁹⁹. To proceed irreversibly, an autocatalytic loop
641 must be fed with energy (Figure X.3) and the reversal of the intermediate I into
642 reactants must be avoided by kinetic barriers^{100,101}. An estimate of the height of the
643 kinetic barrier can be made by considering that the reaction reverting the reactants
644 from intermediate I is slow at the time scale of the reproduction process (generation
645 time). Under these conditions a favourable reproducible variation in the structure of
646 catalyst C would become predominant in a population of replicating systems
647 independently of its initial abundance, provided that the replication process leads to
648 exponential growth⁹⁵.

649

[Insert Figure X.3 here]

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650 This analysis shows that the occurrence of a process mimicking natural selection in
651 simple chemical autocatalytic systems has to meet requirements in terms of distance
652 from equilibrium, kinetic barriers of the reverse process^{47,100,101}, as well as in terms of
653 the quanta of energy provided to the system to surpass these barriers⁸⁸. As soon as
654 these conditions are met and that possibilities of variation are available, the system
655 can only evolve in the direction of an increased kinetic stability, which may include
656 features of organization¹⁰². In other words, the maximization of DKS becomes a
657 driver for evolution in the direction of improved systems that may involve emergent
658 possibilities of self-maintenance and other features of self-organization. At a certain
659 stage these systems might be considered as living according to different arbitrary
660 criterions based for instance on the presence of a metabolism and of a sub-system
661 allowing the storage of information and its use in the reproduction cycle.

662 **X. 3. 4. The Importance of Kinetic Barriers for Kinetic Selection**

663 It therefore turns out that a condition for a system to undergo a selection process
664 working in a way analogous to natural selection rather lies in a limited spontaneous
665 reactivity of activated intermediates than in the presence of catalysts merely making
666 reactions faster. In other words, kinetic selection requires the system to evolve
667 slowly toward the equilibrium state unless no improvement can be made. In biology,
668 this is the case for instance of energy carriers like ATP that are spontaneously
669 almost unreactive at the time scale of usual biological processes but that can
670 undergo fast reactions as a result of enzyme catalysts selected and optimized by
671 evolution¹⁰³. This condition has been clearly stated by Albert Eschenmoser
672 repeatedly⁴⁴⁻⁴⁶. He considered the prerequisite of “a chemical environment held in a
673 non-equilibrium state by kinetic barriers”⁴⁴, as a condition for self-organization in
674 chemical systems. As soon as this condition is met, processes that can circumvent

675 the kinetic barriers (catalysis or autocatalysis) can develop as features of self-
676 organization¹⁰². It turns out that covalent bonds, stronger than many other weak
677 chemical interactions, are associated with significant kinetic barriers. Indeed, any
678 possibility of reaction requires the covalent bonds to be cleaved to a certain degree
679 before a new bond can be formed. Other types of chemical bonds like electrostatic
680 interactions or weak bonds like hydrogen bonds or Van der Waals forces can usually
681 be expressed without necessitating a cleavage of other interactions at a reacting
682 centre. Kinetic barriers, associated with covalent bonds, were considered in previous
683 sections of this review as essential for the stability of organic matter in interstellar
684 space. They may have allowed the delivery of the elements from which organic
685 matter is made at the surface of a telluric planet like the Earth, which may otherwise
686 be missing due to their volatile character.

687 Kinetic barriers are similarly found as critical in the self-organization of life as well.
688 This unanticipated influence of kinetic barriers on two otherwise non-related
689 processes occurring in the evolution of matter in the Universe provides some
690 grounds to the relationship between the abiotic formation of organic matter in space
691 or in the environment of planetary bodies and the development of life. Strong kinetic
692 barriers associated with covalent bonds are needed in both processes as
693 determining factors allowing, on the one hand, for the kinetic selection of stable
694 chemical species in space and, on the other hand, for that of stable features of self-
695 organization.

