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Heat flux across an open pore enables the continuous replication and selection of oligonucleotides towards increasing length

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The replication of nucleic acids is central to the origin of life. On the early Earth, suitable non-equilibrium boundary conditions would have been required to surmount the effects of thermodynamic equilibrium such as the dilution and degradation of oligonucleotides. One particularly intractable experimental finding is that short genetic polymers replicate faster and outcompete longer ones, which leads to ever shorter sequences and the loss of genetic information. Here we show that a heat flux across an open pore in submerged rock concentrates replicating oligonucleotides from a constant feeding flow and selects for longer strands. Our experiments utilize the interplay of molecular thermophoresis and laminar convection, the latter driving strand separation and exponential replication. Strands of 75 nucleotides survive whereas strands half as long die out, which inverts the above dilemma of the survival of the shortest. The combined feeding, thermal cycling and positive length selection opens the door for a stable molecular evolution in the long-term microhabitat of heated porous rock.

From a wide range of exploratory experiments much is known about the capabilities and limitations of chemical replication systems[1–6]. It has become increasingly clear that such replicators are delicate systems that require a suitable supportive microenvironment to host non-equilibrium conditions. These conditions permit the sustainment of molecular evolution and the synthesis of molecules against equilibrating forces[1,7–9]. To the same end, modern cells provide active compartments of reduced entropy that protect genetic information against its thermodynamically favoured decay[8,10]. This is facilitated by sophisticated membrane-trafficking machinery and a metabolism that feeds on chemical low-entropy sources or light energy (Fig. 1a).

It has been known since Spiegelman's experiments in the late 1960s[11] that, even if humans assist with the assembly of an extracellular evolution system, genetic information from long nucleic acids is quickly lost. This is because shorter nucleic acids are replicated with faster kinetics and outcompete longer sequences. If mutations in the replication process can change the sequence length, the result is an evolutionary race towards ever shorter sequences.

In the experiments described here we present a counterexample. We demonstrate that heat dissipation across an open rock pore, a common setting on the early Earth[12] (Fig. 1b), provides a promising non-equilibrium habitat for the autonomous feeding, replication and positive length selection of genetic polymers. Previously, it has been argued that a temperature gradient spanning a submillimetre wide, closed compartment is able to accumulate dilute nucleotides, to enforce their polymerization or to concentrate lipids to form vesicles[13–15].

Here we extend the concept to the geologically realistic case of an open pore with a slow flow passing through it. We find continuous, localized replication of DNA together with an inherent nonlinear selection for long strands. With an added mutation process, the shown system bodes well for an autonomous Darwinian evolution based on chemical replicators with a built-in selection for increasing the sequence length. The complex interplay of thermal and fluid dynamic effects, which leads to a length-selective replication (Fig. 1c, (1)–(4)), is introduced in a stepwise manner.

Results

Accumulation. The accumulation mechanism responsible for counterbalancing the mixing entropy relies on the interplay of thermophoresis and gravitationally driven convection (Fig. 2a and Supplementary Movie 1). In the presence of a temperature difference, thermophoresis drives the molecules horizontally from the warm left side to the cold right side. On a similar timescale, the fluid moves vertically by convection and carries the molecules with it. Convection deflects the horizontal thermophoretic depletion and amplifies it to give a strong vertical molecule accumulation[16,17] (see Methods). This interplay of molecular movement and fluid flow therefore results in an efficient net transport of oligonucleotides to the bottom of the compartment; the experiment is visualized in Fig. 2b (also see Supplementary Movie 2).

For oligonucleotides with a length of 75 bases, concentrations increase by a factor of ten per millimetre pore length, which results in a millionfold concentration increase for a 6 mm high pore. Larger nucleic acids are exponentially better trapped because their higher charge contributes quadratically to the achievable accumulation[18,19]. This length-selective accumulation bias can be directly detected experimentally (Supplementary Fig. 3). The accumulation counterbalances diffusional dilution and offers a solution to the concentration problem associated with the origin of life.

