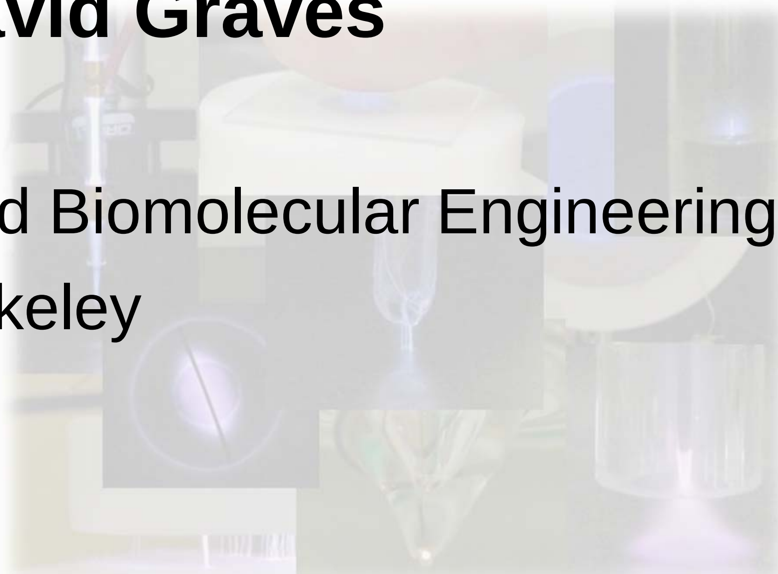
Atmospheric pressure gas plasmas for biomedical applications

Yuki Sakiyama and David Graves

Department of Chemical and Biomolecular Engineering
University of California, Berkeley



Outline

1. Overview of Plasma medicine

- Recent progress in *Plasma Medicine*
- Plasma sources for biomedicine
- Wound healing and cancer treatment
- ROS/RNS in gas plasmas and biomedicine

2. RF plasma needle – bacteria interaction

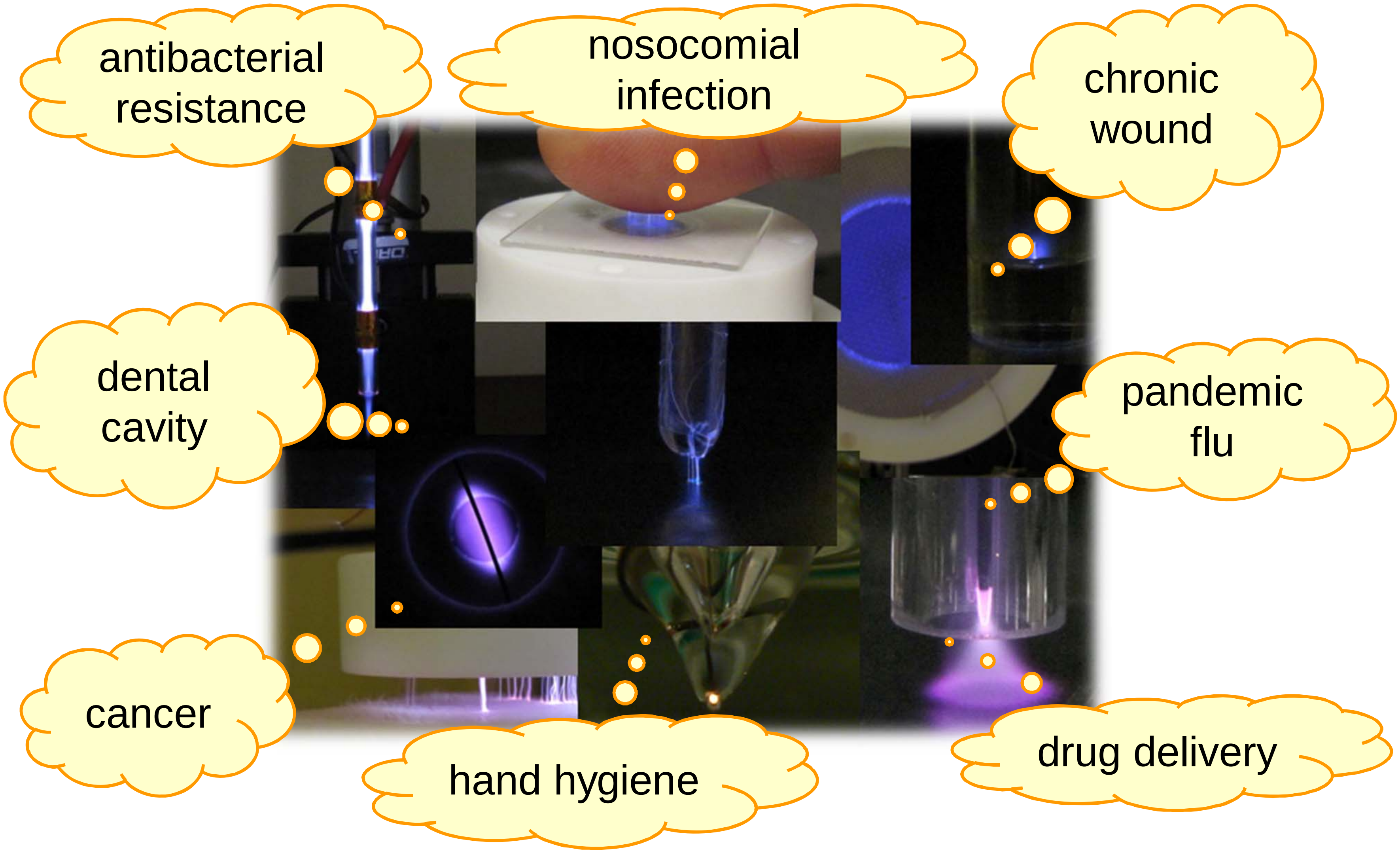
- Ring-shaped killing pattern
- Fluid model
- TALIF measurement

