Singlet delta oxygen production by plasmas

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MOTIVATION

Aim: SDO production at atmospheric pressure for biomedical applications

Why Singlet Delta Oxygen $O_2(a^1\Delta_g)$?

SDO is well known to:

- play a major role in several biological systems and processes
- generate **oxidative damage** to a variety of biological components

[N.I. Krinsky, *Singlet Oxygen*, Academic Press, New York, 1979]

[L. Packer and H. Sies, *Methods in Enzymology, Singlet Oxygen, UV A and Ozone*, Academic Press, New York, 2000]

However, SDO is rather **difficult** to produce and to detect!

development of a plasma source for the controlled production of high fluxes of SDO at atmospheric pressure

including

accurate quantification of SDO fluxes reaching biological targets

INTRODUCTION

- **$O_2(a^1\Delta_g)$:**

  ✓ a very **stable** excited (0.98 eV) molecular state → **easy** to transport
  (long radiative lifetime ~74 min (in gas phase) and low quenching probability)
  [A.A. Frimer, *Singlet Oxygen*, CRC Press, Boca Raton, 1985]

  ✓ detection is rather **challenging** ($A=2.2\ 10^{-4}\ s^{-1}$) [S.M. Newnan et al., J. Chem. Phys. **110** (1999) 10749]

  ✓ efficient production by electric discharge is **difficult** → low E/N required
  (E/N_{opt} = 10 Td vs E/N_{ss} = 100 Td (in pure O_2))

INTRODUCTION

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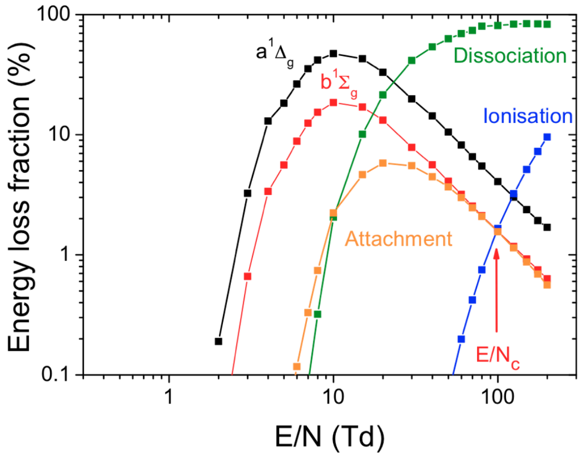
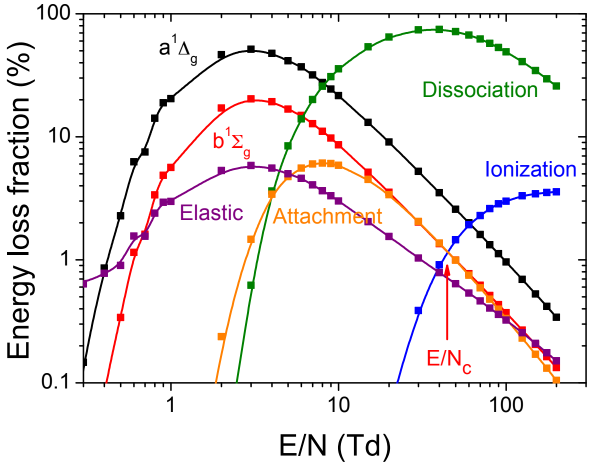
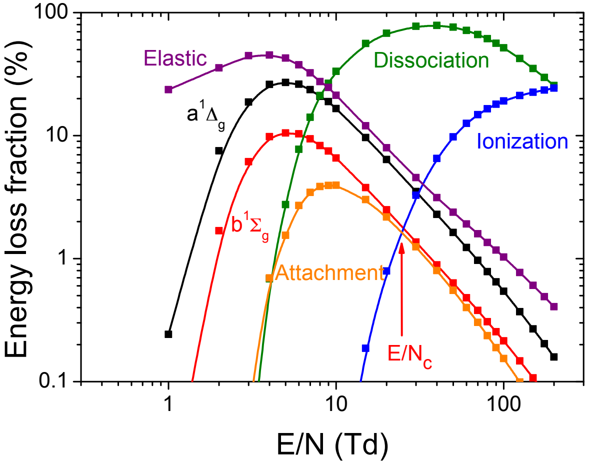
O_2 pure



Ar/O_2 – 10% O_2



He/O_2 – 10% O_2



FTOUL [P. Segur and M.C. Bordage in *Proceedings XIX ICPIG* 1989 Belgrade]

$1\ Td = 10^{-17}\ V.cm^2$

INTRODUCTION

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✓ efficient production by electric discharge is **difficult** → low E/N required
(E/N_{opt} = 10 Td vs E/N_{ss} = 100 Td (in pure O_2))

✓ high yield requires **high specific deposited energy** (~ 4-5 eV/O_2)
[M.J. Kushner, *J. Phys. D: Appl. Phys.* **38** (2005) 1633]

Potential applications:

- **Lasers**: pumping of the oxygen-iodine laser [A.P. Napartovich, *J. Phys. D: Appl. Phys.* **34** (2001) 1827]
- **Biological applications**

INTRODUCTION

How do we generate SDO at amospheric pressure by electric discharges?

- electric discharge operating at low reduced electric field

Efficient SDO production requires to separate:

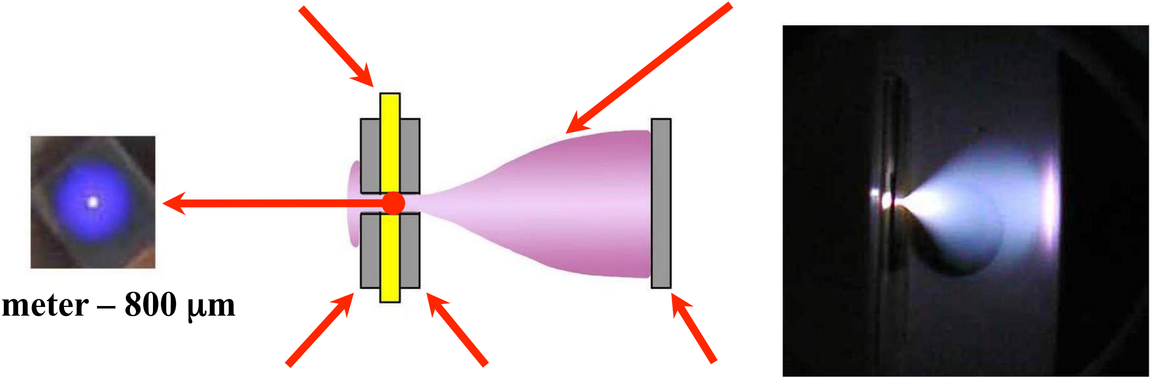
  - **plasma production**: high E/N
  - **SDO excitation**: low E/N

- stable electric discharge at high pressure and high power loading

Solutions to answer these two big issues:

- non-self-sustained discharges [A.E. Hill in Proceedings LASERS 2000]
- **DC microdischarges: MHCD+MCSD** [G. Bauville et al., Appl. Phys. Lett. **90** (2007) 031501]

MICRODISCHARGES



Ionization Zone
Sandwich – 700 µm
Micro-Hollow Cathode Discharge
(MHCD)

Excitation Zone
MCSD plasma – 5 to 10 mm
Micro-Cathode Sustained Discharge
(MCSD)

Diameter – 800 µm

C
Cathode

A1
Anode

A2
Anode

[R.H. Stark and K.H. Schoenbach, *J. Appl. Phys.* **85** (1999) 2075]

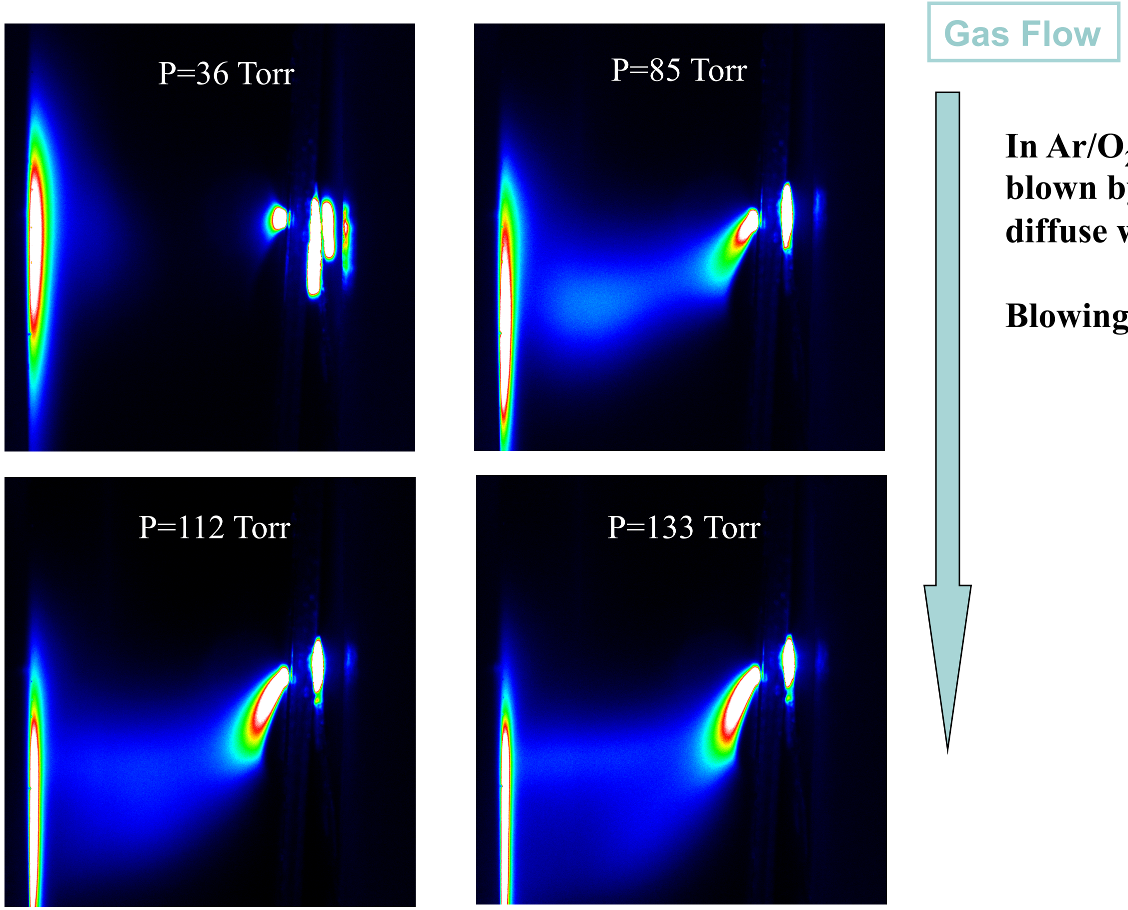
- ➢ MCSD is similar to a **positive column**:
  - ✓ **low E/N** and **Tgas**
  - ✓ **stable** at **high pressure** and **high power loading**

- ➢ MCSD have been proven **efficient for $O_2(a^1\Delta_g)$ generation**:

2007 (G. Bauville et al, Appl. Phys Lett **90**, 031501)	**10^{15} cm^{-3} in Ar/O_2 @ 100 mbar**
2008 (J. S. Sousa et al, Appl. Phys Lett **93**, 011502)	**10^{16} cm^{-3} in He/O_2/NO @ 1000 mbar**
2010 (J. S. Sousa et al, Appl. Phys Lett **97**, 141502)	**10^{17} cm^{-3} in MCSD arrays**

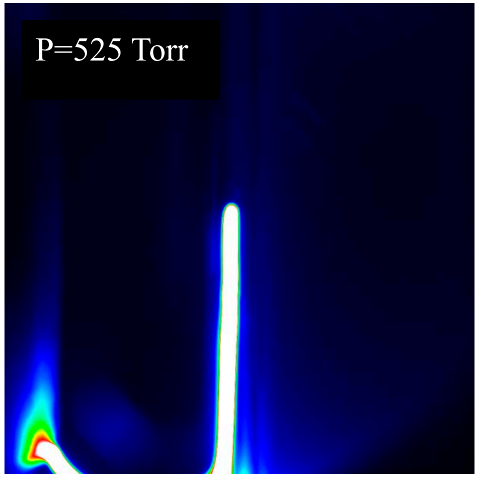
PLASMA DEVELOPMENT in Ar/O_2 MIXTURES

O_2=5 torr, I=0.5 mA, Q(Ar)=430 sccm



In Ar/O_2 mixtures, MCSDs are blown by the gas flow but remain diffuse with a large radial expansion

