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Review Article

A liquid crystal world for the origins of life

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Nucleic acids (NAs) in modern biology accomplish a variety of tasks, and the emergence of primitive nucleic acids is broadly recognized as a crucial step for the emergence of life. While modern NAs have been optimized by evolution to accomplish various biological functions, such as catalysis or transmission of genetic information, primitive NAs could have emerged and been selected based on more rudimental chemical–physical properties, such as their propensity to self-assemble into supramolecular structures. One such supramolecular structure available to primitive NAs are liquid crystal (LC) phases, which are the outcome of the collective behavior of short DNA or RNA oligomers or monomers that self-assemble into linear aggregates by combinations of pairing and stacking. Formation of NA LCs could have provided many essential advantages for a primitive evolving system, including the selection of potential genetic polymers based on structure, protection by compartmentalization, elongation, and recombination by enhanced abiotic ligation. Here, we review recent studies on NA LC assembly, structure, and functions with potential prebiotic relevance. Finally, we discuss environmental or geological conditions on early Earth that could have promoted (or inhibited) primitive NA LC formation and highlight future investigation axes essential to further understanding of how LCs could have contributed to the emergence of life.

Introduction

The origins of life involved many steps, from the formation of Earth [1], to chemical reactions of prebiotic reactants [2,3], to the emergence of functional polymers [2], to the evolution of these polymers [4,5], and to the assembly of primitive compartments that eventually became modern cells [6,7]. Each of these steps resulted in (or required) an increase during chemical complexity. At one point in the emergence of life, functional polymers acquired a prominent role. Such polymers might have included peptides [3], nucleic acids [8,9], polyesters [10], depsipeptides [11], or others [12], each of which could have been synthesized through prebiotic methods such as wet–dry cycles. In particular, it is unclear whether peptides [3], nucleic acids [8,9], or another type of polymer [13] was most essential to the emergence of life. In fact, it may be that different polymers co-existed and co-evolved on early Earth [14]. Nevertheless, it is still helpful to understand the potential mechanisms by which each type of primitive polymer could have been synthesized, assembled, and functioned on early Earth in isolation. Specifically, given the reliance of modern biology on nucleic acids for genetic information storage and gene expression regulation, let us further examine the relevance of nucleic acids to the emergence of life.

Primitive nucleic acids could have accomplished two functions essential to evolving primitive chemical systems: genetic information storage and chemical reaction catalysis. Because these topics have been covered by other studies and review articles [8,9], we focus here on another aspect of nucleic acids: self-assembly. Modern biochemists discovered that NAs can form supramolecular structures when specifically designed sequences are allowed to co-assemble. Broadly termed DNA nanotechnology, complex multi-strand structures with designed shape (cubes, rigid and flexible scaffolds, empty

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shells, flat tiles, etc.) also capable of directed motion, can be obtained by mixtures of DNA oligomers with designed sequences which multiply bind to each other via Watson–Crick base-pair formation [15]. Supramolecular structures can also be obtained with additional forms of interactions that do not require such high amounts of sequence control, including kissing loops [16], G-quadruplexes [17], and modular ribozymes [18]; such supramolecular NA structures have important regulatory or catalytic properties, showing their importance to both modern biology and prebiotic chemistry. One specific type of supramolecular NA structure has been the focus of recent studies revealing their potential relevance to the origins of life: NA liquid crystals (LCs) [19,20]. LCs can be formed not only from NAs, but also from other molecules such as lipids [21], peptides [22], or even small molecules [23], and are present in biology [24]; connecting primitive LCs with modern LCs could reveal structural or functional relevance of LCs at the origins of life.

Here, we review basic NA LC structure and assembly. The relevance of NA LCs to the emergence of life, specifically in the aspects of primitive polymerization/ligation and compartment formation, as well as the prebiotic environments or mechanisms required for such LCs to form, are then discussed in the context of a 'liquid crystal world' (previously proposed [25]) where primitive LCs played an essential role in the emergence of life.

Structure and assembly of primitive nucleic acid liquid crystals

LCs are partially ordered phases in between a disordered liquid phase and an ordered crystalline phase, having properties of both. LCs are well known for use in engineering applications, such as displays, due to their ability to change orientation when subjected to electric fields [26]. Recent engineering developments have also applied LCs to responsive self-assembled soft materials, as LCs can change their molecular order based on external stimuli such as temperature, concentration, or light [27,28].