3. Concluding remarks

A brief history of gas plasmas in biomedicine

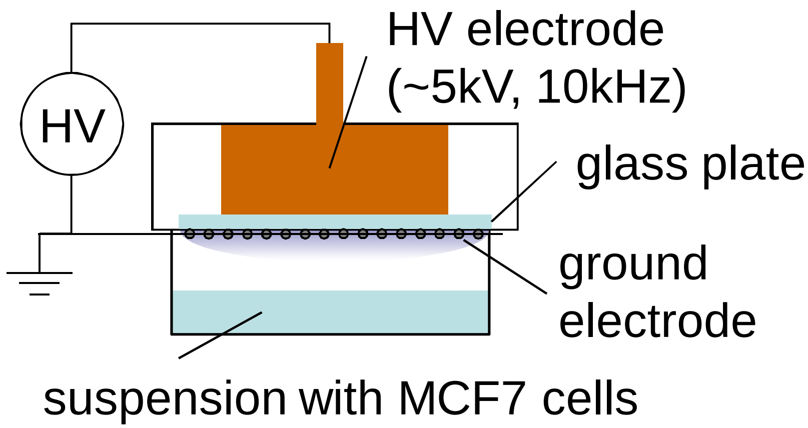
- 2010 G. Isbary: clinical trial for wound healing (MW Ar plasma)
- 2007 G. Fridman: *in vitro* cancer cell treatment (Air DBD)
- 2003 E. Stoffles: non-destructive cell handling (He plasma needle)
- 1999 M. Laroussi: E. coli sterilization (He DBD)
- 1995 APC (ERBE GmbH): Ar plasma for endoscopic surgery
  Coblation (Arthrocare Co): discharge in saline solution
- 1940 Hyfrecator (Birtcher Co): low power and no ground pad
- 1926 Bovie knife: the first clinical use of a electrosurgical device
- 1893 A. d’Arsonval: compatibility of HF with nerve and muscle

Potential applications

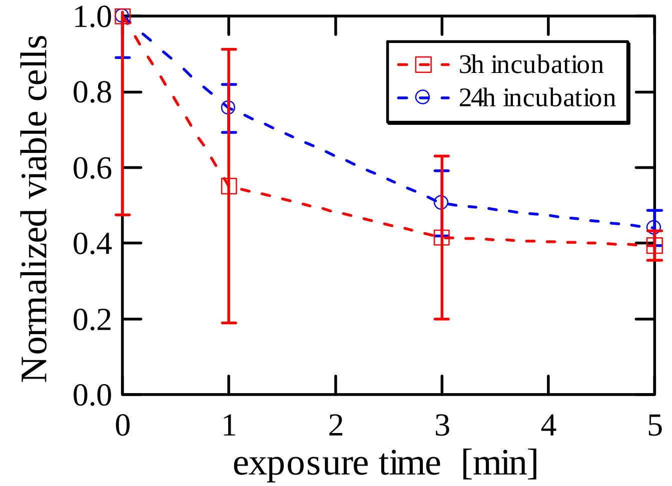


Cancer cell treatment

indirect-mode air DBD (*in vitro*)

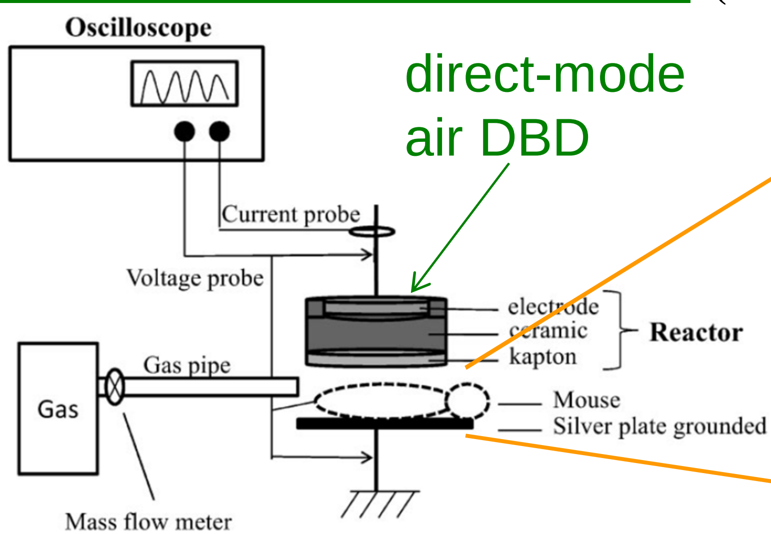


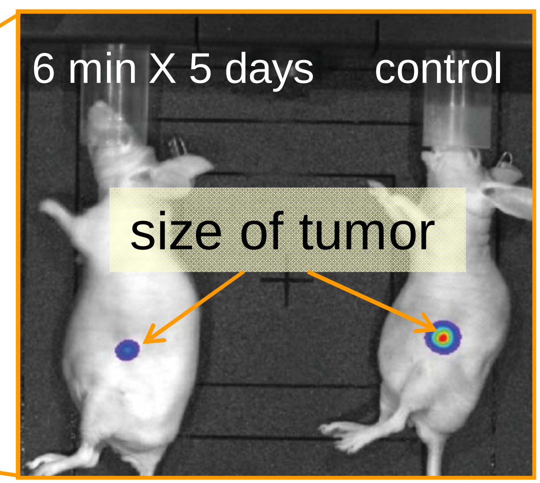
Trypan blue viability assay



(M. Vandamme, *Plasma Process. Polym.* **7** (2010) 264)

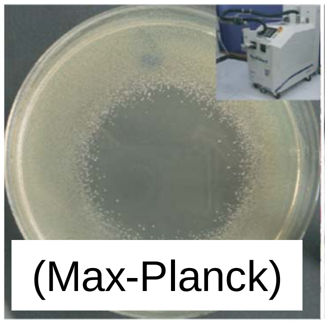
direct-mode air DBD (*in vivo*)

