DNA NANOTECHNOLOGY

The world's smallest assembly line

Two separate studies show how DNA tiles can be used in automated assembly processes: one system self-replicates, the second assembles the output of a molecular computation.

Greg van Anders and Sharon C. Glotzer

At the dawn of the twentieth century, humankind began to make mechanical parts in large quantities, and manufacturers assembled them into early automobiles. The development of the assembly line by Olds and by Ford[1] led to mass production on a scale that allowed the automobile to shift from a boutique product to a consumer good.

Today's nano-scientists find themselves in a similar position to that of Olds and Ford. New methods allow for the synthesis of a diverse array of nano-sized and colloidal 'parts', which would in principle only need blueprints and an assembly line for their large-scale use to construct the next generation of materials and products. What might such an assembly line look like on the nanoscale? In two recent papers, Nadrian Seeman and co-workers provide a first glimpse into how this might work, through two systems based on DNA.

DNA strands consist of sequences of four complementary bases (A, C, G and T), which preferentially pair up as CG and AT through hydrogen bonds. A single strand of DNA with a particular arrangement of letters will therefore bind strongly to a strand with the complementary arrangement of letters. DNA tiles or materials bound to DNA (for example, gold nanoparticles) can thus be endowed with highly specific interactions, a characteristic that has been exploited in the field of DNA nanotechnology to construct a variety of assemblies and dynamic systems[2].

Writing in *Nature*, Seeman and colleagues have now described[3] a system that uses DNA in two different ways to create a prototype assembly that can self-replicate. Several DNA double helices were first arranged into previously designed[4] molecular tiles ('bent triple crossover' motifs). The tiles were given specific edge-to-edge as well as face-to-face interactions, through the complementarity of protruding DNA strands called 'sticky ends'. This led to four types of tiles — A, B and complementary A′ and B′. A and B′ tiles were also tagged with either a biotin–streptavidin label or hairpin loops so that they can be easily observed through atomic force microscopy imaging.

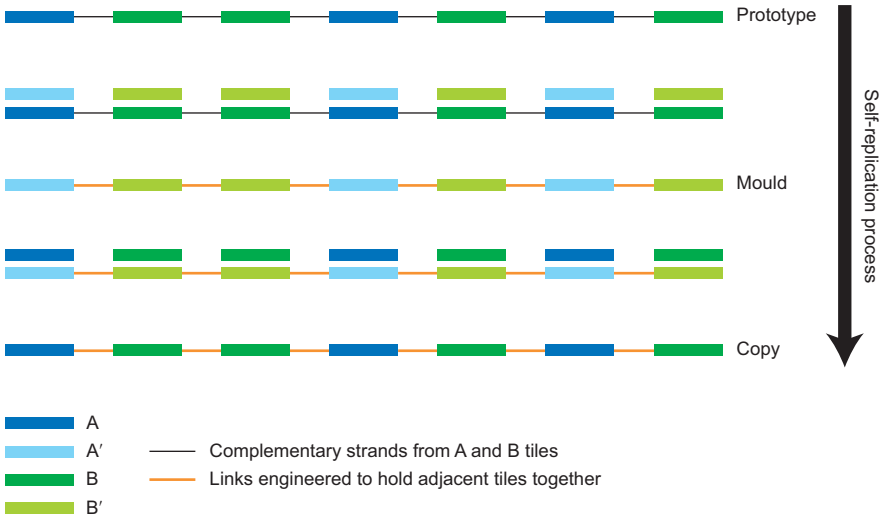

Figure 1 | DNA tiles (A and B) are programmed to assemble into a prototype pattern through hybridization. Face-to-face interactions with complementary tiles A′ and B′, respectively, are then used to construct a 'mould' pattern. This mould is consolidated with linkers and subsequently used to assemble further A and B tiles — this time lacking the complementary edge strands that would bring them together — in the same pattern, thus forming a copy.

A string with a prototype pattern (ABBABAB) was first prepared, and replication then occurred through a two-step process (Fig. 1). In the first step, the prototypes were copied by immersion in a bath of complementary tiles, somewhat reminiscent of impression moulding. The complementary tiles arrange in an A′B′B′A′B′A′B′ fashion through face-to-face interactions with the prototype, and are subsequently linked together through edge-to-edge interactions by the addition of a linking strand (complementary to two adjacent tiles) — these represent the mould, which is then separated from the prototype. In the following step, the mould was 'filled' by immersion in a set of tiles similar to the original set (A and B) — but which now lack the specific edge-to-edge interactions so that they do not form the ABBABAB pattern on their own. In the presence of the mould, however, they arrange in this fashion through face-to-face interactions, producing a copy of the original string. This copy is subsequently rigidified by addition of a linking strand (in the same manner as the mould was held together in the previous step) and separated from the mould. As long as the correct tiles are present in solution, the process can be repeated, and the mould re-used, to copy the original prototype several times.