Size-selective trapping from feeding flow. To establish efficient feeding with replication-relevant monomers, we opened the pore at both ends. This permitted an upwards feeding flow through the pore that originated from the overall large-scale upwards flow in a hydrothermal situation. Interestingly, this led to all-or-nothing

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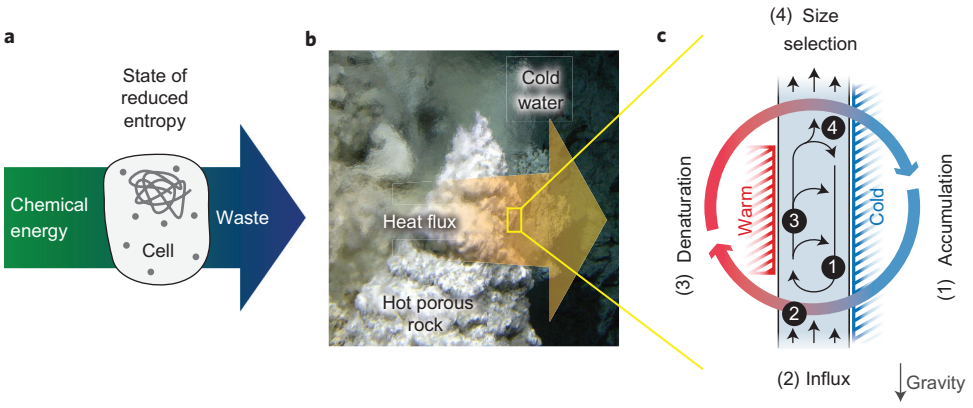

Figure 1 | Reduction of local entropy is key for living systems and can be caused by the flux of thermal energy. a, Modern cells feed on chemical energy, which enables them to host, maintain and replicate information-coding polymers, processes necessary for Darwinian evolution. **b**, The flux of thermal energy across geological cracks near a heat source (the white smoker[28] is adapted from an image courtesy of Deborah S. Kelley). **c**, (1) A thermal gradient across a millimetre-sized crack induces the accumulation of molecules by thermophoresis and convection. (2) A global throughflow imports nutrients into the open pore. (3) Exponential replication is facilitated by the local convection, which shuttles the molecules repetitively between warm and cold, and thus induces the cyclic denaturation of nucleotides. (4) The combination of influx, thermophoresis and convection selectively traps long molecules and flushes out short ones. The inflow speed determines the cut-off size of the resulting length selection. Mechanisms (1) to (4) are described in detail in this article.

trapping characteristics that depend on the strand length. We loaded an oligonucleotide ladder (20–200 base pairs (bp) dsDNA) in a 3.5 mm high and 70 μm wide pore and introduced an upwards flow with a velocity of 6 μm s^{-1}. Using gel electrophoresis, we observed that nucleic acids above a certain threshold length were trapped inside the pore, whereas shorter strands followed the upwards flow and were washed out of the pore (Fig. 3a and Supplementary Movie 3).

For a given velocity, this sharp length fractionation had a transition between 80 and 100 bp and can be understood by the interaction of the flow profile inside the trap with the thermophoretic concentration profile. The upwards feeding flow superimposes on the internal convection pattern, which generates an asymmetrical flow profile inside the trap (Fig. 3b). Long strands are pushed by thermophoresis into the descending flow at the cold side, transporting the molecules downwards. These are then localized against the upwards feeding flow at the bottom end of the heated section. Shorter strands experience weaker thermophoresis and the overall upwards flow drags them out of the trap.

The flow rate at which the solute nucleic acids start to move upwards and leave the pore depends monotonically on the strand length. Consequently, a gradual increase of the flow rate with time results in the sequential release of longer strands (Fig. 3c). The existence of the observed threshold length might come as a surprise, but a finite-element model that combines flow, diffusion and thermophoresis reproduces the behaviour of the trap in detail (Fig. 3d and Methods).

