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with DNA, therefore, it has not been possible to visualize the details of how these drugs interact with the enzymes' active site, much less to seriously consider applying rational design to their development.

Hare *et al.*[1] now change that situation. Their structure succinctly shows how integrase inhibitors displace the 3′ end of the viral DNA from the enzyme's active site, thus blocking its integration activity. Furthermore, they find that the active site, which seemed to lie in a featureless landscape in the earlier structures of the catalytic domain alone, is partially buried in a rugged surface — features that may afford potential sites for anchoring inhibitors.

Despite the giant leap forward that this study[1] takes our understanding of retroviral integrases, questions remain. First, four of the domains in the integrase tetramer are disordered. Are they involved in the interaction with the host DNA, as Hare *et al.* suggest? Do they mediate another function, or are they simply redundant? Also, the target host DNA is not present in the structure, although there seems to be only one place for it to go without drastic structural rearrangement.

The stark contrast between reality and the now-redundant previous models cautions against embarking on exuberant model building with few constraints imposed by experimentation. That said, the integrase enzymes of HIV-1 and PFV are sufficiently similar to justify the use of PFV integrase in complex with both viral DNA and antiviral inhibitors for reliably modelling the binding of these inhibitors to the HIV-1 enzyme. ■

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50 & 100 YEARS AGO

50 YEARS AGO

Strange World of the Moon. An Enquiry into Lunar Physics. By V. A. Firsoff — Persistent observers of the Moon, many of them amateurs with small instruments and little scientific training, have often reported changes of various kinds in the appearance of the lunar surface; these have tended to be met with scepticism by most professional astronomers ... The present book, which attempts to interpret changes seen by the author and other observers in terms of known physical and chemical laws, is timely ... in view of the increased interest in the Moon resulting from the new facilities offered by space rockets ... Mr. Firsoff attributes ray systems to erosion by running water, fed from large deposits of ice accumulated below the spongy surface rocks, and he suggests that the maria, also, are filled by impure ice ... Basically, however, the author's arguments only show that his ideas are barely possible; he has certainly not shown that they are at all likely. In particular, the idea that water is present on the lunar surface is highly implausible.
From *Nature* 12 March 1960.

100 YEARS AGO

Survival of Man. A Study in Unrecognised Human Faculty. By Sir Oliver Lodge — To most people the question of the survival of human personality is the greatest problem of life ... At present the chief interest of the subject centres round the theory of cross correspondences, emanating chiefly from the so-called controls that are manifested in certain well-known and much discussed automatic scripts, and claim to represent the surviving personalities of Myers, Hodgson, and others ... Similarly, indications of known personalities, examples of typical intellectual activities continuing after earthly existence has ceased, may accumulate to such intensity that no hypothesis is so simple or so effective as that which involves the acceptance of the belief in their manifest survival.
From *Nature* 10 March 1910.

ATMOSPHERIC CHEMISTRY

Wider role for airborne chlorine

Roland von Glasow

Unexpected chlorine chemistry in the lowest part of the atmosphere can affect the cycling of nitrogen oxides and the production of ozone, and reduce the lifetime of the greenhouse gas methane.

When people hear about chlorine in the atmosphere, many probably think of the chlorine that comes from man-made chlorofluorocarbons (CFCs) and harms the ozone layer in the stratosphere, some 25 kilometres above Earth's surface. However, on page 271 of this issue, Thornton *et al.*[1] report their observations of large amounts of reactive chlorine compounds at Earth's surface, in the middle of the continental United States.

The authors' measurement site is far from known natural chlorine sources, such as the ocean, or strong anthropogenic sources (for example, coal combustion or steel production). These findings are important because they reveal a previously unconsidered chemical pathway that generates a large amount of chlorine radicals in the troposphere (the lowest 10 kilometres or so of the atmosphere). Such radicals will react with many volatile organic compounds (VOCs), including the potent greenhouse gas methane (CH_4), speeding up their removal from the atmosphere. Furthermore, this pathway will extend the lifetime of nitrogen oxides, the main precursors for ozone production in the troposphere. Ozone is central to atmospheric chemistry, but can also be a pollutant — in high concentrations it is toxic to animals and plants, and it acts as a greenhouse gas.