In a second experiment, described in *Chemical Science*, Seeman and other collaborators take algorithmic assembly to the nanoscale[5]. It is known that DNA tiles can be used to perform computations[6]. Tiles are designed so that strands protruding at an edge (sticky ends) differentiate the binary digits '0' and '1', and whether the digits are part of the input, output or intermediate computation. Combining these specially designed tiles causes them to be assembled in a programmed way so that they act as a computational unit. Now, Seeman and collaborators have extended this idea in two ways: they have implemented a DNA computation step that could be applied to different inputs, and have also cast the output in terms of non-DNA species (Fig. 2).

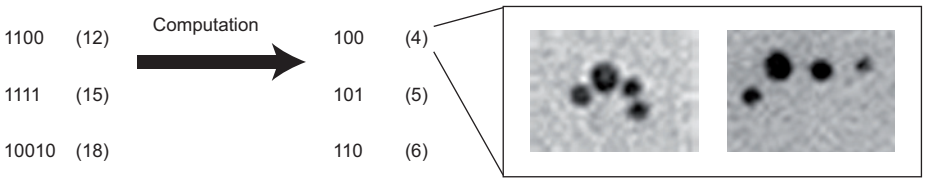

Figure 2 | An assembly of DNA tiles is able to divide by three binary numbers represented by DNA tiles, with sticky-ended DNA strands representing '0' and '1' domains. Gold nanoparticles are attached — small ones (5 nm) to the 0 domains and bigger ones (10 nm) to the 1 domains — so that the output (result of the division) can be imaged by transmission electron microscopy. Two (0100) outputs obtained for the division of 12 by 3 are shown here; reproduced with permission from ref. 5, © 2012 RSC.

Various input strings were assembled that are the binary representation of decimal numbers, 1100, 1111 and 10010 for 12, 15 and 18. The researchers used a set of DNA tiles that bind to the input strings to perform the computation — in this case, division by three. On mixing the input strings with the computational tiles, output strings are formed that correspond to the input numbers divided by three (here, 100, 101 and 110, respectively). Furthermore, 5 nm gold particles were attached to the tiles containing domains corresponding to the binary digit 0, and 10 nm nanoparticles attached to those corresponding to 1, which means that the output sequences could be read using transmission electron microscopy. Although DNA-based self-assembly has been performed before, here different structures were assembled based on a repeatable computation.

Through the first experiment mentioned above, Seeman and collaborators have provided a very important proof of concept of a nanoscale version of a familiar assembly process. After cleverly self-assembling their prototype using specially designed components, they were able to replicate it using parts that were 'off-the-shelf' — rather than specifically pre-programmed to assemble in this way through hybridization. As a process, it should not only be limited to DNA. We can envisage that particles with different programmable interactions, for example through particle patchiness or shape[7,8], could allow generalizations to other systems. Of course, the procedure isn't without its kinks. For example, only about 31% of the copies at the end of the process were identical to the prototype — the researchers compare this to the design of the first cars, airplanes and computers, which have undeniably come a long way in a few decades, to suggest that this replication process may in future be more efficient. Similarly, a shortcoming of the second experiment is that temperature cycling over a nine-hour period was required to ensure tiles would link correctly to achieve high fidelity in the computation process. In the history of automobile assembly it took almost a decade from Olds's mass production of the Curved Dash to Ford's moving assembly line that made the Model T a legendary commercial success. Here's hoping the next crucial leap in nanomaterials assembly lines comes more quickly. ❐

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DYNAMIC MATERIALS

The chemistry of self-healing

A reversible covalent reaction in which two oxygen-insensitive radicals combine to form a carbon–carbon bond provides the mechanism by which a polymer gel can self-heal at room temperature without the need for any external stimulus.

Marek W. Urban

Polymer gels represent an exciting group of materials whose components can be tailored to achieve a desirable spectrum of properties. They exhibit liquid-like flow as well as solid-like elasticity behaviours, which reflect complex physico–chemical relaxation mechanisms during macromolecular chain rearrangements. When the polymer chains interact physically with one another, solid-like properties are obtained, which can be further enhanced when chemical crosslinkages are introduced. During this process, weak self-associated networks are replaced by robust structures held together by covalent bonds. If the formation of covalent crosslinks is reversible and occurs without any side reactions, this can lead to materials that are not only strong but can also be repeatedly reconfigured and healed in response to damage.

Now, as they describe in *Angewandte Chemie International Edition*, Hideyuki Otsuka and co-workers[1] have made a polymer gel that can be healed without the need for an external stimulus. They have capitalized on the reversible formation of diarylbibenzofuranone (DABBF) crosslinkers from the dimerization of stable arylbenzofuranone (ABF) radicals (Fig. 1a). The polymer network (Fig. 1b) was made by reacting tetrahydroxy-functionalized DABBF building blocks with a modified poly(propylene glycol) (PPG) bearing an isocyanate group at each end. As shown in previous studies of polyurethane networks[2], a key feature of this system is the ability of the free radicals formed on mechanical damage to reform covalent bonds. When DABBF dissociates to give pairs of ABF radicals, it is critical that they exhibit little or no sensitivity to oxygen[3]. If they did,