Blowing occurs for Q>100 sccm

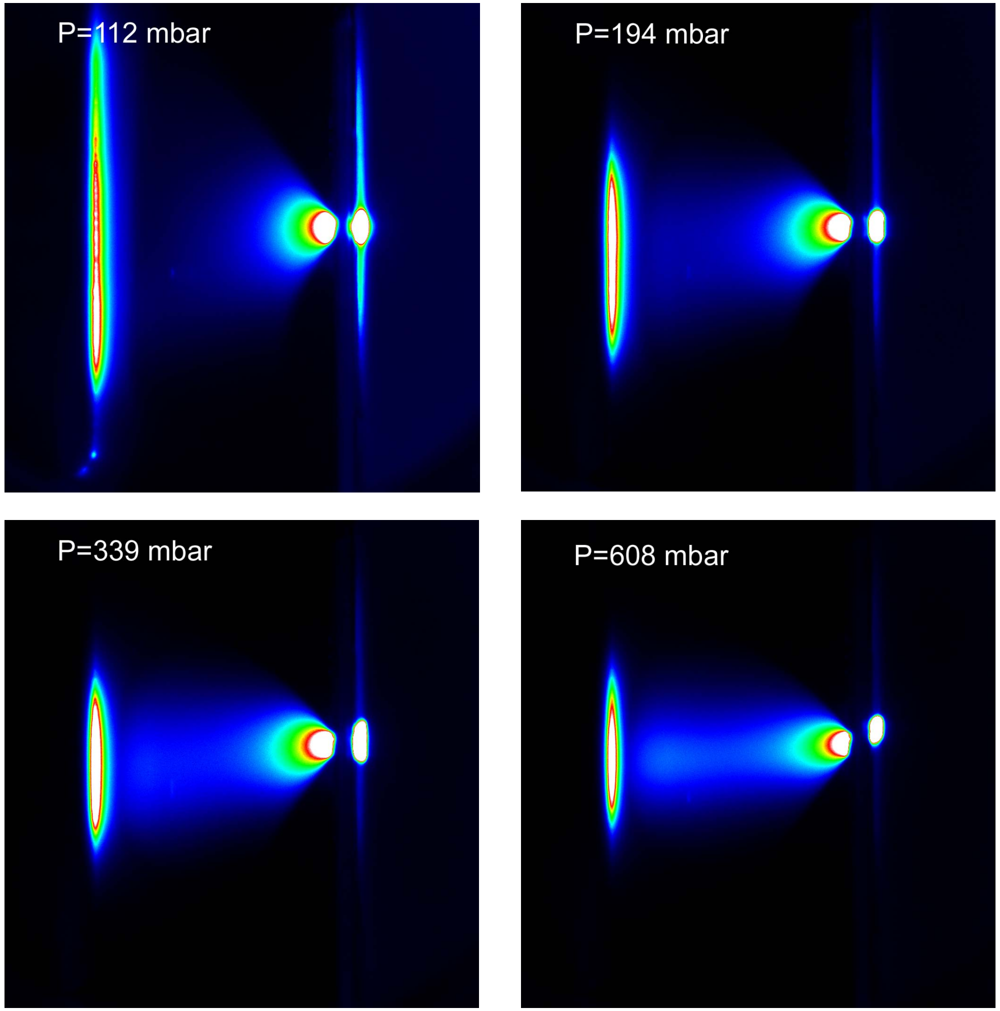


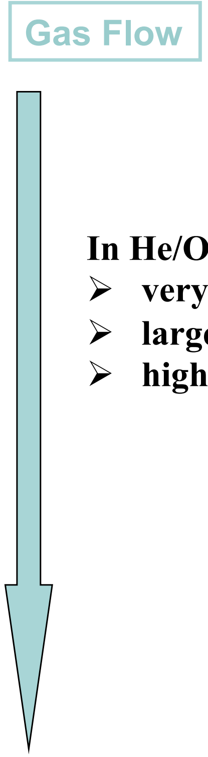
dramatic at higher pressures

[J. S. Sousa et al, *IEEE Trans. Plasma Sci.* **39** (2011) 2680]

PLASMA DEVELOPMENT in He/O_2 MIXTURES

O_2=7 mbar, I=0.5 mA, Q(He)=430 sccm





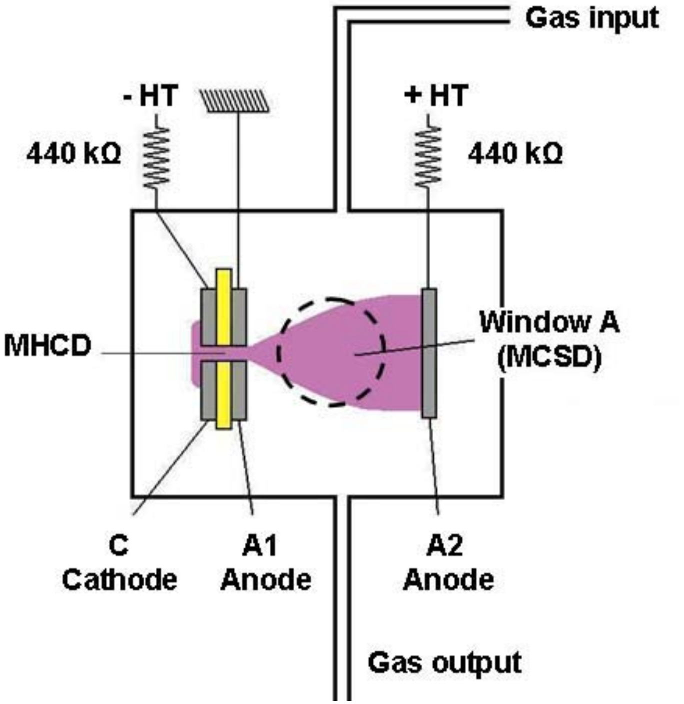
In He/O_2 mixtures, MCSDs are

- **very diffuse**
- **large radial expansion**
- **highly on axis symmetric**

[J. S. Sousa et al, *IEEE Trans. Plasma Sci.* **39** (2011) 2680]

MCSD CHARACTERISATION

➢ **MCSD characterisation by different optical diagnostic techniques:**



❑ **$O_2(b^1\Sigma^+_g)$: OES @ 760 nm**

✓ Tgas : 300 – 500 K

❑ **O_3 : OAS @ 254 nm**

✓ $10^{13} – 10^{16}$ cm^{-3}

❑ **n_e : Stark broadening** (in collaboration with Nader Sadeghi (LSP))

✓ 10^{13} cm^{-3} in pure Rg
✓ non measurable in Rg/O_2

❑ **O-atoms : TALIF** (in collaboration with Lionel Magne (LPGP))

✓ confined to the discharge chamber

❑ **$O_2(a^1\Delta_g)$: OES @ 1.27 µm**

✓ dominated by Rg emission

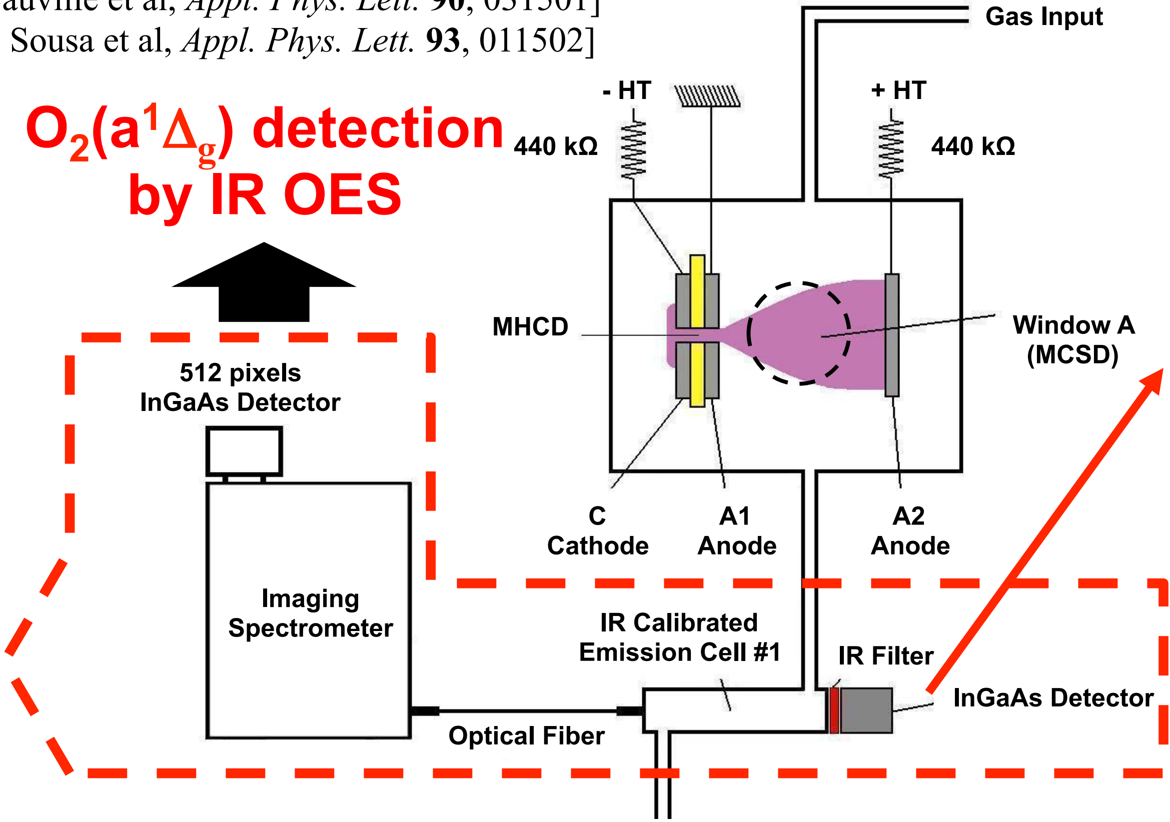
BUT

long lifetime ➡ afterglow measurements

AFTERGLOW

[G. Bauville et al, *Appl. Phys. Lett.* **90**, 031501]
[J. S. Sousa et al, *Appl. Phys. Lett.* **93**, 011502]