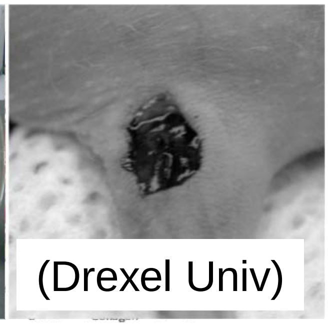


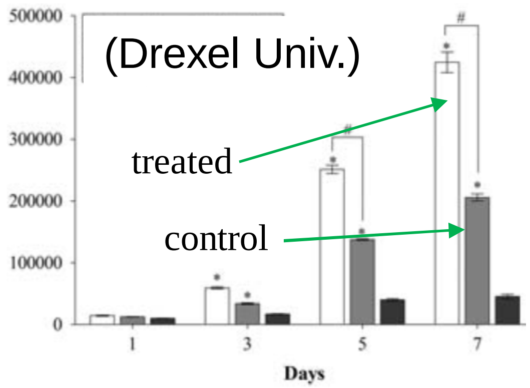


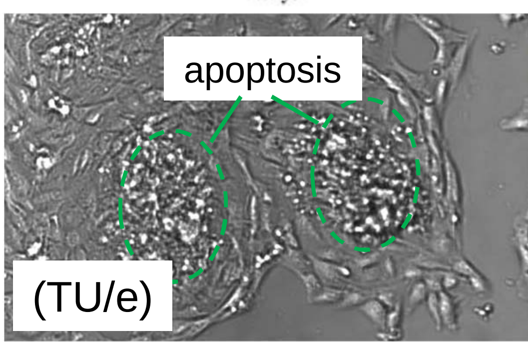
Wound healing: *in vitro* study

R. A. Bryant, et al., *Acute and Chronic Wounds* (Mosby, Missouri, 2006).
G. C. Gurtner., Nature **453** (2008) 314.









Inflammatory phase

- ~48 hours
- bacteria sterilization/debris removal
- blood coagulation

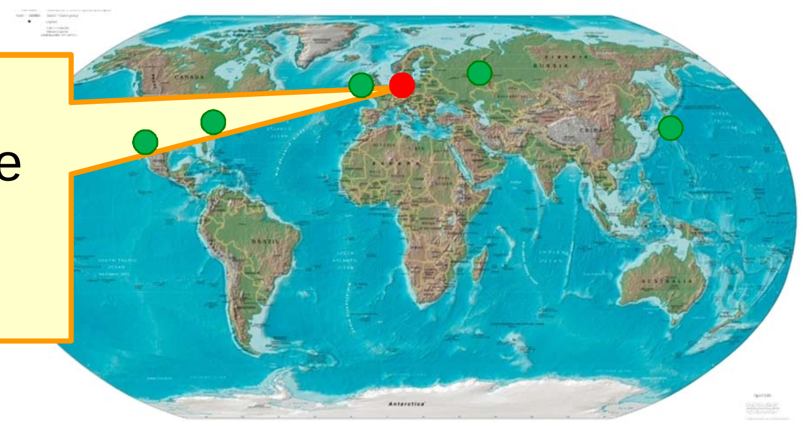
Proliferative phase

- 2~10 days
- blood vessels generation
- collagen deposition from fibroblasts

Remodeling phase

- 1 year
- tissue reorganization/realignment
- apoptosis of unnecessary cells

Wound healing: clinical study

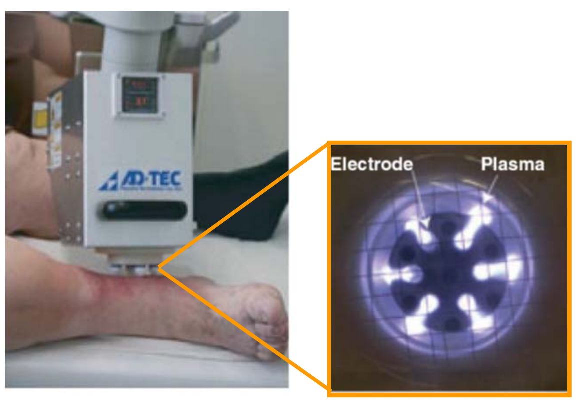


- *Plasma health care* project
- lead by G. Morfill at Max-Planck Institute
- 19 PhDs, 11 MDs
- Germany, UK, Russia, Japan, USA

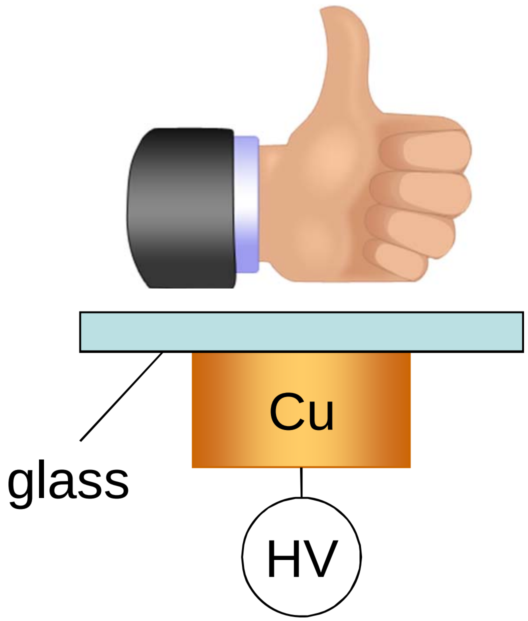
Phase-I clinical study

J. Heinlin, *JDDG* **8** (2010) 968, G. Isbary, Br. J. Dermatol. 163 (2010) 78

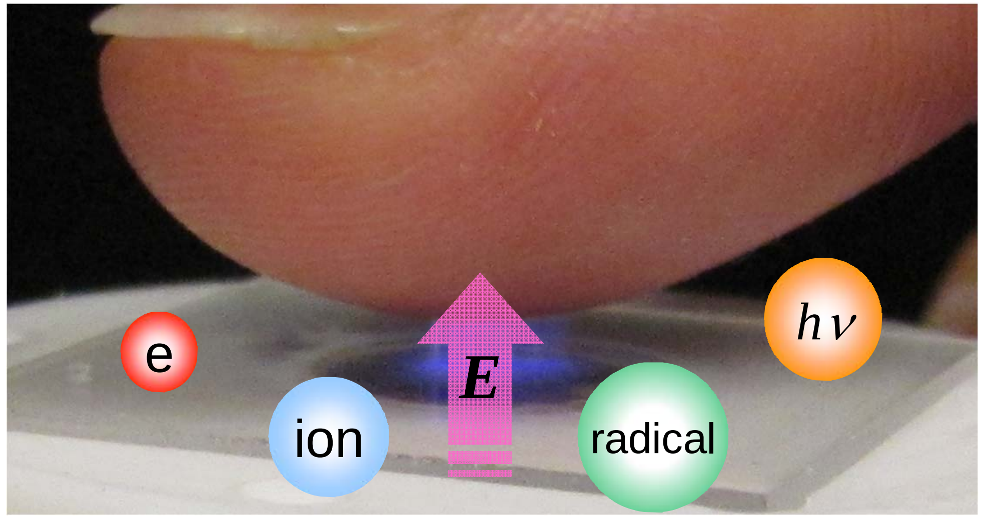
Microwave Ar plasma torch



Plasma-biomaterial interaction: possible agents (1)