To understand the relevance of Thornton and colleagues' discovery, it is necessary to briefly explain the general role of nitrogen oxides in the atmosphere. Nitrogen oxides are released from anthropogenic combustion processes (for example, in cars and power plants) or the burning of biomass, but are also produced naturally by lightning. In the troposphere, the light-induced reaction of nitrogen dioxide (NO_2) is the only way to form ozone. Nitrogen dioxide can also react with ozone to produce nitrate radicals ($NO_3^{\bullet}$), which can then react with more NO_2 to form dinitrogen pentoxide (N_2O_5). In other words, two molecules of NO_2 are 'stored' in one molecule of N_2O_5.

Dinitrogen pentoxide is stable only at low temperatures in the absence of light. If exposed to sunlight, the two molecules of NO_2 stored within it are released and can continue to produce ozone. It has been shown[2,3] that a strong loss process for N_2O_5 is its reaction on the surface of aerosol (Fig. 1) — tiny omnipresent particles in the atmosphere that originate from sources such as combustion processes, dust and salt from the oceans.

Thornton and colleagues' atmospheric measurements[1], taken at night just outside Boulder,

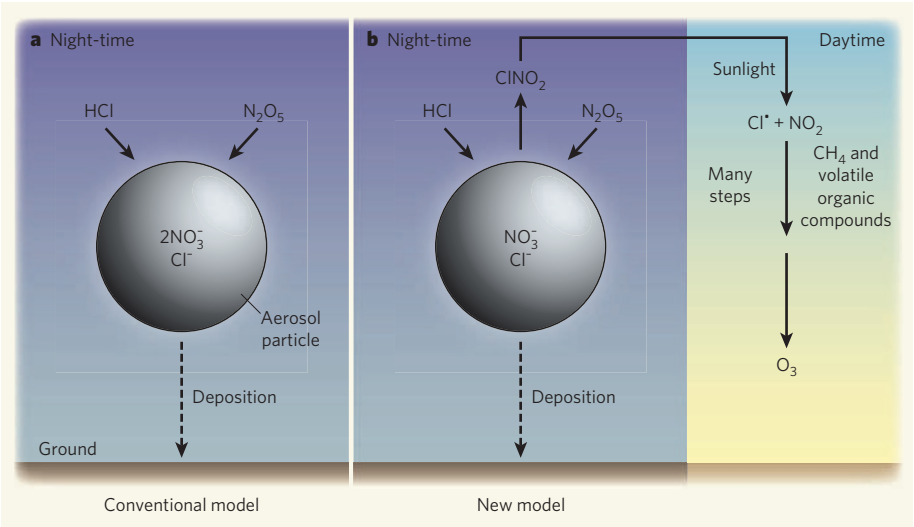

Figure 1 | Schematic of the uptake of N_2O_5 on aerosol particles. **a**, Conventional picture of aerosol uptake of hydrochloric acid (HCl) and dinitrogen pentoxide (N_2O_5), leading to chloride (Cl^-) and nitrate (NO_3^-) ions, respectively. In the absence of further reactions both are eventually deposited on the ground with the aerosol particle. **b**, Mechanism supported by the measurements of Thornton *et al.*[1]: nitryl chloride ($ClNO_2$) is formed at night in the reaction of N_2O_5 on particles containing chloride. The next day, sunlight breaks $ClNO_2$ into chlorine radicals ($Cl^\bullet$) and nitrogen dioxide (NO_2). The chlorine radicals can then attack the greenhouse gas methane (CH_4) and volatile organic compounds, and the resulting peroxy radicals and NO_2 lead to the formation of ozone (O_3).

