Genetic Material under a Magnifying Glass

The genetic alphabet contains four letters. Although our cells can readily decipher our genetic molecules, it isn't so easy for us to read a DNA sequence in the laboratory. Scientists require complex, highly sophisticated analytical techniques to crack individual DNA codes.

Volker Deckert and his team at the Institute for Analytical Sciences (ISAS) in Dortmund have recently developed a method that could provide a way to directly sequence DNA. Their process is based on a combination of Raman spectroscopy and atomic force microscopy. As reported in the journal *Angewandte Chemie*, Deckert and Elena Bailo have successfully analyzed DNA's closest relative, RNA.

Direct sequencing means that the letters of the genetic code are read directly, as if with a magnifying glass. A DNA or RNA strand has a diameter of only two nanometers, so the magnification must be correspondingly powerful. Deckert's team uses an atomic force microscope to achieve this degree of magnification. Steered by the microscope, a tiny, silvered glass tip moves over the RNA strand.

A laser beam focused on the tip excites the section of the strand being examined and starts it vibrating. The spectrum of the scattered light (Raman spectrum) gives very precise information about the molecular structure of the segment. Each genetic "letter", that is, each of the nucleic acids, vibrates differently and thus has a characteristic spectral "fingerprint".

The direct resolution of individual bases has not been attainable, but is also not necessary. The tip only has to be moved over the RNA strand at intervals corresponding to about the base-to-base distance. Even if the measured data then consist of overlapped spectra from several neighboring bases, the information can be used to derive the sequence of the RNA.

If this method, known as tip-enhanced Raman spectroscopy (TERS), can be extended to DNA, it could revolutionize the decoding of genetic information. Previous methods for sequencing DNA are highly complex, work indirectly, and require a large sample of genetic material. In contrast, the TERS technique developed by Deckert directly "reads" the code without chemical agents or detours. It also requires only a single strand of DNA. "DNA sequencing could become very simple," says Deckert, "like reading a barcode at the supermarket."

Citation: Volker Deckert, Tip-Enhanced Raman Spectroscopy of Single RNA Strands: Towards a Novel Direct-Sequencing Method, *Angewandte Chemie International Edition*, doi: 10.1002/anie.200704054

Source: Angewandte Chemie