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Technical Comments

Formation of Ozone by Irradiation of Oxygen at 248 Nanometers

Slanger *et al.* (*1*) report that 248-nm KrF laser radiation produces ozone from oxygen, even though this wavelength is longer than 242.4 nm, the conventionally accepted threshold for the photodissociation of the ground electronic state $X^3\Sigma_g^-$ of O_2 (*2*). Slanger *et al.* (*1*) have demonstrated that the production of O_3 is initially inefficient and slow, but subsequently becomes efficient and rapid, in an autocatalytic fashion. They have shown that the latter efficient mechanism involves the 248-nm photodissociation of previously formed O_3 to yield atomic oxygen and $O_2(X^3\Sigma_g^-)$ in a range of vibrational levels including $v'' = 7,9$; these two levels then absorb the 248-nm radiation, forming $O_2(B^3\Sigma_u^-)$ ($v' = 2,7$), which is known (*3*) to predissociate, efficiently yielding a pair of ground-state oxygen atoms. The atomic oxygen formed directly from the photodissociation of O_3 and indirectly from the predissociation of $O_2(B^3\Sigma_u^-)$ is available to produce more O_3.

The initiating mechanism for the formation of O_3 from O_2 at 248 nm, however, remains somewhat obscure. Slanger *et al.* (*1*) make brief mention of three possibilities for this initial, inefficient step: dissociation of O_2 by two-photon absorption; dissociation of O_2 by radiation of wavelength ~239 nm arising from the anti-Stokes Raman shifting of the 248-nm radiation; and dissociation of $(O_2)_2$ dimers at 248 nm. The first and second suggestions seem unlikely with the unfocused radiation used, and no convincing evidence exists for the third process, in so far as the continuous attenuation of radiation incident on oxygen at 1 atm pressure at wavelength greater than 242.4 nm is mainly due to Rayleigh scattering. Slanger *et al.* (*1*) conclude that the initial formation of O_3 occurred in some undefined manner.

We suggest that a highly probable initiating step is the absorption of the 248-nm radiation by $O_2(X^3\Sigma_g^-)$ ($v'' = 1$), of which the fractional Boltzmann population at 300 K is ~0.057%, The photodissociation threshold for absorption into the Herzberg continuum $O_2(A^3\Sigma_u^+)$ by $O_2(X^3\Sigma_g^-)$ ($v'' = 1$) is 251.9 nm, compared with 242.4 nm for $O_2(X^3\Sigma_g^-)$ ($v'' = 0$), so that the 248-nm laser radiation can photodissociate the former but not the latter. The importance of the absorption of radiation by O_2 ($v'' = 1$), even at a concentration ~0.057% at 300 K, is well established in other spectral regions (*3, 4*).

In view of the facts (i) that the Franck-Condon factor for the (11,1) Herzberg I absorption band at 252.5 nm is ~5 times greater than that of the (11,0) band at 243.0 nm (*5*), and (ii) that the cross section for absorption from $v'' = 0$ into the Herzberg continuum near 242 nm is $\sim 1.0 \times 10^{-24}$ cm^2 (*2*), we estimate that the cross section for absorption of 248-nm radiation from $v'' = 1$ into the Herzberg continuum is $\sim 5 \times 10^{-24}$ cm^2. This estimation ignores the additional pressure-dependent cross section (*2*), which, at 1000 torr (the pressure of the experiment of Slanger *et al.*), could contribute an extra 2.7×10^{-24} cm^2, if we assume the pressure dependence for absorption by $O_2(v'' = 1)$ at 248 nm is the same as that for O_2 ($v'' = 0$) at 242 nm. In the experiment of Slanger *et al.* (*1*), a single laser pulse of 145 mJ corresponds to $\sim 1.8 \times 10^{17}$ photons, so that at the stated 10 Hz repetition rate $\sim 9.0 \times 10^{15}$ photons cm^{-3}s^{-1} are injected into the 200 cm^3 cell. Corresponding to the cell length of 15 cm and, for the $O_2(v'' = 1)$, a partial pressure of 0.6 torr and our estimated absorption cross section of $\sim 5 \times 10^{-24}$ cm^2, the optical depth in I_0/I is $\sim 1.4 \times 10^{-6}$, so that 1.3×10^{10} photons cm^{-3}s^{-1} are absorbed by O_2 ($v'' = 1$) and produce 2.6×10^{10} O_3 molecules cm^{-3}s^{-1}. After 10 min, a typical time for equilibrium to be reached (*1*), 1.6×10^{13} O_3 molecules cm^{-3} would have been produced, compared with O_3 densities of $\sim 1 \times 10^{16}$ cm^{-3} observed by Slanger *et al.* Thus, the process described, involving the absorption of 248-nm radiation by O_2 ($v'' = 1$), seems acceptable as the seeding mechanism that initiates the autocatalytic production of O_3 referred to in the first paragraph.