$O_2(a^1\Delta_g)$ detection by IR OES

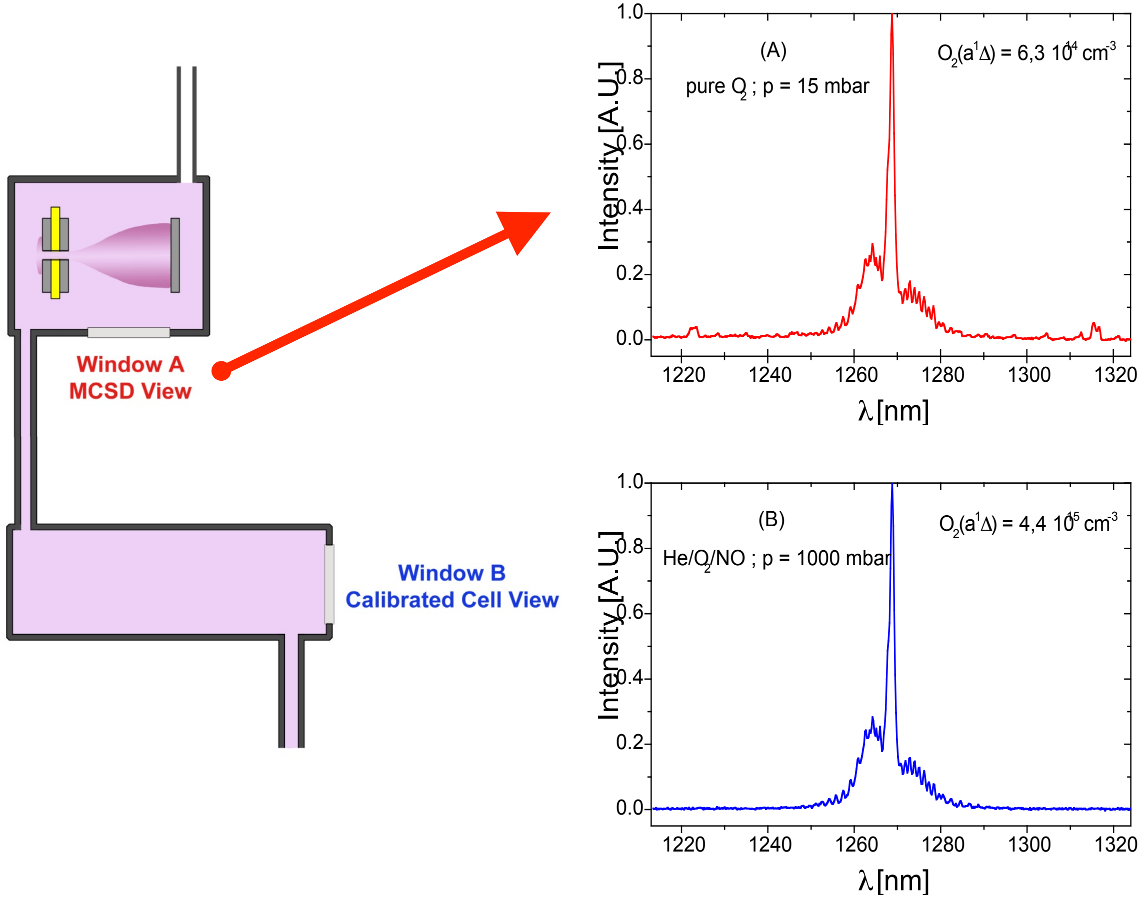


IR Filter + InGaAs + OpAmp
calibration: QTH lamp

 # photons reaching the detector
vs
total emission of the cell:
calculated by MC code including all geometrical factors

$O_2(a^1\Delta_g)$ – IR OES

- **Measurement of the radiative emission of $O_2(a^1\Delta_g)$ at 1.27 µm**



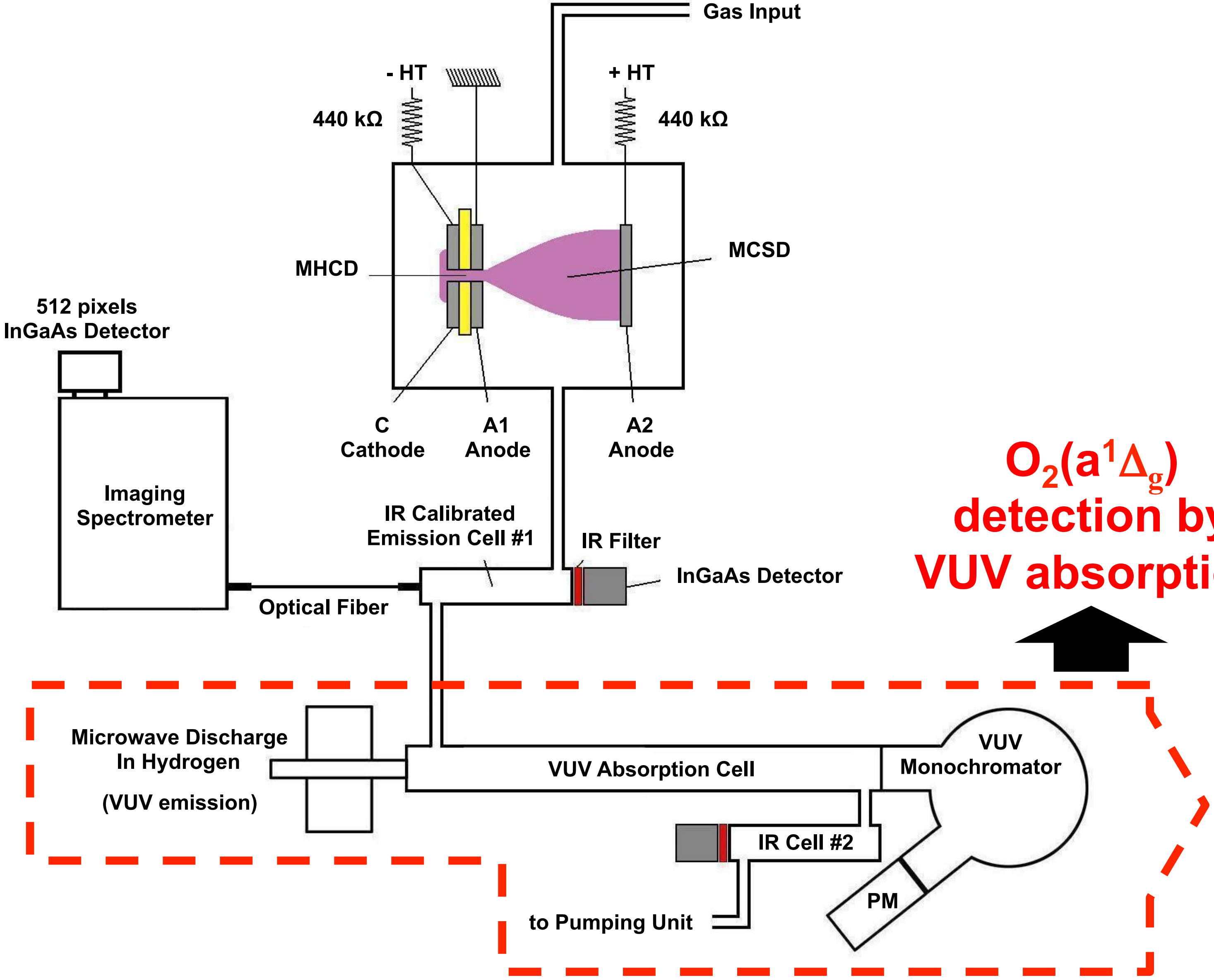
- **Same normalized spectra**
  - ✓ in the MCSD operating in pure O_2 at low pressure
  - ✓ in the afterglow (~25cm) in He/ O_2/NO at atmospheric pressure

no spurious signals due to NO*, NOx*

only $O_2(a^1\Delta_g)$ radiative emission

but what about the induced collision emission: (A=2.2 10^{-4} s^{-1} ↗ A=10^2 s^{-1} in solvents)

AFTERGLOW



$O_2(a^1\Delta_g)$ detection by VUV absorption

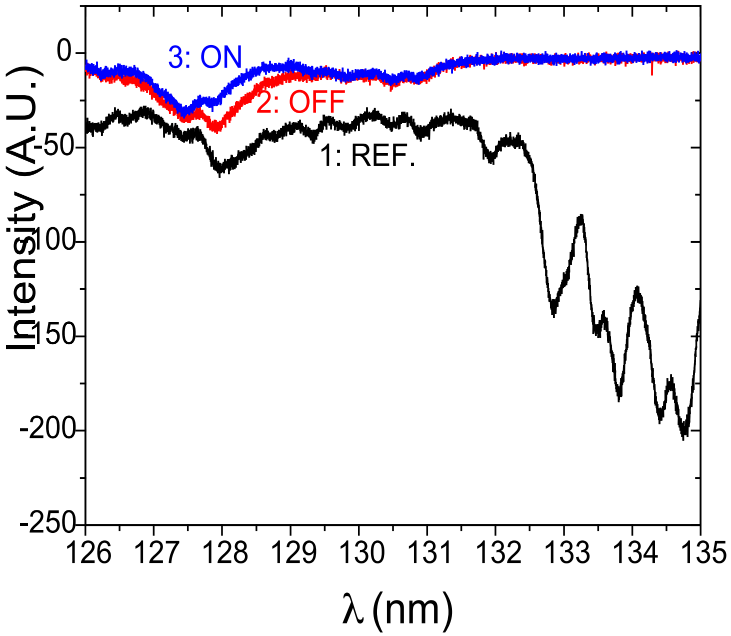
$O_2(a^1\Delta_g)$ – VUV OAS

- **Measurement of the $O_2(a^1\Delta_g)$ number density**
  - ✓ **VUV diagnostic to exclude any possibility of induced-emission collision**
  - ✓ $O_2(a^1\Delta_g)$ largely contribute to the light absorption between 125 and 130 nm

At 128.5 nm

$\sigma_a[O_2(a^1\Delta_g)] = 1.67\ 10^{-17}$ cm^2 **40 times greater than** $\sigma_X[O_2(X^3\Sigma_g)] = 4\ 10^{-19}$ cm^2

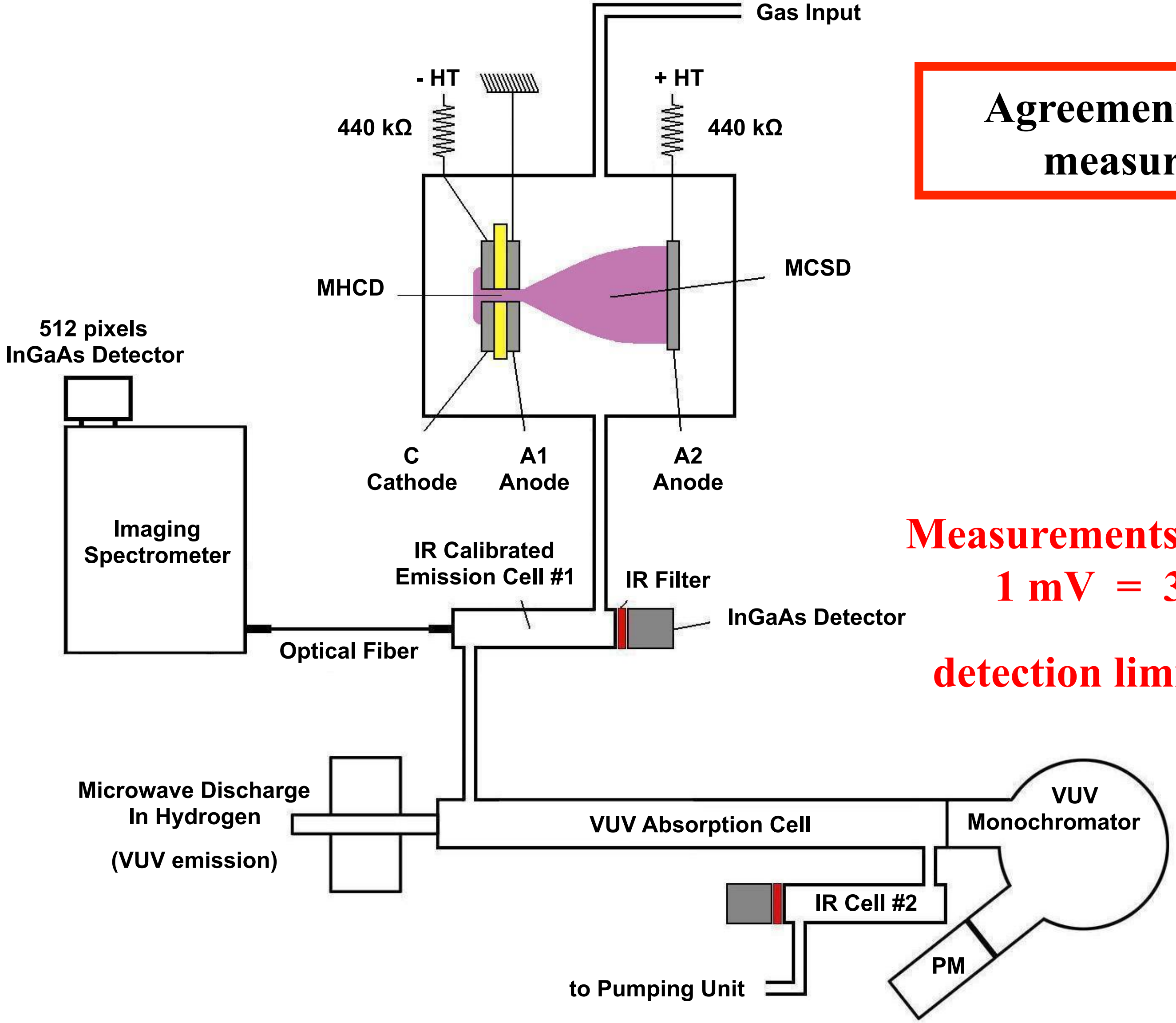
[S. Ogawa, Can. J. Phys. **59** (1975) 1845]



$O_2(a^1\Delta_g)$ number density deduced by the relation:

$\ln(I_0/I) = [O_2(a^1\Delta_g)]\ .\ \sigma_a\ .\ L + [O_2(X^3\Sigma_g)]\ .\ \sigma_X\ .\ L$

$O_2(a^1\Delta_g)$ MEASUREMENTS



Agreement between IR and VUV measurements within 15%

⇩

Measurements in the flowing afterglow:
1 mV = 3.8 10^{15} $O_2(a^1\Delta_g)$ cm^{-3}

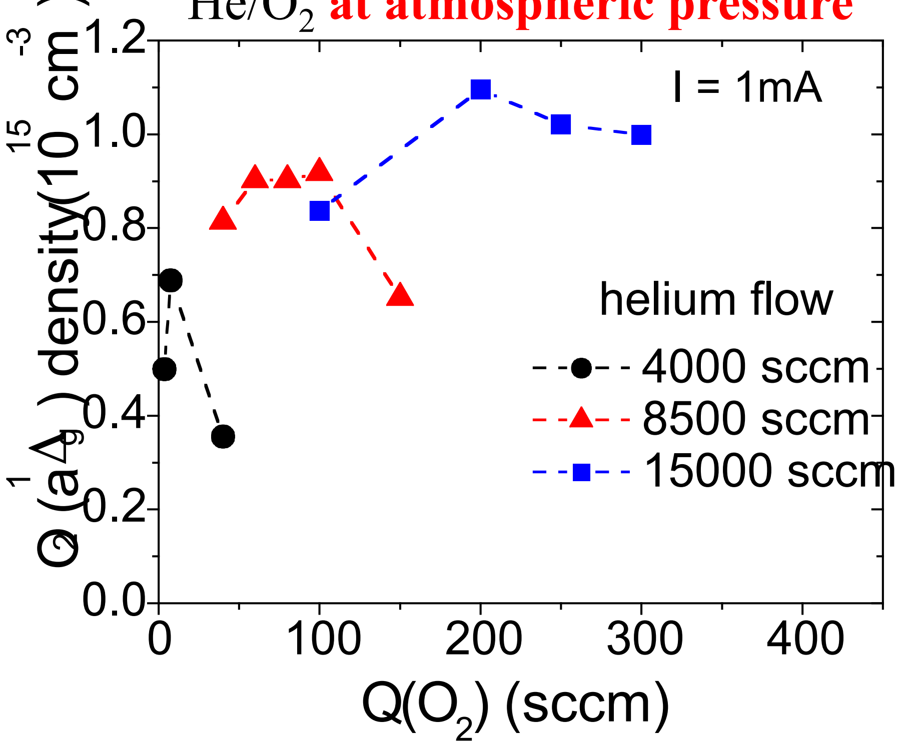
detection limit: 10 µV→ 3.8 10^{13} cm^{-3}

$O_2(a^1\Delta_g)$ PRODUCTION

INFLUENCE OF FLOW

[J. S. Sousa et al, *J. Phys. D: Appl. Phys.* **46** (2013) 464005]

He/O_2 **at atmospheric pressure**



In He/O_2 mixtures **at atmospheric pressure**:

- **$O_2(a^1\Delta_g)$ quenching by O-atoms and O_3** for long residence time
- **main destruction channels:**