696 The identification of a relationship between the generation time of a self-reproducing
697 chemical system and the possibility of initiation of a process similar to natural
698 selection leads to that of a quantitative threshold allowing for the emergence of
699 kinetically based self-organization processes. The occurrence of a cycle working

700 irreversibly as in Figure X.3 (right) is dependent on the barrier of the reverse
701 reaction, which requires being high enough. The dissipation of the free energy
702 content of an energy carrier, i.e. its conversion into heat, to which the cycle is
703 coupled, ensures the necessary irreversibility. The barriers can be assessed using
704 the Eyring equation relating temperature, kinetic barriers and rates constants. The
705 values of these three parameters are therefore bound to each other for systems in
706 which selection of the more kinetically stable variants is effective, i.e. evolving
707 according to a maximization of replicating DKS. An assessment was made using the
708 following reasonable hypotheses:

- 709 - Considering the temperature at which water is in its liquid state, which is
710 essential for the development of its specific properties of hydrophobic
711 interactions¹⁰⁴.
- 712 - Considering generation times of seconds to 100 years

713 This assessment resulted in an order of magnitude of the kinetic barriers of ca. 100
714 kJ mol^{-1} (Refs. 100,101), close to 0.96 eV, expressed using a unit referring to
715 microscopic events. Taking into account the need of additional energy for the system
716 to perform chemical work a value of ca. 150 kJ mol^{-1} (1.45 eV) has been assessed
717 for a chemical reproduction cycle based on simple autocatalysis. Feeding an
718 autocatalytic cycle with several quanta of energy having a lower potential could not
719 be considered as equivalent⁸⁸. A cycle fed by such degraded forms of energy cannot
720 proceed irreversibly unless a very specific process is available for upgrading these
721 quanta into a more potent one and thus for compensating for the associated entropy
722 loss. This compensation is required to meet the Second Law and can only result
723 from the operation of a kind of thermodynamic engine⁸⁸.

724 The emphasis made on the importance of kinetic barriers as a prerequisite for self-
725 organization was above noticed as an indication that, in principle, catalysis should
726 not be crucial for an evolutionary process ruled by an increase in DKS. This
727 statement seems in contradiction with the usual description of biochemical
728 processes that assigns an enzyme catalyst to almost every unitary step. Moreover,
729 the evolution of enzyme structures constitutes an ideal example in which the
730 efficiency of genetically encoded biochemical processes can be monitored and
731 optimized^{105,106}. Indeed, enzyme efficiency is classically described by the
732 complementarity of the enzyme structure with that of the transition state of the
733 reaction stabilizing the later^{107,108}. Autocatalysis can indeed arise when a genetically
734 encoded product or intermediate of a reaction constitutes a catalyst for its own
735 formation. Evolution can therefore make a selection among a set of different variants
736 acting on this process (Figure X.4, left panel). The presence of a well-identified
737 catalytic step is not needed for observing autocatalysis (Figure X.4, right panel).
738 There are others and actually simpler means through which autocatalysis can be
739 brought about. Actually, the autocatalytic property of a chemical reaction network is
740 rather related to a stoichiometric behaviour than to a catalytic one. The requirement
741 for an autocatalytic cycle lies in the outcome of one round of the cycle that results in
742 the formation of more than a stoichiometric amount of a given component (Figure
743 X.4, right). As a result, the total amount of each component of the cycle should
744 increase as the reaction proceeds, which can be observed from a variety of network
745 architectures^{109,110} without any need for a direct catalytic step.

746 [Insert Figure X.4 here]

747 The mechanism of the formose reaction¹¹¹, converting formaldehyde into
748 carbohydrates, indeed constitutes a classical example of network in which

749 autocatalysis does not result from a clearly identified catalytic step (Figure X.5).
750 However, the condition that autocatalysis can be observed provided more than one
751 entity of a component of the network is produced at every round of the cycle should
752 take into account side-reactions that have been omitted on Figure X.5. This
753 drawback introduces a limit on the complexity of the network but may also be
754 compensated by cross-catalysis or other additional features of complexity. In relation
755 with this observation, it is worth mentioning that catalysis can be brought about by
756 the activity of organic compounds^{112,113} and is not limited to metallic ions or surfaces
757 that can hardly be considered as components of a network of organic reactions.