However, while LCs are often used in photonics and material science (even NA-based ones [29–31]), they can be obtained in different biomolecular solutions *in vitro* and are also present in biological systems *in vivo* [24]. For example, intracellular lipid droplets composed of triacylglycerols and cholesteryl esters can transition into an LC phase (highly enriched in cholesteryl esters) upon cellular starvation due to triacylglycerol consumption, directing intracellular lipid exchange and availability [32]. Similarly, bacterial plasmid DNA supercoils into LC phases at physiological conditions [33]. While LCs in general have been discussed to a small extent previously in the context of the origins of life [34], NA LCs in particular have only been investigated in this context within the last few years, leading to the formulation of the 'liquid crystal world' [25] scenario which hypothesizes the potential importance of NA LC phases as a mechanism to produce the required substrate for the 'RNA world' [8,9] to start.

The propensity of DNA to organize in LC phases was first reported into the literature in 1961 by Robinson, although the data were not included in the original publication [35]. In 1980, Senechal, et al. [36] characterized cholesteric DNA phases. However, DNA LCs were only made more well known in the mid-1980s by the pioneering work of Françoise Livolant, which characterized cholesteric (N*) [37], blue (B) [38], and columnar (Cu) [37,39] LC phases in highly concentrated solutions of long double-stranded DNA (dsDNA) from calf thymus. Specifically, long NA duplexes form LC because they possess enough rigidity to behave as 'rod-like' objects with a sufficiently high aspect ratio, i.e. length/diameter, which is a requirement for the LC phase transition, according to Onsager's rule [40,41]. Indeed, long-strands of DNA duplexes have a persistence length of ∼50 nm in 100 mM sodium chloride [42].

However, it is very unlikely for DNA, especially long double strands, to have existed on early Earth. It may have been more likely for RNA [8], RNA–DNA chimeras [43], or other nucleic acids (such as 'pre-RNA') [13], to have been present, but conceivably still in short oligomeric form — too short to provide the selective catalytic activity to bootstrap self-replication. Clark and Bellini discovered that end-to-end stacking of short, palindromic DNA duplexes of short length (down to 6 bp) resulted in the assembly of long linear aggregates that in turn are capable of forming LC [19]. Similarly, RNA oligomers [44] as well as mixtures of DNA and RNA 14-mers with terminal single-strand overlapping sequence 'sticky ends' [45] could also achieve LC formation. More recent studies have found that DNA as short as tetramers with 'sticky ends' exhibit LC ordering [46,47]; in such systems, duplex formation and LC phase transition happen simultaneously in a single self-assembly step in a process in which linear aggregation proceeds by the pairing of nicked-self-templeting DNA tetramers.

The previous studies all utilized pre-determined sequences including self-complementary palindromic sequences or those with engineered 'sticky ends'. Such sequence design would have been impossible on early

Earth before the advent of enzymatic polymerization, and most primitive NAs were likely random or semi-random sequences [48]. Thus, prebiotic relevance would require the investigation of NAs with sequences that are less 'engineered' and more random. This was the aim of more recent works, which showed that random-sequence DNA 20-mers [49] and even mixtures of NA monomers [50] exhibit enough end-to-end interactions to result in LC assembly too (Figure 1A–C).

In particular, nucleotide triphosphates can self-assemble into duplex pairs of stacked aggregates that long-range order into chromonic columnar LC phases. The resulting assemblies feature strongly cooperative intermolecular interactions producing a first-order transition to the columnar LC phase and physical separation of distinct molecular species into LC droplets under Watson–Crick (A with T, G with C) selectivity [50]. These features indicate that the combination of selective H-bonding, molecular packing, and nano segregation, driven by chromonic amphiphilicity, can generate the essential structural characteristics of polymeric duplex DNA by

