studies. In linkage experiments a fraction of the samples that contain two sperm and which have amplified only one of the two alleles at each locus will generate 'false recombinants'. We expect that the frequency of false recombinants can be minimized by careful attention to sperm isolation and the enhancement of sperm lysis and amplification efficiency. If very large numbers of sperm could be analysed with great reliability, some mutational events which cannot be analysed by conventional methods might eventually be studied.

Our ability to haplotype sperm at the DNA level will provide a fundamentally new approach to studying human recombination and may also be useful in determining the physical order of DNA polymorphisms which are so tightly linked that they cannot be resolved by additional family analysis. This may be especially significant in the case of random RFLPs tightly linked to disease-causing loci. The genetic distances between the random RFLPs could be accurately determined and the RFLPs ordered with respect to one another by three point crosses, provided that simultaneous amplification of 3 marker loci could be made efficient enough for single sperm experiments. Such fine structure maps might be of great value in attempts to locate the disease-causing locus itself. Of course because sperm do not exhibit disease phenotypes, an unknown disease locus cannot be directly mapped relative to polymorphisms in this way.

The analysis of single sperm in species that cannot be extensively bred or have exceptionally long generation times may be the only practical way of making genetic maps for these species.

One immediate practical application of the analysis of individual sperm is in the area of forensic medicine. *HLA* typing for paternity determinations or identification of criminals is often hampered by the inability to determine the haplotype of the suspected individuals because this would require the analysis of close relatives. *HLA* analysis of individual sperm from a suspect would allow the linkage phase of the *HLA* markers to be unambiguously determined and thus increase the probability of inclusion or exclusion.

Finally, the ability to study DNA sequences in individual diploid cells will make it possible to study cell-to-cell variation in developmental processes involving DNA rearrangements or other genetic alterations. It is also likely that analysis of messenger RNAs in single cells would be possible if efficient reverse transcrption could be carried out before PCR was initiated. Prenatal diagnosis on a single cell derived from a preimplantation embryo resulting from *in vitro* fertilization is also conceivable.

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LETTERS TO NATURE

No cometesimals in the inner Solar System

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Ultraviolet measurements made by Voyager 2, apparently showing a rapid decrease in hydrogen Lyman-α emission with distance from the Sun, were taken by Donahue *et al.*[1] as evidence for a source of atomic hydrogen in the very local interstellar medium (VLISM). The suggested source[1] is a class of small comets, at solar distances of ~1 AU, that produce atomic hydrogen as their icy mantle is evaporated. This claim has been adduced as evidence for a theory[2] that the Earth is subject to a large influx of cometary material, significantly affecting atmospheric evolution. Here we analyse again the Voyager 2 data, and show that no source of hydrogen in the VLSIM is required other than the inflow of neutral atoms; the original analysis was apparently flawed by an erroneous transcription of tabulated data (T. M. Donahue, personal communication).

Although Donahue *et al.*[1] claimed to find a cometary source of hydrogen, the estimated flux was ~seven orders of magnitude smaller than required by the theory of Frank *et al.*[2]. But by postulating a different and more numerous kind of comet, Frank *et al.* have claimed[3] that the Voyager data, the most important direct evidence for small comets and the crucial data in obtaining limits on sources of volatile compounds such as H_2O, can be made to agree with their theory.

The observations in question are obtained with Voyager 2 shortly after launch[1]. Figure 1 shows the observing geometry looking down on the north pole of the Solar System. A number of observations, in a direction approximately downstream with respect to the inflowing VLISM neutral gas, were obtained with the spacecraft located near 1 AU. Further measurements were obtained with the spacecraft located at $r_0 \sim 1.3$ AU and beyond, with all observations approximately downstream as shown in Fig. 1. The analysis of these data by Donahue *et al.*[1] indicated that the measurements near 1 AU in a direction amost tangential to the Earth's orbit demonstrated intensities in excess of a normal VLISM model. The excess near 1 AU was attributed to the influx of cometesimals. We argue that the stronger signal obtained near 1 AU is simply a consequence of observing geometry.

