Medieval chainmail motif stabilizes DNA nanostructures

The field of nanotechnology refers to all objects in the size range between 1 and 100 nanometers, which correspond to one billionth of a meter. This dimension is hard to imagine and it can be defined as the length that a fingernail grows in one second. At this scale the forces and the properties of nanomaterials are different from the ones characteristic for bulks; gases, liquids and solids may create stronger structures, have different magnetic properties or have better electrical conductivity for instance. This novel technology has several application fields such as chemistry, medicine, biology, materials science, electronics or energy production. Among those, the emerging DNA nanotechnology uses DNA not anymore as carrier of genetic information, but as a building material to create structures at the nanometer scale.

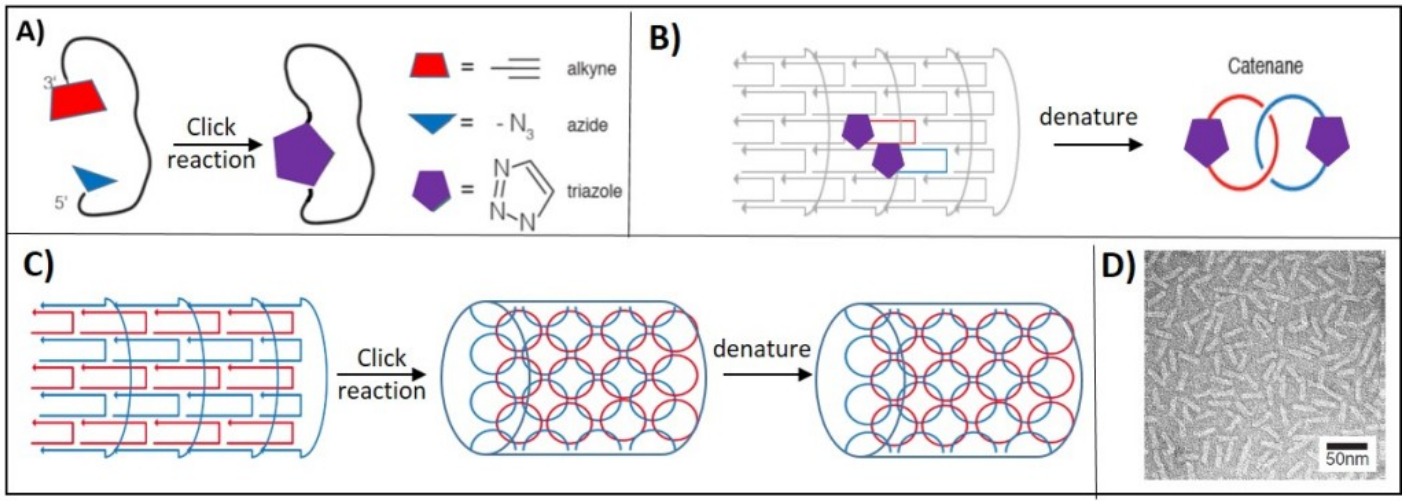

Fig. 1. A) Cu(I) catalyzed Azide-Alkyne cycloaddition forming a DNA ring connected via the new formed 1,4-triazole. B) Formation of two topologically interlocked DNA rings (DNA catenane) via click reaction within the nanotube. C) Formation of 24-membered DNA catenane. After denaturation the structure withstand as monodisperse object. D) TEM image of chainmail DNA nanotubes after heating at 65°C and submitted to 3 hours ExoI digestion.

DNA nanostructures are rationally designed so that a specific arrangement of nucleic acids results in defined secondary structures. The original idea originated by Nadrian C. Seeman in 1982 and from that moment on an enormous number of structures was created especially after the advent of DNA origami and Single-stranded Tile (SST) methods. DNA origami is a technique inspired by the Japanese art to fold paper. A long single-stranded DNA, called “scaffold”, is folded in the desired shape using more than hundreds of short DNA filaments, named “staples”. The SST approach is based on the hybridization of a smaller number of synthetic single stranded DNA in absence of any scaffold. The ability of scientists to synthetize structures made of DNA is not anymore recognize as

a mere exercise of design, but is exploited to create functional and beneficial objects. The main advantages of using DNA as building material is its easiness to handle, commercial availability, biocompatibility and the possibility to control the design with a nanometric precision. Anyhow, DNA nanostructures suffer from instability in certain environments where conditions like low cation concentration or extreme pH values can have adverse effects on the objects and cause their disruption.

In their recent paper Cassinelli et al. set out to overcome these limitations and demonstrated the creation of an ultra-stable DNA nanostructure. The small nanotube, only 27 nm long, is stabilized by click chemistry. This class of reactions join two molecules in an easy-to-handle and very efficient way. The starting nanotube design is composed of 24 single-stranded DNA which are modified by introducing two click reactive groups respectively at the two ends of each strand (Fig. 1A.). Thanks to the click reaction and the spatial preorganization of the strands in the design, each short DNA filament undergoes intramolecular cyclization forming a ring. If two adjacent strands within the nanostructure are modified with azide and alkyne groups one at each end, the click reaction product is a DNA catenane (from the Latin *catena* = chain). Here two strands are topologically interlocked as shown in Fig. 1B.

In case the whole set of 24 DNA strands are modified by azide and alkyne moieties, the one-pot click reaction generates a 24-membered DNA catenane (Fig. 1C.). This is the biggest artificial DNA catenated structure achieved so far and can resemble the chainmail used by the medieval knights. In similarity to the metal chainmail dressed by the medieval knights where those protections made the difference between an injury and the death, the chainmail DNA saves the original nanostructure from DNA denaturing events such as high temperature, organic solvents and depletion of positive ions concentration. The unwavering tube maintains the intact shape after 24 hours incubation in cell culture medium and is also resistance towards enzymes as shown in the Transmission Electron Microscopy analysis (Fig. 1D.).

The strength against these biological factors encourages the application of this stabilization technique in objects addressed to drug delivery and other purposes. The demonstrated method paves the way to application for the creation of DNA catenanes of several sizes and geometries or as assembly platform for a non-enzymatic gene synthesis.

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