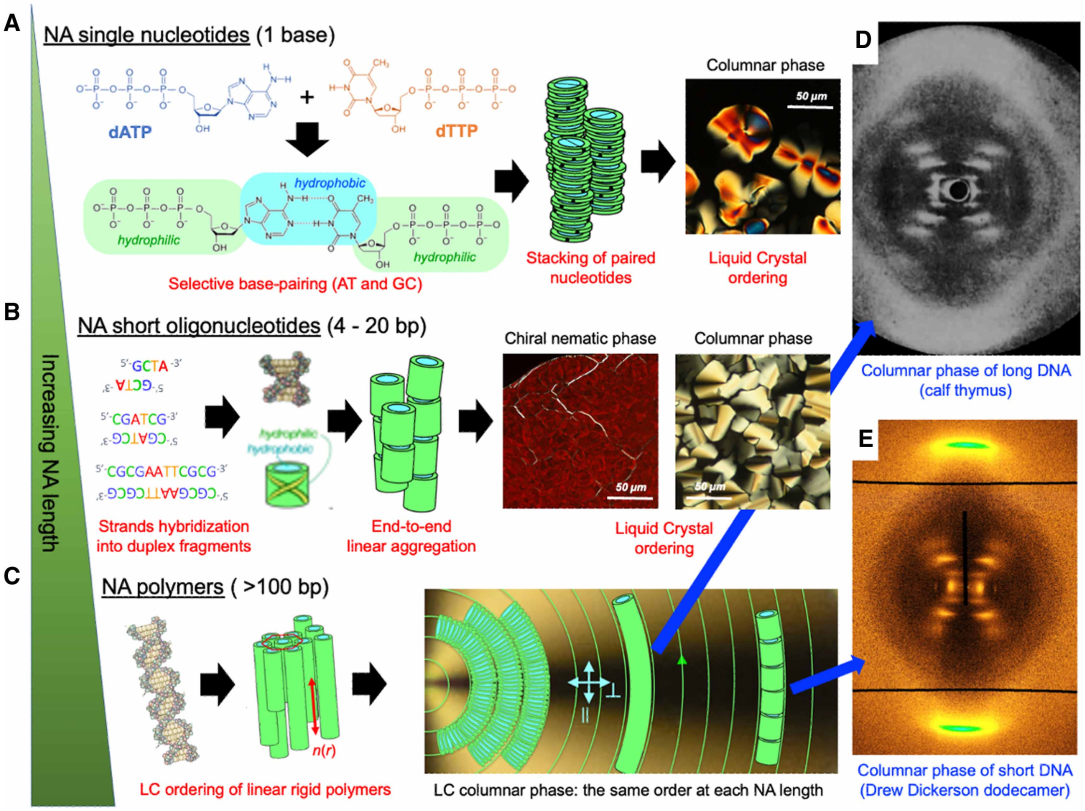

Figure 1. Liquid crystal ordering takes place in a broad and biologically relevant NA length range with different self-assembly mechanisms.

(**A**) LC assembly of the single NA nucleotides dATP and dTTP by stacking of Watson–Crick-paired nucleotides leading to columnar phases. (**B**) LC ordering of linear aggregates of short NA oligonucleotides (4–20 bp) assembled by end-to-end attractive interactions (blunt-end stacking or sticky-end pairing) between NA duplexes. (**C**) LC phases of long double-stranded DNA (>100 bp) by ordering of anisotropic stiff 'rod-like' polymers [50]. Diffuse X-ray scattering from hydrated and oriented duplex B-form DNA samples at room temperature. (**D**) A system similar to one captured by the Franklin–Gosling 'Photo 51' [51], from a fiber of hydrated calf thymus long DNA [52]. (**E**) Microbeam WAXS pattern of an oriented 2 µm ×25 µm monodomain of the columnar liquid crystal phase of the Drew Dickerson dodecamer 5′-CGCGAATTCGCG-3′ [53] (courtesy of G. P. Smith, et al.). Comparing the patterns indicates that the double helix structure in the self-complementary dodecamers, which duplex to form a ~single turn of the helix and then spontaneously stack into columns form the 'columnar' DNA liquid crystal phase, is very similar to that of long calf thymus DNA. One can infer from this that the Franklin–Gosling sample was a columnar liquid crystal. (**A**–**C**) reprinted and adapted with permission from [50] Copyright Smith et al., with an exclusive License to Publish to NAS. (**D**) Reproduced from [52] with permission of the International Union of Crystallography.

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the hierarchical self-assembly of small molecules. A key feature of this self-assembly is that stacking of more units strongly stabilizes LC ordering, with melting temperatures increasing from near freezing to near boiling as the length of the self-assembled molecules increases from NA monomers to, for example, NA dodecamers [50]. Thus, conditions promoting the stacking of more units also promote the stability of LC ordering. Particularly interesting in this regard are conditions under which the LC ordering can itself promote NA polymerization, in which case chromonics which developed polymerization would have an evolutionary advantage in a quest to develop and grow LC order. Such systems would have the potential for liquid crystal autocatalysis (LCA), in which LC ordering stabilizes and expands itself by selecting molecules and catalytically promoting their ligation, as discussed in the next section.

Finally, it is intriguing to consider that DNA and LCs have had a deep connection historically since the discovery of the double-helix: the famous Franklin–Gosling 'Photo 51' was obtained from columnar LC samples of long calf thymus DNA [39,51,52], from which the structure itself of the double-helix was unveiled. The same X-ray pattern is obtained from the columnar LC phase of NA oligomers following their linear aggregation (Figure 1D–E)! LC ordering thus should be considered an intrinsic property of a broad ensemble of NAs molecules, including both modern DNA and those prevalent on early Earth. Although LC formation has not been investigated on other types of prebiotically relevant NAs, these studies suggest that short, random-sequence duplex-forming primitive non-DNA/RNA NAs (or monomers) could also potentially assemble into LCs. We suggest this to be an active area of study in the future.

