If Mercury truly has ice caps, where would the water be coming from? Despite Mercury's magnetic field, the solar wind occasionally reaches the surface, so hydrogen could be implanted into the surface. Mercury's abundant silicate crustal rocks contain oxygen, so there is a theoretical chance that some hydrogen and oxygen could get together and form water. More likely, the water has come from the comets and carbonaceous asteroids that have been bombarding Mercury since the planet's formation until the present day. Some water may still be outgassing and there is certainly continual replenishment from space.

Obviously, in Mercury's hot, radiative environment, the vast majority of water molecules near its surface are quickly dissociated and lost to space. But some small fraction of them may find their way to the planet's polar cold traps and diffuse downwards to subsurface ice traps. Despite Thomas's 1974 suggestion, little subsequent research on Mercury's atmospheric processes has considered the possibility of polar ice caps. Already, new calculations are underway and we may soon expect some revisionist models of Mercury's atmosphere.

Lest we get carried away, however, it remains unproved that the reflective deposit at Mercury's north pole is due to water ice. The Magellan spacecraft's fantastic radar maps of Venus's surface have also revealed anomalously bright units that can hardly be made of ice. The coincidence of Mercury's cap with its north pole (and the hint of a similar feature near its south pole) clearly points to a temperature-sensitive substance as the culprit.

On the one hand, we can see now that our 'broiling Mercury' *gestalt* had inhibited our thinking about ice on Mercury, and ice may be shown to be perfectly reasonable once all the calculations of sources, sinks, transport processes and stability are done. On the other hand, we live on an exceptionally watery planet that happens to have a mean temperature very near the freezing point of water, so there is a possibility that ice comes too readily to our minds. Until we understand the radar reflectivity properties of all other plausible materials, we will not know for certain that there is ice right under the Sun. □

Clark R. Chapman is at the Planetary Science Institute, 2421 East 6th Street, Tucson, Arizona 85719, USA.

OLIGONUCLEOTIDE DRUGS

A change of backbone

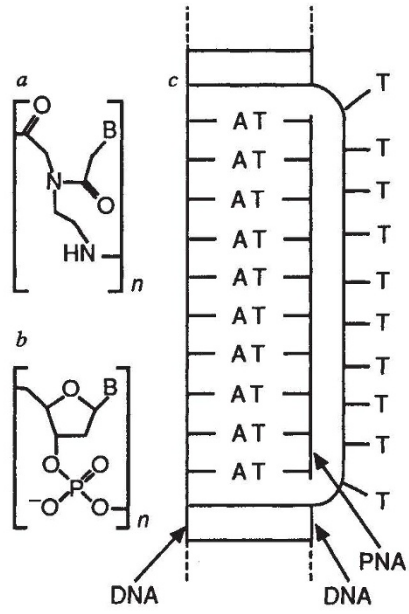
Maxim Frank-Kamenetskii

STUDY of chemically engineered analogues of natural oligonucleotides is all the rage, not least because of their potential as therapeutic agents which act by selectively blocking gene expression. The most radical departure to date from natural oligonucleotides is now reported by Peter Nielsen and colleagues (*Science* **254**, 1497–1500; 1991), who replaced the entire sugar-phosphate backbone of a stretch of DNA with a polyamide chain, preserving only the bases from the DNA prototype. Such protein–DNA chimaeric oligonucleotides form extremely stable heteroduplexes with complementary single-stranded DNA.

The promise of synthetic oligonucleotides is in their potential ability to silence particular genes at the level of messenger RNA (the antisense strategy) or that of double-stranded DNA (the triplex strategy); see *Nature* **350**, 442–443 (1991) for a brief review. They are also finding application as sequence-specific markers on both single- and double-stranded DNA. Increasing evidence has been accumulating to the effect that such 'gene-drugs' make it possible to affect gene expression in both isolated cells and entire organisms.

In genetically engineered organisms, it has proved feasible to incorporate special constructions that yield natural RNA oligonucleotides endogenously. But for clinical application one has to look to synthetic analogues of oligonucleotides that can penetrate cell walls and be efficiently attached to intracellular DNA or RNA. In the search for such analogues, which could improve the accessory properties of oligonucleotides such as nuclease resistance and cell penetration, various groups have been working on modification of the oligonucleotide sugar-phosphate backbone. It is a tricky business, though, because the replacement of even a single atom can significantly decrease the stability of the complex between the oligonucleotide and single- or double-stranded DNA. The achievement of Nielsen *et al.* is to show that whereas small changes in the backbone may be profoundly destabilizing, big changes need not be.

Nielsen *et al.* used computer modelling to design their polyamide nucleic acid (PNA), completely replacing the sugar-phosphate backbone with a polyamide chain. The only common element between their ersatz oligonucleotide and the normal one is the base (designated as B in the figure). They then synthesized oligo-PNAs containing from six to ten thymines. When they mixed the product



a, The structure of polyamide nucleic acid (PNA), in which the sugar-phosphate backbone of DNA (*b*) is replaced with a polyamide chain; only the base (B) remains the same. *c*, Strand displacement of the T-strand of linear plasmid DNA by oligo-PNA. (From Nielsen *et al. Science* **254**, 1497–1500; 1991.)

with dA_{10}, a nucleotide string of ten adenines, duplexes formed. Quite amazingly, the melting temperature of this heteroduplex was 50 °C higher than the melting temperature of the normal DNA duplex formed between dT_{10} (ten thymines) and dA_{10}.

The next experiment further emphasized the unprecedented stability of the PNA–DNA heteroduplex. When oligo-PNA was mixed with linear plasmid DNA carrying a dT_{10}–dA_{10} tract, it was found that, rather than forming a triplex, oligo-PNA displaced the T-strand and formed a duplex with the A-strand (part *c* of figure). This was convincingly demonstrated in a series of experiments involving enzymatic and chemical probing. It remains to be seen whether oligo-PNAs with an arbitrary sequence will form such a strong complex, although it seems likely that they will.

The availability of this new sequence-specific agent with such strong affinity for single-stranded DNA (and, most probably, for RNA) seems to open a cornucopia of opportunities. Among them are synthesis of much more potent antisense oligonucleotides, of markers that bind to specific sites independently of whether they are in duplex or single-stranded form, and of artificial restriction enzymes for any sequence. But a pivotal question remains: will such strong affinity be associated with significant loss of the sequence specificity? □

Maxim Frank-Kamenetskii is in the Institute of Molecular Genetics, USSR Academy of Sciences, Moscow 123182, USSR.

© 1991 Nature Publishing Group