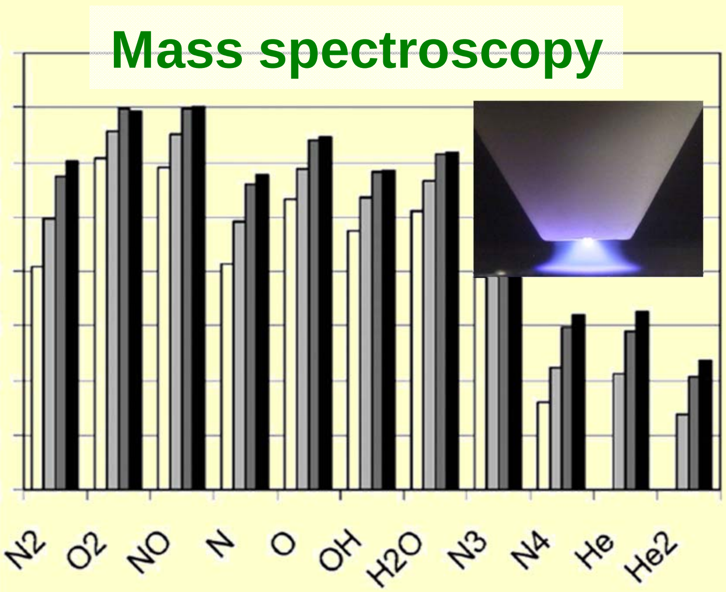
Plasmas in ambient air at room temperature



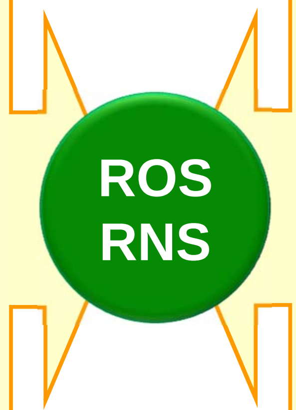
	physics	chemistry	electrostatic
effects	• DNA damage • etching • sputtering	• oxidation • signaling	• membrane disruption ($\sim 10^9$ V/m) • stimulation

Plasma-biomaterial interaction: ROS/RNS

- **ROS** (reactive oxygen species): O, O_2^*, O_3, O_2^-, OH, H_2O_2
- **RNS** (reactive nitrogen species): NO, NO_2, $ONOO^-$



E. Stoffels et al.,
IEEE Trans. Plasma Sci. **36** (2008) 1441.



D. Trachootham, *Nat Rev Drug Discovery* 8 (2009) 579.
M.A. Kohanski, *Cell* 130 (2007) 797.
Abbas, Celluar and Molecular Immunology (Elsevier, 2005).

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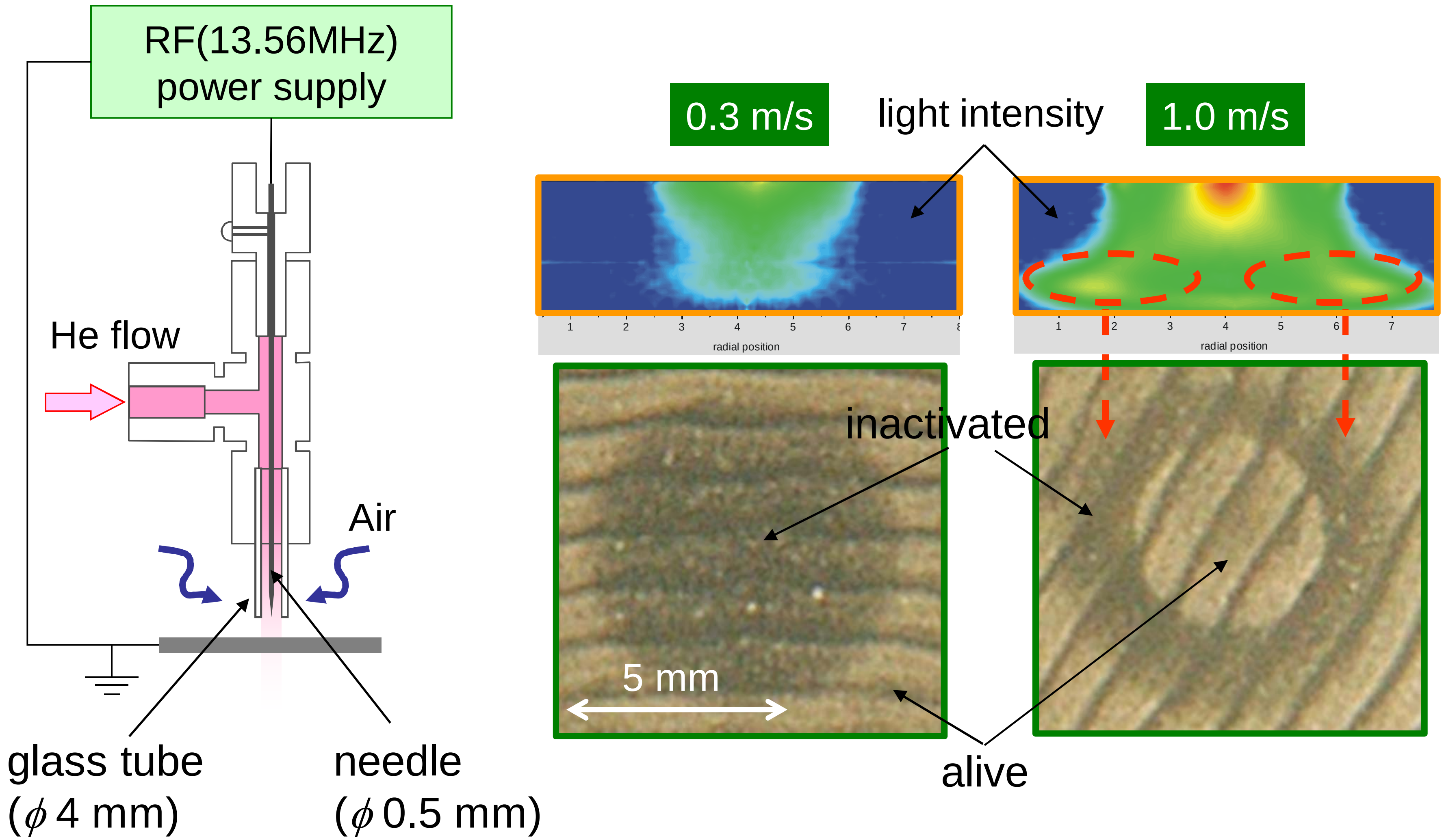
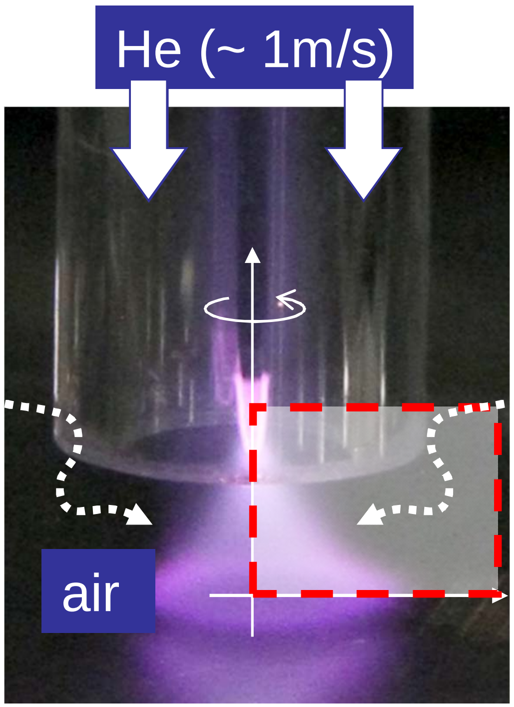
3. Concluding remarks