Functional roles of nucleic acid liquid crystals at the origins of life

Primitive ligation

NAs can hold genetic information and perform catalysis (such as through ribozymes [9]), with both of these functions linked *via* the primary NA sequence. Specifically, the evolution of the sequence information of NAs to achieve more relevant functions (catalytic or otherwise) would have been essential to the emergence of life [9]. However, while NAs can polymerize in a template-dependent manner, how such NAs can replicate (a prerequisite for selective NA evolution) is still not completely understood. Polymerase or ligase ribozymes could have assembled at some point on early Earth [9], but how could these ribozymes have assembled in the first place without their own catalytic activity? While many proposals have been made, including wet-dry cycles [54], mineral-catalyzed polymerization [8,9], *in situ* chemical activation [8,9], and non-enzymatic chemical polymerization [8,9], understanding how primitive NAs can arise from short oligomeric fragments or monomers and replicate is still a major area of focus within the origins of life research community.

One feature of NA LCs is their ability to assist in non-enzymatic ligation due to its unique structural features, which keep the termini of NA fragments in the right geometrical conditions to allow phosphodiester bond formation, thus playing a similar role of modern ligase enzymes (Figure 2). It was shown that 1--Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC)-activated palindromic DNA 12-mer duplexes could assemble into an LC phase through end-to-end stacking interactions, resulting in stacked DNA duplexes. This phase allowed each activated DNA to react with the adjacent DNA duplex in the absence of an enzyme, which resulted in modular ligation of 12-mer sections to form a long covalently linked DNA chain [55]. A study using similar starting materials (EDC-activated DNA), except with 14-mer DNA duplexes that aggregated through 'sticky end' pairing interactions rather than blunt end-to-end interactions, also showed similar ability for non-enzymatic ligation within an LC phase [25]. Further research has even shown the ability for non-enzymatic ligation of 6-mer or 12-mer RNA (both D- and L-RNA) with both blunt and sticky ends within an LC phase to form long RNA chains nearly 100-bases long, with a similar mechanism as the DNA ligation studies mentioned above [56]. These studies suggest that LC phases could have been primitive microreactors which drove primitive reactions, such as ligation, in the absence of enzymes on early Earth; the fact that both DNA and RNA ligation can be driven by LC phases suggests that other types of NA ligation may also be possible. Interestingly, even if EDC is not a prebiotically plausible molecule, it can be replaced by other more prebiotically relevant phosphate activation chemistries such as imidazole or imidazole-derived activation chemistry [8,9], without affecting the templating role of LCs. More advanced prebiotically relevant functions or phenomena within LC phases that take advantage of favorable LC properties, such as gap-filling of nicked DNA 20-mers within an LC phase [57], akin to primitive DNA repair, should be explored going forward. The authors also suggest that template-directed single-base polymerization of both DNA and RNA could also be