$O_2(a^1\Delta_g) + O + He \rightarrow O_2(X^3\Sigma_g) + O + He$

$O_2(a^1\Delta_g) + O_3 \rightarrow O + O_2(X^3\Sigma_g) + O_2(X^3\Sigma_g)$

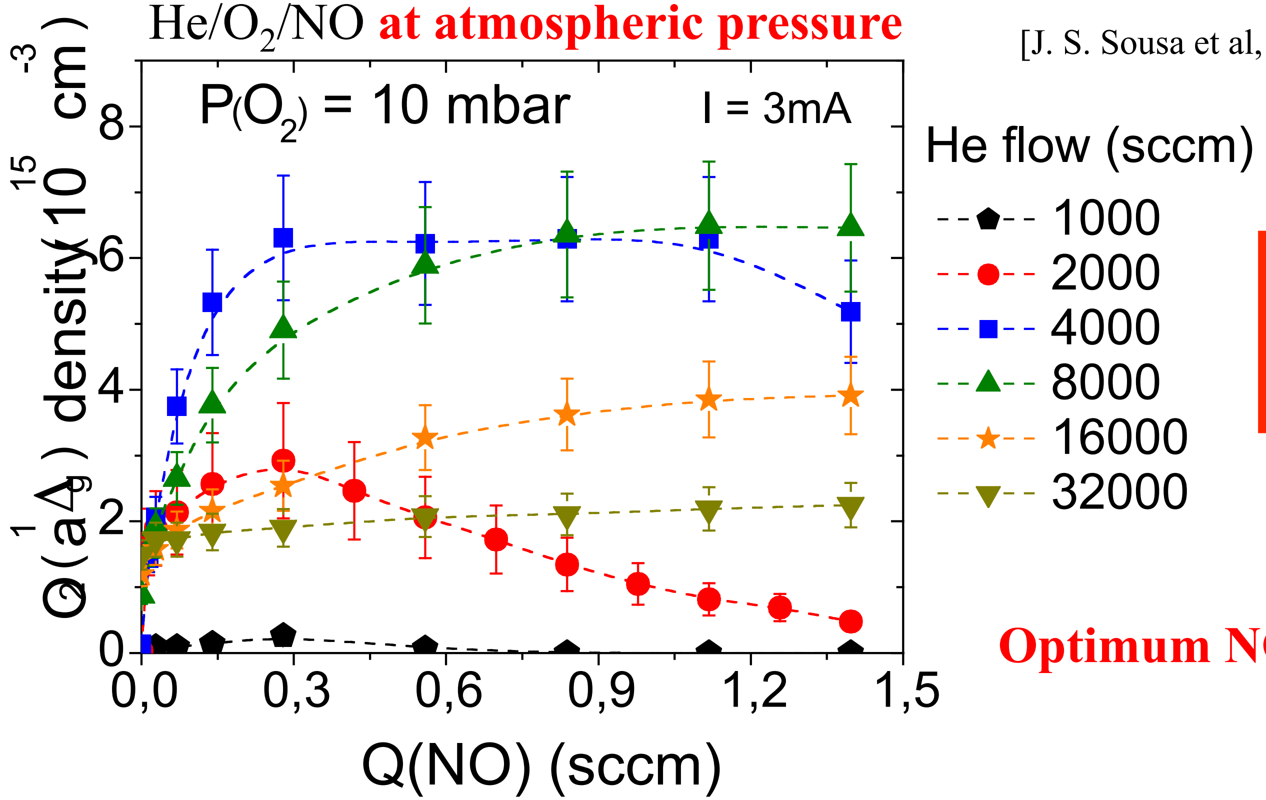
- **$O_2(a^1\Delta_g)$ density ~10^{15} cm^{-3}**, whenever:
  - ✓ helium flow > 10000 sccm (very high gas flow)
  - ✓ O_2 concentration ~2%

In order to obtain greater $O_2(a^1\Delta_g)$ densities:

- **addition of O-atom and O_3 scavengers: NO**

INFLUENCE OF NO

He/O_2/NO **at atmospheric pressure**



[J. S. Sousa et al, *J. Phys. D: Appl. Phys.* **46** (2013) 464005]

However, NO and NO_2 molecules also have a quenching effect on $O_2(a^1\Delta_g)$

Optimum NO concentration depends on:

- gas flow
- O_2 partial pressure
- **energy deposited per O_2 molecule (P/Q)**

Influence of **adding NO** molecules at low concentration:

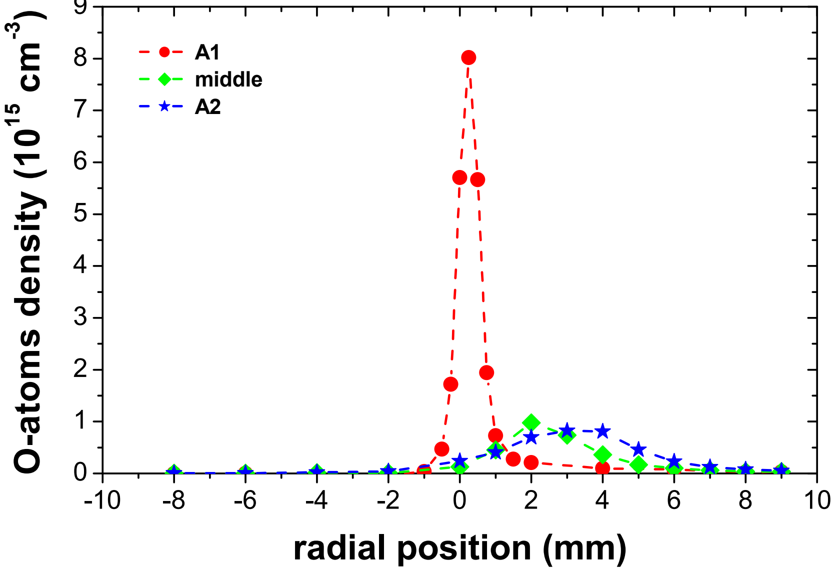
- **decrease of the O-atom density**

$$O + NO + He \rightarrow NO_2 + He$$

- **large increase of $O_2(a^1\Delta_g)$ density** (x6)
- **$O_2(a^1\Delta_g)$ densities higher than 10^{15} cm^{-3}**

INFLUENCE OF NO: O-ATOMS*

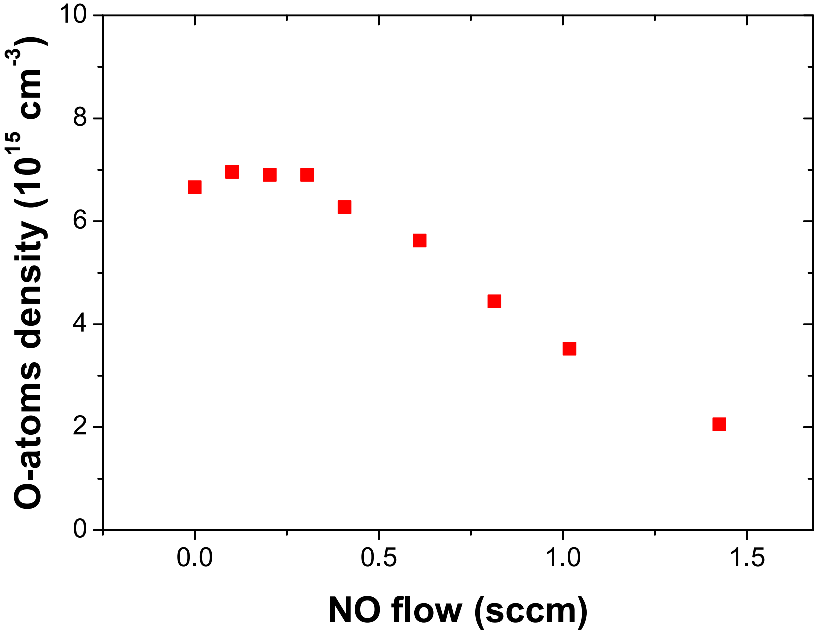
[J. S. Sousa et al, *J. Phys. D: Appl. Phys.* **46** (2013) 464005]


He/O_2 mixtures

- O-atoms confined to the discharge volume

- adding NO molecules at low concentration
  - **decrease of the O-atom density**

$O + NO + He \rightarrow NO_2 + He$

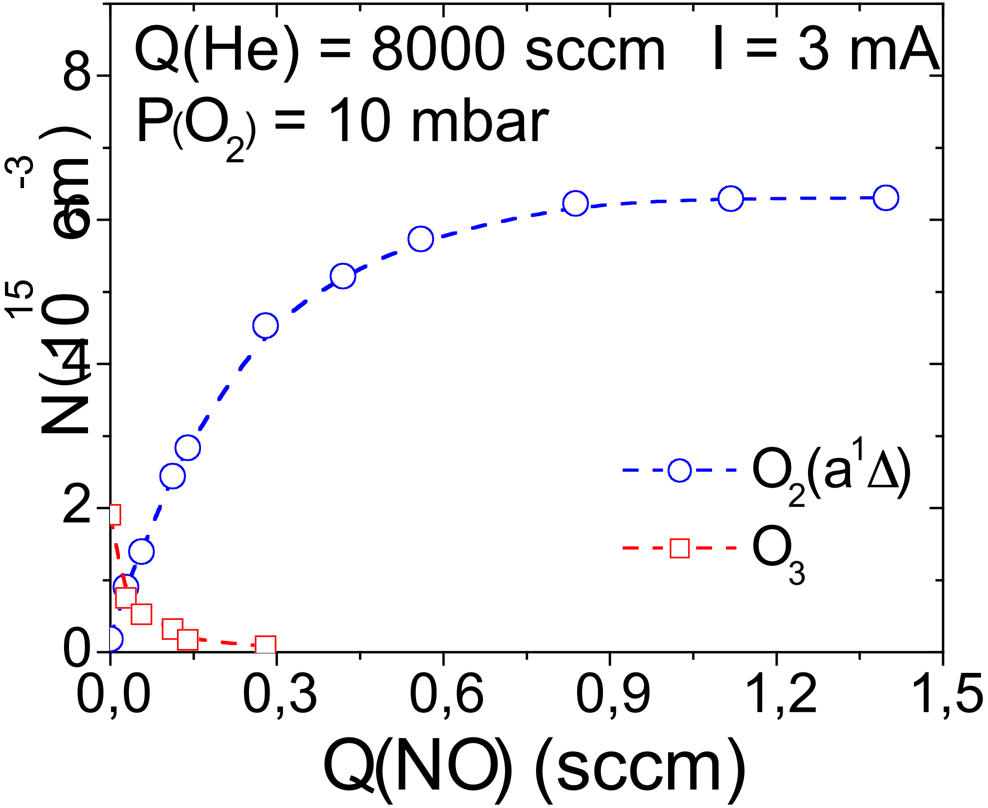

He/O_2/NO mixtures
close to MHCD

* in collaboration with Lionel Magne and Pascal Jeanney (LPGP)

INFLUENCE OF NO: O_3

- **Measurement of the O_3 number density by UV absorption**
  - ✓ O_3 largely contribute to the light absorption at 254 nm : $\sigma[O_3] = 1.15\ 10^{-17}\ cm^2$

He/O_2/NO **at atmospheric pressure**



Influence of adding
small concentrations of NO:

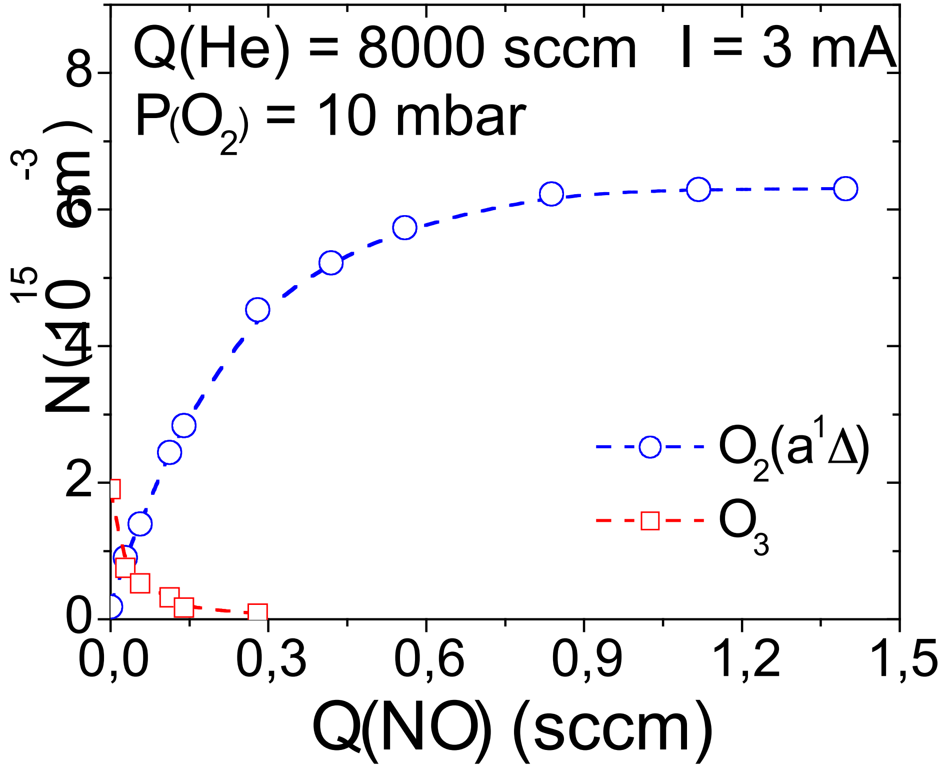
- **large increase of $O_2(a^1\Delta)$ density** (up to 50 times more)
- **huge reduction of O_3 density** (up to its complete destruction)

[J. S. Sousa et al, *J. Phys. D: Appl. Phys.* **46** (2013) 464005]