Plasma needle: observed killing pattern

J.Goree, et al, *J.Phys.D.* **39** 3479 (2006) and *IEEE Trans.Plasma Sci*. **34,** 1317 (2006)



Plasma needle: fluid model



Neutral Gas flow (He, Air)

$$\nabla\cdot(\rho\mathbf{u})=0,\nabla\cdot(\rho\omega_{\mathrm{air}}\mathbf{u}-\rho D\nabla\omega_{\mathrm{air}})=0 \qquad \text{(mass conservation)}$$

$$\nabla\cdot(\rho\mathbf{u}u_i)=-\nabla p-\nabla\cdot\overline{\overline{\boldsymbol{\tau}}}+\sum q_i n_i\mathbf{E} \qquad \text{(momentum conservation)}$$

$$\nabla\cdot(-\lambda\nabla T+\mathbf{u}c_{\mathrm{p}}T)=\Phi+\sum q_i\boldsymbol{\Gamma}_i\mathbf{E}+Q_{el} \qquad \text{(energy conservation)}$$

ion momentum
collisional heating

temperature
velocity
species density

Plasma dynamics

$$\frac{\partial n_i}{\partial t}+\nabla\cdot\boldsymbol{\Gamma}_i=S_i \qquad \text{(mass conservation)}$$

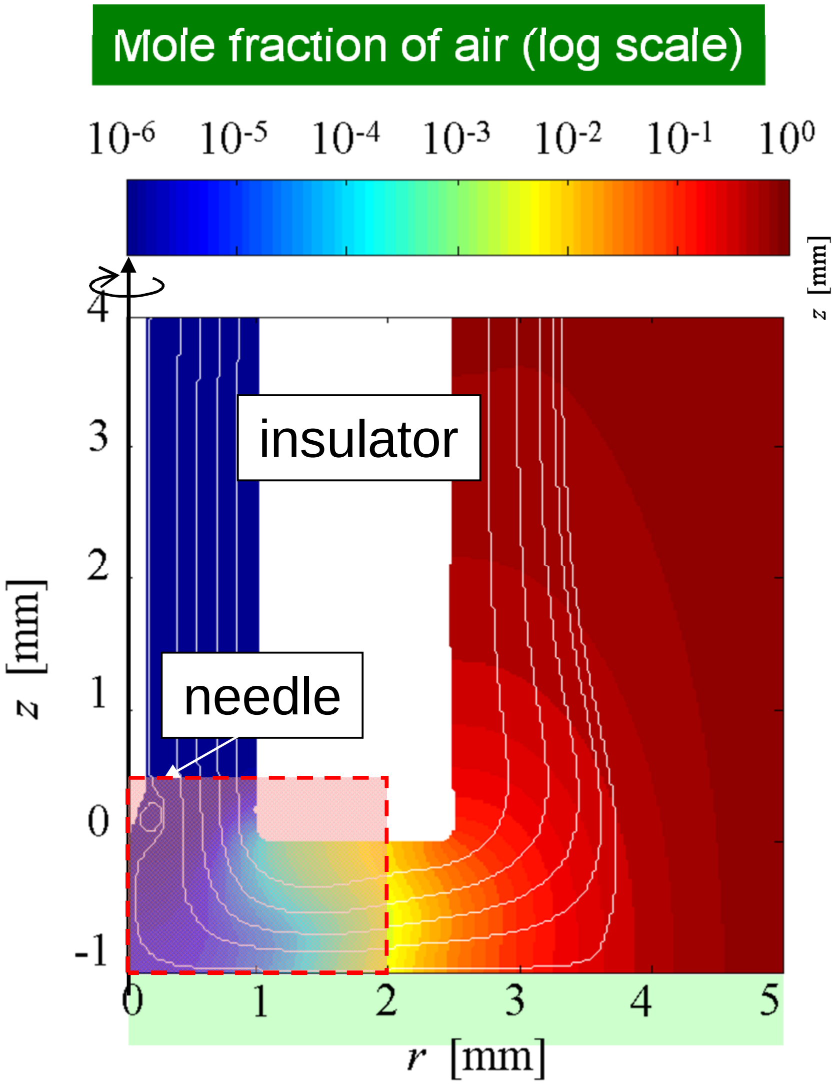
$$\boldsymbol{\Gamma}_i=\mathrm{sgn}(q_i)n_i\mu_i\mathbf{E}-D_i\nabla n_i+n_i\mathbf{u} \qquad \text{(drift-diffusion)}$$

