Eighth International Conference on Atomic and Molecular Data and Their Applications
(ICAMDATA 2012)
NIST, Gaithersburg, Maryland, 1~4 October, 2012

Chemically reactive species in liquids generated by atmospheric-pressure plasmas and their roles in plasma medicine

Satoshi Hamaguchi
Osaka University

Acknowledgements

1. Numerical Simulation: Tatsuya Kanazawa, Michiro Isobe
2. Atmospheric-pressure plasma experiments: Katsuhisa Kitano
3. Plasma application experiments for biological systems: Hideki Yoshikawa, Akira Myoui, Yu Moriguchi, Kazuto Masuda, Dae-Sung Lee

“Handbook of Atomic and Molecular Processes in Plasmas”

ed. by S. Hamaguchi, I. Murakami, and D. Kato
(Osaka University Press, 2011)

The list of authors also includes
Alex M Imai
Fumihiro Koike
.....

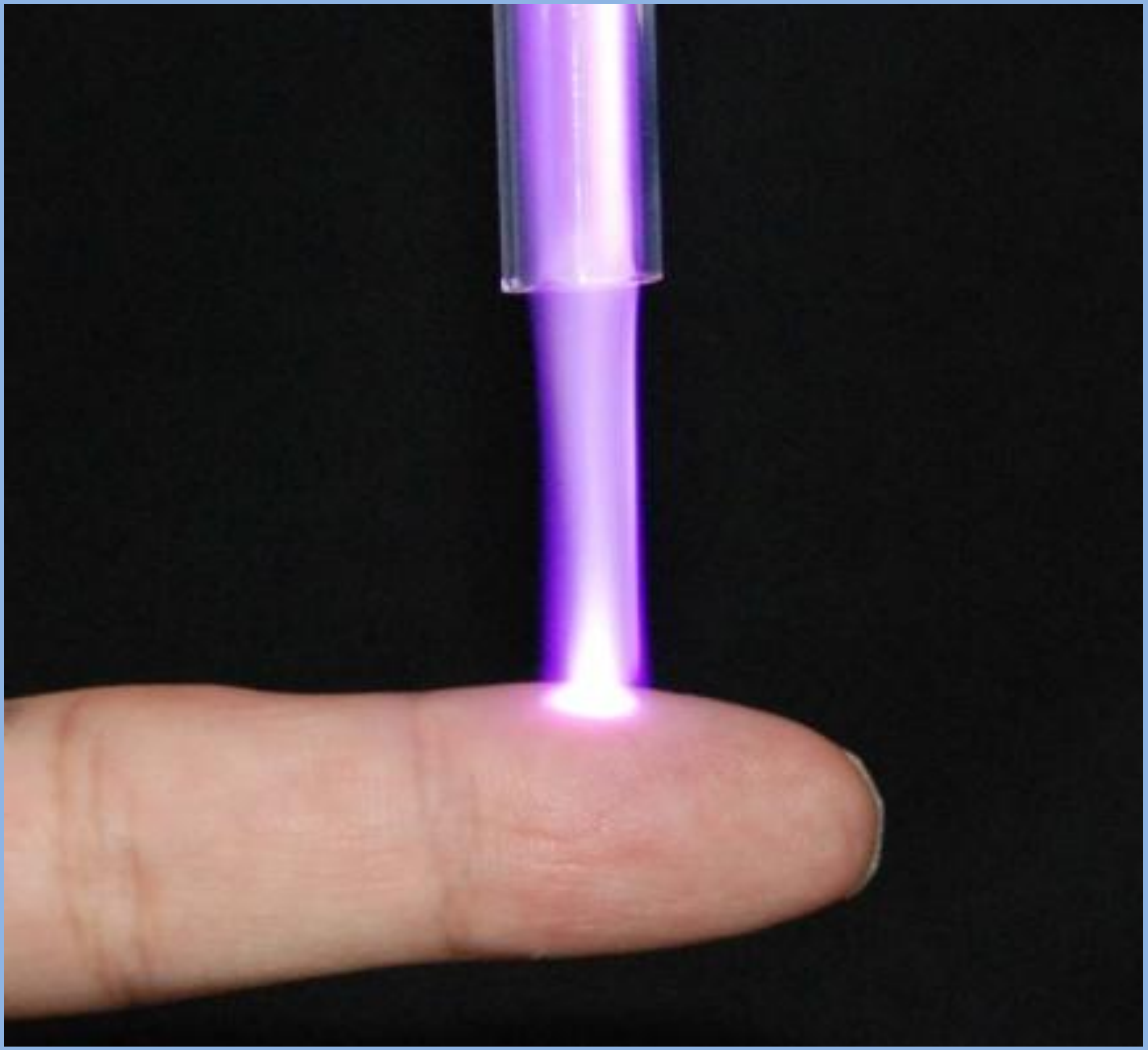
No Data in this “Handbook”

Chap 1 – 10: physics background for data
Chap 11-17: applications

Outline

1. Motivation and background: plasma technologies for medicine
2. Model system: ROS/RON generation in water exposed to low-temperature atmospheric-pressure plasma
3. Sample simulations

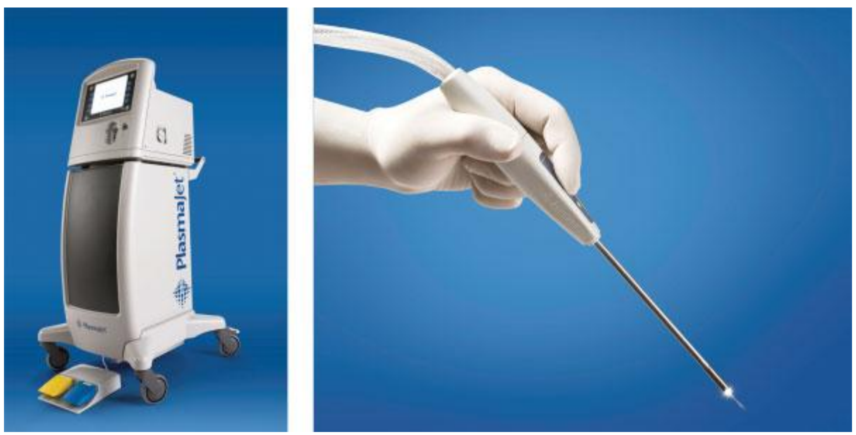
Low-temperature atmospheric-pressure plasmas



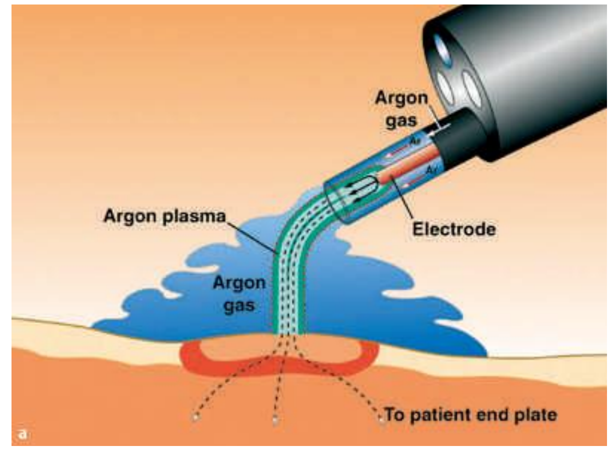
Argon Plasma Coagulator (APC)

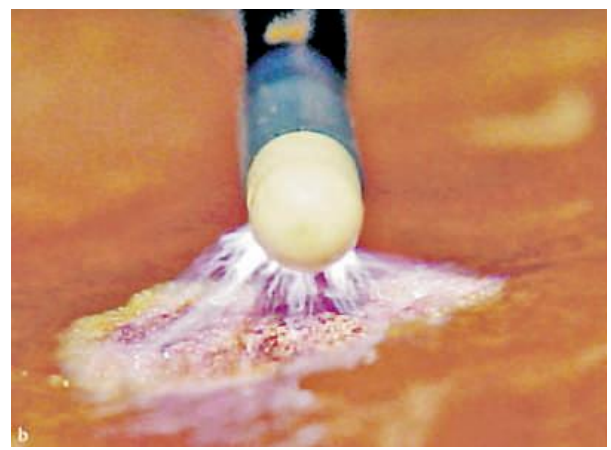
Argon Plasma Coagulator (APC)

cauterization by thermal plasma



Plasma Surgical PlasmaJet System
(from Plasma Surgical Limited)
G. Lloyd, et al., Plasma Process. Polym.
7 (2010) 194.



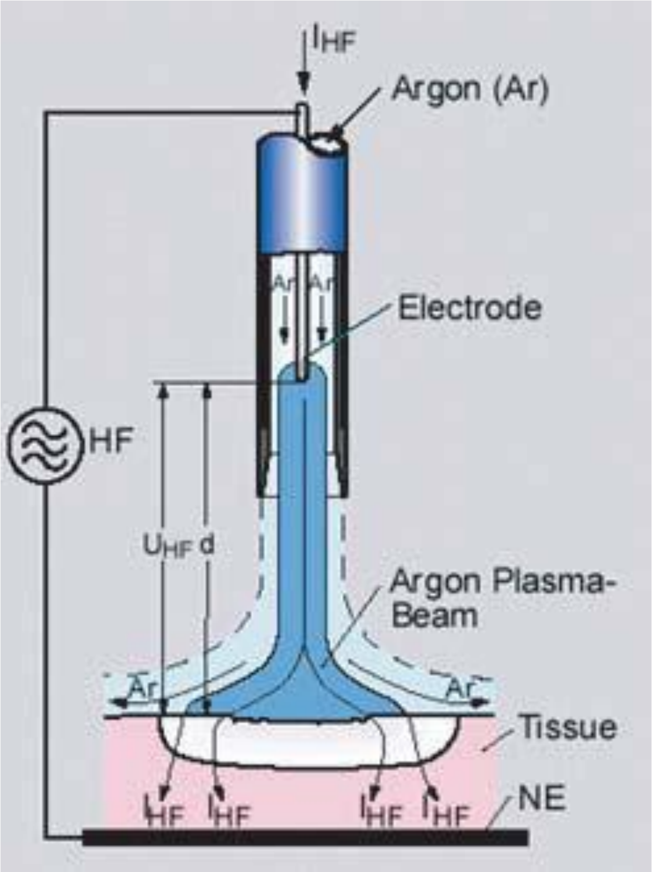


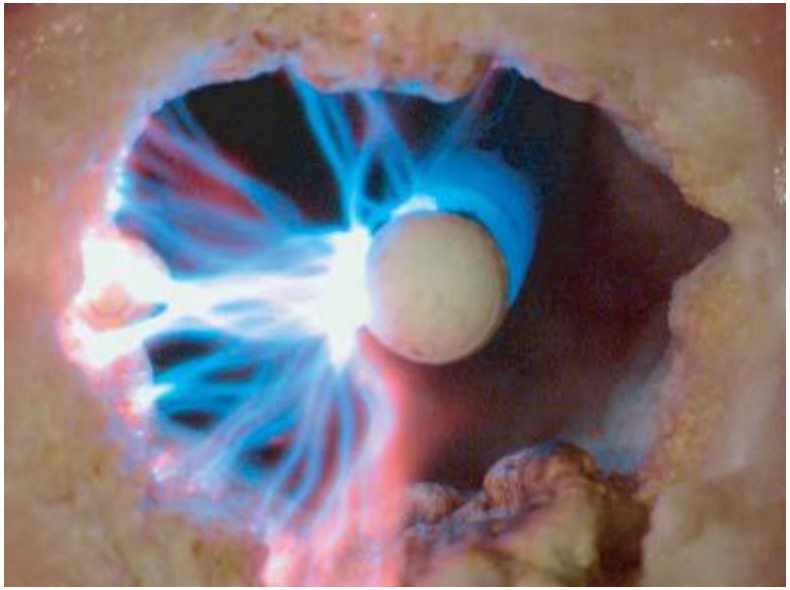
APC basic principles

A. Postgate *et al*., Endoscopy **39** (2007) 361

APC

ERBE (Germany)
power consumption:(50-100 W)
frequency: 350 kHz
plasma temperature : 100°C
(current flows in the tissue)





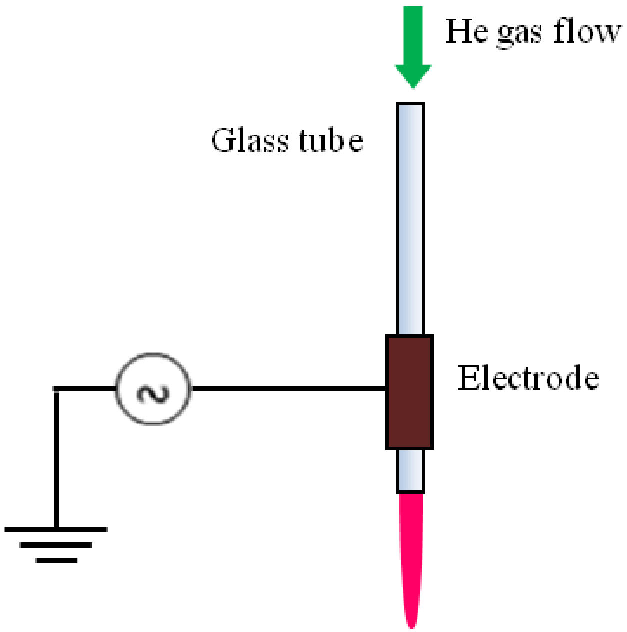
High-frequency Argon Plasma Coagulation unit; left – schematic view, right – interaction with tissue .