758 [Insert Figure X.5 here]

759 The example of the formose reaction illustrates how the occurrence of catalysis by
760 organics, organocatalysis^{112,113}, may have played a specific role in the selection of
761 positive feedback before the emergence of encoded catalysts (Figure 3). Some of
762 these processes can be highly efficient. For instance, intramolecular reactions, in
763 which neighbouring groups are located in a proper position to react, can benefit from
764 a substantial part of the rate enhancement provided by enzymes¹¹⁴, which has been
765 assigned to an entropic origin¹¹⁵. Certain organocatalytic processes, involving a
766 transient formation of a covalent adduct, can take advantage of a similar situation.
767 This process of induced intramolecularity^{116–119} can result in rate increases
768 representing several orders of magnitude, which may be easily available in a
769 prebiotic context¹¹⁶. Though having a scope limited to compounds presenting a
770 favourable structure, the advantage of this kind of catalysis in the origin of life
771 context is its simplicity that does not require the occurrence of multiple weak
772 interactions with transition states in a properly defined three-dimensional structure
773 that is responsible for enzyme efficiency¹²⁰. It may also have orientated chemical

774 evolution in the direction of multifunctional compounds like amino acids or
775 nucleotides for which some reactions can take place through 5- or 6-membered
776 cyclic transition states. However, the disadvantage of these systems as well as other
777 metabolic pathways is their limited evolvability, which should have been overcome
778 by the recourse to polymers of defined sequence to allow for a wider range of
779 variations^{121,122} and eventually open-ended evolution¹²³.

780 **X. 3. 5. Favourable Environmental Conditions for the Origin of Life**

781 Liquid water is commonly considered as a prerequisite for life. There is substantial
782 support to this assumption that includes its large abundance in the Universe as
783 justified by cosmic abundance constraints given above, the wide temperature range
784 in which it remains liquid, its very specific properties in inducing hydrophobic
785 interactions, or its ability in establishing hydrogen bonds and allowing proton
786 transfers¹⁰⁴. The requirement for liquid water defines a temperature range for the
787 occurrence of life based on organic matter. However, life is not compatible with the
788 whole range at which water is present as a liquid (below 647 K, the value of its
789 critical point). No life form has ever been observed to grow above 122 °C (395 K)
790 and most living beings are adapted to temperatures below 50 °C (323 K), with the
791 exception of thermophilic and hyperthermophilic microorganisms¹²⁴. Only the lower
792 range in which water is liquid is therefore favourable to life as we know it and very
793 probably to its origin. The requirement for kinetic barriers sufficient to hold the
794 system in a far from equilibrium state^{44–46} may account for this observation. Indeed,
795 raising the temperature from 300 to 400 K requires the barriers to be increased by
796 ca. 40 kJ mol⁻¹ for the system to have a similar lifetime^{100,101}. The rates of most
797 chemical reactions of covalent bonds increase in a non-selective way at high
798 temperatures rendering more difficult to meet the condition on kinetic barriers.

799 Breakdown processes leading to the equilibrium state can indeed become
800 predominant at the expense of very specific metabolic pathways that allow living
801 organisms to avoid the relaxation towards the equilibrium state. The lower range of
802 temperatures at which water remains in the liquid state (below or close to 300 K)
803 therefore constitutes the *most favourable* conditions for the origin of life. Under these
804 conditions, the relationship between the height of the kinetic barriers holding the
805 chemical environment at distance from equilibrium and the potential energy feeding
806 the system led to consider a potential equivalent to that of visible or UV light as a
807 requirement. Under these conditions, reproducing chemical entities made of covalent
808 bonds with generation time equivalent to that of most living beings on Earth^{100,101} can
809 undergo a process mimicking natural selection. The set of parameters values
810 (temperature, energy and timescale) deduced from the above analysis is matching
811 the conditions that were likely present at the surface of the early Earth. Even though
812 an origin of life under less favourable conditions cannot be ruled out, this
813 correspondence must not be considered as fortuitous and is on the contrary an
814 indication of the relevance of our analysis. It is worth noting, once again, that the
815 kinetic barriers associated with covalent bonds are also responsible for the stability
816 of organic matter in interstellar space, a matter which is easily formed by irradiation
817 of icy grains. That process was indeed considered above as essential for trapping
818 otherwise volatile elements like CHNOPS into interstellar ice grains for periods
819 exceeding that of the timescale of planetary systems formation and later for their
820 delivery on the surface of rocky planets. Kinetic barriers associated with covalent
821 bonds are then involved in processes as different as the origin of life and the
822 differentiation of environments like that of the surface of the early Earth. Hence, one
823 of the most important features of organic matter is related to its kinetic behaviour.