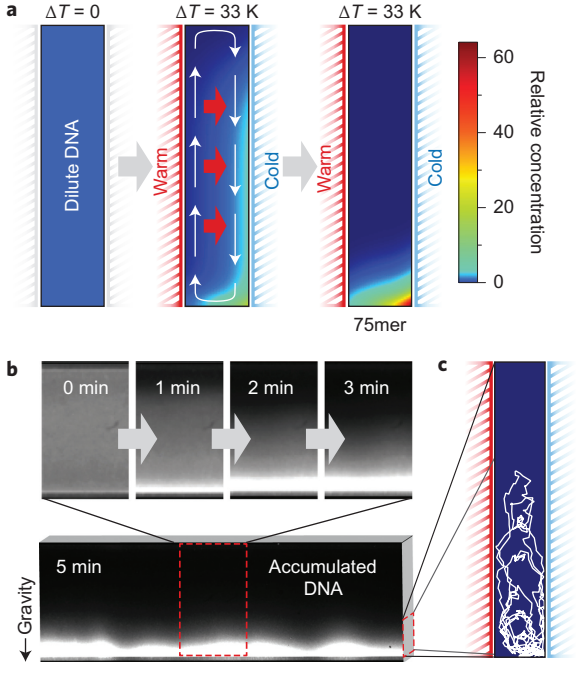

Figure 2 | Accumulation of oligonucleotides. a, The temperature gradient drives oligonucleotides horizontally from warm to cold by thermophoresis and simultaneously triggers the vertical thermal convection of water. Its combination results in a length-dependent accumulation at the bottom of an elongated pore within minutes (see Supplementary Movie 2). **b**, The accumulation of dilute double-stranded oligonucleotides (100–1,000mer) at the bottom is monitored within a 100 μm thin and 2 mm high capillary via SYBR Green I fluorescence. **c**, The accumulation is dynamic: the nucleotides cycle between the warm and cold sides, visualized in white for a single 500mer of DNA.

Exponential replication by convective thermal cycling. Besides continuous feeding and length-selective trapping, the asymmetrically heated pore offers another important feature relevant to the origin of life: laminar convective temperature cycling of the accumulated nucleic acids[20,21]. This opens the door to Watson–Crick-type replication mechanisms, which are otherwise hindered by the considerable energy costs required to separate double-stranded oligonucleotides[22]. The thermal cycling can be predicted from a fluid dynamics model that includes thermophoresis and diffusion (Fig. 4a). It is sufficient to separate cyclically double-stranded DNA (dsDNA) to drive exponential base-by-base replication with duplication times on the order of minutes, as documented by SYBR Green I fluorescence (Fig. 4b and Supplementary Movie 4). Our focus was to study the boundary conditions that enable early chemical systems for oligonucleotide replication. For this, we chose the polymerase chain reaction (PCR) as a fast and well-characterized placeholder for the large family of template-directed replication mechanisms that depend on temperature oscillations for long substrates[2–6].