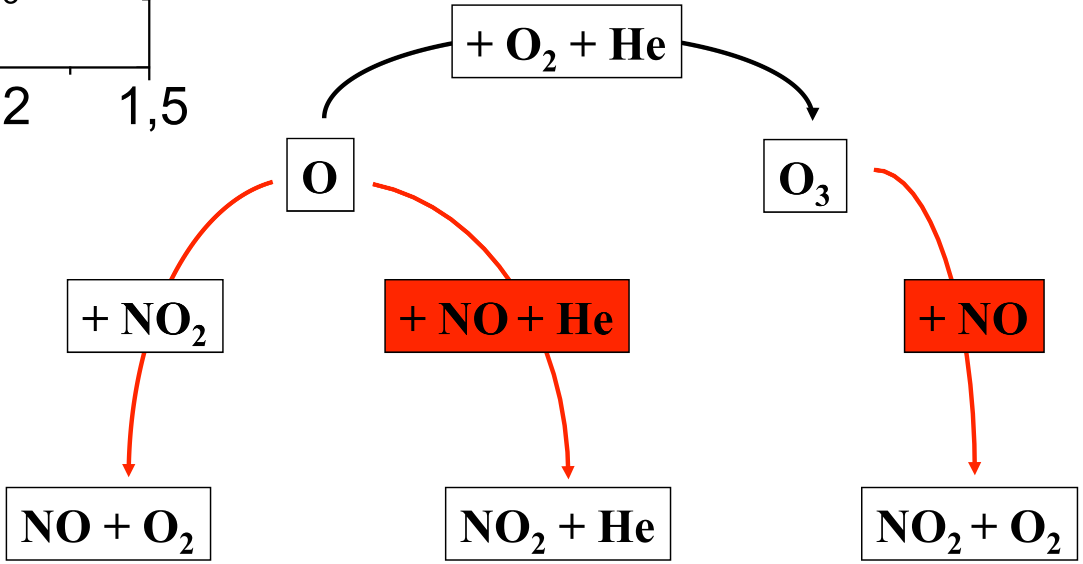
INFLUENCE OF NO: O_3

He/O_2/NO **at atmospheric pressure**

[J.S. Sousa et al., *Eur. Phys. J.: Appl. Phys.* *47* (2009) 22807]



- **$O_2(a^1\Delta)$ is quenched by O in the discharge and by O_3 in and after the discharge**
- the effect of **NO** is to **quench O and O_3** and hence to **reduce losses of $O_2(a^1\Delta)$**



+ O_2 + He

O **O_3**

+ NO_2 **+ NO + He** **+ NO**

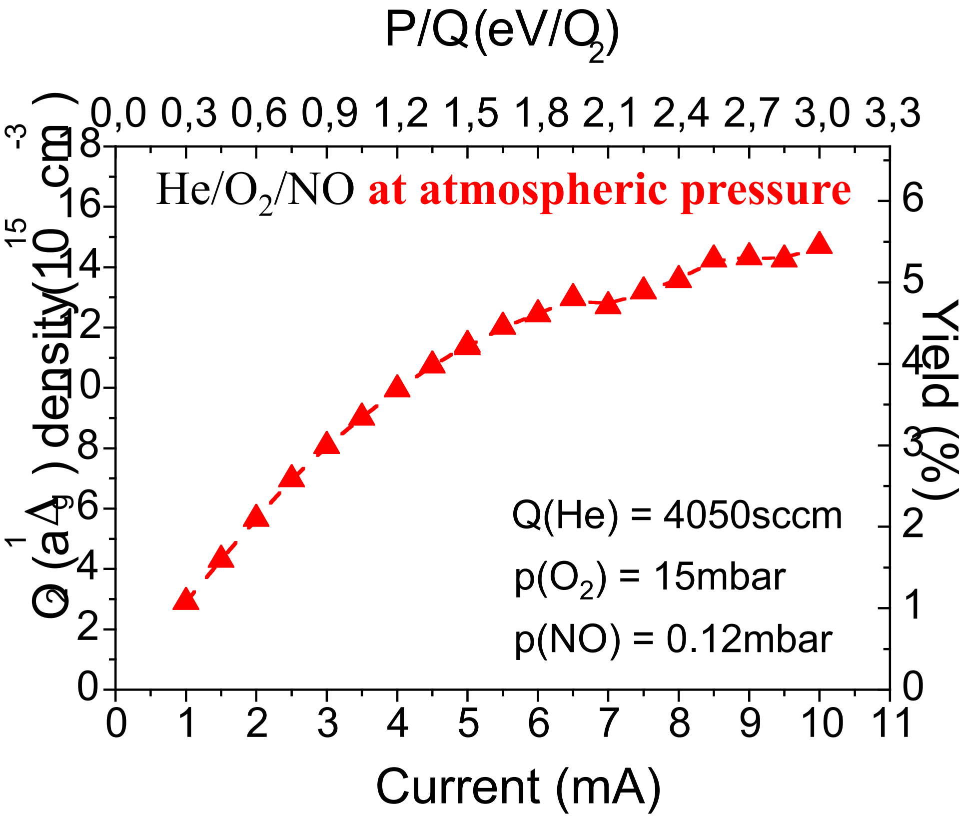
NO + O_2 **NO_2 + He** **NO_2 + O_2**

- NO is not lost in the process, but rather it is recycled in collisions:

$$NO_2 + O \rightarrow NO + O_2$$

INFLUENCE OF CURRENT

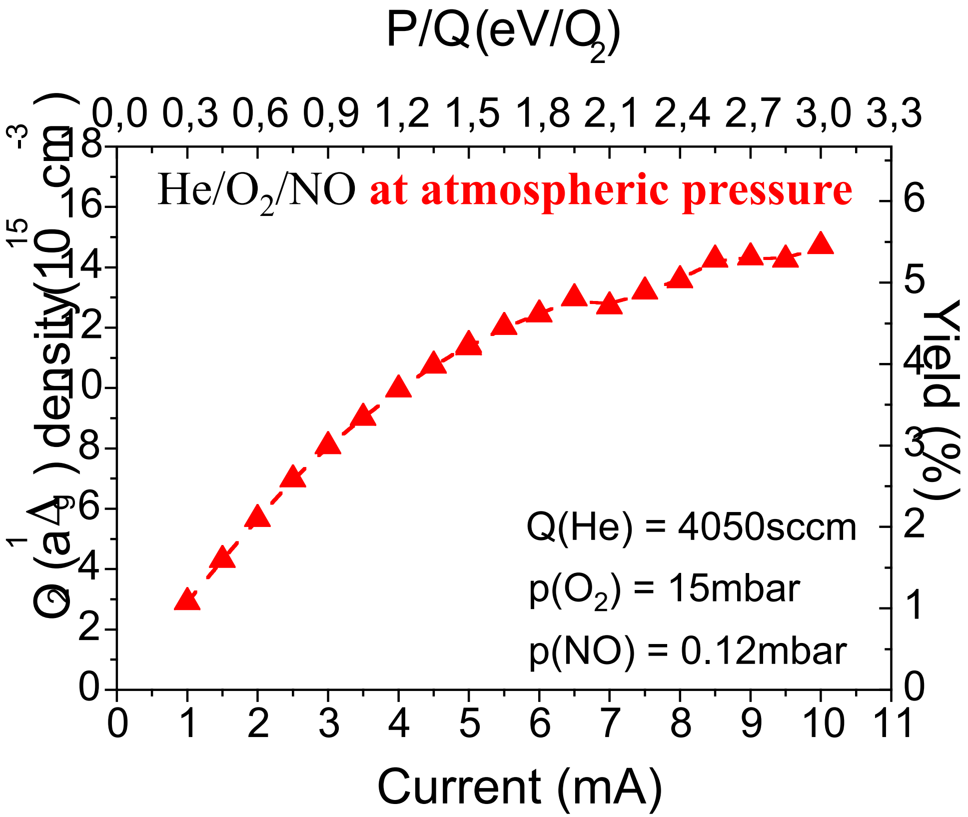
[J. S. Sousa et al, *J. Phys. D: Appl. Phys.* **46** (2013) 464005]



- ➢ $O_2(a^1\Delta_g)$ density increase is nearly linear up to 3 mA
- ➢ $O_2(a^1\Delta_g)$ density begins to saturate at higher currents

INFLUENCE OF CURRENT

[J. S. Sousa et al, *J. Phys. D: Appl. Phys.* **46** (2013) 464005]



$O_2(a^1\Delta_g)$ densities higher than 10^{16} cm^{-3} at atmospheric pressure

for producing **$O_2(a^1\Delta_g)$ densities greater than 10^{16} cm^{-3}**, **higher currents seem to be needed, but P/Q is near its optimum value**

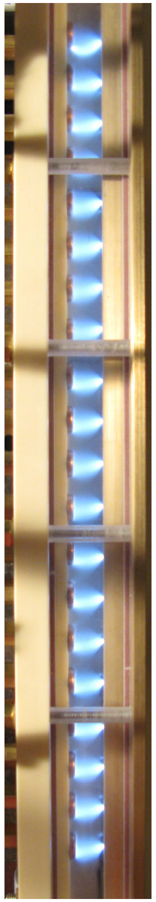
high current →

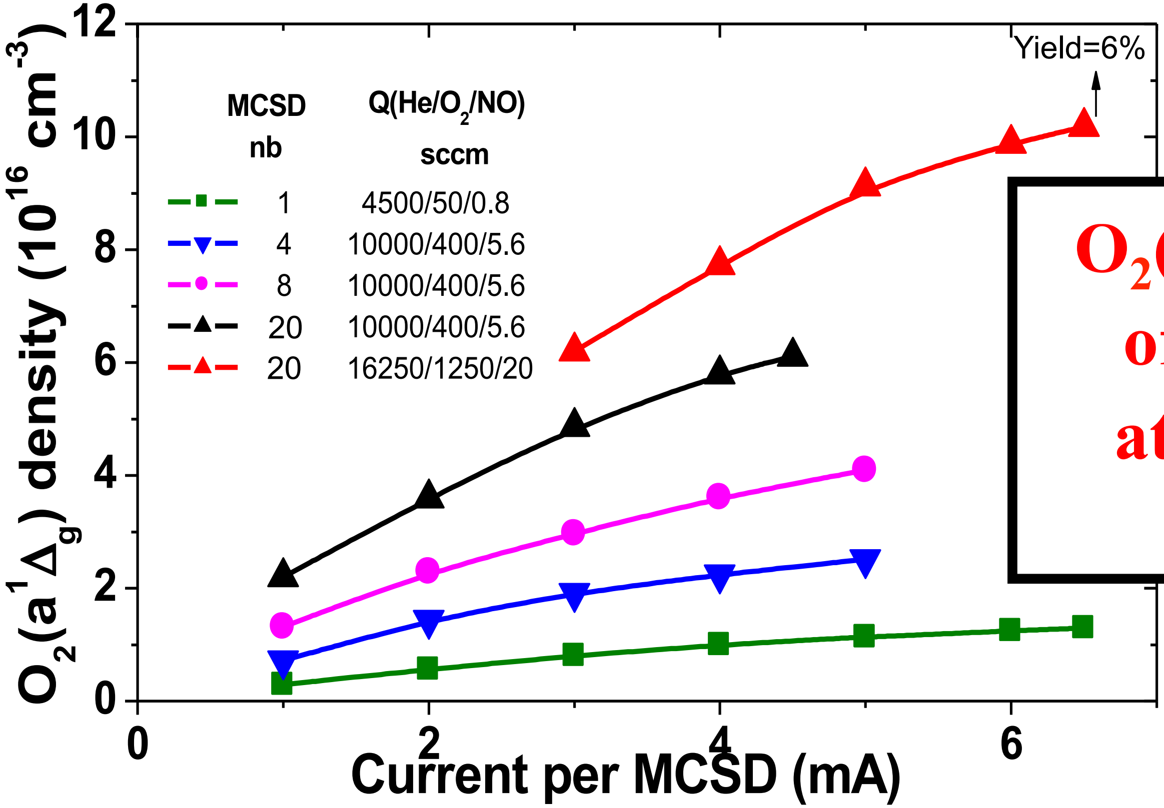
shorter MHCD lifetime

less MCSD liability

$O_2(a^1\Delta_g)$ generation can be improved by using arrays of several MCDS's

MCSD's IN SERIES





He/O_2/NO at atmospheric pressure

$O_2(a^1\Delta_g)$ densities of ~1 10^{17} cm^{-3} at atmospheric pressure

For the same gas composition,
$O_2(a^1\Delta_g)$ density increase is linear up to:

- **2-3 mA/MCSD**
- **6-8 MCSD's in series**

$O_2(a^1\Delta_g)$ fluxes greater than 100 mmole/h can reach bio targets

[J.S. Sousa et al., *Plasma Sources Sci. Technol.* **22** (2013) 035012]

MCSD's IN SERIES

[J.S. Sousa et al., *Plasma Sources Sci. Technol.* **22** (2013) 035012]