824 The low reactivity of covalent bonds at low and moderate temperatures, on the one
825 hand, allows the delivery at the surface of rocky planets of otherwise volatile
826 elements under some form rich in chemical components of prebiotic potential. On the
827 other hand, this low reactivity avoids chemical systems to rapidly evolve towards the
828 equilibrium state opening the possibility of complex reaction pathways that may
829 include non-linear kinetic behaviours.

830 **X. 3. 1. New Directions for Research**

831 It turns out that DKS in chemical systems can express its power of directing the
832 evolution of the system towards a higher degree of stability by selecting the
833 kinetically more efficient reproducing entities when the system is held at sufficient
834 distance from equilibrium. Such a distance implies that the reproduction cycle
835 proceeds irreversibly. Experimental research in the field of the origin of life should
836 therefore concentrate on processes more or less closely related to autocatalysis or
837 including positive feedback that can express a non-linear behaviour under far from
838 equilibrium conditions when the transformation in the reverse direction is negligible.
839 However, in many cases identifying autocatalysis, or similar kinetic behaviours, turns
840 out to be difficult. Autocatalysis could be defined as the kinetic outcome of a reaction
841 cycle or network in which more than one entity could be produced after one round.
842 Its definition is therefore stoichiometric. It is worth emphasizing the need of accuracy
843 in kinetic measurements since a second order kinetic law might escape a rough
844 analysis and could be overlooked by using non-accurate analytical methods or a
845 limited range of experimental data¹²⁵. Another issue is related to the fact that no
846 theoretical rule limits the size of the chemical network required for autocatalysis.
847 Furthermore, this kinetic behaviour appears as an emergent property of the whole
848 network that requires to be analysed as such. It has even been considered that the

849 probabilities of autocatalysis may grow faster than the size of the network¹²⁶.
850 However, an increased size requires higher yields to achieve the condition that the
851 self-replicating entity is produced in more than 1 stoichiometric equivalent at every
852 round. That threshold could additionally depend on various experimental parameters
853 including temperature, concentrations, pH, etc. Identifying an authentic *emergent*
854 autocatalytic network therefore needs a wide range of conditions to be analysed.
855 Moreover, the behaviour of complex systems involving several reactants are more
856 difficult to figure out than straightforward chemical processes. This is the source of
857 one of the most important barriers hindering the identification of autocatalytic
858 processes. It lies in the fact that the whole network of reactions must be performed
859 for the autocatalytic behaviour to be expressed. Indeed, autocatalysis is a property of
860 the network not that of a single reaction, whereas the usual custom of chemists
861 consists in isolating reaction steps, usually for increasing specific yields in a
862 synthetic approach, rather than considering systems of reactions. This custom,
863 though usually highly efficient, is likely to fail when looking for autocatalytic
864 properties of networks. These remarks constitute a strong indication in favour of
865 using a *Systems Chemistry*^{127–129} approach to the emergence of self-organization.
866 This approach means that chemical systems made of different components,
867 reactions, or even sub-systems should be considered to tackle self-organization with
868 the intuition that the most important features should emerge from the combination of
869 parts of the systems rather than from a fully reductionist approach.
870 With respect to an autocatalytic behaviour, the fact that it often results from a
871 collective behaviour of a network means that studying the whole system could be
872 compulsory for its detection instead of analysing its parts separately. Several
873 examples involving the use of original methods for the detection of autocatalytic

874 behaviour have been reported for processes that are related to the origin of life.
875 Weber¹³⁰ indeed identified an autocatalytic property of the product in the reaction of
876 trioses with ammonia by iterating reactions in the presence of the crude product of
877 preceding experiments. This procedure allows the detection of the catalytic activity of
878 a product or side-product without needing the prior knowledge of its nature and is
879 therefore adapted to the identification of autocatalysis as a systems property^{131,132}. It
880 is reminiscent of the usual way through which strains of microorganisms can be
881 isolated in biology or of serial transfer experiments in which replicable biopolymers
882 can be evolved in test tubes¹³³. A similar procedure has also been checked to
883 identify solid surface environments able to select kinetic products out of mixtures by
884 iteratively seeding the product mixture in a fresh reaction medium¹³⁴.