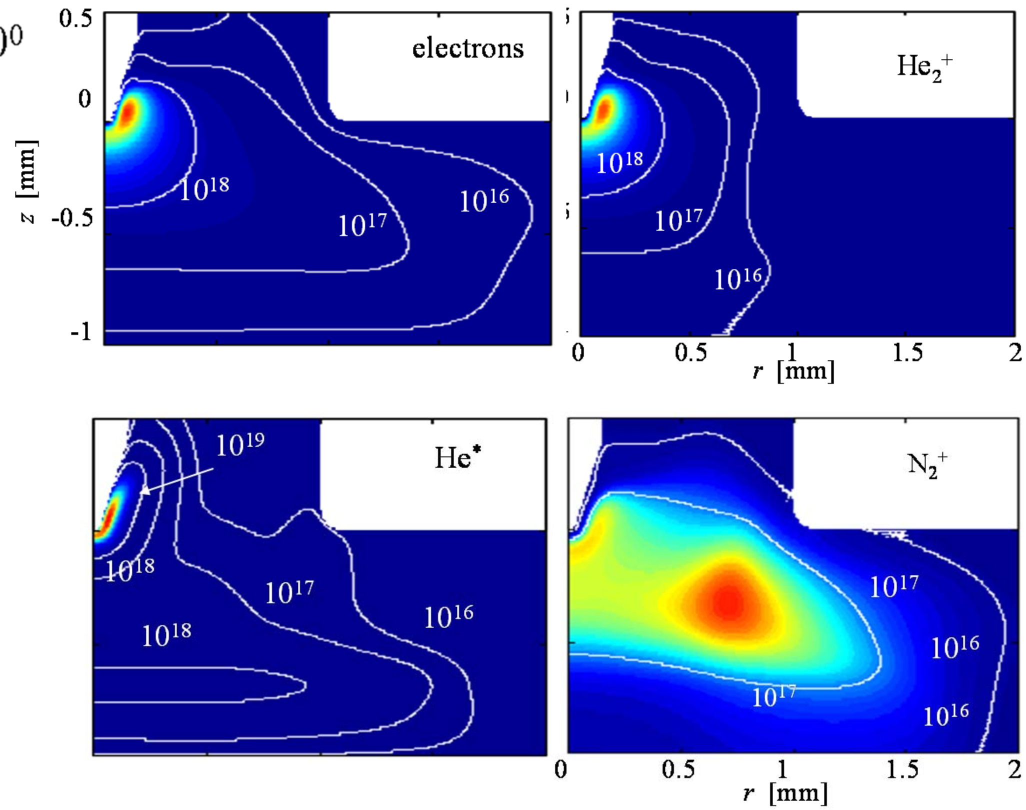
$$\frac{\partial(n_e\varepsilon)}{\partial t}+\nabla\cdot\left(\frac{5}{3}\varepsilon\boldsymbol{\Gamma}_e-\frac{5}{3}n_eD_e\nabla\varepsilon\right)=-\boldsymbol{\Gamma}_e\cdot\mathbf{E}-Q \qquad \text{(electron energy)}$$

$$\varepsilon_0\nabla\cdot\mathbf{E}=\sum q_i n_i \qquad \text{(Poisson's equation)}$$

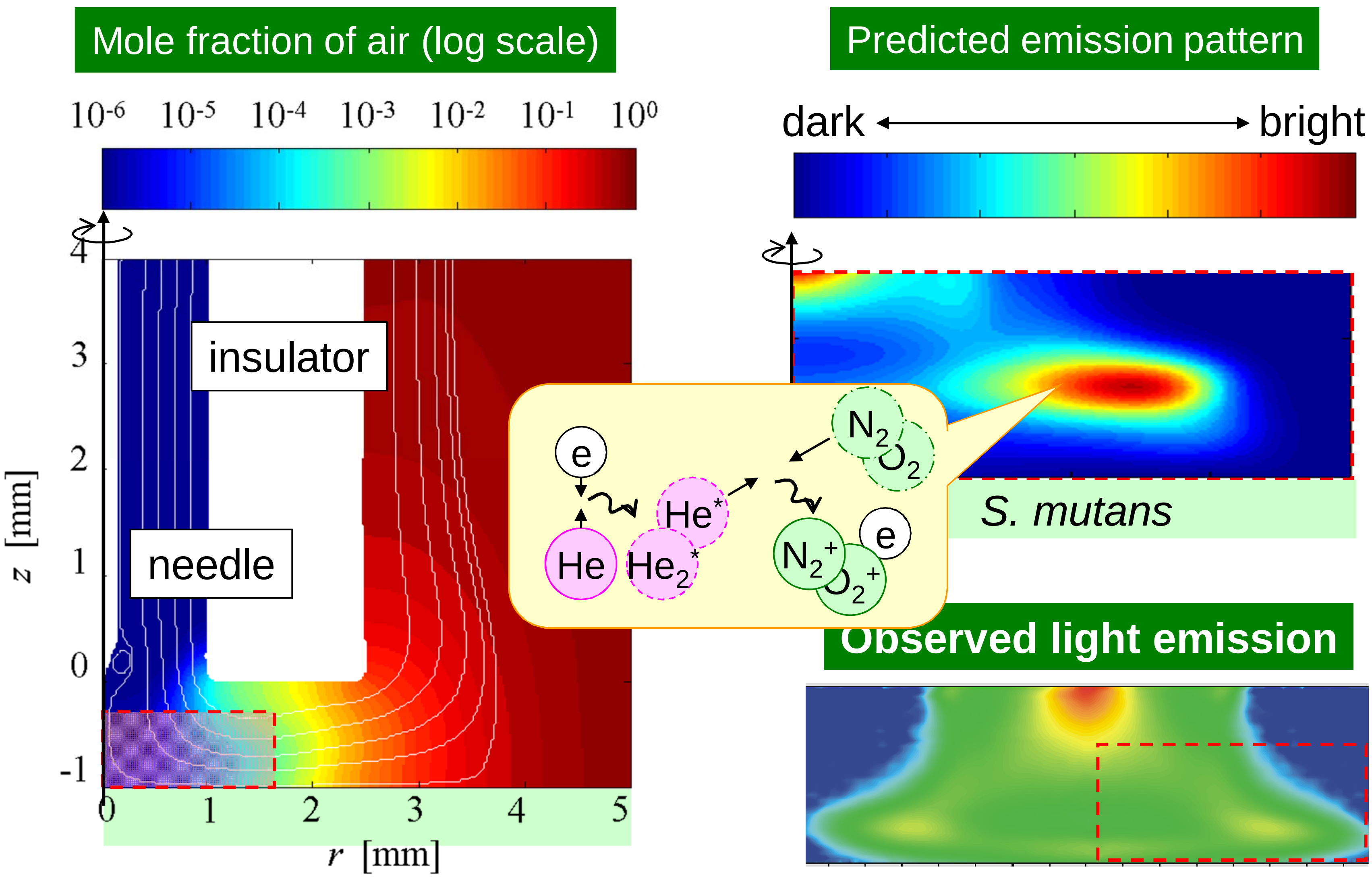
Y. Sakyiama et al, J. Appl. Phys. 101 (2007) 073306, J. Phys. D 41 (2008) 95204

