CHEMISTRY

Metals line up for DNA

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The versatile DNA molecule has found many applications beyond biology. In its latest role, it serves as a self-assembling scaffold to arrange different metal ions in a row, like pearls on a string.

The days when DNA was the exclusive purview of molecular biologists are over. Since the discovery of DNA's double-helix structure in 1953, numerous disciplines have embraced this biomolecule — from medicine to materials science, by way of classical chemistry and biotechnology. Reporting in Nature Nanotechnology, Tanaka et al.1 describe an application of DNA that clearly stems from inorganic chemistry: they have modified DNA so that it serves as a scaffold for one-dimensional arrays of metal ions. Each array is a combination of copper and mercury ions, arranged in an order defined by the DNA sequence. Such precise control over the assembly of these arrays would be necessary for their potential applications as nanomagnets2, as self-assembling molecular wires or as catalysts in chemical reactions.

Single strands of DNA comprise a sugarphosphate chain decorated with organic
bases. A natural DNA double helix consists of
two single strands, with the sugar-phosphate
backbones on the outside and the bases on
the inside (Fig. 1a). Each base forms hydrogen bonds with just one other kind of base
— a complementary base — on the opposite
strand. It is the complementarity of these bases
that drives the reliable self-assembly process of
double-helix formation.

Tanaka et al. replaced the natural bases of DNA with artificial ones. Each of these substitute bases has a high affinity for a particular metal ion — either a copper ion (Cu²+) or a mercury ion (Hg²+). The modified DNA can form a double helix only if the opposing bases have a preference for the same metal ion and if both bases bind to such an ion. Given an appropriate base sequence, a duplex can form that contains one or more metal ions along its central axis (Fig. 1b).

The incorporation of metal ions into an artificial DNA duplex has previously been reported, but with only one kind of metal at a time, typically in systems with a few modified base pairs interspersed between longer rows of natural ones³⁻⁸. What is remarkable about Tanaka and colleagues' work1 is the formation of double helices containing long stretches of two different metal ions. Not only did the authors selectively incorporate more than one kind of metal ion into artificial DNA, but they also used more than one kind of artificial base, in various sequences. This is a tremendous advance towards the goal of making metalcontaining, self-assembling nanomaterials with desirable properties that can be tuned on

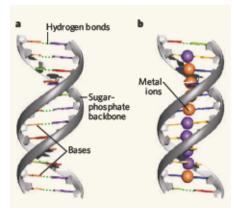


Figure 1| Artificial DNA that incorporates metal ions. a, Single strands of DNA consist of a sugar-phosphate backbone decorated with organic bases. A double helix forms when the bases of one strand form hydrogen bonds to complementary bases on another strand. b, Tanaka et al. have replaced bases in natural DNA with artificial ones that bind specifically to copper ions (Cu²⁺, purple spheres) or mercury ions (Hg²⁺, orange spheres). A duplex forms only when opposing bases bind a metal ion between them. The sequence of metal ions is determined by the sequence of artificial bases.

the basis of the order of the metal ions. The beauty of Tanaka and colleagues' work is that it exploits the self-assembly of DNA, where the two strands come together, a process that has been optimized by evolution over several billion years. Furthermore, automated DNA synthesis permits quick and easy access to any desired sequence of artificial DNA, provided that a certain length of molecule is not exceeded.

So how could these artificial DNA structures be used? One possible application is in organic chemistry, as catalysts for enantioselective reactions9 - that is, reactions that proceed with precise control of the three-dimensional structure of the products. Such catalysts are essential for the synthesis of biologically active compounds, but tailoring the interactions between a catalyst and a reactant to achieve this precise control is far from simple. Natural catalysts, such as enzymes, are excellent at directing enantioselective reactions, but from a chemist's perspective their range of reaction conditions is very restricted. Synthetic metal catalysts can be optimized to work under more typical laboratory conditions and on an industrial scale, but they are often less efficient than enzymes. Metal-ion-containing DNA catalysts

represent a biologically inspired approach that could combine the best of both of these catalytic worlds.

It has been found that, in a short artificial DNA duplex containing an array of five consecutive copper ions, the ions interact magnetically with each other2; this helix can be thought of as a self-assembled nanomagnet. Using Tanaka and colleagues' approach1, specific combinations of metal ions might be incorporated into DNA to fine-tune the magnetic properties of such devices. The electrical properties of DNA are also of interest. Unmodified DNA lacks sufficient electrical conductivity to be used in molecular electronic devices10 To address this problem, DNA has previously been prepared with metals attached to its exterior, but this modification prevented the DNA from reversibly self-assembling11. Tanaka and colleagues' structures1 might provide a way forward, as they incorporate metal ions in the centre of a DNA double helix that retains its ability to self-assemble.

But difficulties might be encountered when scaling up the authors' technique to build larger molecules. As DNA duplexes form, intermediate double helices can be produced in which the bases are not perfectly matched. But every metal ion incorporated into the artificial DNA increases the stability of the final aggregate. This effect could stabilize the intermediate helices so much that they no longer rearrange to form a perfect duplex, so introducing errors during DNA self-assembly.

Perhaps more importantly, automated DNA synthesis can only prepare sequences of up to about 100 bases. To build larger structures, biological techniques must be developed that either splice together short artificial DNA strands or allow the synthesis of longer strands. Such methods exist for natural DNA, but these would have to be modified to tolerate artificial bases and metal ions. Finally, more work is needed to determine the electrical properties of metalion-containing DNA - is it a conductor or a semiconductor? Future research should focus on this question, and investigate the factors that influence conductivity. It seems that the quest for a functioning molecular device based on metal-ion-modified DNA is about to begin. Jens Müller is in the Department of Chemistry, University of Dortmund, Otto-Hahn-Straße 6, 44227 Dortmund, Germany.

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