The search for a local source of hydrogen in the Voyager data was limited by Donahue *et al.*[1] to observations in the VLISM downstream direction (Fig. 1). The observations obtained with the spacecraft positioned near 1 AU were necessarily at a high angle ($\beta \approx 90°$; see Fig. 1) to the antisolar direction because the spacecraft was positioned in the vicinity of 0° right ascension (α) (Fig. 1). Later observations with the spacecraft positioned near 2 AU were obtained with a viewing direction more closely aligned with the antisolar direction. A non-negligible fraction

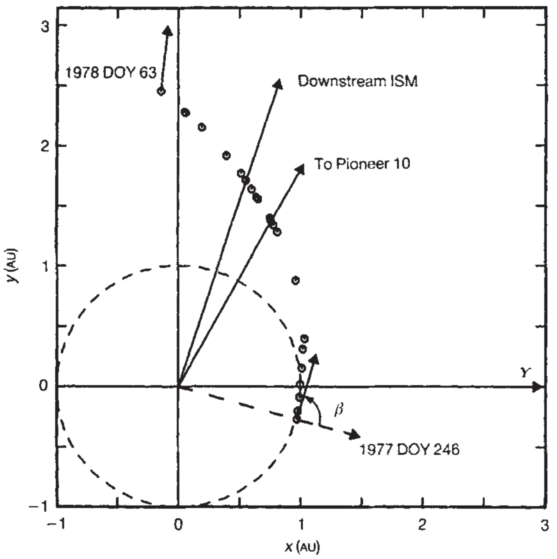

Fig. 1 Voyager 2 spacecraft locations and pointing directions as viewed from the north pole of the Solar System. Y indicates the $\alpha = 0$ reference direction. The positions refer to the data used by Donahue *et al.*[1]. The observational direction for the Voyager ultraviolet spectrograph is shown for 3 September 1977 (DOY 246) and 4 March 1978 (DOY 63). The direction of the Pioneer 10 spacecraft position (at ~15 AU) and mean observational direction (dashed arrow) during this period, and the direction of the flow of the neutral VLISM gas are also indicated. DOY = day of year. The dashed arrow denotes the antisolar direction for the first Voyager obervation used in the analysis.

of the observed hydrogen Lyman-α (Lyα) signal is due to scattering from the inner cavity region. If one approximates the hydrogen distribution in this region as a constant density, this fraction is roughly proportional to $(\beta/\sin\beta)$. Because the observational angle β approaches 90° in the data obtained near 1 AU, the signal produced in the downstream direction is significantly larger than expected relative to the measurements made later near 2 AU, where $\beta \sim 0°$. In other words, the data show a deceptively large signal near 1 AU because of observing geometry. Figure 2 shows the calculated ratio of the Voyager 2 intensity data, $I_{Ly\alpha}$, to the predicted signal based on the model of Ajello *et al.*[4], I_{M1}, after correction for the variation in the solar Lyα flux. The ratio is normalized to $I_{Ly\alpha}/I_{M1} = 1.00\ (\pm 0.05)$ in the averaged data points for 28 January to 4 March 1978 (days of year (DOY) 28-63), corresponding to a heliocentric distance $r_0 \geq 2.0$ AU. The data obtained in the time span 3-15 September 1977 (DOY 246-258) corresponds to a spacecraft position near $r_0 = 1.0$ AU. The value of $I_{Ly\alpha}/I_{M1}$ during this latter period scatters around the value 1.04 ± 0.09; this scatter appears to be limited by our ability to accurately define the solar flux during the integration time of the measurement. But the scatter in the $I_{Ly\alpha}/I_{M1}$ values in Fig. 2 is generally consistent with our estimated 1σ statistical error of ±4%. The Ajello *et al.*[4] model is based on the Thomas[5] spatial structure of atomic hydrogen determined by assuming the only source of neutral gas to be the inflowing VLISM. Figure 3 shows a plot of Voyager intensity data against model predictions as a function of spacecraft radial position. The model calculation includes a correction for variation in solar Lyα flux defined by the Pioneer 10 data shown in Fig. 4. We conclude that the Ajello *et al.*[4] model accounts for the data within errors.

