appeared on 9th May 2008

Designer molecules come of age

Blueprints to create structures using groups of atoms are becoming reality, says S.Ananthanarayanan.

From the state of living in rocky overhangs and caves, man has progressed to create functional, modular abodes, using ready-made components like blocks of stone or bricks. The science of civil engineering, apart from the use of particular materials, consists of the design of basic components and presenting the manner of putting the components together, to create complex structures.

But in the science of creating very small, nano-sized structures, we have not had the capacity to first create the components, which can then be assembled. Even for assembling complex chemicals, we cannot create components and we need to use exisiting chemical groups. Some special and useful chemical forms are developed by specific plants and much of the pharmaceutical industry is engaged in isolating and extracting these chemicals, for use as medicine.

Molecular blueprints

How the plant synthesises particular molecules, or animals assemble specific enzymes, of course, is with the help of the genetic instructions, or roadmaps, contained in the DNA. For optimum efficiency in managing life, the DNA, which are contained in each living cell, have evolved to spell out the creation of just 20 amino acids, the building blocks of proteins. And the formula of a protein is the sequence of amino acids to be combined – as spelt out in the sequence of groups of atoms strung together in portions of the DNA super-molecule.

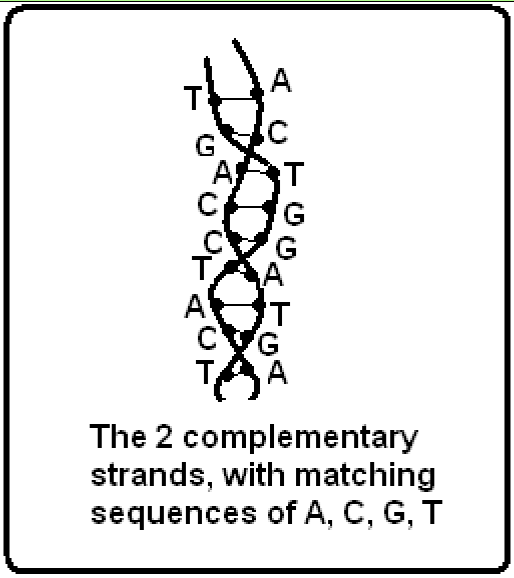
Study of this super-molecule in recent years has led to understanding a remarkable 'group-of-atoms-level' set of components that can be assembled, both to blueprint creation of proteins as well as to arrange themselves in different, exact shapes.

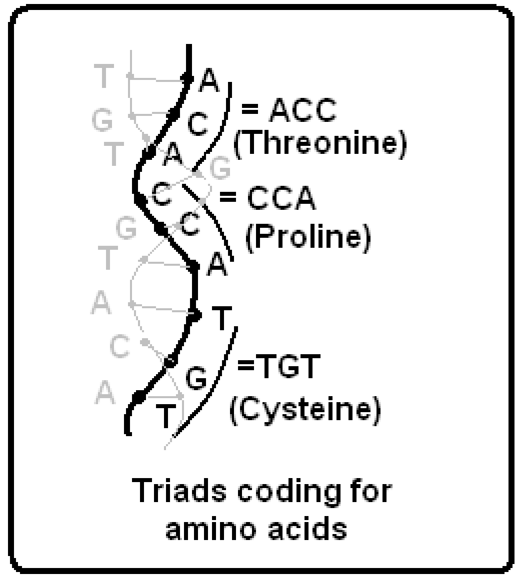
DNA origami

Origami is the Japanese art of paper folding. Using just a few basic paper folding patterns, a skilled artist can create myriad interesting shapes, flowers, animals, geometric shapes and even 3 dimensional objects. The techniques used to manipulate the components of the DNA to create shapes and forms has become known as ***DNA origami***.

The tremendous variety and versatility of nature owes itself to the elegant and simple device that compresses into a single molecule the structure of millions of different proteins, which then enable the existence of the countless species of animals and plant organisms. This device is the DNA molecule, which also has the capacity to replicate itself from just the random 'soup' of chemical elements in which it is immersed.