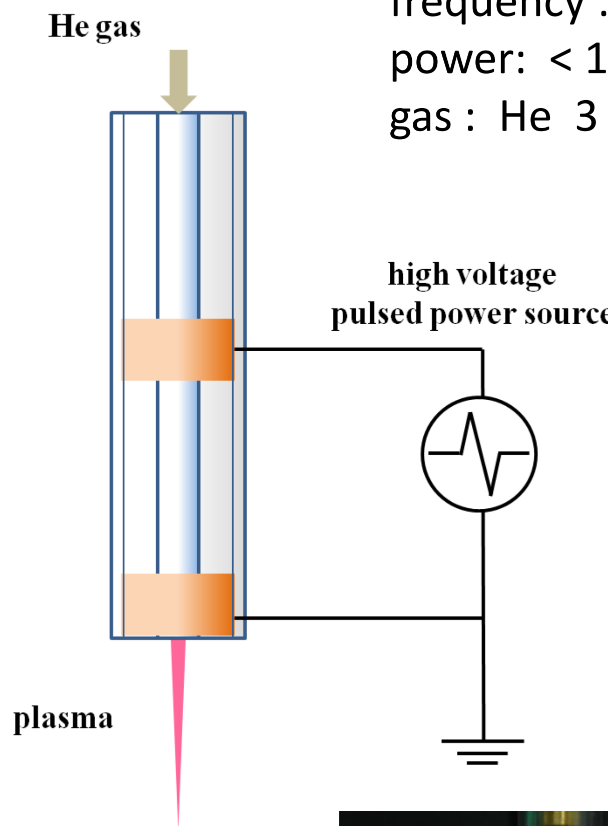
E. Stoffels, Contrib. Plasma Phys. **47**, 40 – 48 (2007)

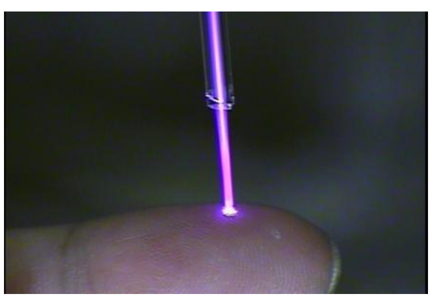
low-temperature atmospheric-pressure plasmas