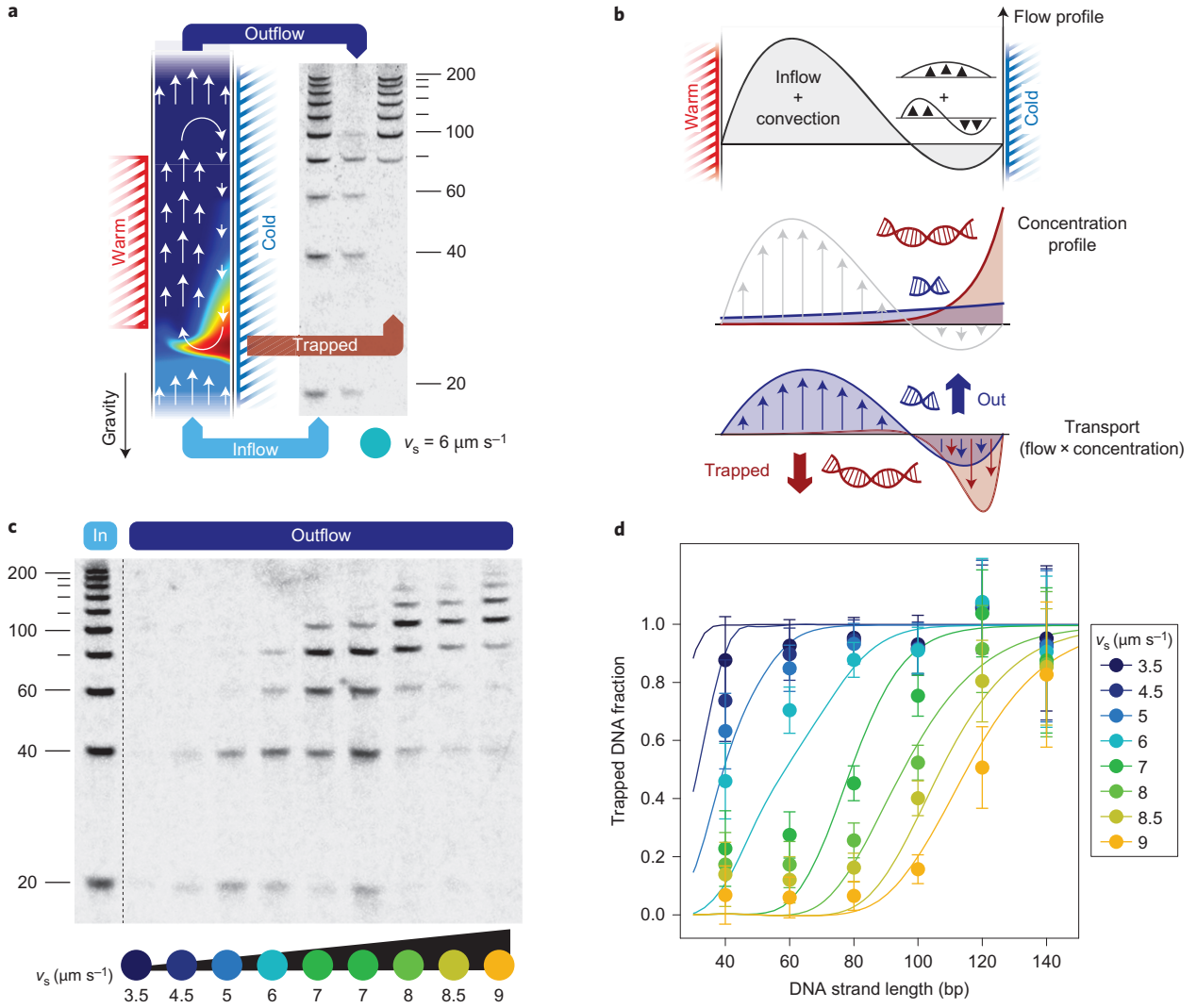

Figure 3 | Heat-driven filter selecting for strand length. a, A steady upwards feeding flow is triggered by opening the asymmetrically heated pore. A ladder of dsDNA (20–200 bp, 20 bp steps) was injected into the trap. Subsequent flushing of the capillary with pure buffer at a single velocity (v_s = 6 µm s^{-1}) revealed the filter's thresholding characteristics—lengths ≲80 bp flow through the pore whereas longer strands are trapped. **b**, An asymmetric flow pattern is generated by the superposition of the upwards flow and the convection. Thermophoresis pushes the long strands into the downwards flow and traps them. Short strands are subjected to the overall upwards flow and leave the pore. The trapping is a function of the feeding flow speed. **c**, The velocity of the external flow v_s tunes the fractionation of nucleic acids. As in the experiment before, a DNA ladder was initially introduced at a low flow velocity, which was then sequentially increased. The released DNA was measured using gel electrophoresis. **d**, The fraction of trapped DNA obtained from the electrophoresis gel constitutes a selection landscape of this thermal habitat in favour of long oligonucleotides. The velocity-dependent trapped fraction is described by a fluid dynamics model (see Methods). Error bars reflect the signal-to-noise ratio of the gel images (see Supplementary Fig. 11 for details).

Differential survival of replicating strands. Combining all of the above, we show how the joint thermally induced trapping and replication enables this arrangement to overcome Spiegelman's evolutionary dilemma of the degeneration of strand length and therefore loss of genomic information[11]. We followed the composition of a heterogeneous DNA population that replicates continuously inside the open pore. A 2.5 mm short capillary was seeded with a population of unlabelled template DNA strands with identical primer binding sites and a binary length distribution of 36 bp and 75 bp at a concentration of 1 nM each.

A temperature gradient from 61 °C to 94 °C was applied to a continuous upwards flux of template-free PCR buffer that contained nucleotides, polymerase and 7 nM fluorescently labelled primers and was run through the system at a speed of 6 µm s^{-1}. Over the course of the experiment (seven hours), the trapping volume was exchanged approximately 150 times with the template-free feeding buffer. Aliquots that contained the product of the continuously running reaction were taken from the outflow and analysed using gel electrophoresis. As the primers carried the labels, only replicated DNA strands were detected (Fig. 4c).

We observed that only the long strands were able to replicate sufficiently to withstand the diluting flow through the pore. This determined the increase of the relative concentration of the long, viable strands with respect to the total amount of DNA (Fig. 4d, yellow). The twofold shorter strands became diluted and then extinct.

This competitive replication and selection of two genetic polymers in favour of larger molecular lengths can be understood easily with a simple model. The determinants of the growth kinetics $dc_i/dt = (\mathrm{rep}_i - \mathrm{dil}_i)c_i$ for either the short or the long species $i = \{S, L\}$ are given by the replication rates rep_i and the dilution rates dil_i. Expressing the relative concentration of the long strands yields $c_L/(c_S + c_L) = (1 + Ae^{-\Delta kt})^{-1}$. $A = c_S^0/c_L^0$ is the initial