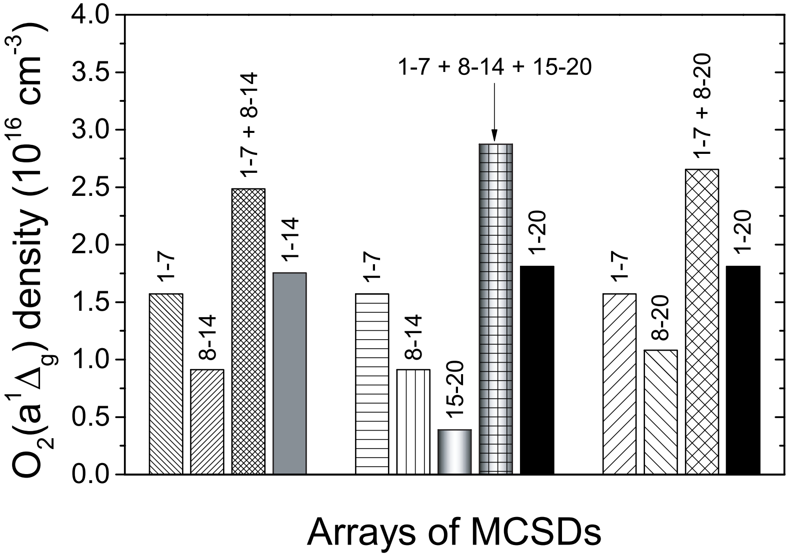
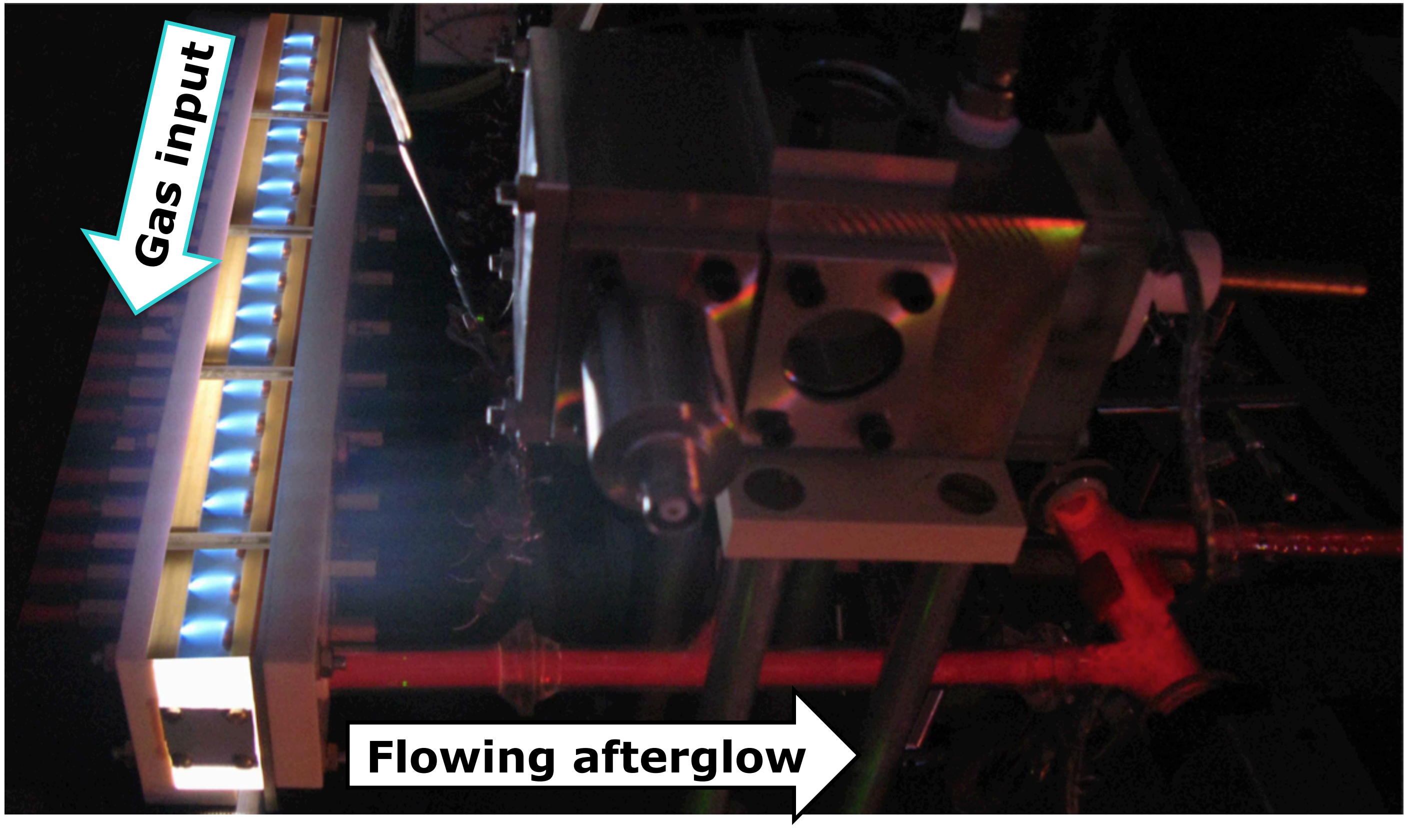


Figure 10. $O_2(a\,^1\Delta_g)$ density measured in the effluent, at 30 cm downstream of the last MCSD, while operating six different arrays of MCSDs (1–7, 8–14, 15–20, 8–20, 1–14, 1–20) at 3.5 mA per MCSD in He/O_2/NO mixtures, at a total gas flow of 4.6 slm and O_2 and NO partial pressures equal to 11 and 0.17 mbar, respectively. The theoretical sum of the $O_2(a\,^1\Delta_g)$ densities obtained with several arrays of MCSDs is also shown in columns 3, 8 and 12. Note that the number of active discharges increases with increasing distance to the detection cell, i.e. MCSD #1 and #20 are located at 30 and 53.75 cm upstream of the detection cell, respectively.

SDO dimol

[J.S. Sousa et al., *Plasma Sources Sci. Technol.* **22** (2013) 035012]



SDO dimol

[J.S. Sousa et al., *Plasma Sources Sci. Technol.* **22** (2013) 035012]

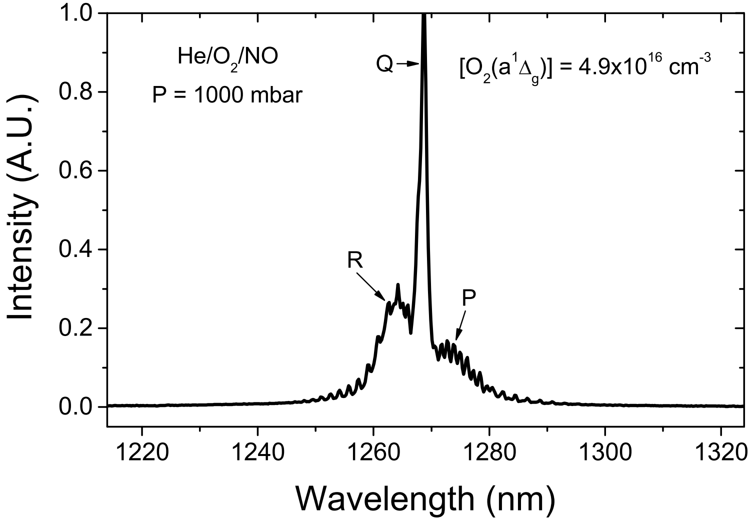


Figure 4. Infrared spectra measured in the flowing effluent (30 cm downstream of the last MCSD) while operating 20 MCSDs in a He/O_2/NO mixture at atmospheric pressure; spectral resolution of 0.7 nm.

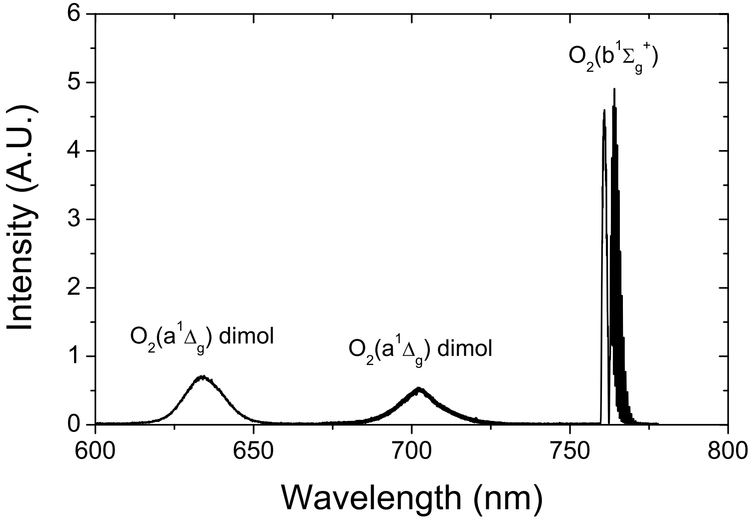


Figure 5. $O_2(a\,^1\Delta_g)$ dimol emission around 634 and 703 nm and $O_2(b\,^1\Sigma_g^+)$ emission around 762 nm in the flowing effluent (30 cm downstream of the last MCSD), while operating 20 MCSDs (3 mA per MCSD) in a He/O_2/NO mixture at atmospheric pressure (10 slm of He, 3.8% of O_2 and 358 ppm of NO); spectral resolution of 0.13 nm.

SDO dimol

[J.S. Sousa et al., *Plasma Sources Sci. Technol.* **22** (2013) 035012]

$$O_2(a\,^1\Delta_g)(V=0)+O_2(a\,^1\Delta_g)(V=0)\rightarrow O_2(X\,^3\Sigma_g^-)\\ \times(V=0)+O_2(X\,^3\Sigma_g^-)(V=0)+h\upsilon\ (634\,\mathrm{nm})$$

$$O_2(a\,^1\Delta_g)(V=0)+O_2(a\,^1\Delta_g)(V=0)\rightarrow O_2(X\,^3\Sigma_g^-)\\ \times(V=1)+O_2(X\,^3\Sigma_g^-)(V=0)+h\upsilon\ (703\,\mathrm{nm}).$$

$$O_2(a\,^1\Delta_g)+O_2(a\,^1\Delta_g)\rightarrow O_2(X\,^3\Sigma_g^-)+O_2(b\,^1\Sigma_g^+)\\ \rightarrow O_2(X\,^3\Sigma_g^-)+O_2(X\,^3\Sigma_g^-)+h\upsilon\ (762\,\mathrm{nm}).$$

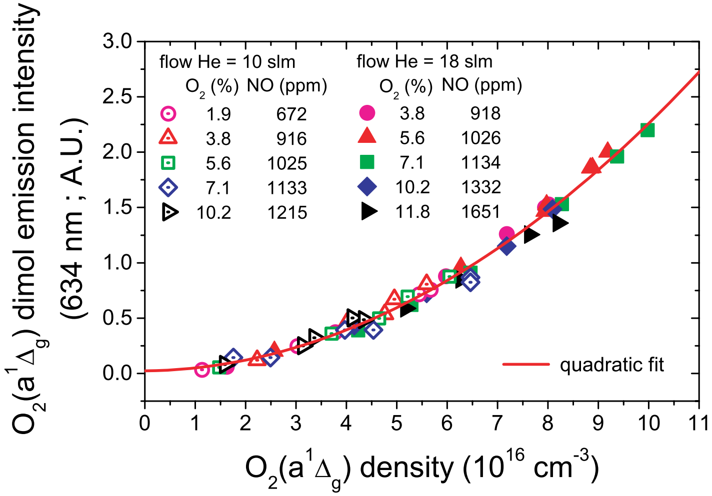


Figure 13. Evolution of the intensity of the $O_2(a\,^1\Delta_g)$ dimol emission (in arbitrary units) versus the $O_2(a\,^1\Delta_g)$ densities obtained in the effluent at 30 cm downstream of the last MCSD for several experimental conditions.

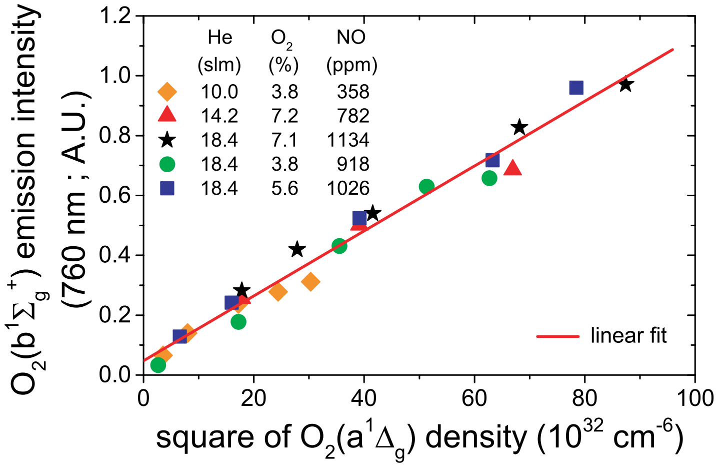
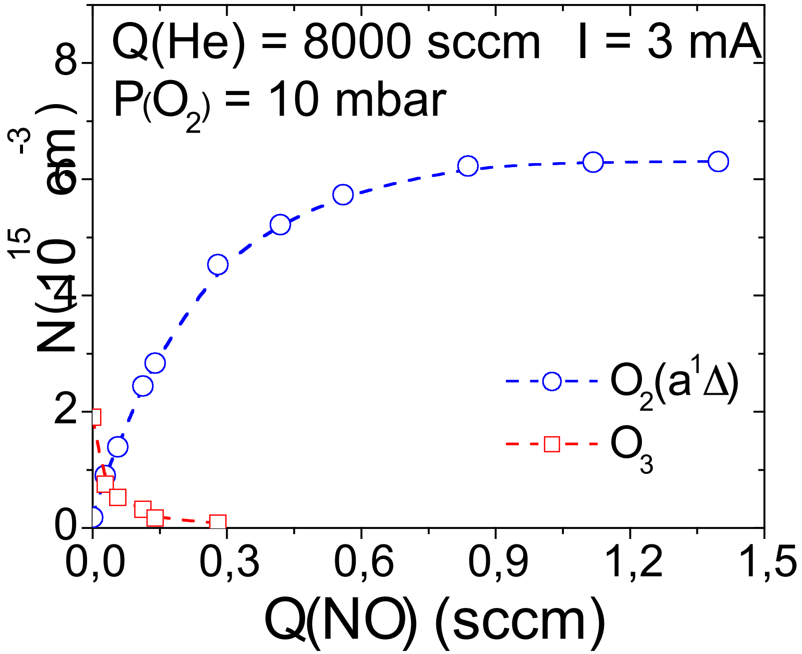
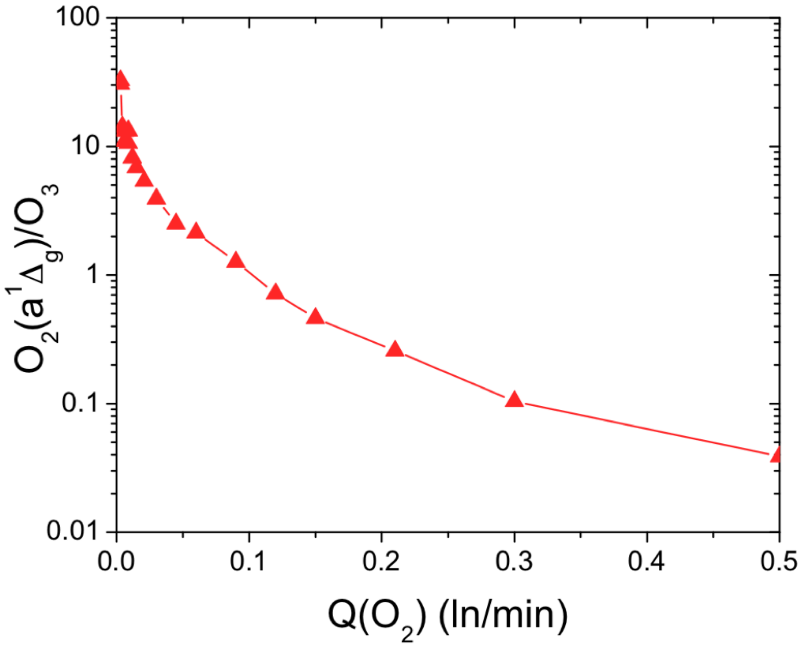


Figure 14. Evolution of the intensity of the $O_2(b\,^1\Sigma_g^+)$ emission (in arbitrary units) versus the square of the $O_2(a\,^1\Delta_g)$ densities obtained in the effluent at 30 cm downstream of the last MCSD for several experimental conditions.