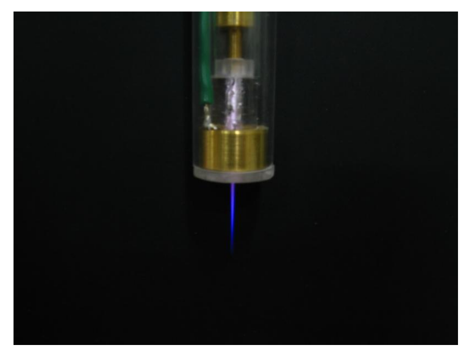
Plasma jet systems

voltage: 1 ~ 10kV
frequency : 10 ~ 30kHz
power: < 1 W
gas : He 3 l/min



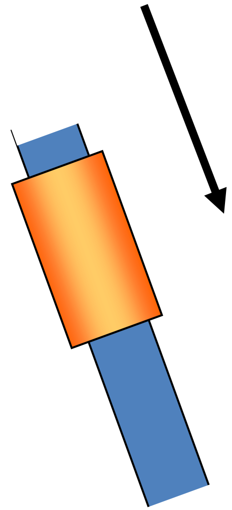






hand-held plasma jet device

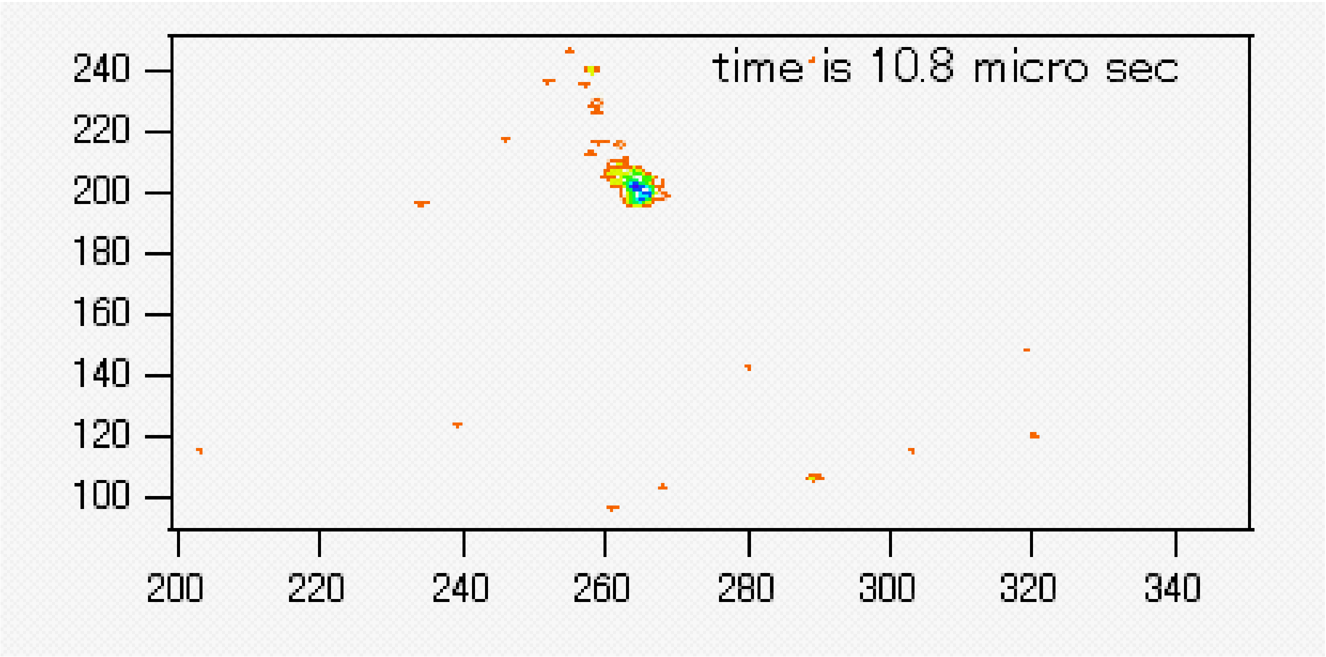
High-speed camera observation



direction of plasma jet injection

plasma bullet : speed（ ≒10km/s）≫ gas velocity

exposure time: 0.1μs
shot at every 0.2μs

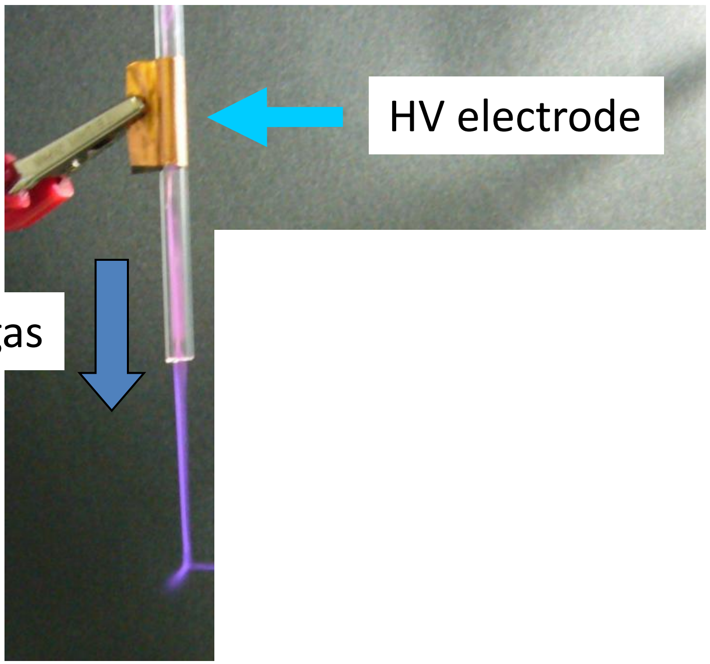


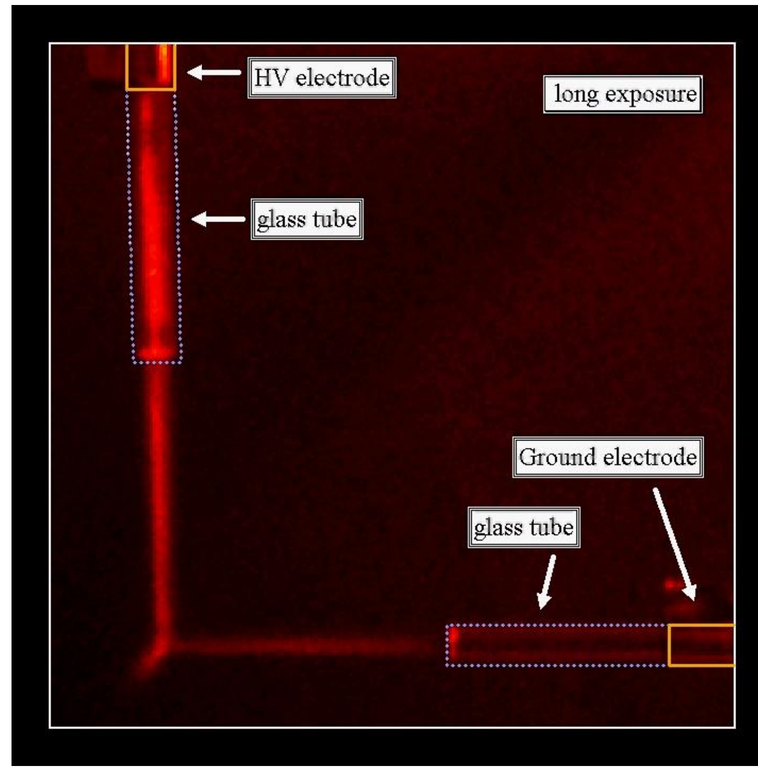
Cross Jet

Cross jet

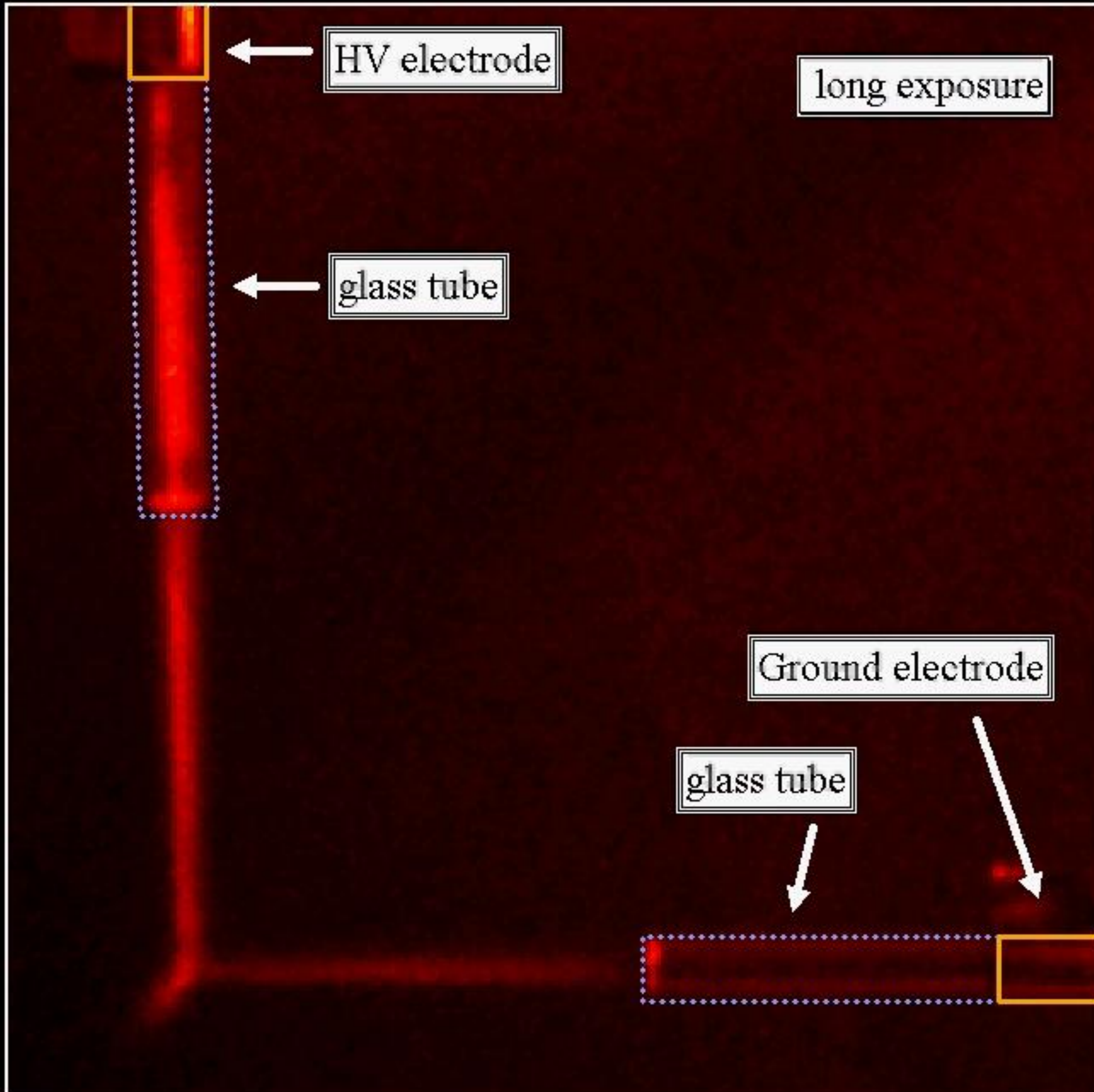
High speed ICCD camera

Exposure time 50ns
Time step 50ns





The ionization front travels along the crossing gas flows


HV electrode
long exposure
glass tube
Ground electrode
glass tube

Medical Tools

Plasma medicine

traditional surgical devices

scalpels･electrical scalpels

mechanical force/ heat

radiations

X-ray, heavy ions

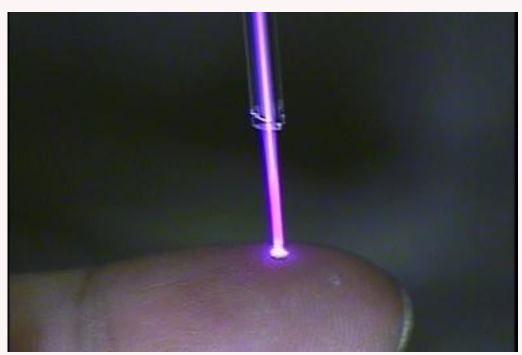
ionization

low-temperature plasma

new generation of plasma device

free radicals, ROS, RON

blood coagulation, would healing, local sterilization, cell proliferation etc.



laser

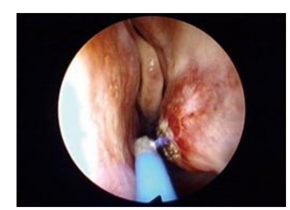
laser scalpels

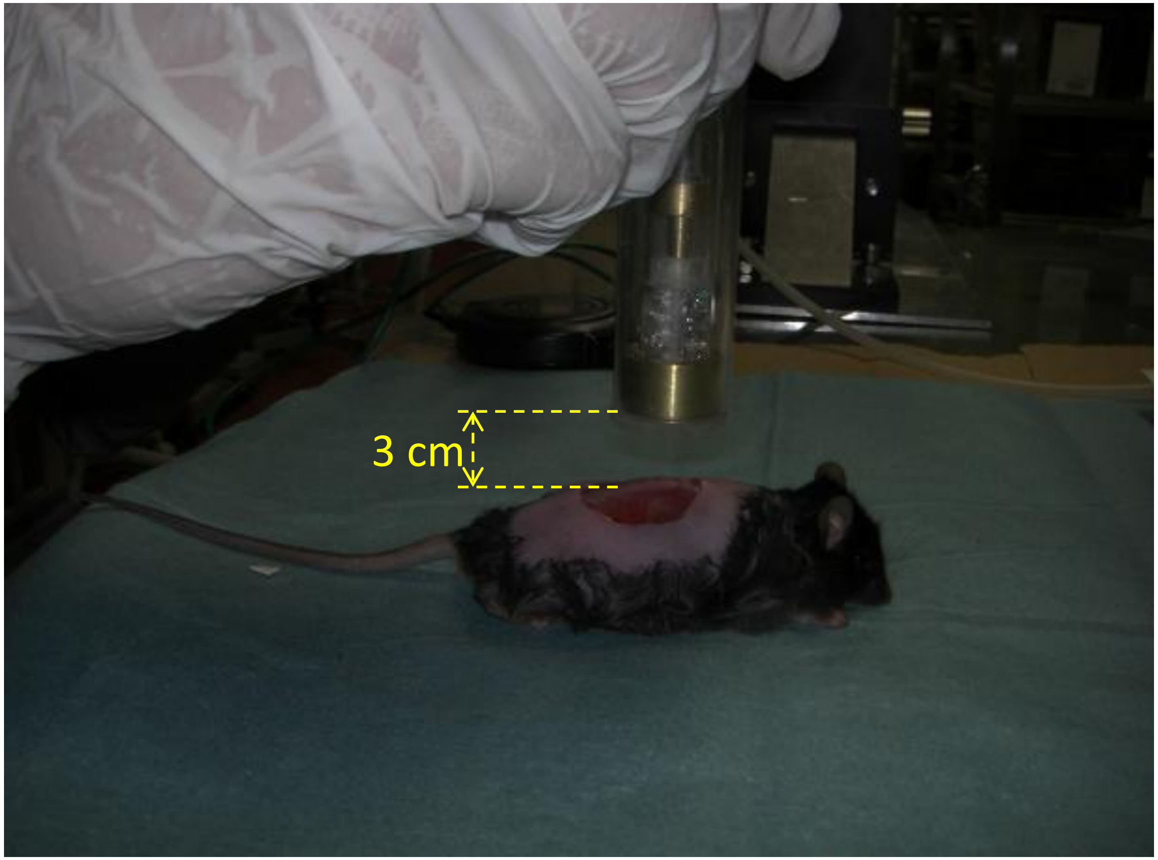
heat

thermal plasma

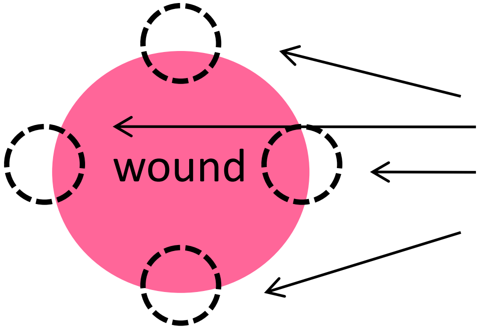
argon plasma coagulator

heat





Application Method



1 min plasma application each
in Day 0 and Day 1 (twice)

Day 0 (before plasma application)

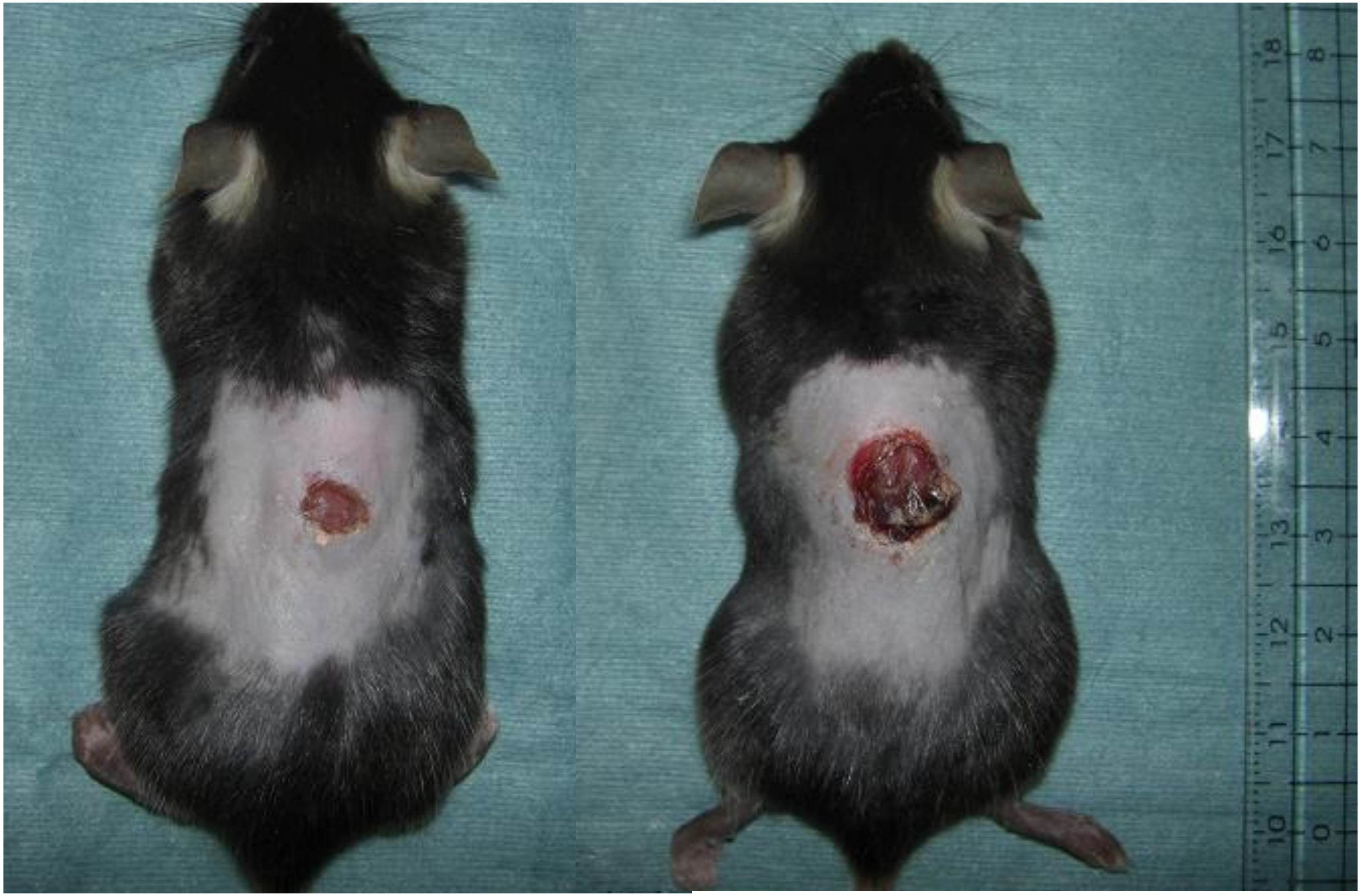
Before Plasma Application

area = 89 units (arb)

Control

area = 111 units

Day 6

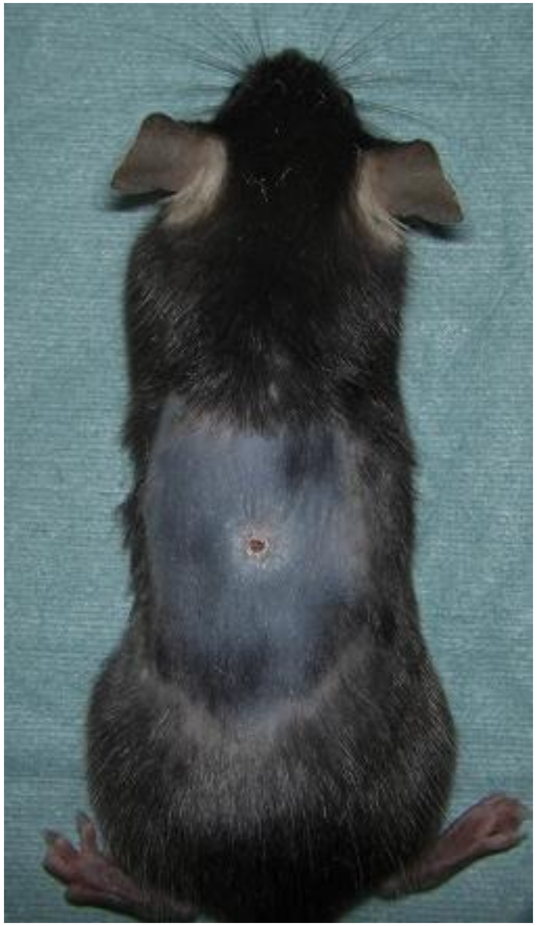


plasma treated: area = 25 units (28%)		untreated: area 87 (78%)

Day 10

plasma treated: area = 12 units (14%)