As stated by Donahue *et al.*[1], the major uncertainty in establishing the observed distribution is the determination of the appropriate value of solar flux ($\mathscr{F}_0$Lyα) used for normalization. We have used the value obtained from Pioneer 10 (P10) $I_{Ly\alpha}$ data. The P10 spacecraft was located at $r_0 \approx 15$ AU and $\alpha \approx 61°$ during this period and we have applied no phase correction to the data. Figure 4 shows a plot of the P10 solar reference data corrected for a r_0^{-1} variation in signal ($I_{Ly\alpha} r_0$), in comparison with predicted signal $\mathscr{F}_0$Lyα at Earth based on He-10,830-Å equivalent-width measurements (see Donnelly *et al.*[6] and Skinner *et al.*[7]). Using either data set to obtain $\mathscr{F}_0$Lyα produces equivalent results in Fig. 4 after appropriate phase correction. The short-term variability in $\mathscr{F}_0$Lyα indicated in the Atmospheric Explorer-E (AE-E) data used by Donahue *et al.*[1] does not agree particularly well with either data set in Fig. 4, and we regard the AE-E data as unreliable[8]. Nevertheless, reduction of the results using the AE-E data produces the same conclusion as we have obtained above, indicating that using any of these data sets to define $\mathscr{F}_0$Lyα does not alter the basic conclusion, namely that there is no evidence of a measurable local source of atomic hydrogen in the Voyager data.

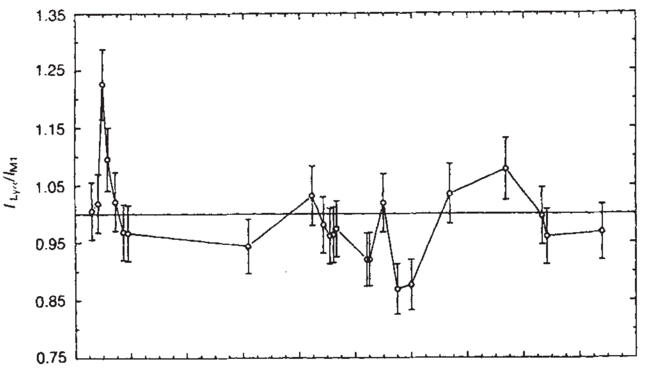

Fig. 2 The ratio of the Lyα intensity measured by Voyager 2 ($I_{Ly\alpha}$) relative to prediction of the VLISM model of Ajello *et al.*[4] (I_{M1}), using the data obtained at points shown in Fig. 1. The ratio $I_{Ly\alpha}/I_{M1}$ is normalized to 1.0 averaged over the data points for 28 January to 4 March 1978 (DOY 393-428). The model includes the variation of the solar flux as defined by the Pioneer 10 data shown in Fig. 4. The mean ratio over the period 3-15 September 1977 (DOY 246-258) is $I_{Ly\alpha}/I_{M1} = 1.04 \pm 0.09$, compared to a mean value $I_{Ly\alpha}/I_{M1} = 1.00 \pm 0.05$ for the period 28 January to 4 March 1978 (DOY 393-428). Note that here DOY refers to days from 1 January 1977.