Colorado, indicate an additional major reaction pathway for N_2O_5 (Fig. 1). If it reacts at night on aerosol particles that contain chloride, then one of the two NO_2 molecules stored within it can form nitryl chloride ($ClNO_2$). This is released to the atmosphere, whereas the other NO_2 molecule forms a nitrate ion (NO_3^-). Under most conditions, nitrate ions remain in the particles and are eventually deposited on the ground. The following morning, $ClNO_2$ is broken down by sunlight into a chlorine radical and NO_2. This effectively extends the lifetime of NO_2, allowing it to produce more ozone and to be transported by air currents away from its source. The chlorine radical, meanwhile, can react with VOCs, including CH_4. The chain of reactions that follows eventually leads to the production of peroxy radicals that (along with nitrogen oxides) are key ingredients of ozone formation.

This reaction pathway for N_2O_5 had already been observed[4] in the laboratory in 1989, but confirmation of its role in the atmosphere didn't occur until 2008, when Osthoff *et al.*[5] observed high $ClNO_2$ concentrations in coastal regions and ship plumes — places where chloride from sea salt meets pollution. Crucially, Thornton *et al.*[1] have now observed the same pathway well away from likely local sources of chloride, and provide compelling reasons to believe that this chemistry is more widespread than previously thought. The authors suggest that the chloride required for the production of $ClNO_2$ could be supplied from a plethora of man-made and natural sources. Long-term atmospheric measurements from deposition networks at many locations in the United States suggest that this might indeed be the case, but the sources and amounts of 'background' chloride need to be better quantified to improve our understanding of where this kind of chemistry might be most prominent.

On this basis, Thornton *et al.*[1] assumed that the ingredients for $ClNO_2$ formation are ubiquitous in the atmosphere of the continental United States and used a computer model of the atmosphere to estimate the continent-wide impact of this reaction. A notable uncertainty in the model is the efficiency of $ClNO_2$ formation, which depends on the available surface area of aerosol particles, the particles' composition (especially their chloride content) and the relative humidity. The authors' simulations suggest that 8–22% of all nitrogen oxides emitted in the United States cycle through the $ClNO_2$ pathway, which will therefore affect the lifetime and transport of those compounds as described earlier. The researchers' estimate of the amount of $ClNO_2$ produced over the continental United States alone is much larger than the first global estimate of the compound's production[6], and is similar to recent estimates of global $ClNO_2$ production in coastal regions[5].

If other continental regions also act as sources of $ClNO_2$, then the cycling of nitrogen oxides and chlorine through this compound is of global relevance. A more thorough investigation of this reaction pathway is therefore warranted, involving many more measurements of $ClNO_2$ and of background chlorine compounds in general. As a large part of the uncertainties in Thornton and colleagues' model relate to the actual reaction of N_2O_5 on aerosol particles, this reaction should also be studied in more detail, in the hope of finding generally applicable parameters for the process.

Numerical models of atmospheric halogen chemistry have to include many compounds to fully describe the various reaction cycles. Yet many of these compounds, including certain key intermediates such as hypobromous acid (HOBr) and hypochlorous acid (HOCl), have so far not been identified in the atmosphere, despite the fact that new instruments have provided much insight into halogen reaction cycles in recent years[1,5]. To keep making progress, scientists working in the laboratory, the field and with numerical models must collaborate at the early stages of projects, to find ways of detecting and quantifying 'new' compounds[7]. Such an approach would be invaluable in answering the questions raised by Thornton and colleagues' study[1]. ■

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SUPRAMOLECULAR CHEMISTRY

Sticking to sugars

Anthony P. Davis

If evolution has had trouble making effective carbohydrate receptors, what hope do humans have of creating synthetic versions? A method for preparing libraries of such receptors boosts the chances of success.

Carbohydrate recognition — the process in which receptors bind to specific carbohydrate molecules — is a difficult task, best left, one might think, to biological molecules that have evolved to do the job. Chemists have nevertheless taken up the challenge of finding synthetic receptors for carbohydrates, and are beginning to succeed. Reporting in *Angewandte Chemie*, Pal *et al.*[1] describe a family of peptide-based receptors that incorporates synthetic, carbohydrate-binding amino acids. By screening 400 variants of these receptors, the authors