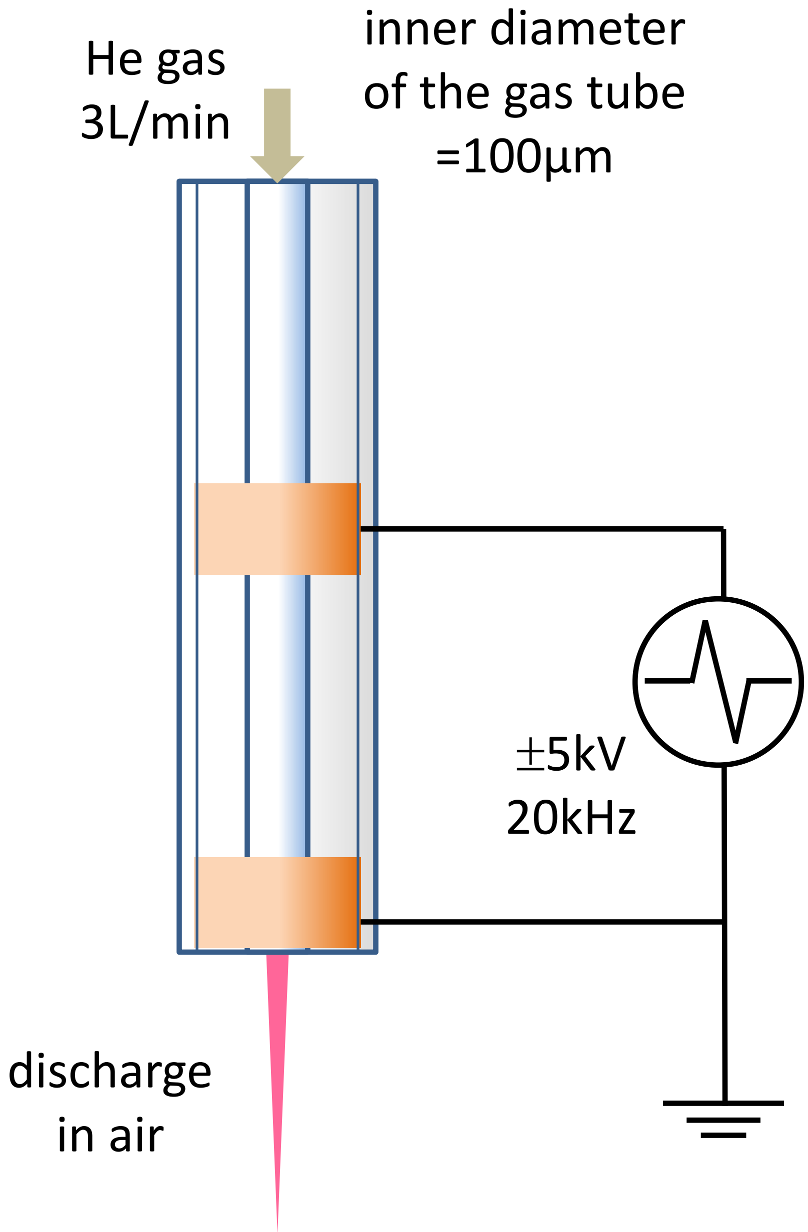
Day 12

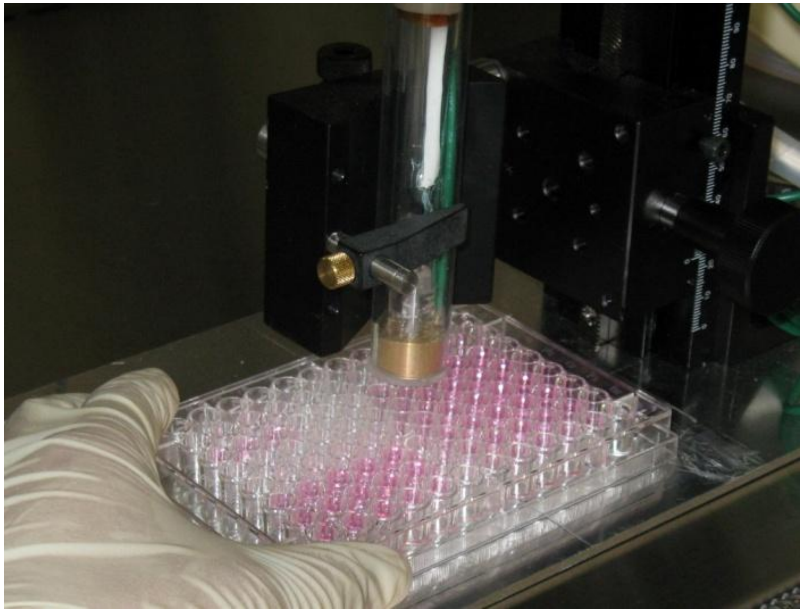


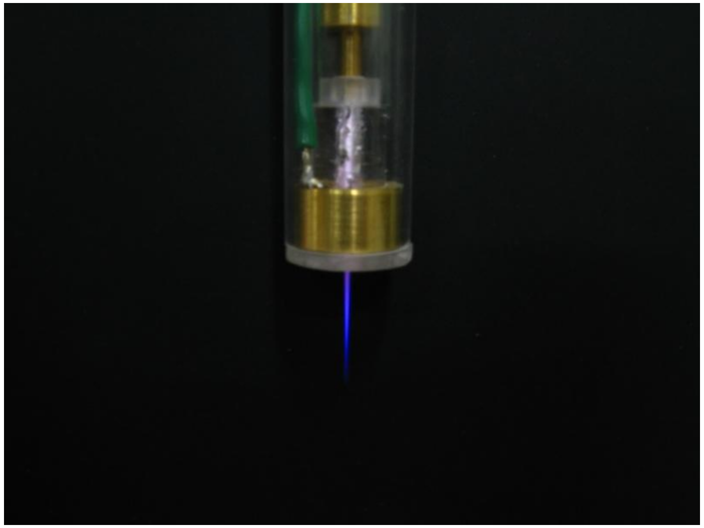
plasma treated

Cell Proliferation

Plasma System

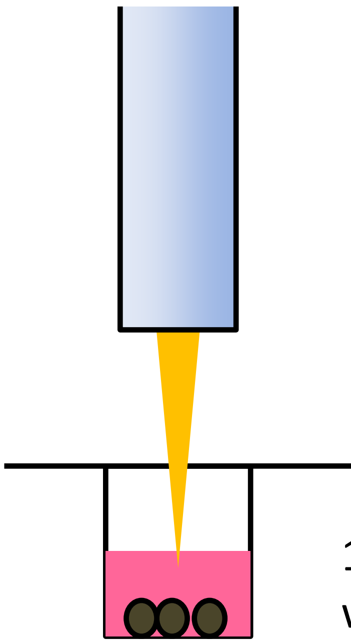


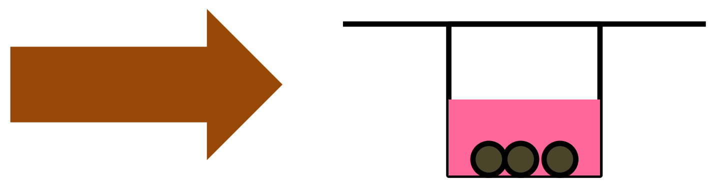




procedure

incubation





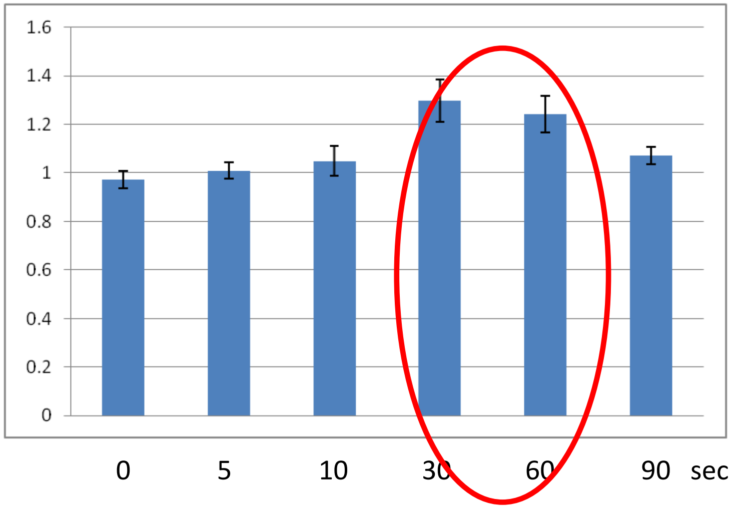
100 μl DMEM
with about 3000 cells
(for a 96 well process)

