

SELF-ORGANIZATION

Dissipative DNA fibres

Self-organization — ubiquitous in living systems — occurs out-of-equilibrium, with dissipation of energy and matter. Researchers have now shown that slow proton dissipation switches the assembly of DNA-based fibres to a growth mechanism that heals their gaps, yielding tight nanocable architectures.

Mathieu Surin

Nature is wealthy in self-organized chemical systems, in which molecular components spontaneously assemble to form organized architectures whose spatio-temporal order imparts emergent functional properties. Indeed, in living systems biomolecular constructs self-organize out of equilibrium — that is, far from thermodynamic equilibrium — since these are open systems with continuous exchanges of energy, matter and information with the environment. To cite one example, the polymerization of actin proteins and the hierarchical assembly of actin filaments are self-organization processes regulated by ATP hydrolysis, acting as a fuel. The dynamics of self-organization is essential for an adaptable network of actin filaments, which are a major component of the cell skeleton.

In contrast, in their attempts to fabricate functional organic materials, researchers

often attempt to organize molecules in space by programming intermolecular interactions to direct their assembly in solution at (or near) thermodynamic equilibrium. This leads to a self-assembly process, which can be monitored by a simple melting or denaturation experiment — that is, the assembly goes from an ordered state to a disordered state when increasing the temperature or by addition of a denaturant. Careful design of the position of interacting groups on the molecules can yield organized systems at the supramolecular level with interesting properties such as self-healing and gelation, but not to a level of sophistication where nature operates, and therefore with limited perspectives in terms of functions.

Writing in *Nature Chemistry*, Hanadi Sleiman and colleagues addressed this issue by developing a new approach to direct the self-organization of DNA-based systems

through an out-of-equilibrium process¹. They describe an oscillatory dissipative pathway to transform short DNA-based fibres into highly organized nanocable morphologies. The starting system is composed of short DNA strands made of exactly 15 adenine bases, mixed in water with a small molecule, cyanuric acid (Fig. 1, left). The hydrogen-bonding interactions between DNA bases and cyanuric acid direct the formation of supramolecular polymers — that is, chains of several DNA strands held together with the small molecule in a ‘triplex’ helical morphology. The formation of these triplex structures was detailed earlier by the same group in *Nature Chemistry*². These triplexes exist as relatively short fibres and have structural defects in the form of gaps along their main axis (Fig. 1).

To heal the gaps of these fibres, the researchers cleverly developed a dissipative

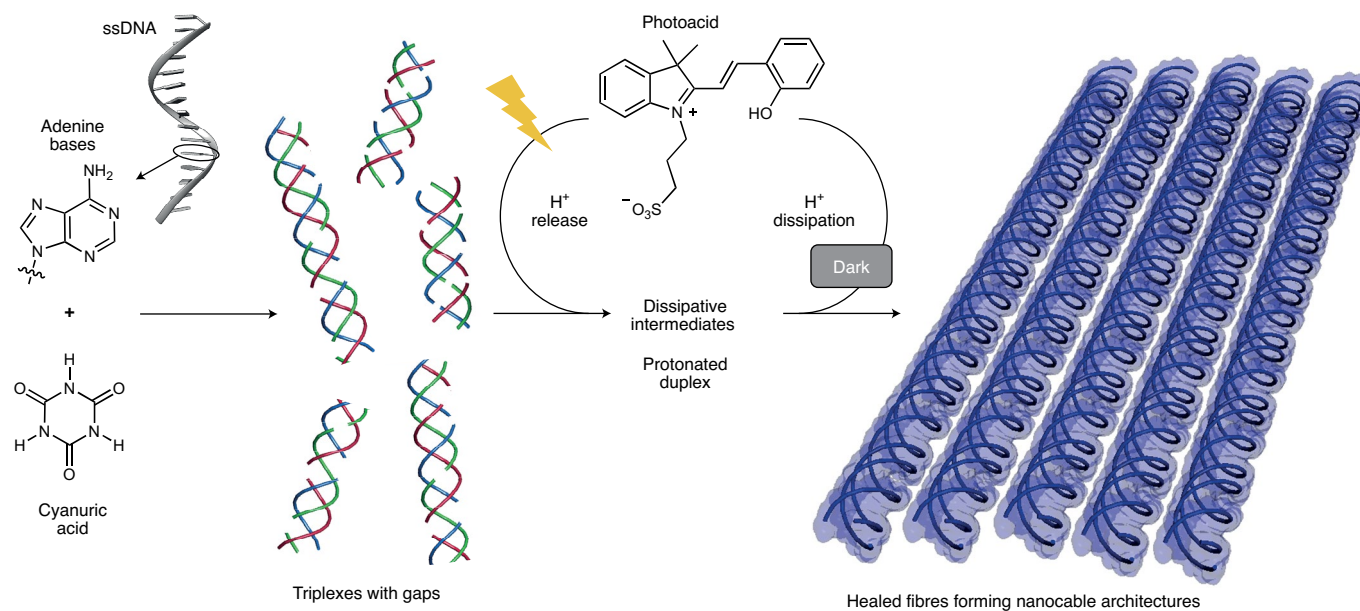


Fig. 1 Sketch of the dissipative self-organization process to heal the gaps of DNA-based fibres. The process is mediated by irradiation of a photoacid followed by slow proton dissipation, transforming triplexes with gaps (assembled from oligo(adenine) and cyanuric acid) into self-organized coaxial nanocables.

approach based on an oscillatory decrease and increase of pH. The use of a photoacid — a merocyanine dye — that releases protons upon light irradiation is original. When irradiating the triplexes in the presence of this photoacid with white light for 10 minutes, the pH of the solution drops below 4. At this low pH, triplexes become unstable and disassemble, freeing the DNA strands, which rearrange in pairs instead of interacting with the cyanuric acid molecule. In other words, the triplexes are transformed into protonated DNA duplexes, which slowly release the protons when left in the dark for 1 hour.