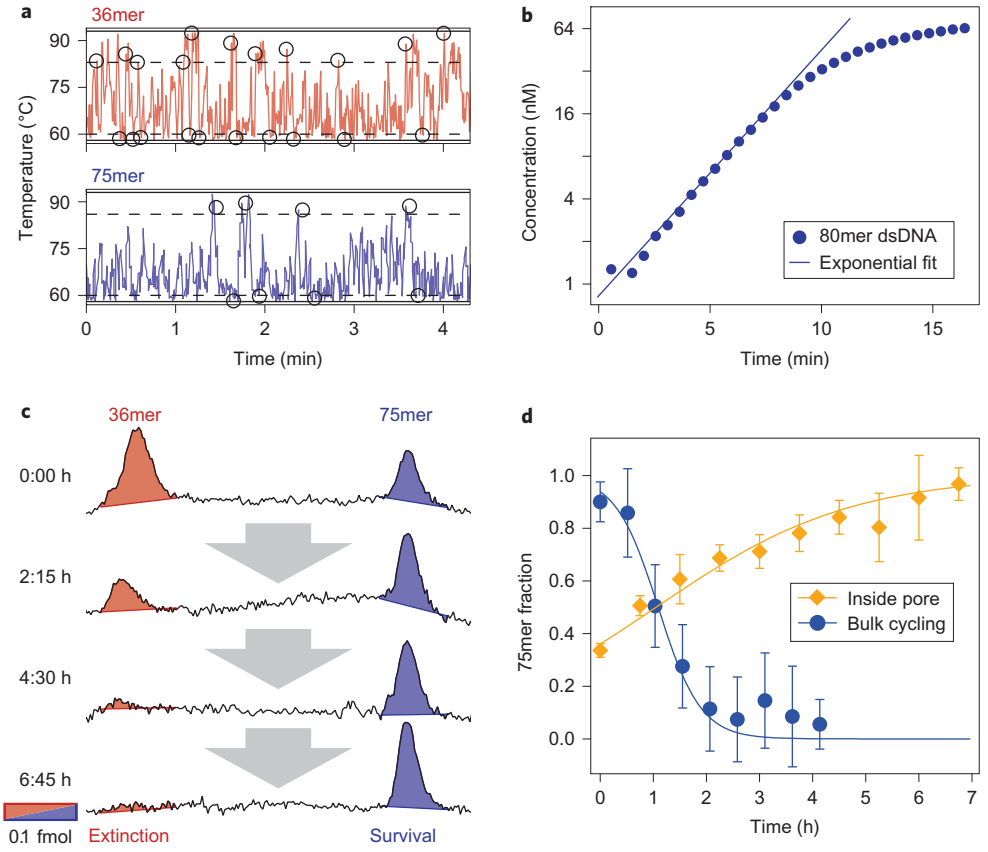

Figure 4 | Selection of a replicating DNA population that occupies the thermal habitat. a, Strands are subjected to temperature oscillations by the combination of thermophoresis, convection, feeding flow and diffusion. Simulations of stochastic molecule traces show that strands of 75 bp cycle inside the system for 18 minutes on average. In comparison, 36mers, owing to their enhanced diffusion, show faster temperature cycles, but are flushed out of the system after five minutes. **b**, Taq DNA polymerase-assisted replication of 80mer dsDNA by convective temperature cycling. Quantitative SYBR Green I fluorescence measurements show an exponential replication with a doubling time of 102 seconds (see Supplementary Movie 4). **c**, An open pore (see Fig. 1c) was seeded with a binary population of nucleic acids. Quantitative gel electrophoresis revealed sustainable replication for only the long strand. Short strands became diluted and then extinct despite their faster replication. **d**, Relative concentrations of the two competing species inside the thermal habitat. The selection pressure of the thermal gradient altered the composition of the binary population with time (yellow diamonds) in good agreement with an analytical replication model. The absolute fitness values were 1.03 and 0.87 for long and short strands, respectively. Without the thermal gradient, the short oligonucleotides won over the long strands (blue circles), analogous to the Spiegelman experiment. Error bars reflect the signal-to-noise ratio of the gel images (see Supplementary Fig. 11 for details).

concentration ratio and $\Delta k = (\mathrm{rep_L} - \mathrm{rep_S}) - (\mathrm{dil_L} - \mathrm{dil_S})$ is the differential growth rate. We experimentally found that, inside the pore, long strands (L) outcompete shorter ones (S) with $\Delta k = 0.55\,\mathrm{h}^{-1}$ (yellow curve). The length-selective fractionation model (Fig. 3c) confirmed that the shorter strands suffer from a fourfold higher dilution rate as compared to the trapped long strands. This selection of the longer replicating strand works best if the mechanism of replication is inefficient, such that the dilution of the short strand occurs before it can be replicated efficiently.