Cell count : WST kit CCK-8
or typan blue & Beckman Coalter Counter

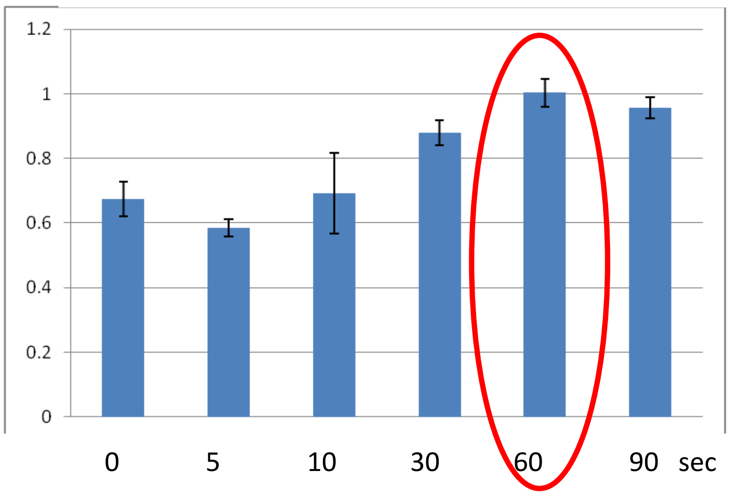
N=3 with a Bonferroni-Dunn test

Human primary culture

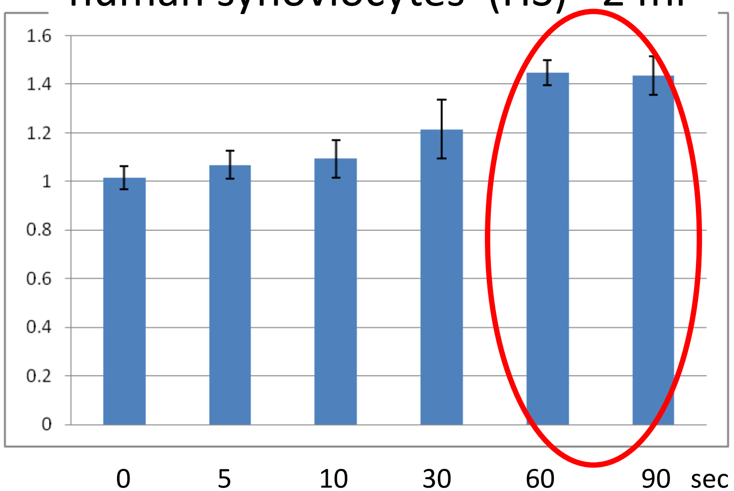
human synoviocytes (HS) 6hr



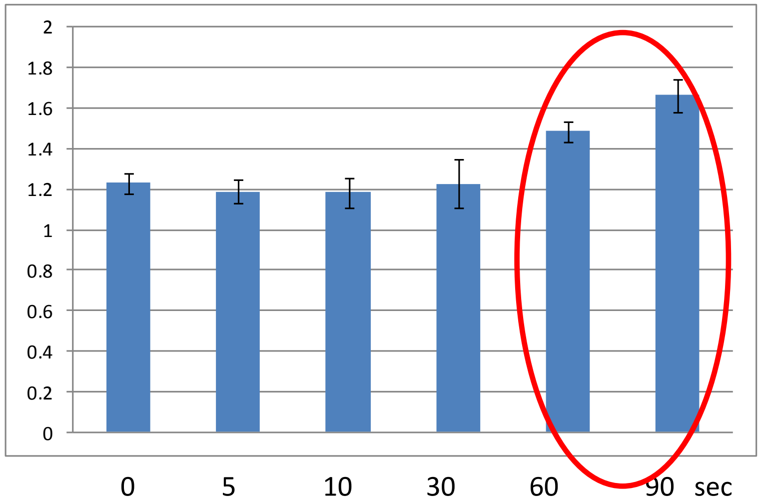
human synoviocytes (HS) 12hr

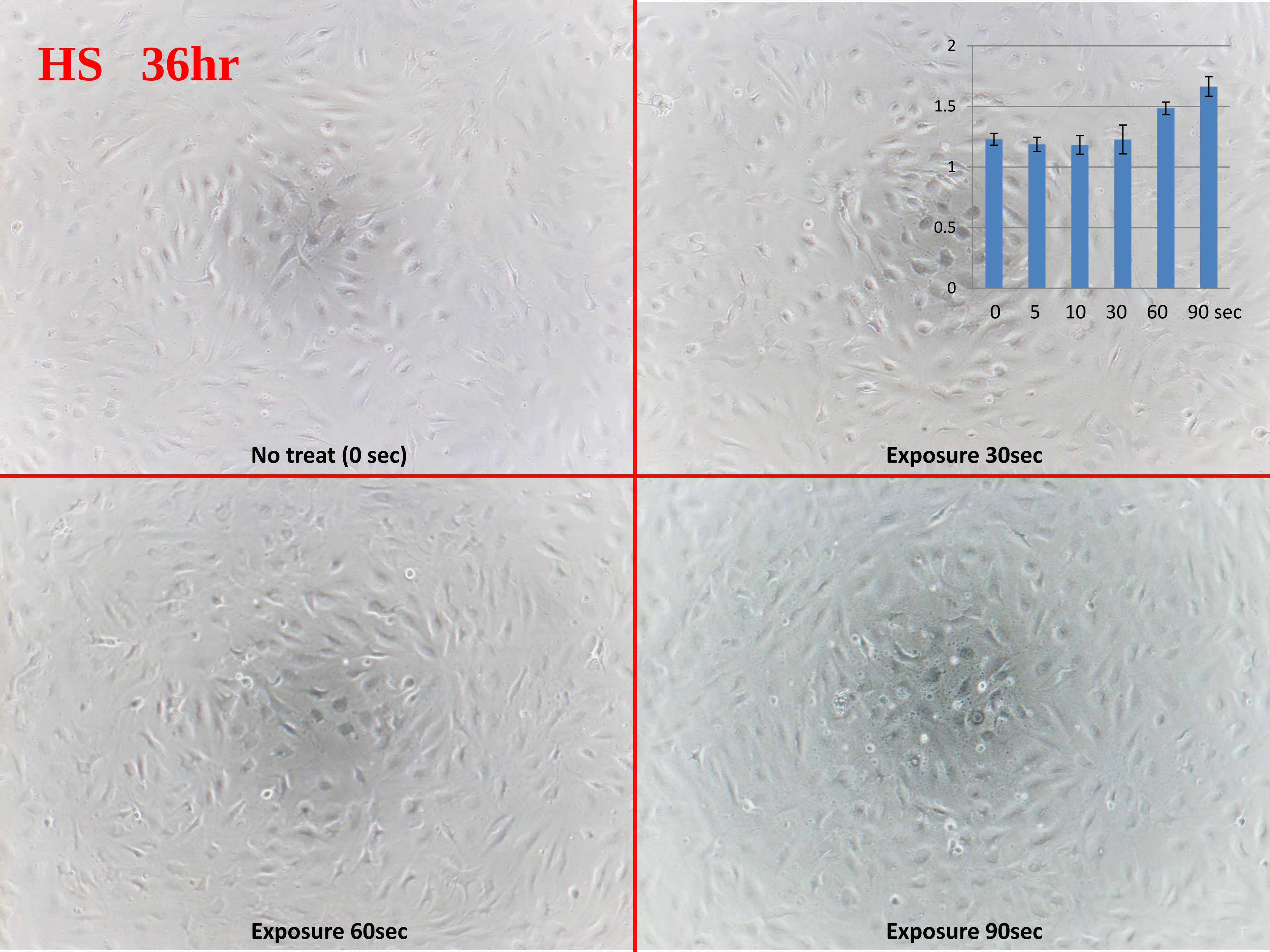


human synoviocytes (HS) 24hr



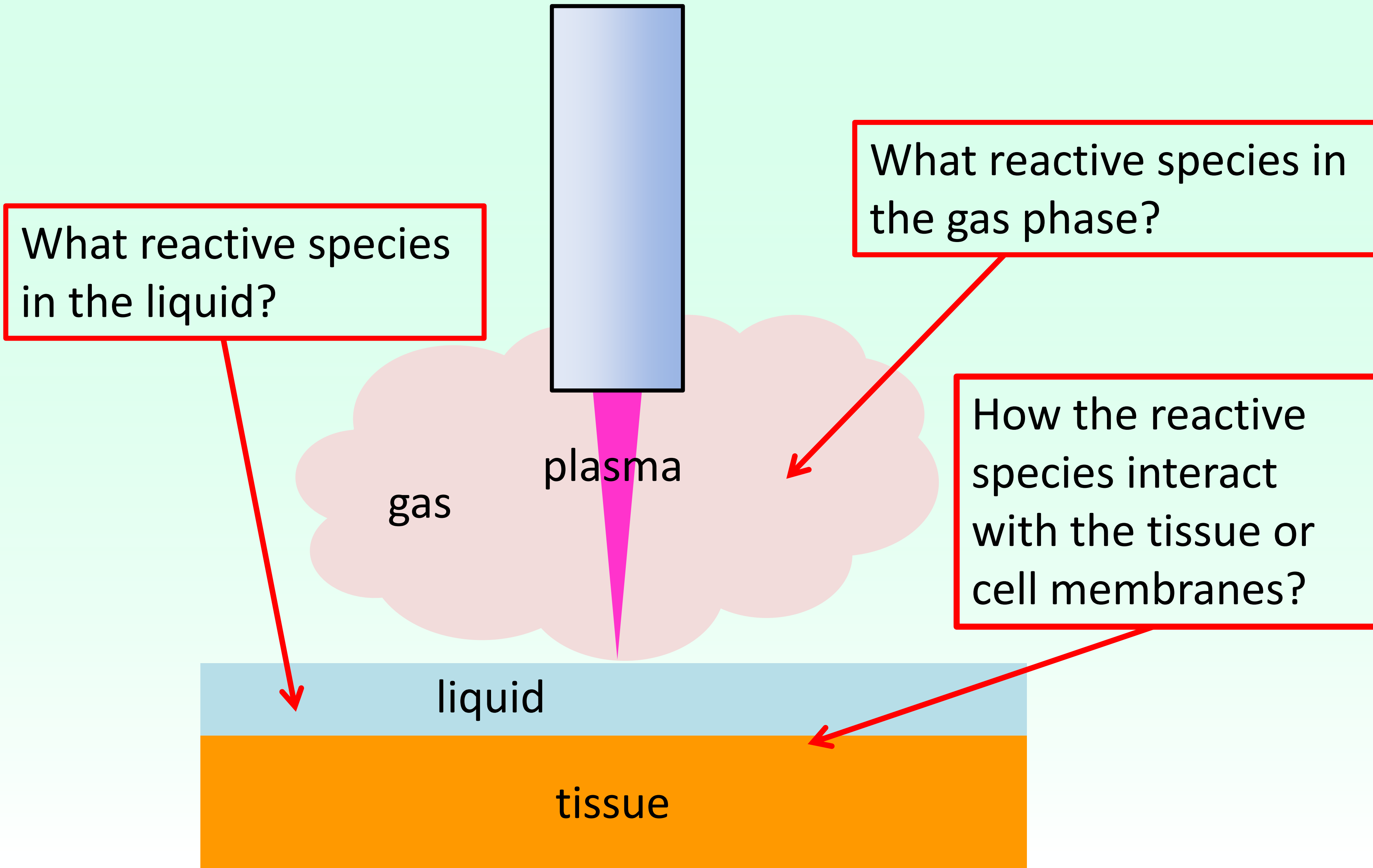
human synoviocytes (HS) 36hr




HS 36hr
2
1.5
1
0.5
0
0
5
10
30
60
90 sec
No treat (0 sec)
Exposure 30sec
Exposure 60sec
Exposure 90sec

model system to study

physics questions

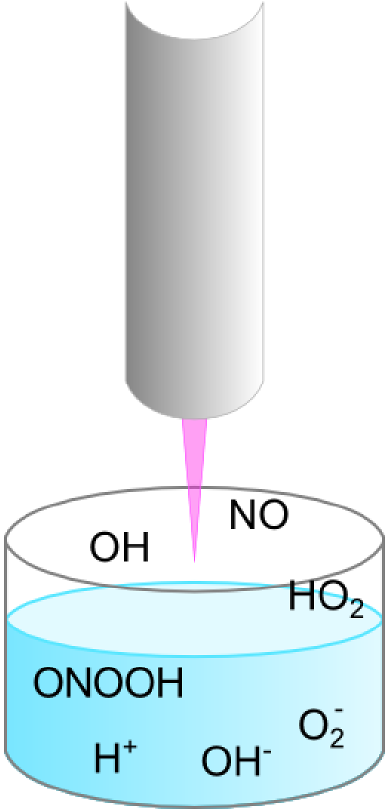


Goal of this study

Chemically reactive species generated in liquid have some strong biological effects

ROS (Reactive Oxygen Species)
OH (hydroxyl radical), O_2^-(superoxide anion radical),
HO_2 (hydroperoxyl radical) etc

RNS (Reactive Nitrogen Species)
NO (nitric oxide), NO_2 (nitrogen dioxide),
ONOOH (peroxynitrite), $ONOOH^-$



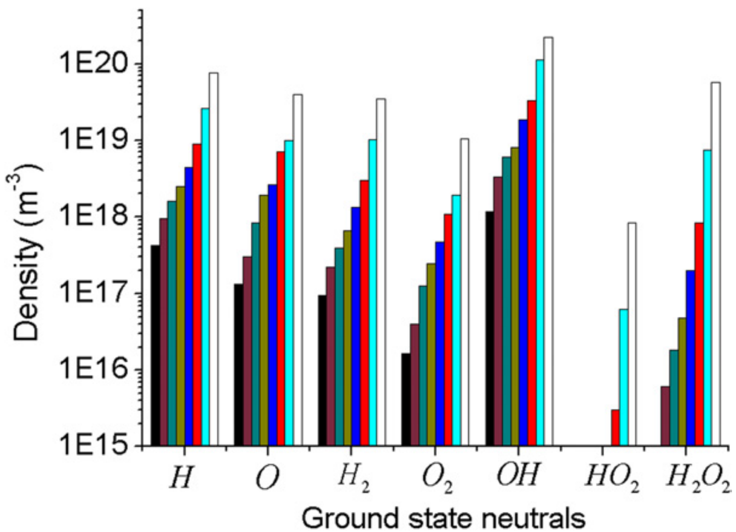
Goal

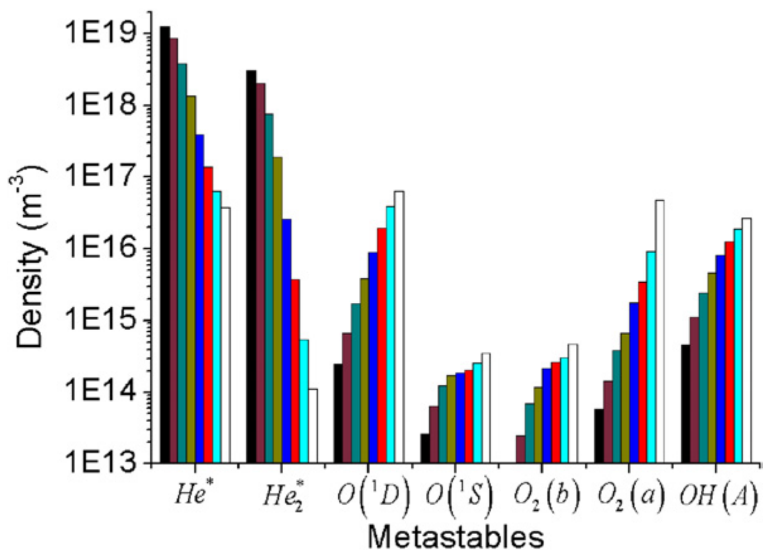
To understand their generation and reaction processes in liquids by numerical simulations