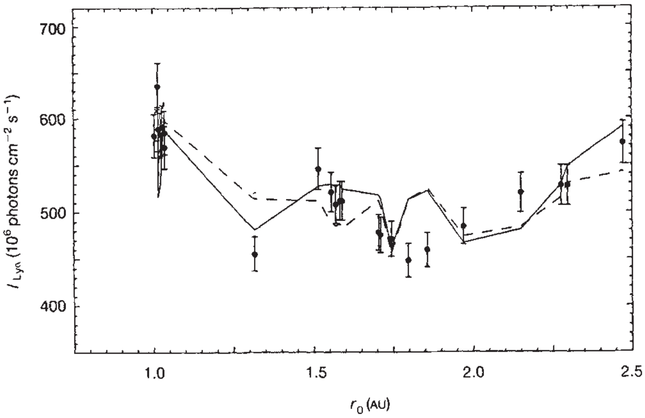

Fig. 3 Voyager 2 intensities for the data examined by Donahue *et al.*[1] as a function of spacecraft heliocentric radial position (solid circles), compared to normalized VLISM model calculations using the Ajello *et al.*[4] model (solid line) and a simplified analytic approximation (dashed line). The model calculations are corrected for the solar Lyα flux variation as defined by the Pioneer 10 data (Fig. 4).

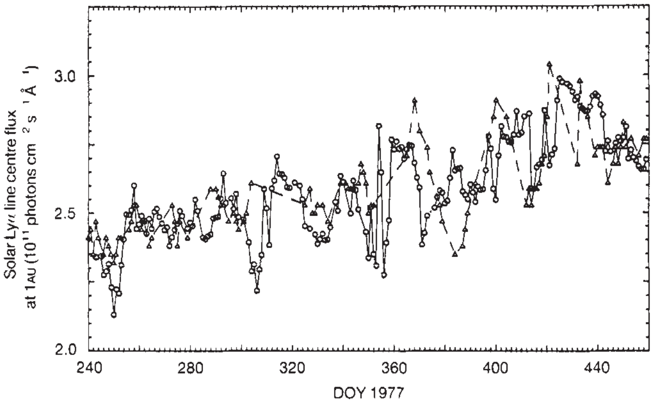

Fig. 4 Variation of the line centre solar Lyα flux as defined by the Pioneer 10 measurements of reflected solar radiation (open circles connected by a solid line) and measured equivalent width of the He-10,830-Å solar absorption feature (open triangles connected by a dashed line) over the period 28 August 1977 to 5 April 1978 (DOY 1977 240–460). The P10 data is proportional to the product $I_{Ly\alpha}r_0$. The P10 spacecraft location is in the range r_0 = 13.5–15.3 AU during this period. The data are normalized to SME reference data during 1982, with a conversion to predicted line centre flux by the factor $I_\lambda = 0.961I$ (photons cm^{-2} s^{-1} Å^{-1}). Solar line shape is assumed constant.

The results obtained here derive mainly from the observing geometry; the sensitivity to VLISM model parameters is minimal. In fact, the Voyager 2 results can be approximated using

$$I_{Ly\alpha} = g_e r_e^2 n_c\left(\frac{\beta}{r_0 \sin\beta}\right) + I_c \qquad (1)$$

where g_e is the Lyα g value at distance r_e = 1 AU from the Sun, n_c is a characteristic inner cavity H I density, r_0 is the spacecraft radial distance, β is the angle between the line of sight and the antisolar direction and I_c is a constant intensity due to backscattering at or beyond some characteristic ionization cavity boundary. The model represented by equation 1 corresponds to the Donahue *et al.*[1] model with their parameter $\gamma = 2$. The model (dashed line) shown in Fig. 3 corresponds to $n_c = 0.008$ cm^{-3} and $I_c = 3.49 \times 10^8$ photons cm^{-2} s^{-1}. The atomic hydrogen distribution in the calculation simply uses a step function H I distribution as an approximation to the detailed Thomas[5] calculation.

We conclude that there is no systematic evidence for a local source of atomic hydrogen in the Voyager data. If such a source were present at 1 AU, it could have a Lyα emission rate no larger than $I_{Ly\alpha} \approx 20$ rayleighs, a factor of eight below the value obtained by Donahue *et al.*[1]. Donahue (private communication) has obtained a similar result using the Thomas[5] tabulated VLISM model and AE-E solar reference data.