On the other hand, in a well-mixed situation, and hence in the absence of the selection pressure of the pore, we recovered Spiegelman's dilemma of the tyranny of the short. In a serial dilution experiment using a conventional thermal cycler with dilution rates that reproduce the pore conditions, the long strands died out rapidly with a differential growth rate of $\Delta k = -2.5\,\mathrm{h}^{-1}$ (Fig. 4d, blue curve).

Discussion

Our experimental findings conclusively show that, at the expense of dissipating free thermal energy, a habitat is created that drives and sustains the replication of long oligonucleotides by exploiting both convective temperature cycling and a selection pressure that supports the long over the short sequences. Therefore, heat dissipation enables the pore to overcome Spiegelman's classic problem for *in vitro* replication systems that create ever shorter genetic polymers, which results in the loss of genetic information.

On the hot early Earth, the pore system we describe was probably widespread because of porous, partially metallic volcanic rock, both near the surface and at submarine sites. As metals have a more than 100-fold larger thermal conductivity than water[23], metallic inhomogeneities near the pores can focus the thermal gradient from centimetres down to a micrometre-sized cleft (Supplementary Fig. 1). The kinetics of replication and selection were realized in the most simple geometrical setting of a single pore section with dimensions of 0.07 mm × 3.5 mm. Metallic inclusions do allow thermal gradients to be focused up to 100-fold to reach the thermal gradients of realistic geological settings (Supplementary Fig. 1). It is, however, important that the steepness of the thermal gradient can be further relaxed by at least one order of magnitude by separating replication and selection into two adjacent pores (Supplementary Fig. 2). At the bottom, a wide pore could provide the necessary temperature difference for replication[24]. At its top, the outflow would be constricted through one or more thin, but longer, selecting

pores. Their increased length of several centimetres instead of 3.5 mm compensates linearly for the reduced temperature difference[13].

Although the demonstrated length-selective trapping requires a temperature difference to work, the average temperature of the trap is not a critical parameter and can be tuned easily to fit the replication reaction. Therefore, the core mechanism of temperature cycling and selection studied here will also work for replication systems that require colder temperatures, including, for example, ribozymes or Q-beta replicase. However, many early replication systems are likely to rely on high temperatures for temperature-induced strand separation. For the PCR reaction used in the experiment, the strand lengths were highly controlled by the primers. In comparison, reactions that involve ligations have a tendency to extend the strands with partial templating[25] and initiate the length extension of the genetic polymers.

To extend this work to achieve Darwinian evolution in the demonstrated system, the replication process requires a significant mutation rate, including changes of the sequence length. The use of error-prone PCR with deep sequencing is therefore an interesting prospect for future experiments. At this point, the amount inside the pore is less than 1 pg, which prevents such an approach: the necessary strong preamplification would highly bias the obtained sequences and obscure their analysis.

Importantly, the thermophoretic selection pressure applies to each individual molecule of the population. As it is ultimately sensitive to the thermophoretic strength, the selection does not only favour the survival of long strands over short strands—it is possible that this mechanism could be tuned to select for the formation of macromolecular complexes or even for binding of aptamers[26].

Conclusion

Our experiments reveal how temperature gradients, the most simple out-of-equilibrium setting, can give rise to local environments that stabilize molecular replication against the entropic tendencies of dilution, degradation and negative length selection. A thermal gradient drives replication of oligonucleotides with an inherent directional selection of long over short sequence lengths. Interestingly, when replication and trapping inside the pore reach their steady state, the newly replicated molecules leave the trap with the feeding flow. This ensures an efficient transfer of the genetic polymers to neighbouring pore systems. Heat dissipation across porous rock was probably in close proximity to other non-equilibrium settings of pH, ultraviolet radiation and electrical potential gradients, all of which are able to drive upstream synthesis reactions that produce molecular building blocks. An exciting prospect of the presented experiments is the possible addition of mutation processes to achieve a sustained Darwinian evolution of the molecular population inside the thermal gradients of the early Earth. Accordingly, the onset of molecular evolution could have been facilitated by the natural thermal selection of rare, long nucleic acids in this geologically ubiquitous non-equilibrium environment.

Methods

Temperature gradients. Temperature gradients were generated across rectangular borosilicate glass capillaries (VitroTubes, VitroCom) with a cross-sectional aspect ratio of 1:20 and a thermal conductivity of 1.2 W m^{-1} K^{-1}. To this end, two different approaches were followed. (1) For the direct observation of the accumulation effect, glass capillaries were coated with a transparent conducting oxide layer that allowed for one-sided heating at a constant electric power with cooling from the other side. (2) Fractionation and replication experiments were performed in capillaries sandwiched between and thermally connected to temperature-controlled metal surfaces (compare the Supplementary Information and the figures therein for details of both approaches).