Plasma needle: phase-averaged species density



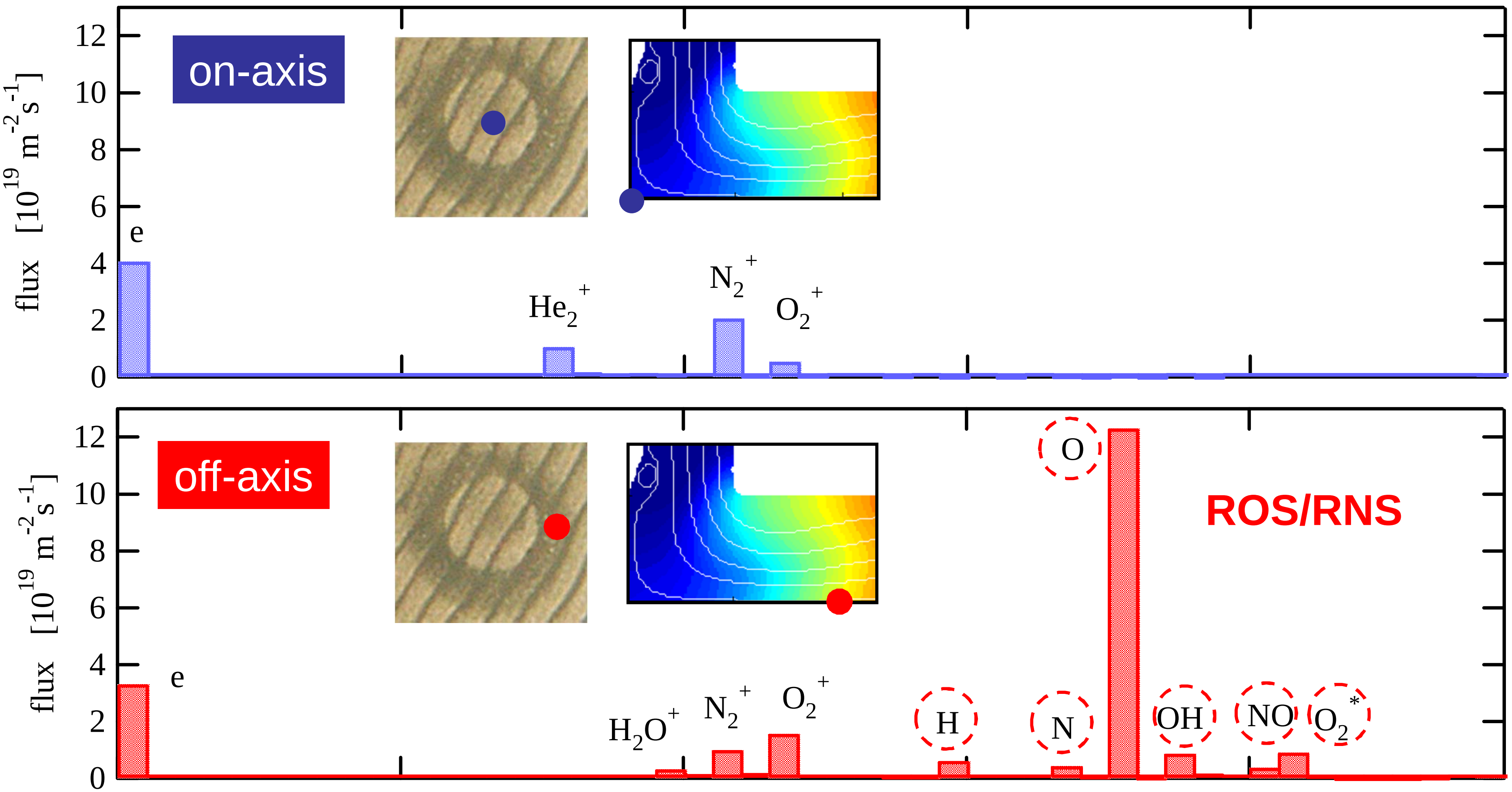


Plasma needle: reproduced ring-shaped emission



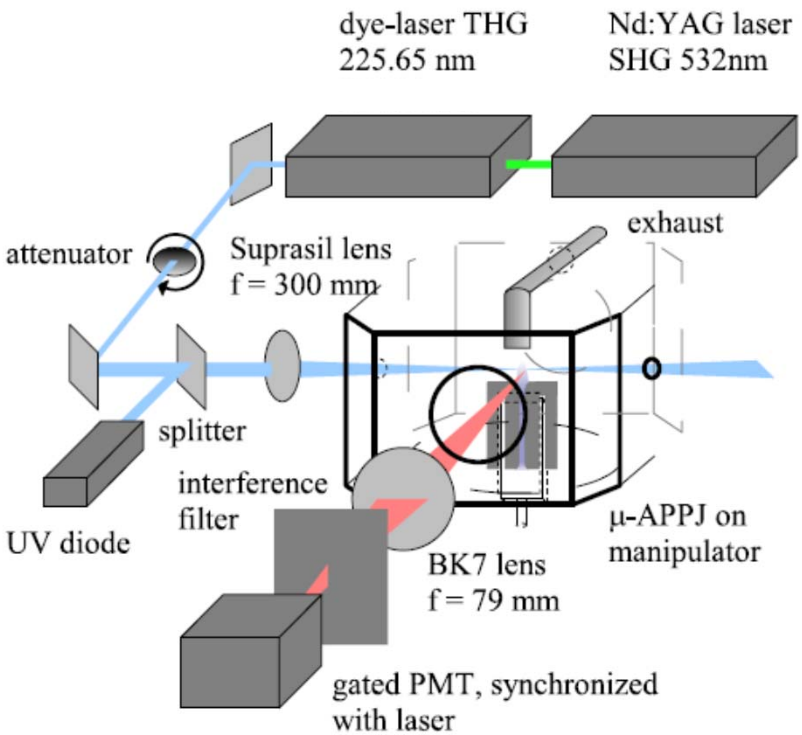
Y. Sakyiama et al, Plasma Sources Sci. Tchnol. 18 (2009) 025022