The proposed initiating mechanism could be tested by measuring the temperature dependence of the rate of formation of O_3 in experiments of the type performed by Slanger *et al.*, but with the cell previously baked in vacuo to achieve outgassing. For example, the fractional Boltzmann population of O_2 ($v'' = 1$) is ~1.1% at 500 K, ~0.06% at 300 K, and ~0.001% at 195 K. Slanger *et al.* noted that warming the cell walls resulted in a marked lowering of the O_3 concentration and attribute this to desorbed water vapor, which is then attacked by O^1D (from the photolysis of O_3 at 248 nm) to form OH, which catalytically destroys O_3. This effect, which is not related to the issue of the initiating mechanism, would be eliminated by prior outgassing of the cell.

The formation of O_3 by irradiation of O_2 at 210 nm (*1*) and 214 nm (*6*) has been observed. The production of O_3 at these wavelengths increases linearly with time and is not autocatalytic in nature. These wavelengths are shorter than 242.4 nm, the

Herzberg continuum photodissociation threshold for O_2 ($v'' = 0$). The pressure dependence of the rate of production of O_3 from O_2 has been studied at 214 nm (*6*) and appears to mirror the pressure dependence of the total absorption cross section of O_2 at that wavelength (*2*). The absorption cross section of O_3 in the region from 210 to 214 nm is continuous and about 20 to 10 times smaller than at 248 nm. The photolytic products of O_3 in this 210- to 214-nm region have not been identified (*7*), but the nonautocatalytic growth rate of O_3 made by irradiation of O_2 at 210 nm and 214 nm suggests that the process of O_3 photodissociation to produce $O_2(X^3\Sigma_g^-)(v'' = 2 - 5)$ and subsequent photoabsorption to the predissociative $O_2(B^3\Sigma_u^-)$ state is inefficient at these wavelengths.

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Response: Our study (*1*) was not designed to investigate the initial seeding process for ozone production in the 248-nm dissociation of O_2. We realized that the S-shaped O_3 production curve necessarily implied autocatalysis, but we left the initiating mechanism to speculation. The process proposed by Freeman *et al.* takes place for the conditions of our experiment at an ozone production rate of 0.048 mtorr min^{-1}, equivalent to their cited rate of 2.6×10^{10} molecules $cm^{-3}s^{-1}$. As our detection limit was about 1 mtorr O_3, this implies an induction period of a few minutes. We observed no such induction time, but it is possible that the experimental procedure we used prevented its observation.

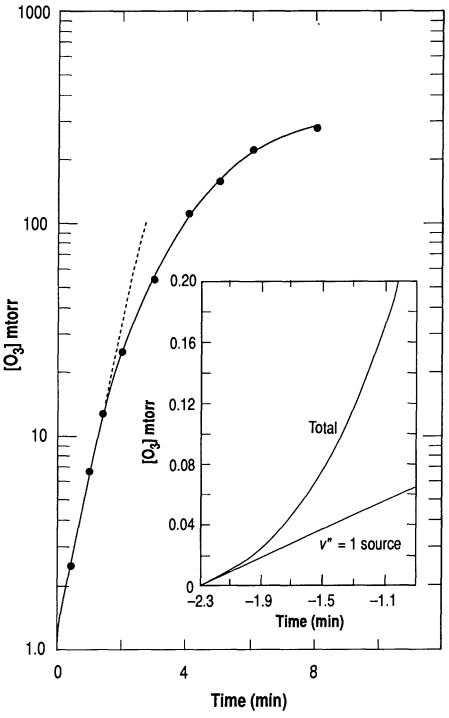

Fig. 1. Observed ozone growth curve for 1000 torr O_2 and 145 mj KrF(248 nm), 10 Hz irradiation. Inset shows calculated early time ozone growth, before "$t = 0$," with the assumption that photodissociation of $O_2(v'' = 1)$ is the initiating mechanism.