Accumulation-only experiments. dsDNA was diluted in 1 × Taq reaction buffer (New England Biolabs) that contained 10 mM Tris-HCl, 50 mM KCl, 1.5 mM $MgCl_2$ and 0.1% Tween20, with a pH of 8.3 at room temperature. A dsDNA ladder (10 μg ml^{-1}, 100–1000 bp, ten equidistant bands, weight equalized) was used in combination with 0.5 × SYBR Green I[27]. The applied temperature gradient from 22 °C to 88 °C resulted in temperatures from 38 °C to 71 °C inside the capillary (inner dimensions, 100 μm × 2,000 μm and 70 μm × 1,400 μm, as specified).

Fractionation experiments. A DNA ladder (20–200 bp, ten equidistant bands) was suspended in a 1 × PCR buffer that included 0.1% Tween20. Fractionation was carried out in a vertically oriented capillary (inner dimensions, 70 μm × 1400 μm) with an internal temperature gradient from 39 °C to 73 °C present over a capillary length of 3.5 mm (see the Supplementary Information for the details). The threshold trapping characterization was determined using a constant flow speed. Gradual fractionation was achieved by increasing the flow rate with time using a feedback-controlled syringe pump (neMESYS, Cetoni; see the Supplementary Information for a detailed protocol).

***In vitro* selection and replication.** Extracellular selection of replicating DNA strands was studied in a temperature gradient from 61 °C to 94 °C inside a thoroughly cleaned (DNA Away, Molecular BioProducts) capillary (inner dimensions, 70 μm × 1,400 μm, heated along 2.5 mm) at a mean solvent velocity of 6 μm s^{-1}. DNA replication was facilitated in a commercially available, glycerol-free master mix (fast cycling PCR Kit, Qiagen) that contained Taq polymerase, free nucleotides and standard concentrations of mono- and bivalent salts. The overall efficiency of DNA replication was reduced to less than 8% by means of a low concentration (7 nM) of each 14mer primer (forward (Cy5) and reverse primers; see Supplementary Fig. 7 for the sequences) in the feeding buffer. Unlabelled DNA templates (36mer, 75mer) were seeded into the region of replication through the system's output, leaving the feeding buffer template free. Reaction products that contained the incorporated Cy5 primer from the feeding buffer were extracted from the output of the artificial pore in 1.5 μl aliquots. Controls were performed in a conventional real-time PCR cycler (CFX96, Bio-Rad). A serial dilution experiment was performed to derive the replication efficiencies of the 36mer and 75mer DNA. Temperature cycles emulated the mean temperature cycle of 75mer DNA inside the pore, consisting of three seconds at 94 °C and 14 seconds at 60 °C (Supplementary Fig. 9). Including transition times, the total cycle time was 46.5 s. The initial concentrations were 2 pM (36mer) and 18 pM (75mer) for the PCR templates and 7 nM for the common primers. Every 40 cycles, the sample was diluted by a factor of 20 to yield a dilution rate of $dil_S = dil_L = 5.8\,h^{-1}$ that counterbalanced the concentration increase of the 36mer DNA within 40 cycles. This scheme prevented a depletion of the primer concentration and ensured that the efficiencies of the PCR reaction stayed constant over all 320 cycles. Replication rates were determined by comparison of the amount of DNA before each dilution using gel electrophoresis (Supplementary Fig. 12). The mean replication rates were determined to be $rep_S = (5.8 \pm 0.6)\,h^{-1}$ (36mer) and $rep_L = (3.3 \pm 0.4)\,h^{-1}$ (75mer).