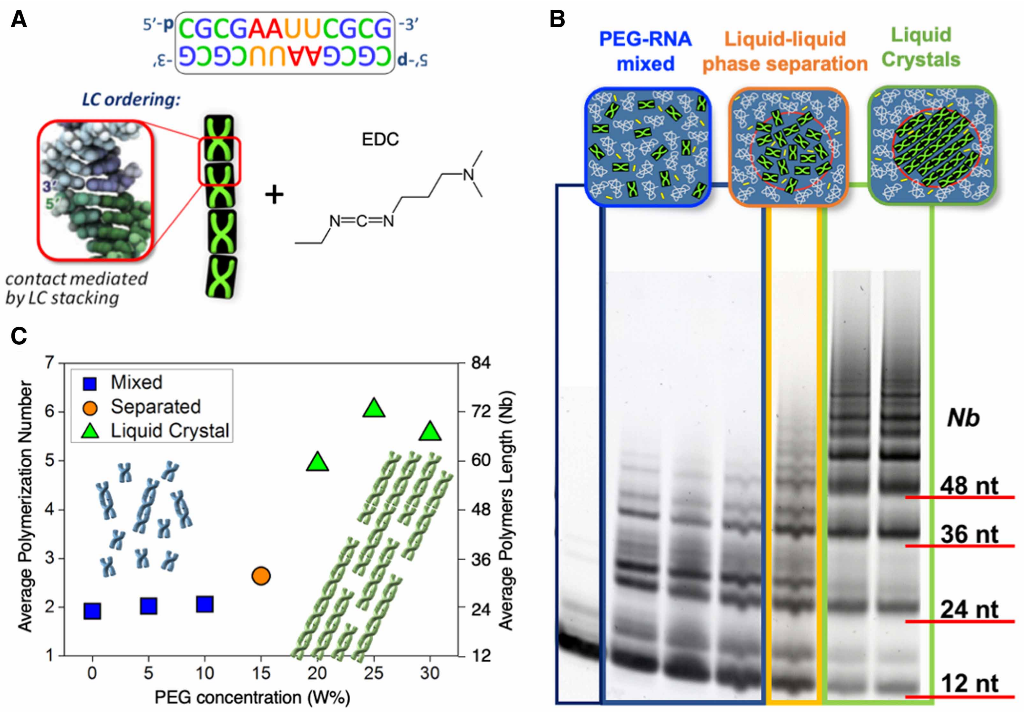

Figure 2. Liquid crystal assisted non-enzymatic ligation of oligoNAs.
(**A**) LC-stabilized end-to-end stacking of short NA duplexes keeps the termini of NA fragments (12 bp) activated by EDC in the correct geometrical conditions to enhance phosphodiester bond formation with the adjacent DNA duplex. (**B**) At increasing polyethylene glycol (PEG) concentrations, the ligation reaction can be performed in a diluted PEG-NA mixture, a liquid–liquid phase-separated structure, and a liquid–liquid crystal phase-separated structure. The formation of phase-separated LC domains boosts the formation of modular longer NA polymers (each 12 bp), as shown by gel electrophoresis. (**C**) The reaction yield is thus phase dependent, with a marked ligation enhancement observed in LC phases. Reprinted and adapted with permission from [56]. Copyright 2018 American Chemical Society.

explored in the context of LC phases, which would give even more insights into the role of LCs in primitive NA polymerization.

Primitive compartment formation

Before the advent of cells, primitive compartments (i.e. protocells) dominated early Earth [8]. Such compartments supplied functions, such as compartmentalization or replication [6], essential for the emergence of an encapsulated primitive chemical system capable of evolution (such as NAs reaction networks), and could have taken many forms including lipid vesicles [7], membraneless phase-separated compartments [58], or other structures like rock pores [59]. It has been postulated that LC assembly or existence within a protocell could further assist an evolving NA system encapsulated within the protocells to achieve more efficient ligation or polymerization (see above). While NA LCs have not to date been observed within lipid vesicles (and should be a target of future studies), they have been observed in coacervates, a type of phase-separated membraneless compartment.

Complex coacervates are often produced from electrostatic interactions of oppositely charged polymers or molecules, such as NAs (negatively charged backbone) and cationic peptides (such as polylysine or polyarginine). Thus, as DNA is a prerequisite of DNA-peptide coacervate assembly, could the DNA also be induced to exhibit LC phase assembly to generate intra-coacervate LC (also known as LLCPS; liquid–liquid crystal phase separation [60])? Theoretical studies supported the plausibility of LC-coacervates [61], while Shakya and King [62] were the first to observe the formation of cholesteric (N*) LC domains within poly-L-lysine (PLL) and 22-mer palindromic poly(GC) or poly(AT) DNA coacervates. Fraccia and Jia next discovered that a self-complementary palindromic 12-mer DNA could form the full range of typical LC mesophases, N*, uniaxial

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columnar (C_u), and crystalline-columnar (C_2), within a DNA-PLL coacervate depending on salt concentration [63,64]. The coacervate droplets underwent continuous reversible transitions upon variations of salinity, hydration, or temperature (Figure 3). Salinity, hydration, and temperature cycles relevant to LC-coacervate mesophase transitions likely would have been present on early Earth and highly relevant for primitive chemistries. Repeated cycles could have led to molecular evolution and emergence of primitive structures with increasing structural (or functional) complexity [65]. Within the LC-coacervates, DNA could be up-concentrated by up to 2–3 orders of magnitude, paralleling the RNA concentration increase observed within other related coacervate systems [66]; such coacervate formation could have been one mechanism for primitive systems to increase encapsulated NA concentration, which could be helpful for speeding up essential primitive chemical reactions (involving the NA).