885 **X. 4. Conclusions**

886 The ideas gathered in the present chapter do not constitute an attempt to define life
887 since it is an arbitrary task. However, they provide new insights on the process
888 through which self-organization may have occurred by favouring kinetically efficient
889 pathways. The transition of kinetic selection into natural selection might therefore not
890 be seen as a sharp transition but as a fuzzy one^{13,14}. Its identification should rather
891 turn out to be arbitrary rather than sharp and clear-cut. Accounting for the whole
892 process would be easier by looking for continuity than by trying to identify sharp
893 transitions. This approach provides an explanation for the specific ability of organic
894 matter in the chemistry of life. It is not directly related to the physical properties of
895 organic compounds as such but to the conditions ruling their transformations or
896 breakdowns. It turns out that a connection can be made between the formation of
897 organic matter in interstellar settings and the origin of life that is not necessarily
898 related to a very specific nature of organic matter *per se* not to a fully deterministic

899 process. Conversely, it must be based on the ability or inability of organic
900 compounds to be transformed. This observation would not constitute a surprise
901 when considering the fact that most constituents of cells are constantly regenerated.
902 The stability of living organisms is less related to the conservation of their
903 constituents than to their continuous exchange with the environment. It is therefore
904 related to organic reactivity, a very specific domain of organic chemistry in which
905 properties emerge from chemical transformations within biochemicals having
906 structures based on covalent bonds¹³⁵. It is not the organic character of the
907 extraterrestrial matter that confers it a prebiotic character but it is its ability to be
908 transformed in favourable environments and to give rise to reaction networks in
909 which complex processes associated with non-linear kinetics can occur. The range
910 of kinetic barriers allowing these properties in aqueous solution, at temperatures
911 compatible with the existence of liquid water, matches the one corresponding to
912 species stable for billions of years at the low temperatures found in interstellar
913 media. This stability may be responsible for the presence of CHNOPS elements at
914 the surface of a rocky planets at the same time as liquid water and therefore of the
915 constitution of environments favourable to the origin of life. Under these conditions,
916 the kinetic selection of systems capable of undergoing exponential growth may
917 become efficient. The non-limited diversity of organic molecules allowed possibilities
918 of non-limited variation in self-reproducing systems reaching eventually systems
919 made of biopolymers allowing an evolution based on natural selection. Emphasizing
920 the kinetic features of the process may be more helpful in the search for systems
921 presenting rudimentary traits of self-organization than looking at reactions able to
922 produce biochemical building blocks. Systems investigations aimed at identifying
923 autocatalysis or at least positive feedback behaviours should therefore be favoured.

924

925

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1129 **FIGURE CAPTIONS**

1130

1131 **Figure X. 1** An abiotic reaction network predating metabolism may have been
1132 involved in the self-organization of life at different stages e.g. by feeding a prebiotic
1133 network of reactions with essential components. Notwithstanding the role of the
1134 environment in fuelling dissipative processes, organisms endowed of a higher
1135 organization degree may also have harnessed such networks by improving them
1136 through the activity of genetically encoded biocatalysts.

1137

1138 **Figure X. 2** Features of self-organization including loops of positive feedback can be
1139 selected as a result of their kinetic advantage in way reminiscent of how natural
1140 selection proceeds. Catalysis is likely to constitute a strong player acting on kinetic
1141 selection. Simple catalysis by metals or inorganic surface may play an early role. An
1142 autocatalytic behaviour can emerge from organocatalysis and natural selection as a
1143 result, for instance, of polymer catalysts encoded by information carriers reproduced
1144 by template replication.

1145

1146 **Figure X. 3** Biological reproduction essentially proceeds irreversibly (left), whereas
1147 an autocatalytic loop must be held far from equilibrium by feeding with low-entropy
1148 energy to become irreversible. **Reproduced from Ref. 88 with permission from**
1149 **Springer Nature, Copyright 2020.**

1150

1151 **Figure X. 4** Examples of autocatalytic cycles. Autocatalytic properties can result
1152 from the catalytic ability of one component on a chemical step involved in the cycle
1153 (left).