gas-phase simulation

with rate equations

0 D (i.e., global) simulation for He & H_2O

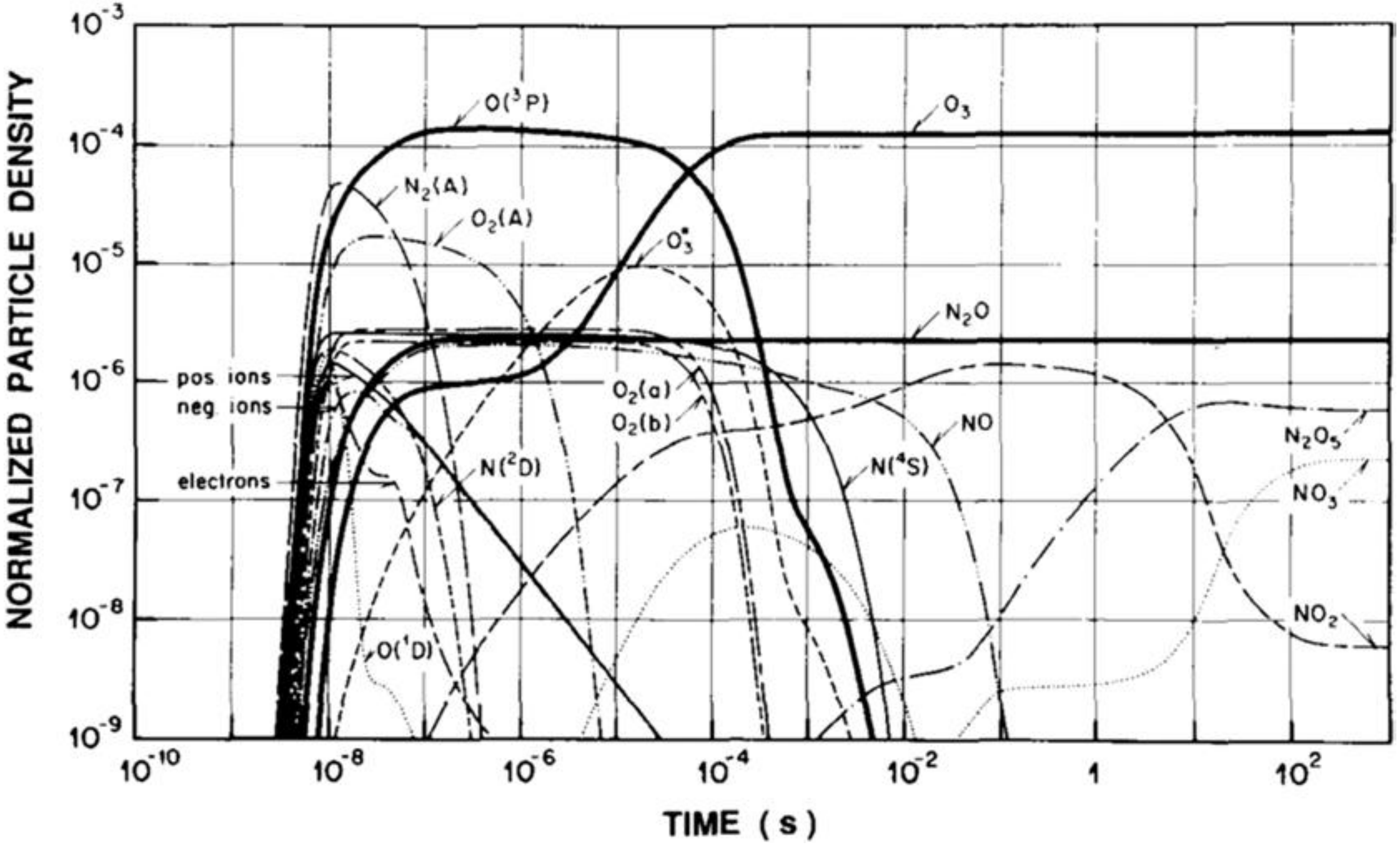




D. X. Liu, P. Bruggeman, F. Iza, M. Z. Rong and M.G. Kong,
Plasma Sources Sci. Technol. 19 (2010) 025018

Reactive species generated in atmospheric-pressure plasmas (simulation : in gas phase)

Eliasson B and Kogelschatz U 1991 IEEE Trans. Plasma Sci.**19** 309

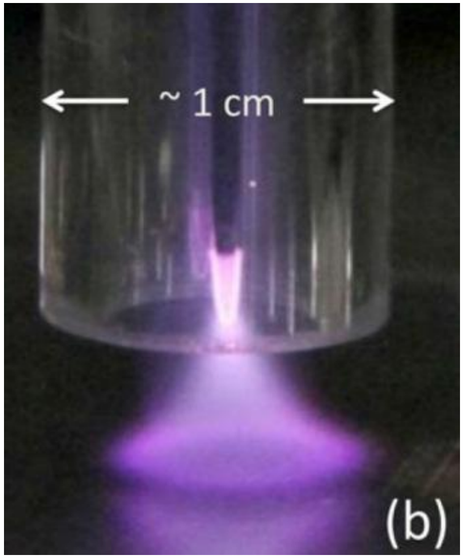


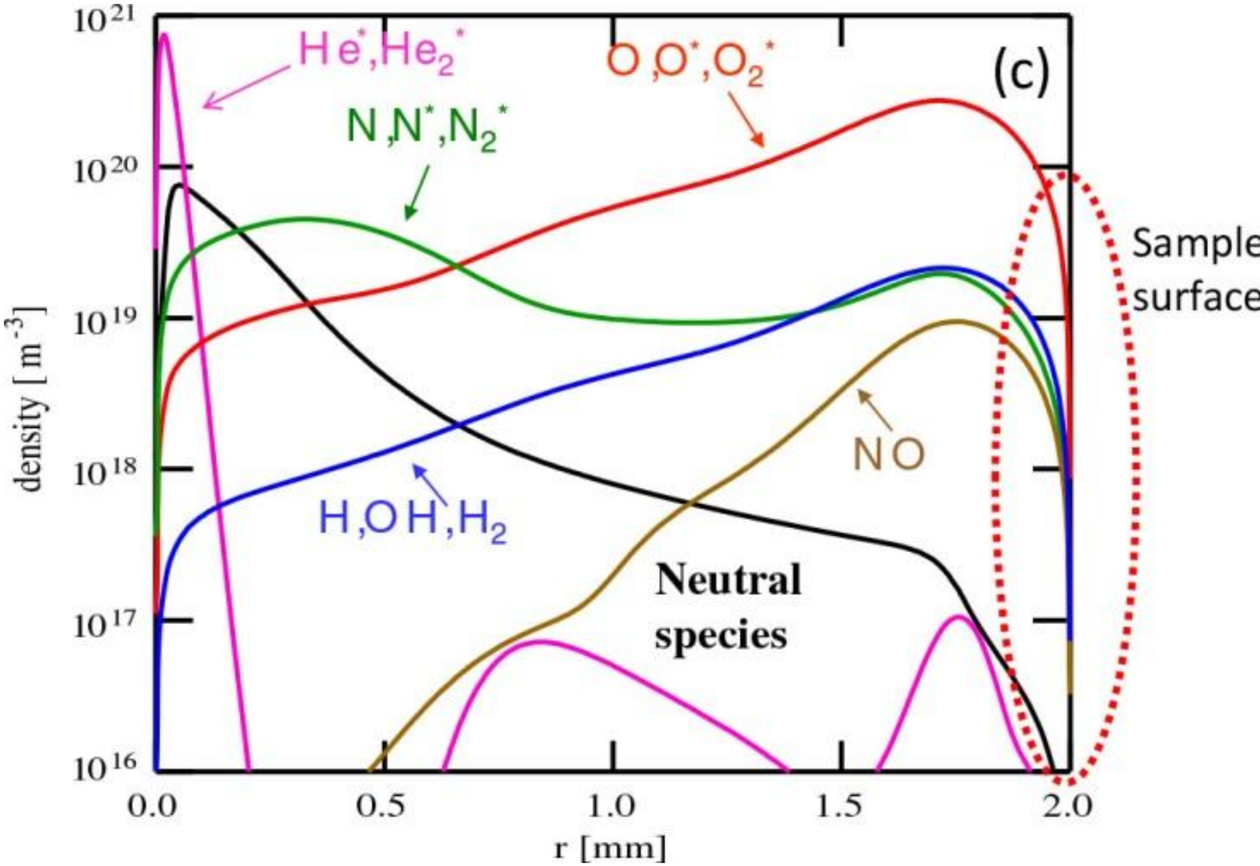
Zero-dimensional numerical simulation of chemical species generated by a microdischarge in a dielectric barrier discharge in air
(80% of N2 + 20% of O2, p = 1 atm, T = 300 K).

gas-phase simulation

Rate equations with transport

1D simulation





D. B. Graves, J. Phys. D: **48** (2012) 263001

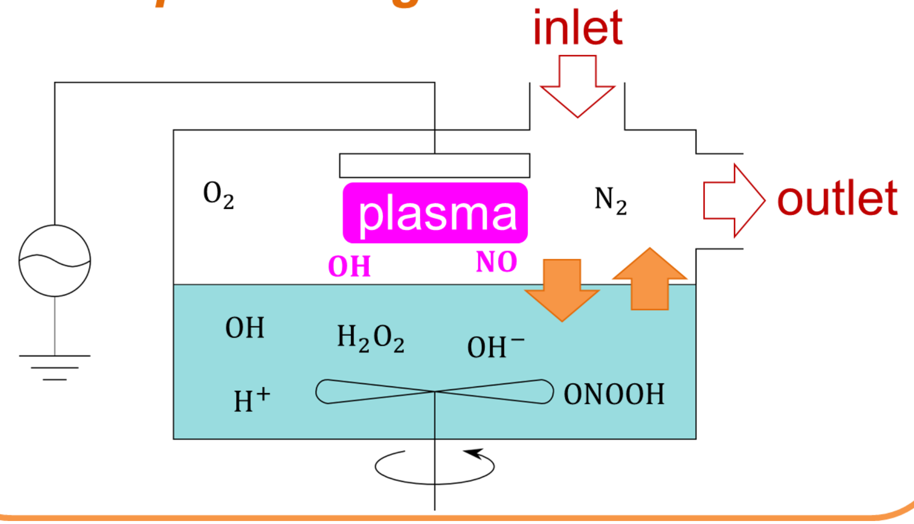
If all gas-phase species – electrons, ions, and neutral (reactive) species – are known, can we predict what species are generated in liquid exposed to the plasma?

Model System

System

- Low temp. Atmospheric Pressure Plasma (APP)
  →provide reactive species
- Pure water (pH=7)

Conceptual Diagram



Computation

- Rate equations／0 D simulation
- No transport (no flow or diffusion) in each phase

(transport of species between the gas and liquid phases)

Henry's law: transport of matters through the gas-liquid interface in equilibrium

Henry's law

$$[OH]_{liq} = k_H P_{OH}$$

$$= k_H [OH]_{gas} RT_g$$

Rate equations

Chemical Reactions (Global Model)
35 chemical species & 98 rate equations

Rate eqn.:
$$\frac{d[H_2]}{dt} = \cdots + \boxed{k_1}\boxed{[e_{aq}^{\ -}][e_{aq}^{\ -}]} + \boxed{k_3}\boxed{[e_{aq}^{\ -}][H]} + \cdots$$

change of density in time = rate const. × **product of densities** + ···

Reaction Scheme	Rate Constant(at 298K) $[M^{-1}s^{-1}]$
$e_{aq}^{\ -} + e_{aq}^{\ -} \rightarrow H_2 + 2OH^-$	$k_1 = 5.1 \times 10^9$
$e_{aq}^{\ -} + H^+ \rightarrow H$	$k_2 = 2.4 \times 10^{10}$
$e_{aq}^{\ -} + H \rightarrow H_2 + OH^-$	$k_3 = 2.5 \times 10^{10}$
$e_{aq}^{\ -} + OH \rightarrow OH^-$	$k_4 = 3.0 \times 10^{10}$

**NDRL/NIST Solution Kinetics Database on the Web*

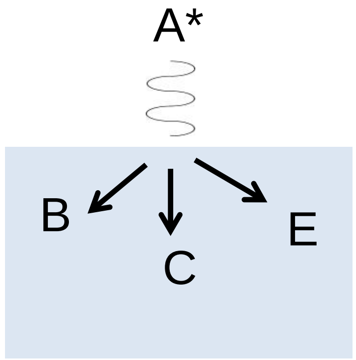
Sample Simulations

To understand what reactive species are generated in liquid by *each* gaseous species

<u>Cases</u>

1. Only OH (hydroxyl) radicals are provided [from the plasma].
2. Only NO (nitric oxide) is provided.
3. Both OH and NO are provides (with nothing else).
4. After OH and NO are provided for 10 sec. and the plasma is turned off.

   → How the reactive species get lost in liquid

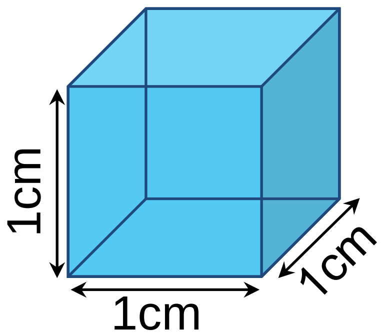


Fluxes of OH and NO (typical values from a plasma)

TABLE 1. Typical relative concentrations of various charged and neutral species generated by non-thermal DBD plasma in gas phase.