In retrospect, the experiment should have been performed by introducing pure O_2 into a baked cell, with the start time being defined by the unblocking of the 248-nm laser. Instead, since we could see that O_3 production started slowly, we assumed that O_3 would not build up in flowing O_2. Thus, the laser irradiated the flowing gas, providing a transmitted intensity through "pure" O_2. We then took the start time as the instant that the flow was stopped, with 1000 torr O_2 in the cell. In each case, we saw immediate O_3 production, commencing slowly and then accelerating.

It is possible that there was a low level of O_3 in the cell, perhaps adsorbed on the walls or made during the starting procedure. Were this the case, no induction time would be expected and O_3 production would be immediately apparent, as observed. Although the lack of an induction time precludes being more specific about the initiating mechanism, such a mechanism exists, and photodissociation of $O_2(v'' = 1)$ is a strong candidate.

If the assumption is made that the original data show no induction time because sufficient ozone is present at "$t = 0$," such that the autocatalytic process is already dominant, one should be able to calculate this amount on the basis of the expectation that early in the buildup the O_3 growth is exponential. In an example of an experimental O_3 buildup curve from our original paper (Fig. 1), the first 2 min of exponential growth are seen, with a time constant of 1.6 min^{-1}. The extrapolated ozone concentration at "$t = 0$" is 1.2 mtorr, an amount that might have been initially present in the cell. The analytical expression for the ozone growth is $d[O_3]/dt = \alpha + \beta [O_3]$, where α is the linear term, 0.048 mtorr min^{-1}, and β is the coefficient of the exponential term, 1.6 min^{-1}. Integration yields $[O_3](t) = (\alpha/\beta)\{\exp(\beta t) - 1\}$. Using this expression, one may determine that the extrapolated "$t = 0$" concentration of 1.2 mtorr occurs 2.3 min after initiation by the $O_2(v'' = 1)$ source. The inset to Fig. 1 shows the $v'' = 1$ source contribution and the calculated ozone production over the first minute, starting at a true $t = 0$. The two sources become equal 45 s after initiation, so that a growth curve that is linear in time, representing the mechanism of Freeman *et al.* (*2*), would be limited to the first 10 s of irradiation.

If the initiation process is to be studied in more detail, it will be necessary to design the experiment in a way that rigorously excludes initial ozone. However, these considerations have little to do with the thesis of our original paper (*1*), that O_3 can be autocatalytically generated by photodissociation of itself and its vibrationally excited O_2 photo product.

To the suggestion of Freeman *et al.* that the $O_2(v'' = 1)$ pumping mechanism could be investigated by changing the temperature, we note that the limiting reaction on O_3 buildup, $O + O_3 \rightarrow 2O_2$, is temperature-dependent. Therefore, changing the temperature should ultimately have an effect on the ozone level. The $O_2(v'' = 1)$ initiating mechanism has a 252-nm threshold, so that if it is the only such mechanism, the overall process should be ineffective at longer wavelengths.

The fact that ozone production proceeds autocatalytically once the ozone density exceeds ~0.01 mtorr is particularly interesting with respect to KrF laser operation in air. Surface concentrations of ozone in clean air (*2*) typically correspond to partial pressures in the range 0.02 to 0.04 mtorr and are often considerably higher in urban air. Thus, no initiation is required, and in an enclosed space ozone concentrations may build up to high levels. For long path lengths, it is possible that the ozone thus generated would interfere with laser transmission; the optical depth at 248 nm is 3 for 10 mtorr ozone with a 10-m path length. For lasers with a high repetition rate, it is conceivable that even in an unconfined space the ozone buildup could be substantial, as the $O + O_2$ recombination time at 1 atm is only 15 μs and diffusion is relatively slow. On the other hand, we note

that our work has been recently duplicated by Guthrie *et al.* (*3*), who find that ozone production in air is much less efficient than in 1000 torr O_2.

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Fetal Brain Grafts and Parkinson's Disease

I have reservations about the enthusiastic tone of the report by Lindvall *et al.* (*1*) and the accompanying Research News article (2 Feb., p. 529) on the effects of fetal brain tissue transplantation in a single human patient. Lindvall *et al.* imply that the changes seen were caused by survival of the transplanted cells and the resultant reinnervation of the host brain. The Research News article implies that the effects were qualitatively different from the effects that have so far been seen with adrenal medulla grafts. Compelling alternative possibilities were not discussed. First, the role of patient expectations may not be trivial. The patient could not possibly have been naïve with respect to the expectations associated with the procedure. In addition to the obvious pitfalls of a study based on a single human subject, the interest and attention accorded this procedure may have contributed to the clinical changes.