1154

1155 **Figure X. 5** An example of autocatalytic loop in the architecture of the reaction
1156 network responsible for the formose reaction¹¹¹. The system meets a first condition
1157 for complexity by the occurrence of kinetic barriers that hinder the direct dimerization
1158 of formaldehyde into glycoaldehyde and hold the system in a far from equilibrium
1159 state. The cleavage of tetramers or pentamers into two shorter reactive
1160 carbohydrates (retroaldolization) able to undergo the reaction with formaldehyde
1161 (aldolization) allow the system to overcome this blockade through an autocatalytic
1162 behaviour.

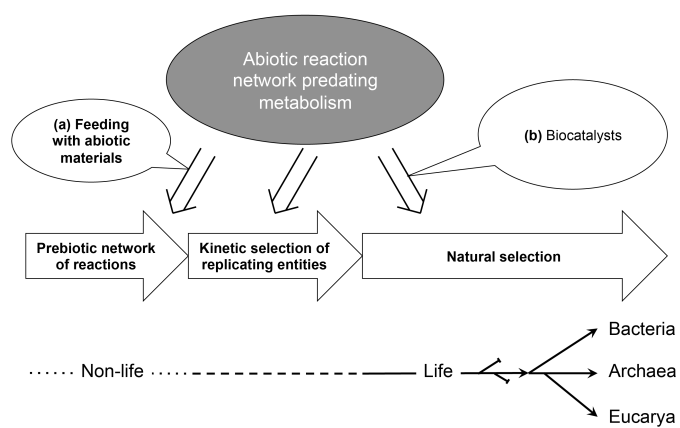
1163 **Table X. 1.** List of observed interstellar molecules. Although identified gas phase
1164 molecules dominate this list, some molecules are also observed in the solid state
1165 under the form of ices (bold). **Adapted from Ref. 53 with permission from the**
1166 **author, Copyright [2013].**

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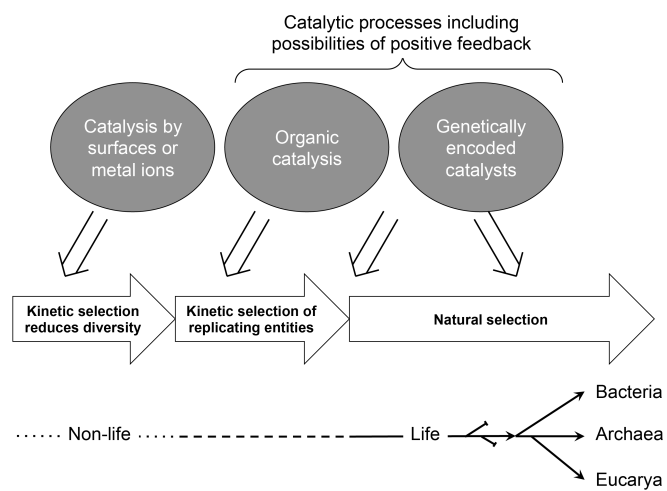
1170 Figure X. 1



1171

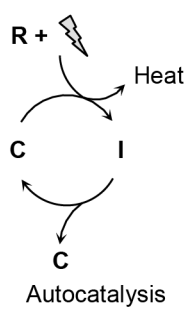
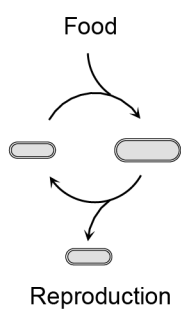
1172

1173 Figure X. 2



1174

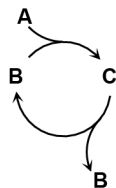
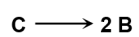
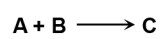
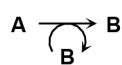
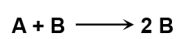
1175 Figure X. 3