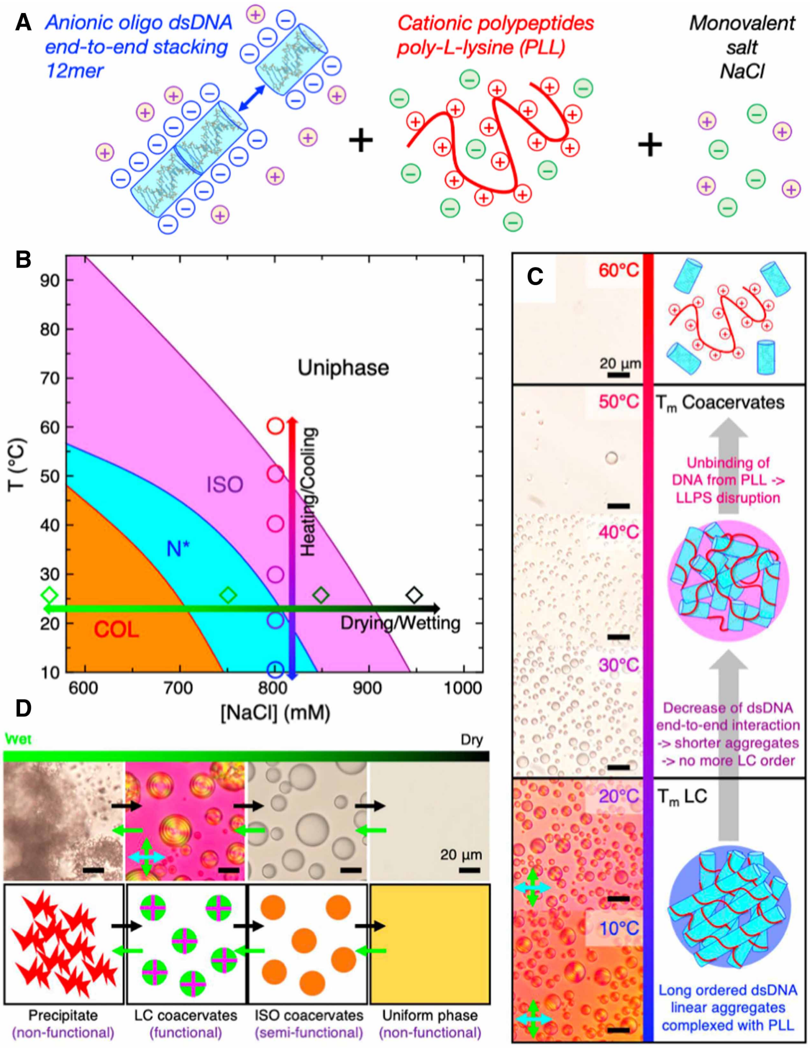

Figure 3. Salt and temperature-dependent phase diagram for liquid crystal coacervates.

(**A**) Liquid crystalline coacervates are formed in solutions of oligo dsDNA, poly-L-lysine, and NaCl. (**B**) Phase diagram of LC-coacervate formation at different temperatures and sodium chloride (NaCl) concentrations; COL: columnar phase, N*: cholesteric phase; ISO: isotropic phase. All transitions could be achieved by reversibly varying temperature or salinity (via dehydration/rehydration). (**C**) Increases in temperature result in a transition of the LC-coacervate to an ISO coacervate (without LC character), and then to a uniform phase. The right side illustrates the plausible interior structure of the DNA and peptides within the coacervate. (**D**) Increasing salinity due to dehydration results in reversible transition from a precipitate to LC-coacervates, to ISO coacervates, to a uniform phase; the reverse phase transition can be achieved through rehydration. Reprinted and adapted with permission from [64] under a Creative Commons license.