Plasma-generated species	Density (cm^{-3})	Density (mol L^{-1})
Superoxide ($O_2^{\bullet-}$)	10^{10} to 10^{12}	
Hydroxyl ($OH^{\bullet}$)	10^{15} to 10^{17}	1.66×10^{-6} to 1.66×10^{-4}
Hydrogen peroxide (H_2O_2)	10^{14} to 10^{16}	
Singlet oxygen ($^1O_{2-}$)	10^{14} to 10^{16}	
Ozone (O_3)	10^{15} to 10^{17}	
Nitric oxide (NO)	10^{13} to 10^{14}	1.66×10^{-8} to 1.66×10^{-7}
Electrons (e^-)	10^{9} to 10^{11}	
Positive ions (M^+)	10^{10} to 10^{12}	

**R.Sensenig et al. Annals of Biomedical Engineering 39 (2011) 674-687*

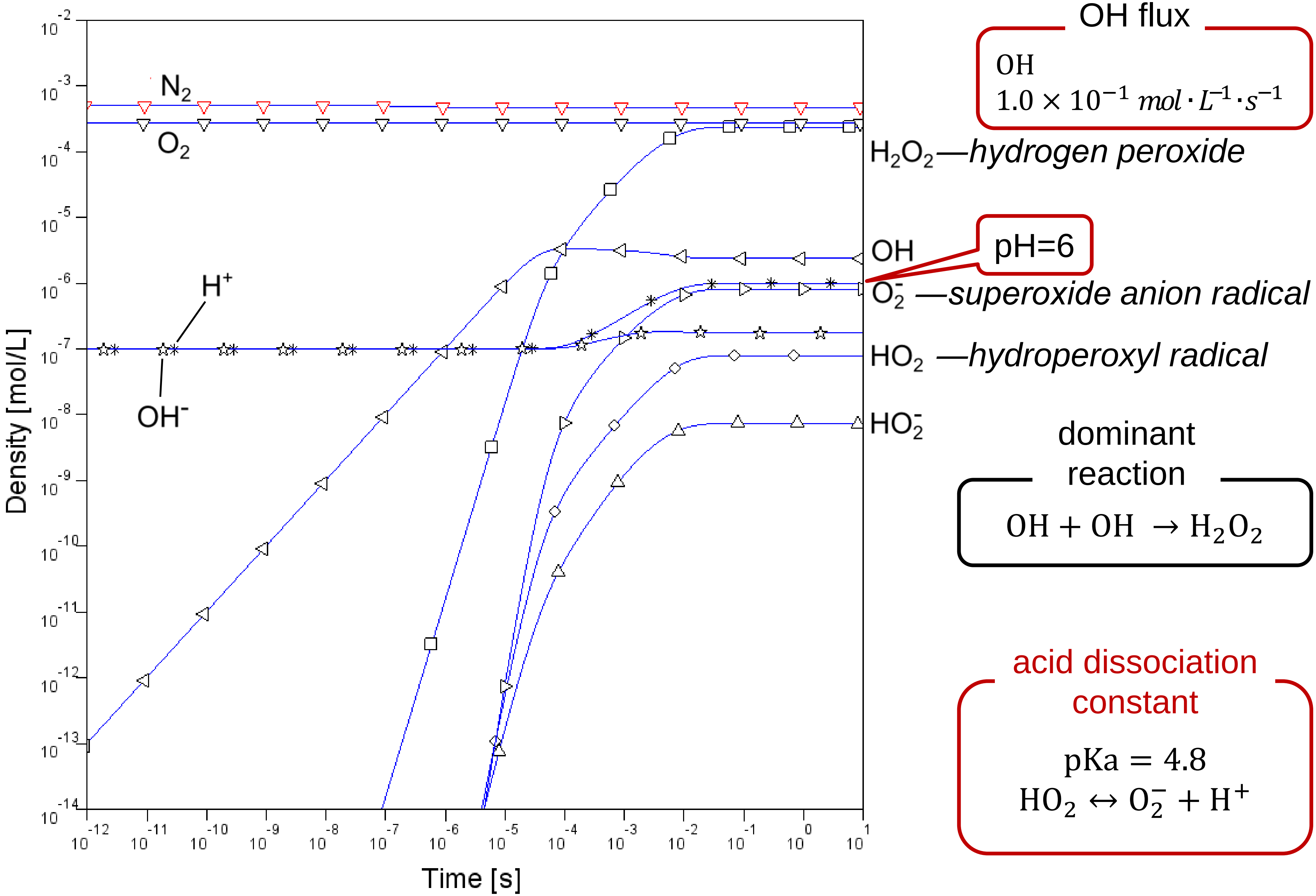


fluxes

$$\frac{S}{V} \cdot \bar{v}_{OH} \cdot [OH]_{gas} = 1.0 \times 10^{-1}\ mol \cdot L^{-1} \cdot s^{-1}$$

$$\frac{S}{V} \cdot \bar{v}_{NO} \cdot [NO]_{gas} = 7.6 \times 10^{-4}\ mol \cdot L^{-1} \cdot s^{-1}$$

Case1 : OH only from the gas phase



OH flux

OH
$1.0 \times 10^{-1}\ mol \cdot L^{-1} \cdot s^{-1}$

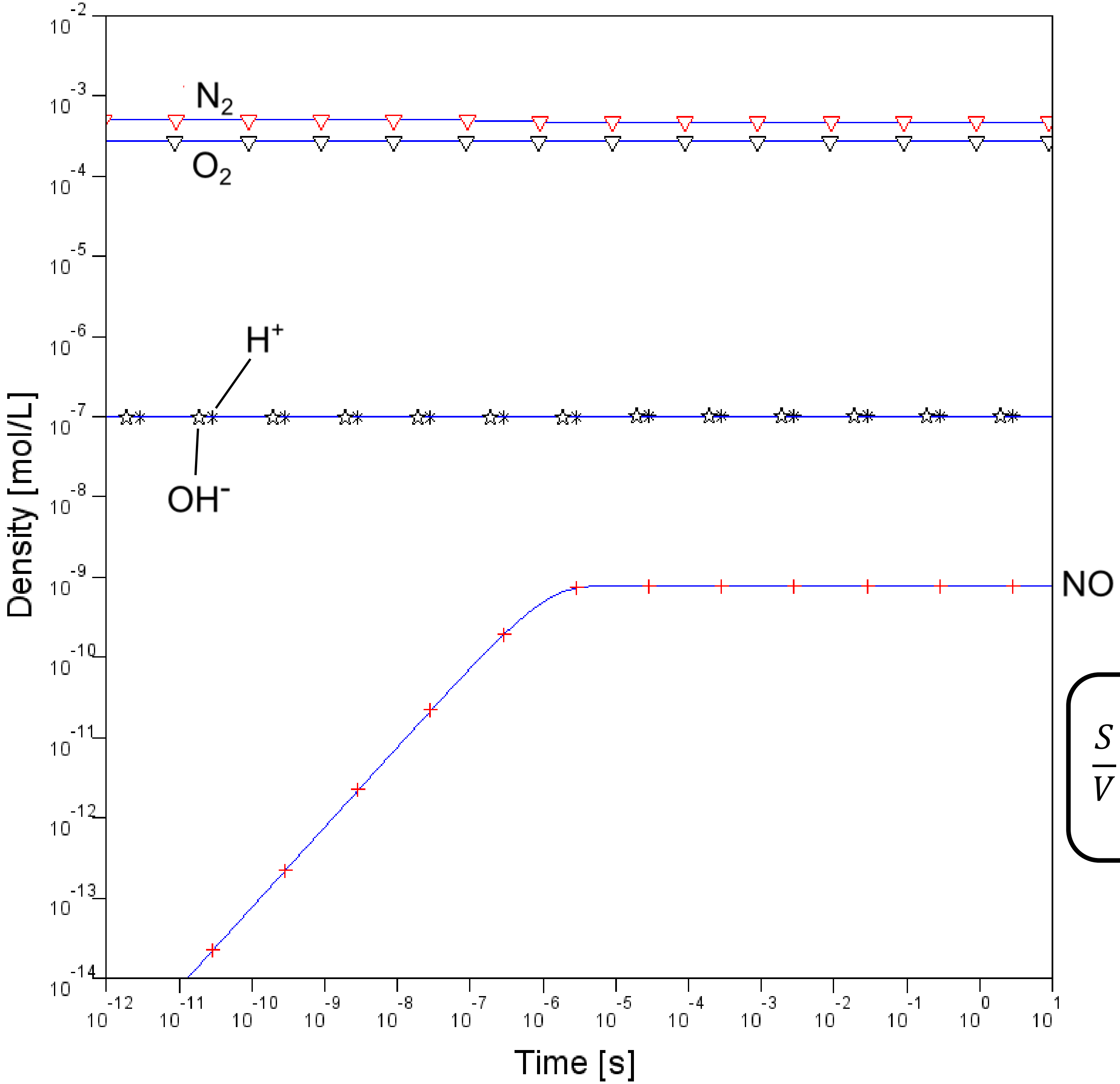
dominant reaction

$\mathrm{OH} + \mathrm{OH} \rightarrow \mathrm{H_2O_2}$

acid dissociation constant

$\mathrm{pKa} = 4.8$
$\mathrm{HO_2} \leftrightarrow \mathrm{O_2^-} + \mathrm{H^+}$

NO only from the gas phase



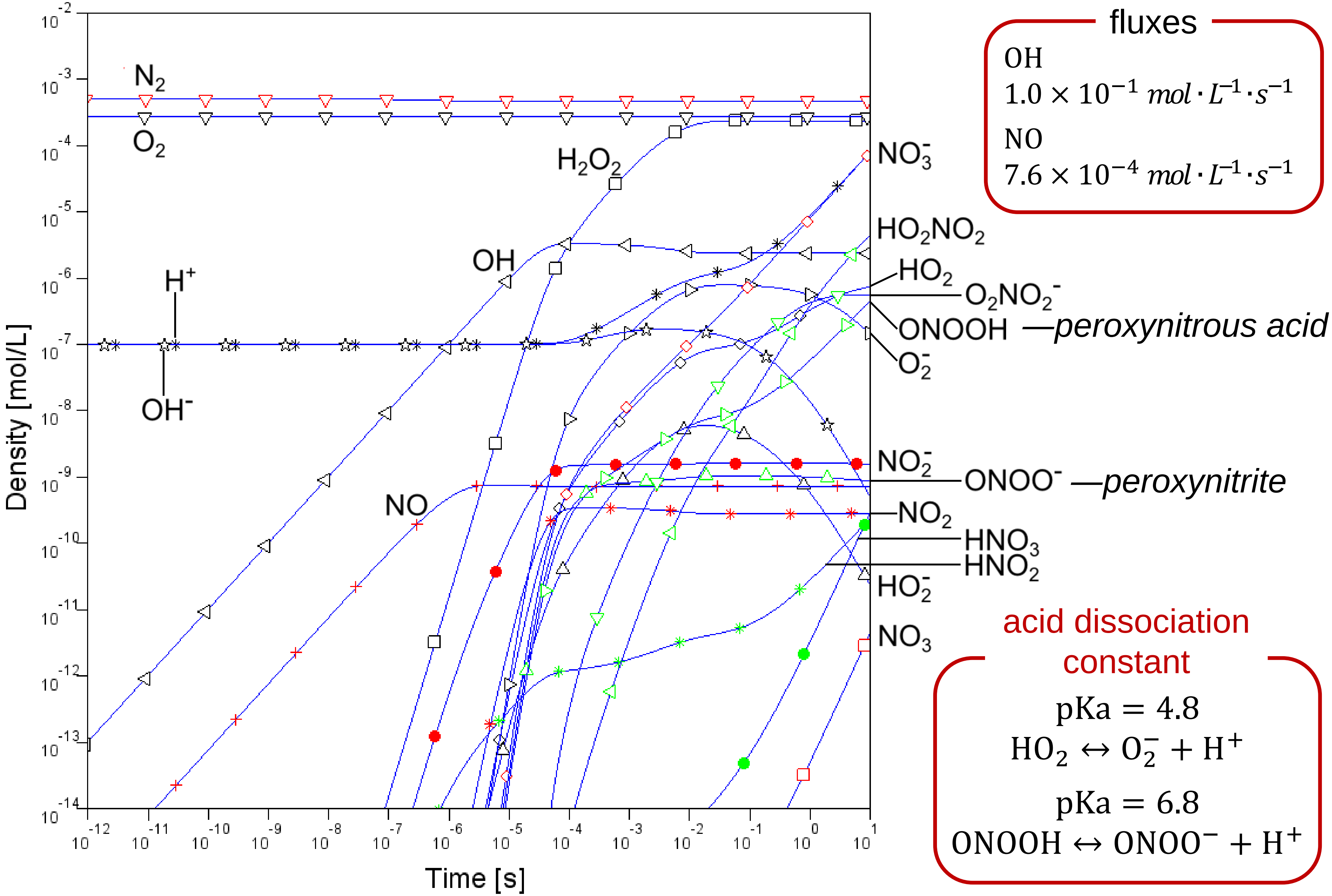
NO flux

NO
$7.6 \times 10^{-4}\ mol \cdot L^{-1} \cdot s^{-1}$

NO flux from the gas

$$\frac{S}{V} \cdot \bar{v} \left([NO]_{gas} - \frac{1}{k_H R T_g} [NO]_{liq} \right)$$