Multiple cycles of light irradiation (for 10 minutes) and dark (for around 60 minutes) produce a dissipative self-organization process in which the slow proton dissipation in the dark permits a gradual release of the DNA strands, which can then reassemble with cyanuric acid at higher pH. This process changes the kinetics of formation of fibres, heals their gaps and elongates the triplexes into unidirectional fibres. High-resolution microscopy techniques clearly show the transformation of short fibres from the self-assembled system — the initial triplexes — to the self-organized out-of-equilibrium system, in which the very long triplex fibres are hierarchically organized into coaxial nanocable architectures (Fig. 1, right). The tightening of the individual fibres can be estimated from their persistence length, which is more than doubled when going from the fibres containing gaps to the nanocables.

This elaborate approach to heal the structural defects in DNA-based assemblies demonstrates that the exploration of out-of-equilibrium dissipative processes can yield unexpected structures or improved morphologies with superior properties. Here, cycles of short white light irradiation followed by longer times in the dark leads to a pH-driven dissipative process yielding highly organized structures that are otherwise inaccessible at equilibrium.

While the shape and length of fibres were characterized with high-resolution microscopies (AFM and cryo-EM), their internal structures at the atomic level remain under debate. Indeed, recent molecular modelling results suggest that triplexes are probably arranged in helicene-like rather than a rosette-like architecture³. Likewise, future efforts should be directed to deeply characterize the conformations and structures of the dissipative intermediates and the nanocable architectures observed here.

One strength of this work rests on the simplicity of the dissipative process, using white light to trigger the proton release from a photoacid, followed by a slow dissipation of protons by intermediates in the dark. This could be used for other types of supramolecular self-assemblies sensitive to pH variations and for which the organization could be improved or tuned by oscillatory light switching in the presence of a photoacid.

This work is one step further towards achieving the high level of structuration

and functionality found in self-organized biomolecular systems. Applied to a DNA-based fibre, this opens new avenues to deal with biomolecular systems, potentially with functional DNA. This will join other works in the emerging field of systems chemistry, a blooming field bridging supramolecular chemistry with out-of-equilibrium processes towards life-like materials⁴, as exemplified by recent examples on ATP-fuelled polymerization of synthetic molecules⁵ or DNA⁶. Interfacing sophisticated synthetic self-organized architectures with natural systems in a dynamic fashion will bring exciting discoveries. □

Mathieu Surin  

Laboratory for Chemistry of Novel Materials, Department of Chemistry, University of Mons – UMONS, Mons, Belgium.

✉e-mail: mathieu.surin@umons.ac.be

Published online: 17 August 2021
<https://doi.org/10.1038/s41557-021-00774-3>

References

1. Rizzuto, F. J. et al. *Nat. Chem.* <https://doi.org/10.1038/s41557-021-00751-w> (2021).
2. Avakyan, N. et al. *Nat. Chem.* **8**, 369–376 (2016).
3. Alenaizan, A., Fauché, K., Krishnamurthy, R. & Sherrill, C. D. *Chem. Eur. J.* **27**, 4043–4052 (2021).
4. Mattia, E. & Otto, S. *Nat. Nanotech.* **10**, 111–119 (2015).
5. Sorrenti, A., Leira-Iglesias, J., Sato, A. & Hermans, T. M. et al. *Nat. Commun.* **8**, 15899 (2017).
6. Deng, J., Bezold, D., Jessen, H. J. & Walther, A. *Angew. Chem. Int. Ed.* **59**, 12084–12092 (2020).

Competing interests

The author declares no competing interests.



SYNTHETIC METHODOLOGY

Mastering mono-bond metathesis

Carbon–carbon single bonds are generally among the least reactive chemical bonds. While olefin metathesis reactions are well established, direct metathesis of C–C single bonds is rare. Now, a C–C single bond metathesis reaction has been developed, forming cross-biaryl products from unstrained homo-biaryl compounds.

Michael M. Gilbert and Daniel J. Weix

Catalytic olefin metathesis has created a variety of opportunities in organic synthesis by enabling disconnections based on unpolarized, isolated alkenes. Part of the reason for the rapid adoption of this chemistry is the high chemoselectivity for alkenes in preference to other functional groups that are more nucleophilic or electrophilic. This unusual selectivity

has made olefin metathesis an attractive approach for manipulating the underlying carbon skeleton of complex molecules^{1,2}. Similarly, a chemoselective rearrangement of C–C single bonds would be a transformative advance for organic synthesis.

While the elementary steps needed to accomplish C–C single bond metathesis have been known for years³, implementing

a catalytic strategy for complex molecule synthesis faces the additional challenge of activating a specific C–C σ -bond while avoiding indiscriminate side reactions with more reactive functionalities (Fig. 1a). Balancing high reactivity while maintaining selectivity is difficult for several reasons: C–C bonds (C₆H₅–C₆H₅, 114 kcal mol⁻¹) and C–H bonds (H–C₆H₅, 113 kcal mol⁻¹) have