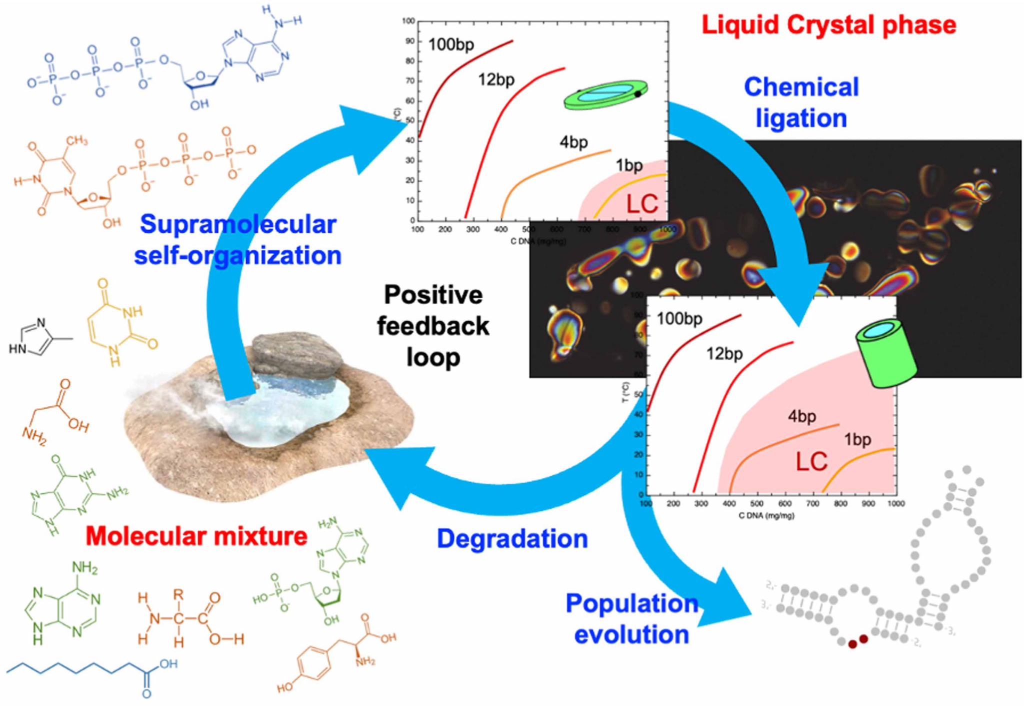

Figure 4. Schematic illustration of the liquid crystal world hypothesis.

(i) In molecular mixtures, NA monomers capable of supramolecular aggregation can form LC phases; (ii) LCs provide selection by segregation and promote abiotic polymerization in the presence of the correct chemistry; (iii) NA elongation increases the stability of LC phases to higher temperature and lower concentration, providing a positive feedback-loop, where longer NAs are most favorably further elongated; (iv) LC domains also protect NAs from degradation, and may support selection and evolution towards catalytic sequences.

However, it is not clear whether the NA liquid crystallinity contributes to coacervation, or whether coacervation (or the results therein) is what contributes to the liquid crystallinity; further studies are needed (and currently ongoing) to more clearly understand the direction of this causation (if any). Additionally, other than NA up-concentration, other functions of LC-coacervates have yet to be explored. The authors challenge the community to investigate other prebiotically relevant functions of LC-coacervates. For example, recent studies have investigated the plausibility of non-enzymatic DNA ligation within LC-coacervates [67], potentially as a mechanism to promote primitive NA polymerization within a protocell. Additionally, the studies reviewed herein only reported DNA LC-coacervates. Given that both RNA [56] and NA monomers [50] can form LCs as well as coacervates [68,69], further studies showing the plausibility of RNA or NA monomer LC-coacervates should be a target of future work.

Conclusion

The liquid crystal world hypothesis

As detailed above, the formation of LC domains of ultrashort NA chains, or even single nucleobases, brings about many features with a high potential of having been instrumental to the formation of longer active NA chains that could have been essential to the origin of life (sketched in Figure 4): (i) symmetry breaking, by which molecules aggregate in one definite direction, offering a template for linear polymerization, without which random chemistry would yield branched and circular structures; (ii) molecular selectivity from phase transitions, by which only molecules that have structural and interaction features (both based on stacking) enable participation in the collective ordering and become part of self-assembled chains, while all other molecules are macroscopically segregated in coexisting phases; and (iii) catalytic effects due to the stabilization, by collective ordering, of stacked bases, providing a constraint to the molecular positioning and orientation that favors the formation of the phosphodiester bonds.

In what follows, taking the original proposal of the 'liquid crystal world' [25], we discuss its plausibility on early Earth, introducing primitive environments or processes that could have promoted (or inhibited) NA LC assembly.

Long, stiff NA rod formation

NAs (excluding monomers) must first be in duplex form to exhibit LC character due to stiffness requirements. Thus, conditions that promoted duplex formation would be favored in a 'liquid crystal world'. Specifically, constant existence in extremely high-temperature geothermal areas such as hot springs (such as Norris Geyser Basin in Yellowstone, with a sub-surface temperature of 240°C [70]) would conceivably result in the NA duplexes to melt and also RNA strands to degrade. Similarly, end-to-end stacking interactions are required for LC formation [63], and may also be disrupted by constant high temperature. Mildly high environmental temperatures which generally inhibit duplex formation could be overcome by strands with greater GC content; early non-enzymatic template-directed RNA polymerization experiments showed that polymerization of G and C was more amenable than A and U [71], although recent innovations in polymerization chemistry have resulted in more equal incorporation of all bases [72].

Additionally, higher salinity and neutral pH are more amenable for NA hybridization [73] (primitive cycling between acidic and neutral pH promotes strand separation in acidic conditions [74]), while viscous media is also inhibitory to hybridization of single strands into duplexes [75] and can force duplexes to fold into non-linear structures (i.e. no longer a long, stiff rod) [76]. Thus, aqueous environments with higher salinity, such as oceans or saline lakes [77], could promote NA LC formation, although high concentrations of magnesium chloride could result in RNA degradation [78]. Conversely, bodies of water such as acid lakes/streams [79] and acidic [80] or alkaline [81] hot springs, or primitive gels with high viscosity [82] could be inhibitory for NA LC formation. However, recent research has shown the plausibility of regions within a multiphase coacervate which are more amenable to duplex stability, while other regions within the same coacervate are destabilizing to duplexes [83], which could be one mechanism to localize LC forming NAs within a specific area of a primitive compartment. Thus, more studies investigating LC formation in a wide variety of prebiotically plausible conditions is necessary to understand which environments could have hosted the 'liquid crystal world' on early Earth.