The DNA molecule is a regular sequence of four different groups of atoms, known as A,G, C and T, attached one after the other, in different combinations, to a 'backbone'. Each group of three consecutive units of these 'attachments' to the backbone form a 'triad', and each triad uniquely determines one amino acid. The number of triads that can be formed with four different things is 4x4x4=64. But this capacity to code in 64 ways is used to code only for twenty amino acids, by allowing for some redundancy, for safety, and also to show where a series of groups of three starts and ends.





Each of these series can be thousands of triads long and thus specify the sequence of extremely complex proteins. The whole DNA molecule has thousands of series and codes for great variety of proteins.

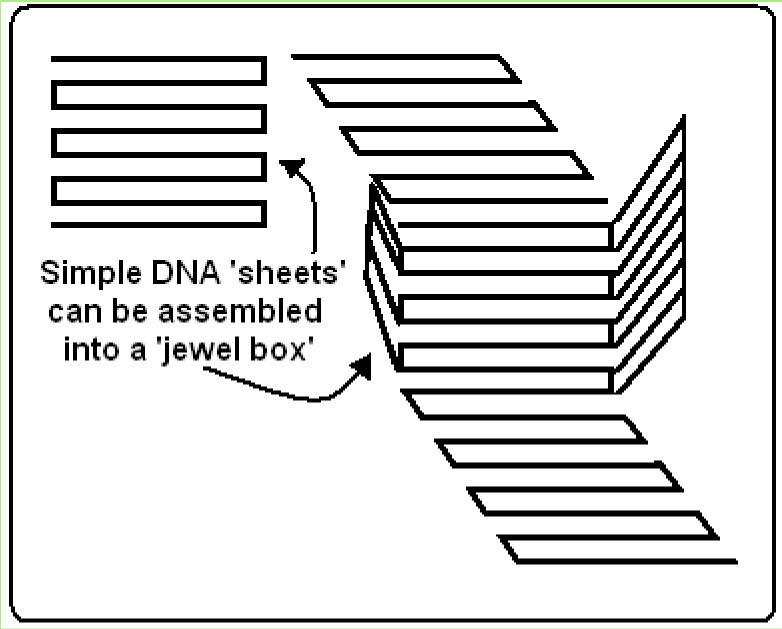
But the interesting thing is that DNA consists not of just of one string of A,G,C,T but of two strings, each being a complement of the other. This happens because each of the 'bases', A,G,C and T has affinity only for one other base – A for T and C for G and vice-versa- and the sequence in one string thus uniquely determines the sequence in the other string and the two strings, which are complements, wind around each other in a helix. If a DNA molecule should split into 2 single strands of DNA, the complements of the A,G,T,C bases from the surrounding raw materials find their counterparts and attach themselves to a backbone - thus creating the respective complementary string and duplicating the original DNA!

DNA Research

Apart from directing the creation of specific amino acids, the different sequences in the DNA also determine in which way the molecule will fold. Recent research has made much progress in this property and the dynamics of how different sequences may bend the series is now fairly understood. Another stride has been the ability to synthesise fairly long sequences, to create a series of about 100 specific A,G, C,T units at a time. It has hence become possible to create the very sequences that are known to bend the molecule in a known way. There are also ways to 'splice' or join together 2 different such strands, which results in a string that will fold in a particular way. The DNA molecule has thus become a powerful instrument for designing nanostructures.

The work of Paul Rothemund of California Institute of Technology, a few years ago, made news when he programmed DNA sequences to fold themselves into predefined shapes – of star shapes, smiley faces and a map of North America, among others. Component 'tiles' of DNA were developed and methods found to join them together, to enable building vast sheets or complex patterns. Rothemund's method was generic and could be adapted to creating nano-scale templates or platforms for arranging other materials.

The journal, ***Nature*** has reported that a group of workers in Denmark and Germany has extended the methods to three dimensions and has created a rectangular box, just 36 and 42 nanometers in size, with a lid! Six DNA scraps, which were folded into 'sheets' were joined together along specific edges, which made the sheets form themselves into the box. Supplying a further strand of DNA, which would unfasten one of the sheets amounted to 'opening' the box.



That the box has been created has been verified using X-rays and electron scattering and a fluorescent marker has been developed to indicate whether the box is open or shut. The concept is very promising and permits delivery of a drug, for instance, in nano-quantities, to be released, when desired, by switching on the mechanism to open the box!