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References

1. Powner, M. W., Gerland, B. & Sutherland, J. D. Synthesis of activated pyrimidine ribonucleotides in prebiotically plausible conditions. *Nature* **459,** 239–242 (2009).
2. Sievers, D. & Von Kiedrowski, G. Self-replication of complementary nucleotide-based oligomers. *Nature* **369,** 221–224 (1994).
3. Mansy, S. S. *et al.* Template-directed synthesis of a genetic polymer in a model protocell. *Nature* **454,** 122–125 (2008).
4. Wochner, A., Attwater, J., Coulson, A. & Holliger, P. Ribozyme-catalyzed transcription of an active ribozyme. *Science* **332,** 209–212 (2011).
5. Paul, N. & Joyce, G. F. A self-replicating ligase ribozyme. *Proc. Natl Acad. Sci. USA* **99,** 12733–12740 (2002).
6. Yang, Z., Chen, F., Alvarado, J. B. & Benner, S. A. Amplification, mutation, and sequencing of a six-letter synthetic genetic system. *J. Am. Chem. Soc.* **133,** 15105–15112 (2011).
7. Szostak, J. W. The eightfold path to non-enzymatic RNA replication. *J. Syst. Chem.* **3,** 1–14 (2012).
8. Pascal, R., Pross, A. & Sutherland, J. D. Towards an evolutionary theory of the origin of life based on kinetics and thermodynamics. *Open Biol.* **3,** 130156 (2013).
9. Powner, M. W., Sutherland, J. D. & Szostak, J. W. Chemoselective multicomponent one-pot assembly of purine precursors in water. *J. Am. Chem. Soc.* **132,** 16677–16688 (2010).
10. Schrödinger, E. *What is Life?* (Cambridge Univ. Press, 1944).
11. Mills, D. R., Peterson, R. L. & Spiegelman, S. An extracellular Darwinian experiment with a self-duplicating nucleic acid molecule. *Proc. Natl Acad. Sci. USA* **58,** 217–224 (1967).
12. Lay, T., Hernlund, J. & Buffett, B. A. Core–mantle boundary heat flow. *Nature Geosci.* **1,** 25–32 (2008).
13. Baaske, P. *et al.* Extreme accumulation of nucleotides in simulated hydrothermal pore systems. *Proc. Natl Acad. Sci. USA* **104,** 9346–9351 (2007).
14. Budin, I., Bruckner, R. J. & Szostak, J. W. Formation of protocell-like vesicles in a thermal diffusion column. *J. Am. Chem. Soc.* **131,** 9628–9629 (2009).
15. Mast, C. B., Schink, S., Gerland, U. & Braun, D. Escalation of polymerization in a thermal gradient. *Proc. Natl Acad. Sci. USA* **110,** 8030–8035 (2013).

16. Clusius, K. & Dickel, G. Trennung von Flüssigkeitsgemischen mittels kombinierter Thermodiffusion und Thermosiphonwirkung. *Naturwissenschaften* **26,** 546 (1938).
17. Debye, P. Zur Theorie des Clusiusschen Trennungsverfahrens. *Annal. Phys.* **428,** 284–294 (1939).
18. Piazza, R. & Guarino, A. Soret effect in interacting micellar solutions. *Phys. Rev. Lett.* **88,** 208302 (2002).
19. Duhr, S. & Braun, D. Why molecules move along a temperature gradient. *Proc. Natl Acad. Sci. USA* **103,** 19678–19682 (2006).
20. Krishnan, M., Ugaz, V. M. & Burns, M. A. PCR in a Rayleigh–Benard convection cell. *Science* **298,** 793 (2002).
21. Mast, C. B. & Braun, D. Thermal trap for DNA replication. *Phys. Rev. Lett.* **104,** 188102 (2010).
22. Rajamani, S. *et al.* Effect of stalling after mismatches on the error catastrophe in nonenzymatic nucleic acid replication. *J. Am. Chem. Soc.* **132,** 5880–5885 (2010).
23. Tritt, T. M. *Thermal Conductivity: Theory, Properties and Applications* (Kluwer Academic/Plenum, 2004).
24. Braun, D., Goddard, N. L. & Libchaber, A. Exponential DNA replication by laminar convection. *Phys. Rev. Lett.* **91,** 158103 (2003).
25. Fernando, C., Von Kiedrowski, G. & Szathmáry, E. A stochastic model of nonenzymatic nucleic acid replication: "Elongators" sequester replicators. *J. Mol. Evol.* **64,** 572–585 (2007).
26. Baaske, P., Wienken, C. J., Reineck, P., Duhr, S. & Braun, D. Optical thermophoresis for quantifying the buffer dependence of aptamer binding. *Angew. Chem. Int. Ed.* **49,** 2238–2241 (2010).
27. Wilhelm, J. & Pingoud, A. Real-time polymerase chain reaction. *ChemBioChem* **4,** 1120–1128 (2003).
28. Kelley, D. S. *et al.* An off-axis hydrothermal vent field near the Mid-Atlantic Ridge at 30° N. *Nature* **412,** 145–149 (2001).

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Author contributions

M.K., L.K. and S.L. contributed equally to this work and performed the experiments. M.K., L.K., S.L and D.B. conceived and designed the experiments, analysed the data and wrote the paper.

Additional information

Supplementary information is available in the online version of the paper. Reprints and permissions information is available online at www.nature.com/reprints. Correspondence and requests for materials should be addressed to D.B.

Competing financial interests

The authors declare no competing financial interests.