NA concentration and length

NA LCs require sufficiently high concentration to form, and thus a 'liquid crystal world' is also dependent on the ability for NA to be concentrated. We have already mentioned the ability for coacervate systems to up-concentrate NAs in their interior hundreds to thousand folds [63,64,66]. Aqueous two-phase systems [84], which have shown some affinity for NA segregation, have also been shown to produce LC phase separate droplets in PEG-NA mixtures [25,55,56,60,85,86]. However, other types of membraneless droplets assembled from phase separation, such as polyester microdroplets [10,87–89], should be considered to probe intra-compartmental LC assembly. Moreover, other primitive processes could also up-concentrate the NAs to a sufficient level to exhibit LC character. For example, dehydration of solutions containing NA strands (or random NA monomers) could occur through evaporation on the banks of a hot spring system or an oceanic beach. Precipitation could result in the dilution of the NA system (resulting in LC disassembly) and another round of drying could recapitulate the NA duplexes. Such cycles of LC formation/disruption can provide a fitness landscape for selecting NAs based on their propensity to form more or less stable LC phases. Similarly, sublimation of a frozen solution containing NAs (akin to lyophilization), such as that which could occur in arctic permafrost [90] or extraterrestrial environments with frozen aqueous media like Enceladus [91] or even comets [92], could also result in up-concentration of NAs (although lyophilization has been shown to potentially cause NA damage as well [93]).

Additionally, there are also geological processes or structures which could promote NA up-concentration. For example, a variety of mineral surfaces have been shown to adsorb NAs including DNA [94], RNA [95], and nucleotide monomers [96]. In fact, longer RNA has been shown to be selected for on mineral surfaces [95], suggesting that mineral surface adsorption could provide an environment for longer NAs (more amenable for assembly of the NA duplexes required for LC) to accumulate. Another type of geological structure that can both up-concentrate NAs and accumulate longer strands are hydrothermal rock pores. Simulated rock pores were first studied in 2007, and were proposed to up-concentrate nucleotide monomers and short RNA strands up to 22-bases long by many orders of magnitude [59]. Subsequent laboratory experiments discovered that such pores could promote enzymatic DNA replication [97] and DNA 'sticky end' ligation [98] through the thermal trap and thermophoretic action. Finally, thermal gradients within rock pores result in the selection of longer DNA duplexes (which more easily form LC phases) via thermophoresis and convection [99], while gas bubbles within the pores contribute both to monomer and RNA accumulation [100] as well as to the selective accumulation of longer DNA strands [101]. Given that hydrothermal rock pores could protect NA photodegradation [102] (by being underwater) and are also compatible with and drive the function of coacervates [103], such geological structures could be a reasonable primitive environment amenable to the emergence of primitive NA LCs and/or LC-coacervates.

Here, we described the assembly and function of LCs in the context of the origins of life and suggest specific environmental or chemical conditions that would be amenable to the formation of a 'liquid crystal world' on early Earth. We challenge the field to further investigate the assembly, structure, function of primitive LCs, particularly LC-coacervates, in a variety of prebiotically plausible conditions. Finally, given their ability to concentrate NAs and monomers and to select for longer NA strands, we suggest that hydrothermal rock pores could be a relevant candidate environment for the assembly of primitive LCs, and deserve more investigation in the context of a 'liquid crystal world'.

Summary

- LCs can assemble from short NA monomers, oligomers, or even random sequences through the assistance of end-to-end stacking and pairing interactions of NA duplexes, which results in the formation and stabilization of physical long linear NA aggregates, whose behavior resembles the one of covalently bonded long-chain NA.
- In molecular mixtures, spontaneous phase separation and LCs ordering contribute to the selection and compartmentalization of NA duplex sequences through segregation or complex coacervation.
- NA LCs have been shown to enhance non-enzymatic NA polymerization through chemical ligation which is a crucial step to generate long and potentially catalytic sequences for the origin of life.
- Further studies on primitive LCs, such as the prebiotic environments they could have formed in or exhibition of 'life-like' properties, could lead to further understanding on the acquisition of complexity via chemical evolution as part of a 'liquid crystal world'.

Competing Interests

The authors declare that there are no competing interests associated with the manuscript.

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Author Contribution

All authors wrote the manuscript.

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Abbreviations

NAs, nucleic acids; LC, liquid crystal; LCA, liquid crystal autocatalysis; EDC, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide; PLL, poly-L-lysine.

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