OH & NO supplied simultaneously for 10s



fluxes

OH

$1.0 \times 10^{-1}\ mol \cdot L^{-1} \cdot s^{-1}$

NO

$7.6 \times 10^{-4}\ mol \cdot L^{-1} \cdot s^{-1}$

acid dissociation constant

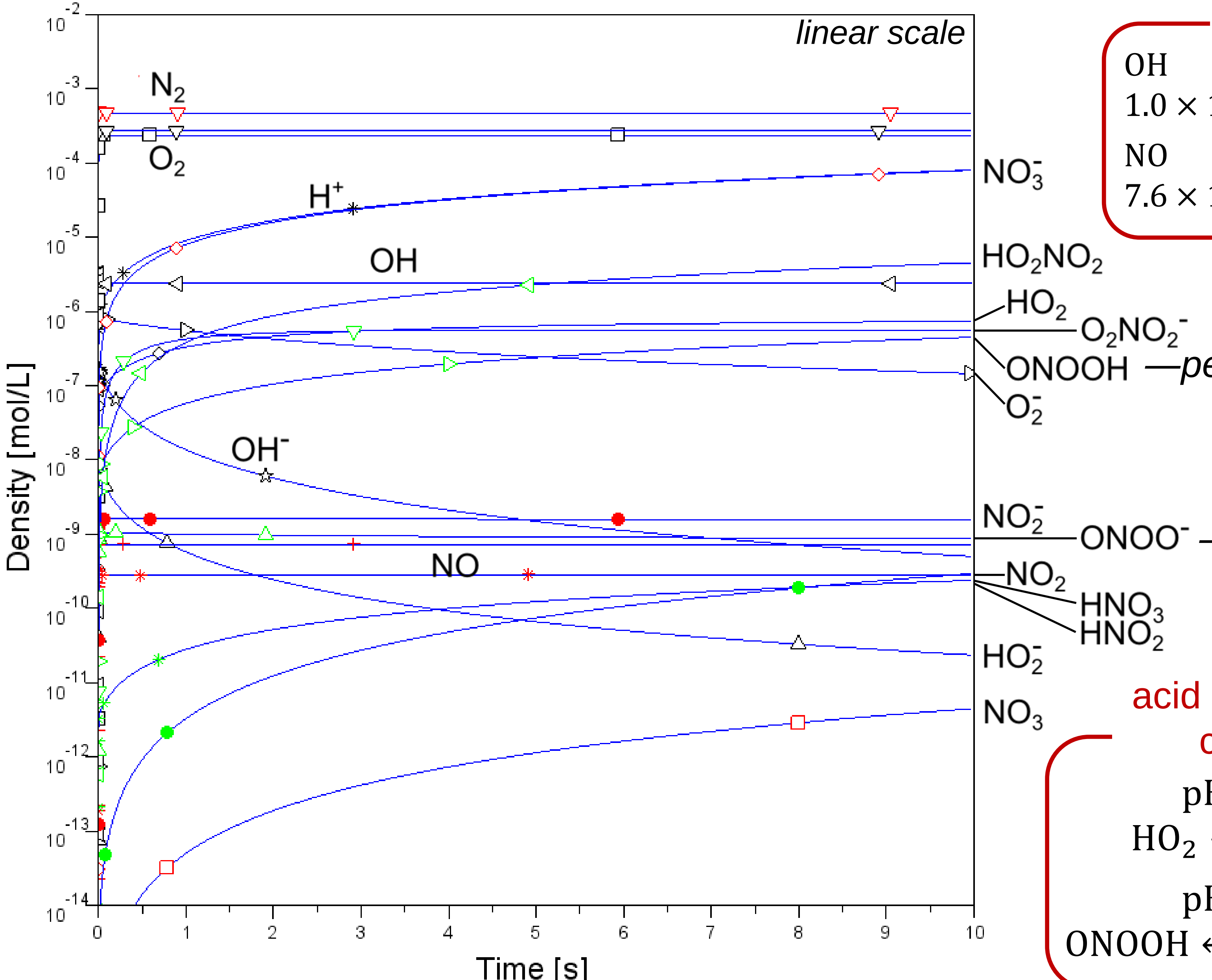
$$\mathrm{pKa} = 4.8$$

$$HO_2 \leftrightarrow O_2^- + H^+$$

$$\mathrm{pKa} = 6.8$$

$$ONOOH \leftrightarrow ONOO^- + H^+$$

OH & NO supply for 10 s (linear time scale)



fluxes

OH

$1.0 \times 10^{-1}\ mol \cdot L^{-1} \cdot s^{-1}$

NO

$7.6 \times 10^{-4}\ mol \cdot L^{-1} \cdot s^{-1}$

acid dissociation constant

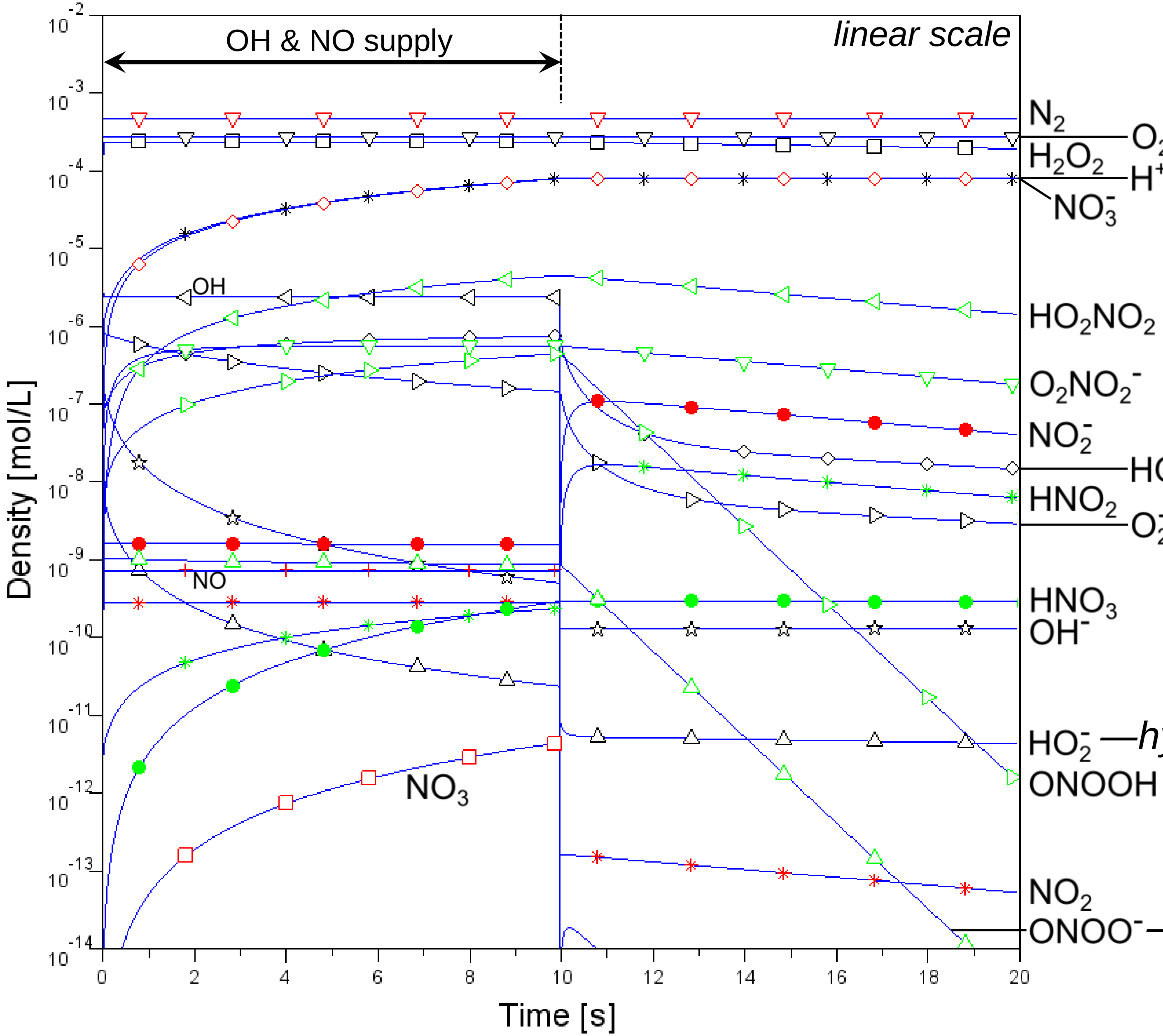
$\mathrm{pKa} = 4.8$

$\mathrm{HO_2} \leftrightarrow \mathrm{O_2^-} + \mathrm{H^+}$

$\mathrm{pKa} = 6.8$

$\mathrm{ONOOH} \leftrightarrow \mathrm{ONOO^-} + \mathrm{H^+}$

OH&NO supplied for 10s and stopped



fluxes

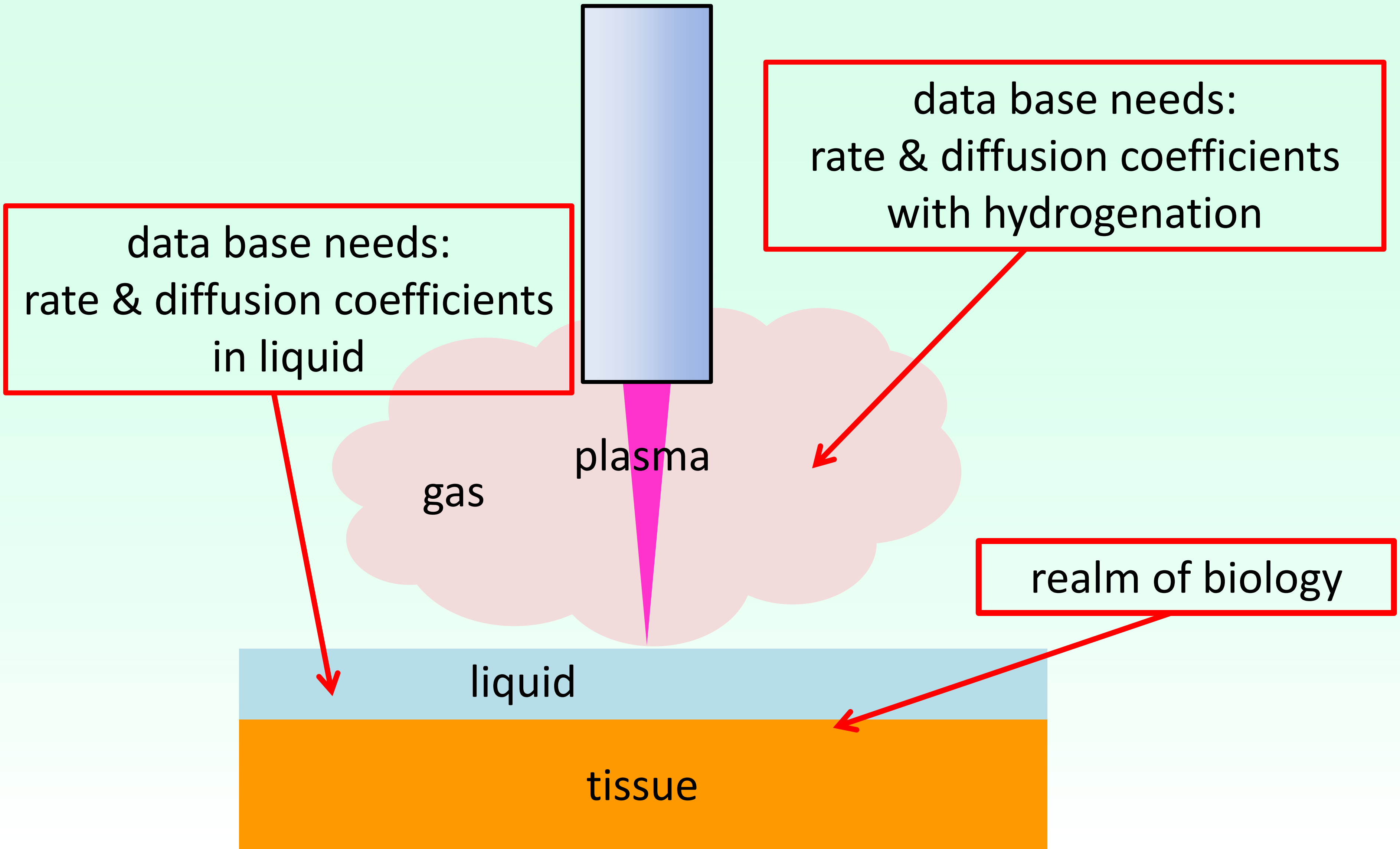
OH

$1.0 \times 10^{-1}\ mol \cdot L^{-1} \cdot s^{-1}$

NO

$7.6 \times 10^{-4}\ mol \cdot L^{-1} \cdot s^{-1}$

Summary


data base needs:
rate & diffusion coefficients
with hydrogenation
data base needs:
rate & diffusion coefficients
in liquid
plasma
gas
realm of biology
liquid
tissue