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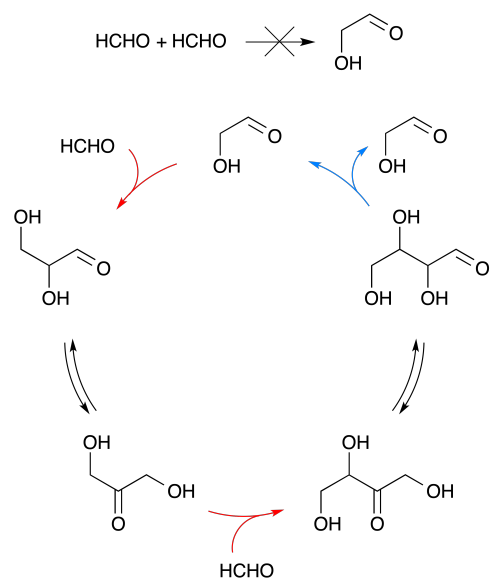
1178 Figure X. 4



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1181 Figure X. 5



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1184 Table X. 1.

2 atoms	3 atoms	4 atoms	5 atoms	6 atoms	7 atoms	8 atoms	> 8 atoms
AlCl	AlNC	C ₃ H	C ₅	H ₂ C ₃ O	C ₂ H ₄ O	H ₃ C ₃ N	CH ₃ C ₄ H
AlF	AlOH	C ₃ N	CH₄	C ₂ H ₄	CH ₃ C ₂ H	OHCH ₂ CHO	H ₃ COCH ₃
AlO	C ₃	C ₃ N ⁻	C ₃ H ₂	CH ₃ CN	CH ₃ NH ₂	HCOOCH ₃	CH ₃ CH ₂ CN
C ₂	C ₂ H	C ₃ O	H ₂ CCN	CH ₃ NC	CH ₂ CHCN	CH₃COOH	CH ₃ CONH ₂
CF ⁺	C ₂ O	C ₃ S	H ₂ C ₂ O	CH₃OH	H ₂ CHCOH	H ₂ C ₆	CH ₃ CH ₂ OH
CH	C ₂ S	H ₃ O ⁺	H ₂ CNH	CH ₃ SH	C ₆ H	CH ₂ CHCHO	C ₈ H
CN	C ₂ P	C₂H₂	H ₂ COH ⁺	C ₄ H ₂	C ₆ H ⁻	CH ₂ CHCN	HC ₇ N
CN ⁻	CO₂	H ₂ CN	C ₄ H	HC ₃ NH ⁺	HC ₅ N	C ₇ H	CH ₃ CHCH ₂
CO	H ₃ ⁺	H ₂ CN ⁺	C ₄ H ⁻	HCONH₂	CH₃CHO	NH ₂ CH ₂ CN	(CH ₃) ₂ CO
CO ⁺	H ₂ C	H₂CO	HC ₃ N	C ₅ H	...	C ₂ H ₆	CH ₃ CH ₂ CHO
CP	H₂O	H ₂ CS	HC ₂ NC	HC ₂ CHO	...	CH ₃ CHNH	CH ₃ C ₅ N
CS	H ₂ O ⁺	HCCN	HCOOH	HC ₄ N	CH ₃ C ₆ H
H ₂	HO ₂	HCNH ⁺	NH ₂ CN	CH ₂ CNH	C ₂ H ₅ OCHO
HCl	H ₂ S	HOCO ⁺	HC(O)CN	HNCHCN	H ₃ COC ₂ H ₅
HF	H ₂ Cl ⁺	HOCN	SiC ₄	C ₆ H ₆
HN	HCN	HOOH	SiH ₄	C ₃ H ₇ CN
HO	HCO	HCNO	CH ₃ O	HC ₁₁ N
KCl	HCO ⁺	HNCO	HNCNH	C ₁₄ H ₁₀ ⁺
N ₂	HCP	HNCS	C ₆₀
NO	HCS ⁺	NH₃	C ₇₀
NS	HNC	SiC ₃	CH ₃ COOCH ₃
NaCl	HN ₂ ⁺	HCOO⁻	HC ₉ N
O ₂	HNO
PN	HCO ⁺
PO	FeCN
SH	KCN
SH ⁺	MgCN
SO	MgNC
SO ⁺	NH ₂
SiC	NH ₂ ⁺
SiN	N ₂ O
SiO	NaCN
SiS	OCS
OH ⁺	SO ₂
FeO	SiC ₂
HCl ⁺	SiCN
TiO	SiNC
...	OCN⁻
...	TiO ₂

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