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The oxygen isotope effect in $Ba_{0.625}K_{0.375}BiO_3$

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The nature of the superconducting pairing mechanism in the high-temperature superconducting oxides is still an open question. Shortly after the discovery of these materials, several groups began an intensive study of the oxygen isotope effect. For a monatomic conventional (BCS) superconductor, the transition temperature T_c is proportional to $M^{-\alpha}$, where M is the mass of the atom and $\alpha = 0.5$, assuming no anharmonicity for the phonon modes and no Coulomb interactions. For a multicomponent material, $T_c \propto M_i^{-\alpha_i}$ with an α_i defined for each ion with mass M_i. Thus, each element contributes to the overall α (which would still equal 0.5) with a weight dependent on the structure of the phonon modes that are important for superconductivity. Because the $^{16}O/^{18}O$ mass ratio is much smaller than the available mass ratios for the isotopes of the other atoms in these materials, the oxygen contribution to α (α_{ox}) should be the largest and thus in principle the easiest to measure. A zero or very small oxygen isotope effect would thus imply an unconventional pairing mechanism, although the suppression of α in normal phonon-mediated superconductors is common. A large value of α (>0.3) indicates conventional (BCS) superconductivity. $Ba_{1-x}K_xBiO_3$ was recently found to be superconducting[1], with $T_c \approx 30$ K. Unlike the planar cuprate supercondors, this material is cubic. Here we report on the ^{18}O isotope effect for $Ba_{0.625}K_{0.375}BiO_3$. We find that this material has a large isotope effect, indicating that the pairing mechanism is conventional (phonon-mediated).

Transition temperatures for $La_{1.85}Sr_{0.15}CuO_4$ (with a nominal T_c of ~38 K) have been found to decrease by 0.3–1 K on substitution of ^{18}O (refs 2–4), which implies a variation in α_{ox} of 0.1–0.37, with a most probable value of 0.2. T_c suppressions of 0–1 K have been reported for $YBa_2Cu_3O_7$ (refs 4–9), giving a much lower value of α_{ox} (0–0.05) than in $La_{1.85}Sr_{0.15}CuO_4$ because of the much higher T_c (91 K) of the former. These large variations in reported α should not be unexpected because for these materials the shift in T_c, ΔT_c, is much less than the superconducting transition width, making the determination (and even the criterion for the determination) of ΔT_c difficult. Synthesizing these materials with sample-to-sample variations that are less than the observed isotope shift is also difficult. But despite large variations in the reported oxygen isotope effects there is no doubt that α_{ox} for $YBa_2Cu_3O_7$ is much smaller than that for $La_{1.85}Sr_{0.15}CuO_4$.

The isotope effect has been measured recently for $BaPb_{1-x}Bi_xO_3$ ($T_c \approx 13$ K for $x = 0.25$) and was found to be large[4], indicating that pairing is phonon-mediated in this material. From the results in ref. 4 (T_c = 11 K, $\Delta T_c = 0.5 \pm 0.1$ K, 60% ^{18}O substitution) α_{ox} is calculated to be 0.6 ± 0.1. This value is unrealistically large, but if 100% substitution is assumed instead, more reasonable values (0.4 ± 0.1) are obtained. It is interesting that the magnitude of the T_c suppression appears to remain constant for these three oxide systems, leading to a monotonic decrease in α_{ox} as T_c increases. This has led to speculation that in these materials there is a continuous transition from phonon-mediated superconductivity (for low-temperature supercondutors) to a dual phonon–electronic boson mechanism (for example, phonon–plasmon) for materials with high transition temperatures[10]. Thus, suppression of the isotope effect could be a measure of the non-phonon contribution to superconductivity. If α_{ox} scales with T_c, we would expect an