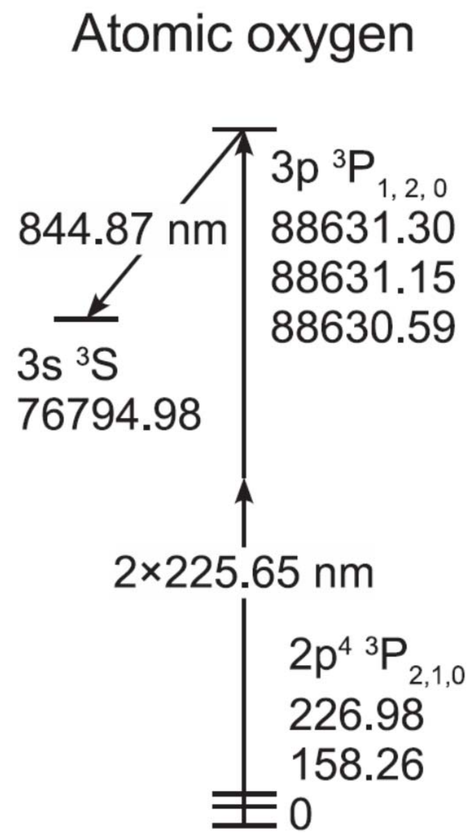
Plasma needle: flux onto bacteria



Model validation: O atom measurement

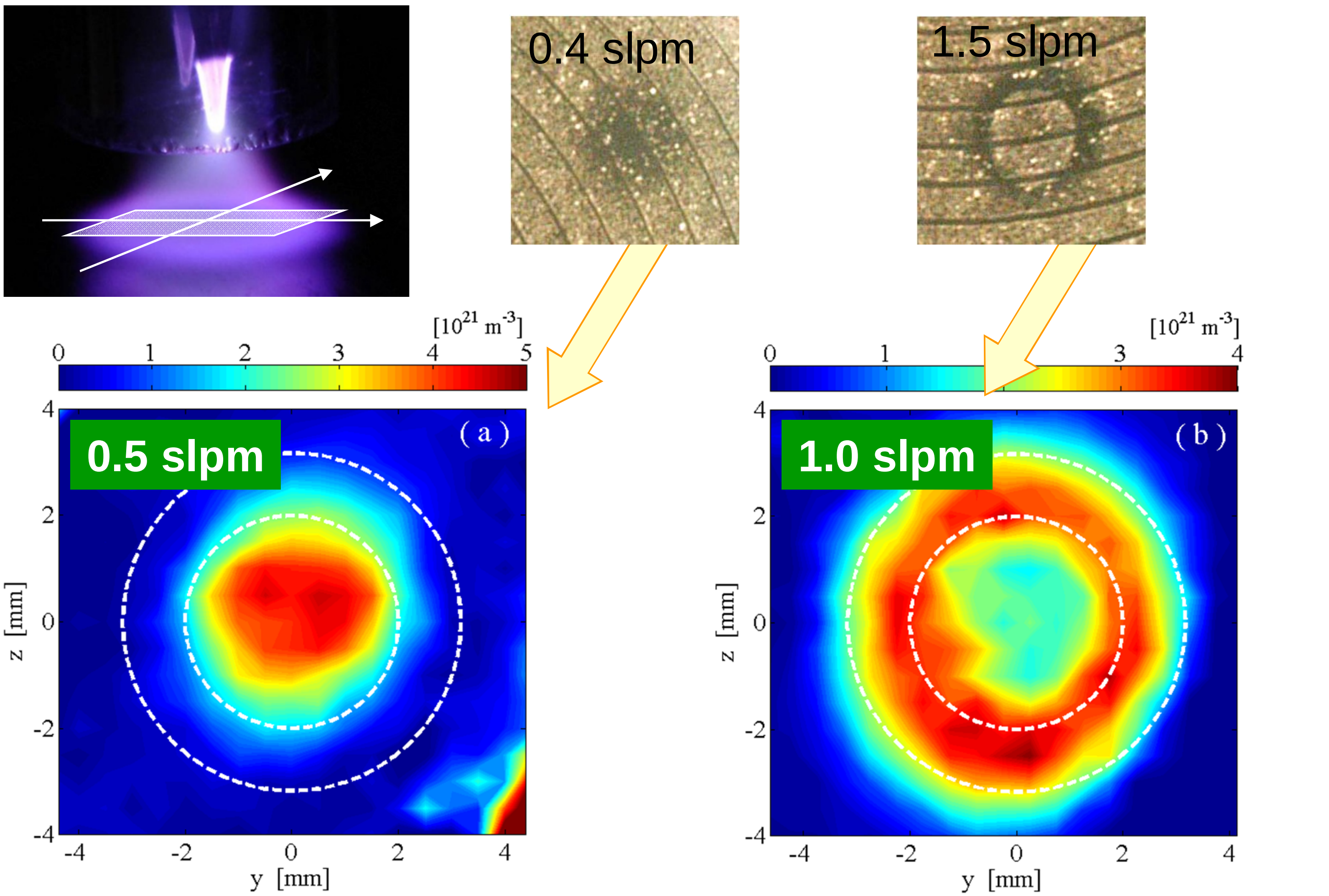
- **TALIF**: two photon absorbed laser induced fluorescence
- collaboration with Ruhr-Universitat Bochum (Germany)





N. Knake, et al, *J. Phys. D: Appl. Phys.* **41** (2008) 194006

Model validation: measured O atom density



Y. Sakiyama, et al., *Appl. Phys. Lett*. **97** (2010) 151501.

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Concluding Remarks

1. Plasma-generated ROS/RNS has enormous potential to open up a new field in biomedicine.

2. Neutral gas flow and air chemistry play significant roles in plasma medicine at atmospheric pressure.

3. Numerical modeling is a powerful tool to investigate plasma-biomaterial interaction and to understand the basic mechanisms of the interaction.

Acknowledgements

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Dr. J. Jarrige and Prof. M. Laroussi (Old Dominion University, US)

Prof. J. Goree (University of Iowa, US)

Dr. E. Stoffels

Related publications

Reviews for plasma medicine

M. Larrousi, *Plasma Process. Polym.* **2** (2005) 391.

G. Fridman, et al., *Plasma Process. Polym.* **5** (2008) 503.

E. Stoffels, et al., *IEEE Trans. Plasma Sci.* **36** (2008) 1441.

M. G. Kong, et al., *New Journal of Physics* **11** (2009) 115012.

Plasma-biomaterial interaction in Graves group

Y. Sakiyama and D. B. Graves, *J. Phys. D* **39** (2006) 3451.

Y. Sakiyama and D. B. Graves, *J. Phys. D* **39** (2006) 3644.

Y. Sakiyama and D. B. Graves, *J. Appl. Phys.* **101** (2007) 073306.

Y. Sakiyama and D. B. Graves, *IEEE Trans. Plasma Sci.* **35** (2007) 1279.

Y. Sakiyama, et al., *J. Phys. D* **41** (2008) 95204.

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Y. Sakiyama, et al., *Appl. Phys. Lett.* **97** (2010) 151501.