BIO APPLICATIONS

[J.S. Sousa et al., *Plasma Sources Sci. Technol.* **22** (2013) 035012]

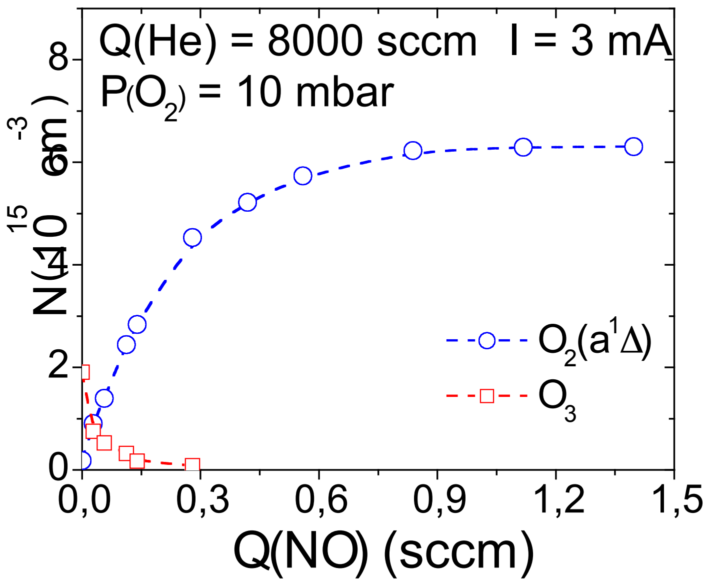


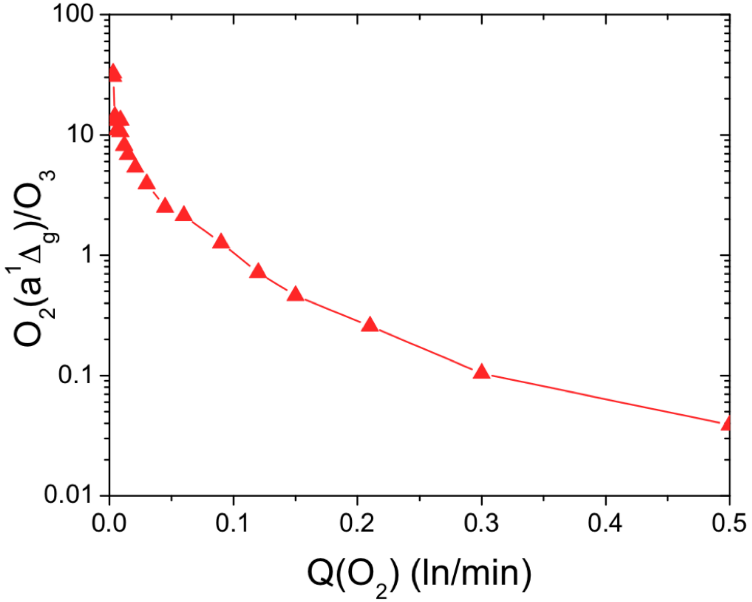


- the density ratio of **$O_2(a^1\Delta_g)$ to O_3** can be easily and **finely tuned through the discharge current, and the O_2 and NO concentration**

- the **maximum** and **minimum** values of the density ratio of **$O_2(a^1\Delta_g)$ to O_3** are obtained using the **detection limits** and are, thus, **underestimated**

BIO APPLICATIONS





Condition A

He/O_2/NO

8000/80/1.4 sccm

I = 3 mA/MCSD

$O_2(a^1\Delta_g) \sim 1.5\ 10^{16}\ \mathrm{cm}^{-3}$

$O_3 < 1.2\ 10^{12}\ \mathrm{cm}^{-3}$

Condition Z

He/O_2/NO

8000/300/0 sccm

I = 2 mA/MCSD

$O_2(a^1\Delta_g) < 1.0\ 10^{13}\ \mathrm{cm}^{-3}$

$O_3 \sim 7.0\ 10^{15}\ \mathrm{cm}^{-3}$

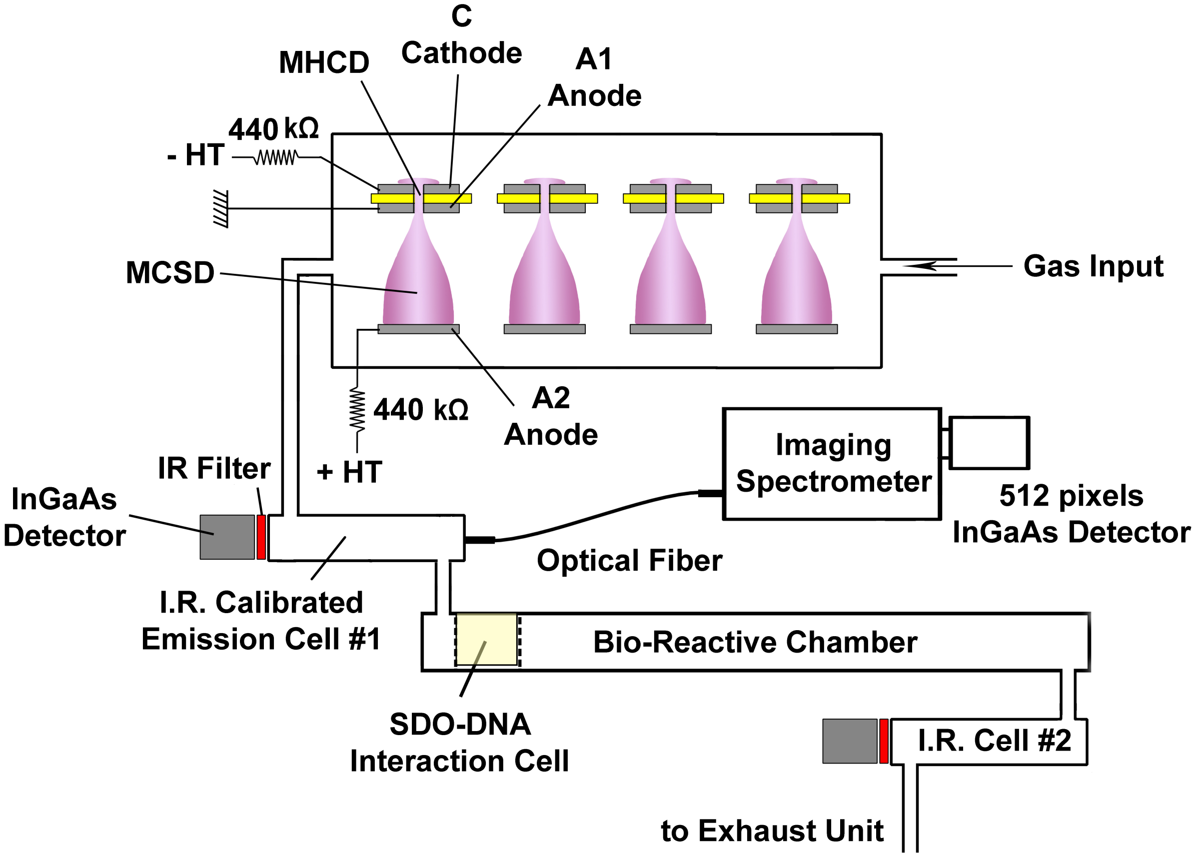
$$\frac{O_2(a^1\Delta_g) - A}{O_2(a^1\Delta_g) - Z} \quad > 10^3$$

$$\frac{O_3 - A}{O_3 - Z} \quad < 10^{-3}$$

- **MCSD's** appear to be very **suitable and useful tools for examining the biological components targeted by these different ROS**

DNA OXIDATION

- **DNA** (in solution) **oxidation by $O_2(a^1\Delta_g)$ and O_3** at ~25cm downstream



2-4 mL 1mM aqueous solution

No O-atoms!

Low NO_x concentration

(< 150 ppm)

PBS buffer

(10 mM KH_2PO_4, pH = 6.8)

Post-treatment analysis:

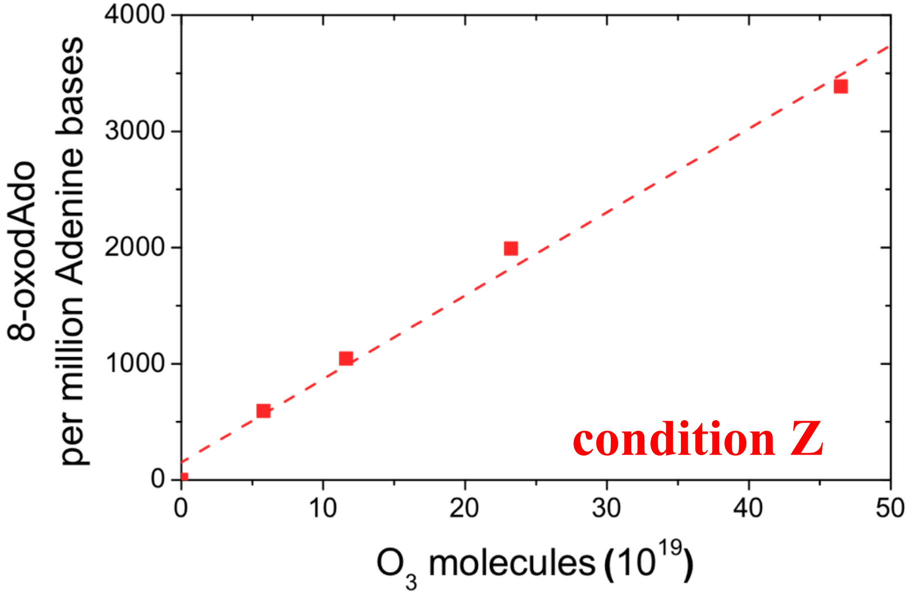
- **Electrophoresis** (in collaboration with P.M. Girard & E. Sage – Curie)
- **HPLC-tandem MS** (in collaboration with J.L. Ravanat – CEA)

DNA OXIDATION

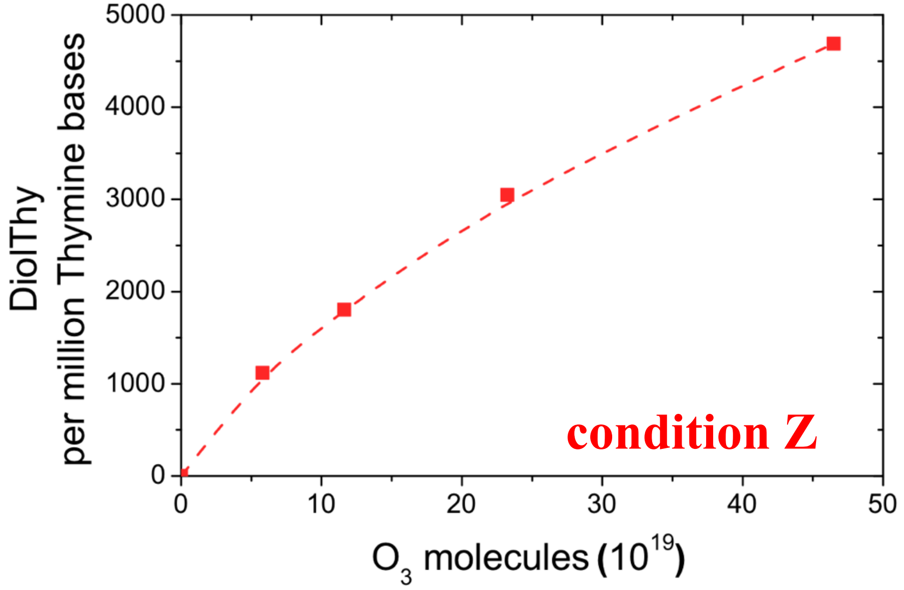
[J. S. Sousa et al, **DOI 10.1007/978-94-007-2852-3_9** (Ch9, pp107– 119), Springer Science+Business Media B.V. (2012)]

