DNA Evolves

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For most of the last 3.5 billion years DNA has performed purely biological functions. The identification of its role as the carrier of genetic information in living cells in 1944,[1] followed by the discovery of its now-iconic double helix structure by Watson and Crick in 1953,[2] laid the foundations for much of modern biology. Molecular biology and biochemistry have led to continuous improvements in the understanding of how DNA actually functions in living systems.

Over the last three decades, however, the robust molecular recognition ability of DNA – the pairing that occurs between guanine (G) and cytosine (C) or adenine (A) and thymine (T) – has inspired scientists to use DNA as a structural material. The specificity of GC/AT Watson-Crick complementary base pairing leads to intra- and intermolecular interactions that are both predictable and programmable. As a result, a whole field of DNA nanotechnology has evolved, aimed at building increasingly complex nanostructures and introducing multiple functionalities as a means to address problems in nanoscience, biological chemistry, and nanomedicine.

When single-stranded DNA molecules with complementary antiparallel sequences encounter one another, they bind to form the familiar double helix or duplex structure. Duplex DNA molecules equipped with complementary single-stranded overhangs (sticky ends), can thus combine together to form larger molecules. However, more complex structures require branching junctions. These do in fact occur in nature, but only transiently during a cell's manipulation of its genetic material. Nadrian Seeman, who first envisioned using 3D DNA lattices to orient other large molecules, constructed the first branched structure – a "four-arm" junction – in 1983.[3] Unlike the similar Holliday junctions found in nature, it is an immobile junction, consisting of four arms of different sequences to fix the junction at a certain position and it can, in principle, assemble into rigid crystalline lattices. Following their initial success, Seeman's group spent more than a decade designing and developing a variety of branched DNA structures including three-, five-, and six-armed junctions, and double-crossover (DX) tiles, finally publishing the first DNA 2D lattices of rigid DX tiles in 1998.[4] Inspired by this work, substantial progress has been made by other groups using tile-based structures to generate a variety of 2D and 3D DNA nanostructures. The next significant breakthrough occurred in 2006, when Paul Rothemund demonstrated a new technique, referred to as DNA origami.[5] The DNA can be manipulated into almost any final origami shape by folding a long single-stranded scaffold DNA in the presence of short "staple" strands. This approach overcomes several drawbacks of the tile-based structures including low yield, the need for purification, and lack of control over the final dimensions.

One of the key goals of DNA nanotechnology is to use the molecularly precise DNA 2D and 3D structures as templates to organize other materials. In the past few years DNA origami in particular has been used as a molecular pegboard to organize a variety of functional materials including metal nanoparticles, semiconductor quantum dots, nanotubes, nanowires, proteins, peptides and virus capsids and to control the distance between them with nanometer precision. The ability to organize such a wide variety of objects opens the door to the creation of highly multifunctional nanostructures.

Some applications depend on having ordered arrays of nanostructures and here the solution-based

synthesis of DNA nanostructures presents a challenge. To address this, in 2009, Caltech and IBM scientists developed a new method of local chemical functionalization to precisely position and orient DNA origami on surfaces[6] and in the following year an alternative method was explored by Hao Yan's group to selectively attach DNA origami tubes onto gold islands on a silicon substrate.[7] Although robust for a biomolecule, DNA is still a complex and sensitive polyectrolyte, and its behavior, including its structural integrity, is strongly affected by the type and concentration of counterions present in the solution. Transferring DNA nanostructures from the assembly medium to a substrate can distort or totally lose the programmed morphology of the lattices. This year, however, Chad Mirkin's group reported "silica encapsulation" of DNA assembled 3D superlattices,[8] demonstrating that both the symmetries and lattice spacings of the solution-phase structure can be preserved and remain stable against distortion, collapse, or dissociation.

DNA technology is capable of more than just producing static nanostructures: molecular robots, based on conformational changes driven, for example, by strand exchange processes, are an active area of research. Recently DNA "walkers" moving on programmed paths constructed from DNA origami have been reported by two groups.[9] These complex systems demonstrate a high degree of functional control, walking along tracks and transferring cargo at the nanometer scale. Other types of nanorobots make use of origami cages that open and release their contents when their lock is activated by a specific antigen key.[10]

Over the last three decades our ability to make complex and even active DNA nanostructures has increased dramatically. While new techniques are still being developed, researchers are now also focusing on issues associated with applications, such as scale-up, yield and biocompatibility. Whichever directions prove most fruitful, one thing is certain: DNA nanotechnology will keep evolving.

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