The magnitude of the clinical changes seen is impressive, although not necessarily more impressive than the changes seen after adrenal medulla transplantation in some studies. For example, in the study of Goetz *et al.* (*2*), in which 18 patients received adrenal medulla grafts by means of the Madrazo *et al.* (*3*) procedure, an average decrease in "off" time from 52% of the waking day before surgery to 22% 3 months after transplantation was seen. This is almost identical to the change seen by Lindvall *et al.* (*1*).

Also, increased fluorodopa uptake seen on a positron emission tomography scan is not entirely equivalent to cell survival. Improvement in the patient for other reasons, including recovery of dopaminergic terminals around the graft site, might result in such a change. There is some evidence, in fact, that recovery of endogenous dopaminergic terminals can contribute to the effects of brain grafts under certain circumstances (*4*).

Lindvall *et al.* conclude that the time course of the patient's improvement was "consistent with the slow development of a growing graft" (*1*, p. 576), but the time course was not entirely consistent with what would be expected for growth of human fetal tissue grafts in situ. In previous experiments by Brundin, Lindvall, and their colleagues in rats (*5*), effects of human fetal tissue grafts implanted in essentially the same way did not appear until after at least 3 months, and generally not until 4 to 5 months after transplantation. In their *Science* report (*1*), substantial improvement was seen as soon as 2 months and was maximal by 3 months. Thus the improvement was almost twice as rapid as in animal studies. In the previous clinical trials of adrenal medulla grafting by Goetz *et al.* (*2*), improvement was minimal after 1 month, while near-maximal improvement was seen by 3 months. This exactly matches the time course of improvement seen by Lindvall *et al.* (*1*).

Lindvall *et al.* also conclude that the effects were not due to tissue damage, in part because no improvement was seen in earlier studies where a larger cannula was used. In their most recent experiment, however, the procedure was improved so that more tissue could be implanted. "Virtually all" of the tissue from the ventral mesencephalon of four fetuses was used. Tissue implantation per se produces damage to the host brain; thus the possibility that the present trial produced greater tissue damage than previous trials cannot be ruled out.

An unfortunate consequence of excessive publicity about brain tissue transplantation has been the application of tissue transplantation as though it were a therapeutic procedure. In some cases, tissue transplantation has even been used for diseases other than Parkinson's disease, including schizophrenia, Huntington's chorea, and progressive supranuclear palsy. Tissue transplantation remains an experimental technique and should be applied to humans only in the course of carefully planned therapeutic trials.

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Lindvall *et al.* (*1*) are to be congratulated for their demonstration that transplantation of fetal tissue may be therapeutic in patients with neurodegenerative and neurotraumatic disorders. Positron emission tomography (PET) with 6-[F18]fluoro-L-dopa (6FD) revealed a 130% increase in the operated putamen's influx constant. The interpretation of Lindvall *et al.* is that this represented reinnervation of the putamen by surviving functional graft. However, another explanation is also consistent with their observations, namely, that the surgical procedure induced sprouting of fibers from endogenous, residual, surviving dopaminergic neurons. That dopaminergic fibers from which sprouting could occur are present pre-operatively is evident from the PET scan presented in figure 3 of their report.

We have conducted a series of experiments grafting different tissues into the basal ganglia of primates with hemiparkinsonian symptoms induced by methyl(phenyl)tetrahydropyridine. We have witnessed the capability of PET with 6FD to detect surviving, viable fetal mesencephalic allografts (*2*). However, we have seen similar alterations of 6FD-derived radioactivity in the area of graft placement that histologically proved to be secondary to neurite sprouting from host dopaminergic neurons (*3, 4*). The changes in the authors' stereotactic technique, which they hypothesize as contributing to a greater survival of the implanted fetal cells (dopaminergic or nondopaminergic) (*4*) could also have resulted in greater stimulus for neurite-promoting factor release or could have created a more favorable balance between neurotrophic and neurotoxic influences. Conceivably, both mechanisms could simultaneously be operating.

PET with 6FD provides an in vivo tool for assessing biochemical changes resulting from grafting procedures. Through histologic correlation, the exact interpretation of changes in measured 6FD-derived activity can be obtained. Although Lindvall *et al.* measured a 130% increase in the operated putamen's influx constant, from the data presented it is not clear to what extent this finding was influenced by the 6FD dose difference between the pre- and postoperative studies. Without information about ra-