- **DNA oxidation by O_3 was achieved!**

Adenine



Thymine

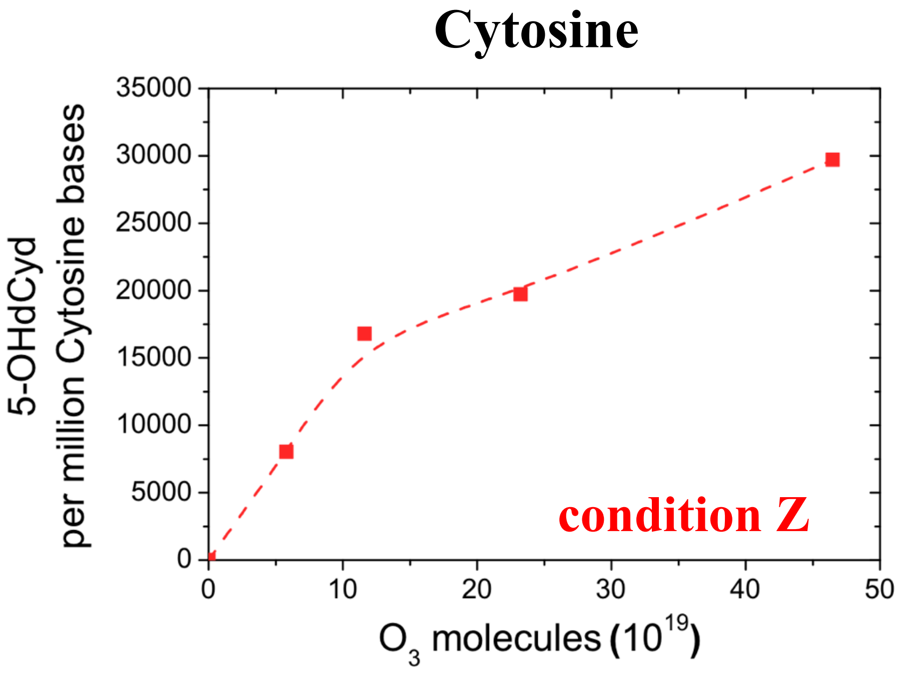


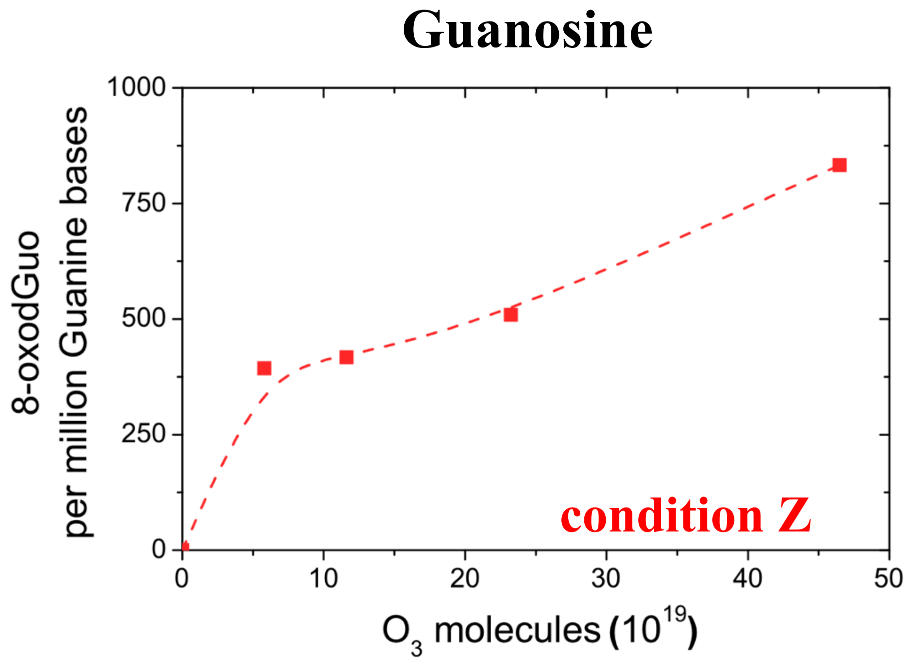
- **oxidized nucleosides** production **increases** almost **linearly** with the **O_3 flow**

DNA OXIDATION

[J. S. Sousa et al, **DOI 10.1007/978-94-007-2852-3_9** (Ch9, pp107– 119), Springer Science+Business Media B.V. (2012)]

- **Actually, O_3 overoxidized DNA!**





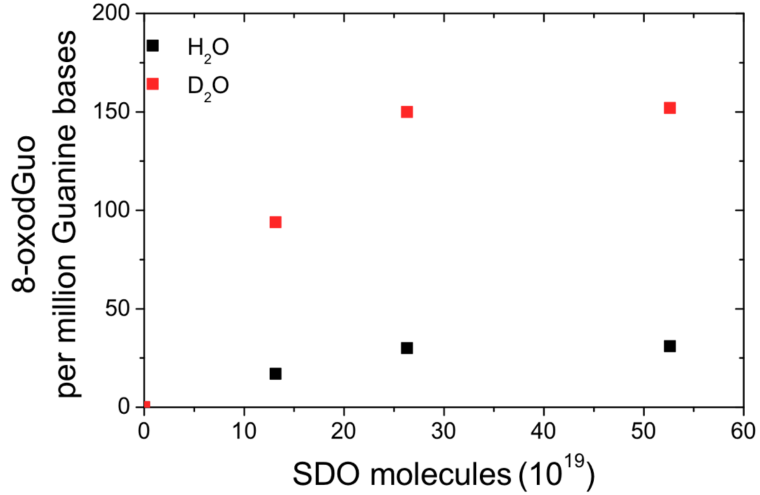
- **5-OHdCyd and 8-oxodGuo are easily oxidized** [T. Douki et al., *Radiat. Res.* **153** (2000) 29]

- **O_3 is very effective on oxidizing Cytosine**

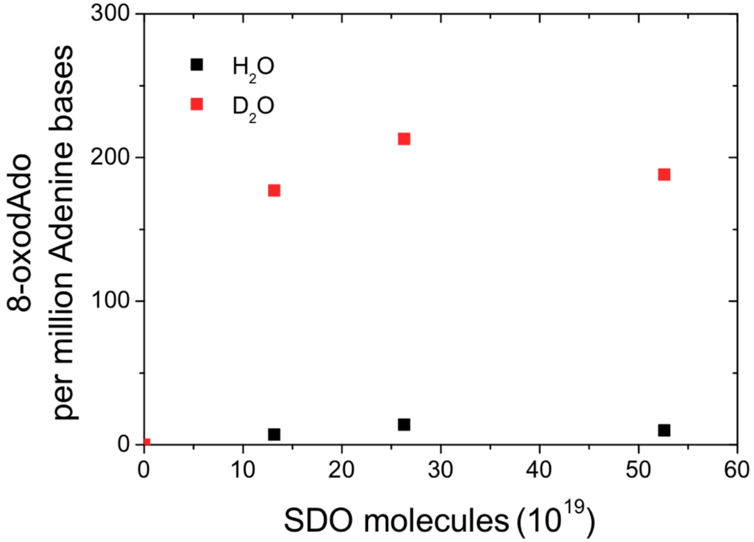
DNA OXIDATION

- **DNA oxidation by $O_2(a^1\Delta_g)$ was also achieved!**

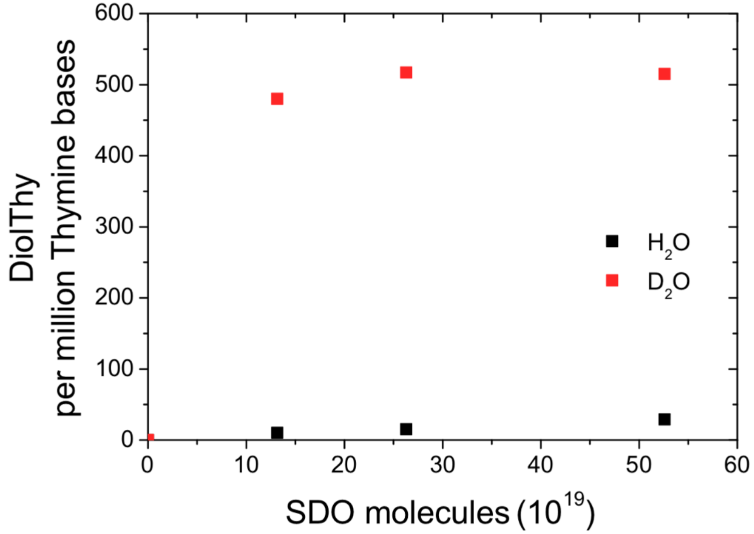
condition A



condition A



condition A



- **$O_2(a^1\Delta_g)$ oxidizes all bases but Cytosine!**
- **Actually, $O_2(a^1\Delta_g)$ overoxidized DNA!**

**Can we conclude that $O_2(a^1\Delta_g)$
is the active species?**

DNA OXIDATION

	A $O_2(a^1\Delta)$ ~ 1.5 10^{16} cm^{-3} O_3 < 8.0 10^{12} cm^{-3}	Z $O_2(a^1\Delta)$ < 1.0 10^{13} cm^{-3} O_3 ~ 7.0 10^{15} cm^{-3}	**O_3 damage / $O_2(a^1\Delta)$ damage**
8-oxoAdo	20	3385	**~170**
8-oxodGuo	30	833	**~28**
DiolThy	40	4689	**~117**
5-OHdCYd	14	29706	**~2122**

- ➢ **10 times more damages in condition A** than those which could be **induced by residual O_3**

BUT

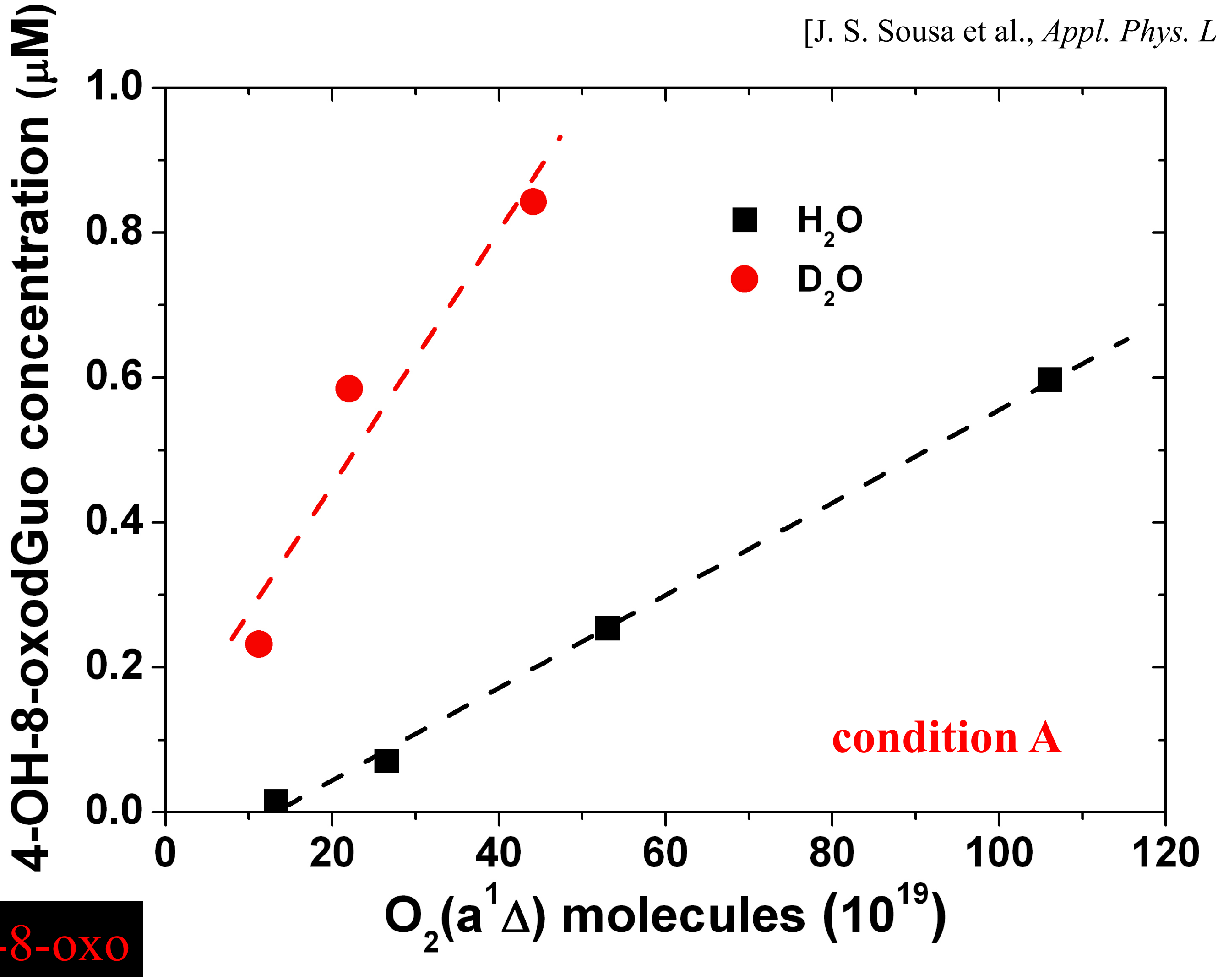
  - ✓ **$O_2(a^1\Delta_g)$ is physically de-excited in water**
  - ✓ possible **role of NO_X → HNO_3 in solution** (under investigation)

- ➢ **both O_3 and $O_2(a^1\Delta_g)$ seem to oxidize DNA**
- ➢ **O_3 seems to be more effective on oxidizing DNA**

More experiments need to be done in order to clearly understand the reactivity of $O_2(a^1\Delta_g)$ and O_3 with DNA

dGuo OXIDATION

[J. S. Sousa et al., *Appl. Phys. Lett.* **97** (2010) 141502]



4-OH-8-oxo

- ➢ results from dGuo oxidation by $O_2(a^1\Delta_g)$?
  - ✓ 4-OH-8-oxo production increases linearly with $O_2(a^1\Delta_g)$ flow