INP FROM IDEA TO PROTOTYPE

PHYSICAL APPLICATIONS IN LIFE SCIENCE

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Leibniz Institute for Plasma Science and Technology (INP), Greifswald, GERMANY

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SPIG 2020

NATIONALES ZENTRUM FÜR PLASMAMEDIZIN

INTERNATIONAL SOCIETY FOR PLASMA MEDICINE

LEIBNIZ HEALTH TECHNOLOGIES

Leibniz Association

FROM IDEA TO PROTOTYPE

PHYSICAL APPLICATIONS IN LIFE SCIENCE

- Physical applications are today‘s reality in nearly all fields of LIFE SCIENCE
- LIFE SCIENCE means biology, medicine, biomedicine, pharmacy, biochemistry, chemistry, molecular biology, biophysics, bioinformatics, human biology, agricultural technology, nutritional science, food research, and also scientific research on biogenic natural resources and on biodiversity…
- Today: Focus on **PLASMA Physical Applications** (Hygiene, Medicine, Agricuture)

Atmospheric pressure plasmas – “tool box“

Non-Thermal (NT) Plasmas		Thermal Plasmas
“Cold“ Non-Thermal Plasmas	Translational (“Hot NT“) Plasmas	
$T_i \approx T_g \approx 300 \ldots 400$ K $T_i << T_e < 10^5$ K (10 eV)	$T_i << T_e \leq 10^4 \ldots 10^5$ K $T_i \approx T_g \leq 4\ 10^3$ K	$T_i \approx T_g \approx T_e$ $T_x < 5\ 10^3 \ldots 10^4$ K

[1] Barrier discharges

[2] Coronas

[3] Microplasmas-Arrays

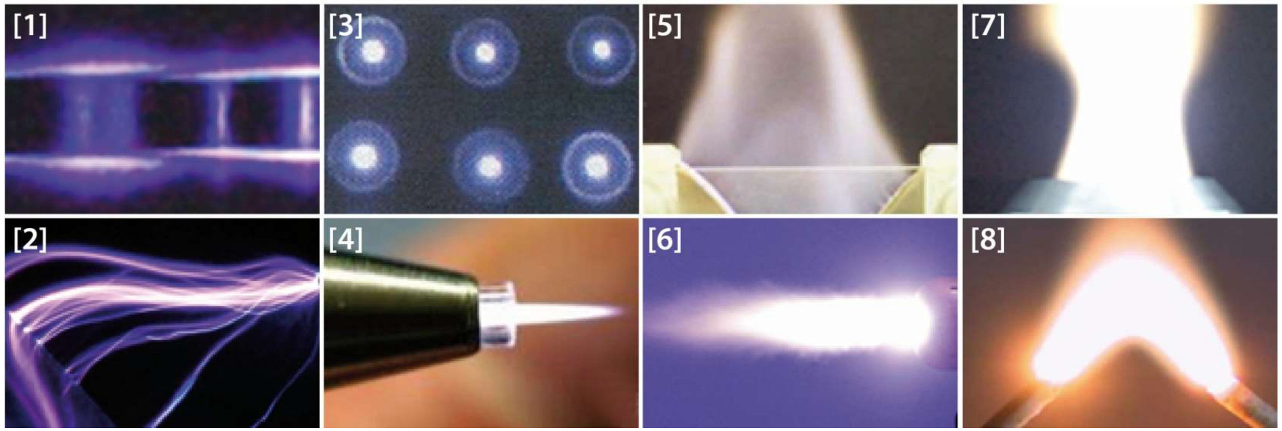
[4] Plasma jets

[5] Gliding Arc

[6] Arc jet

[7] Plasma Torch

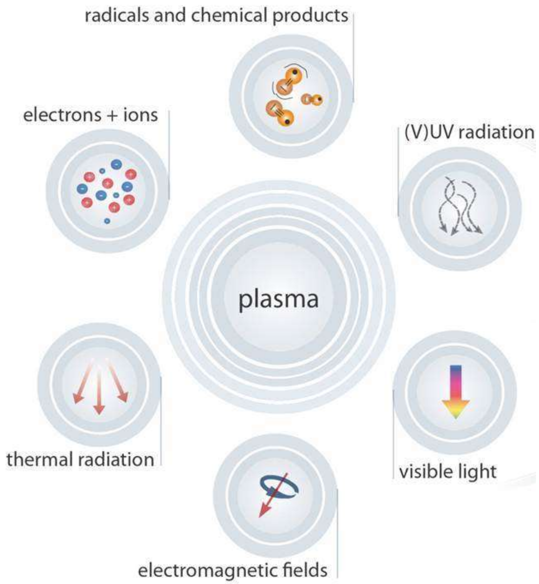
[8] Arc



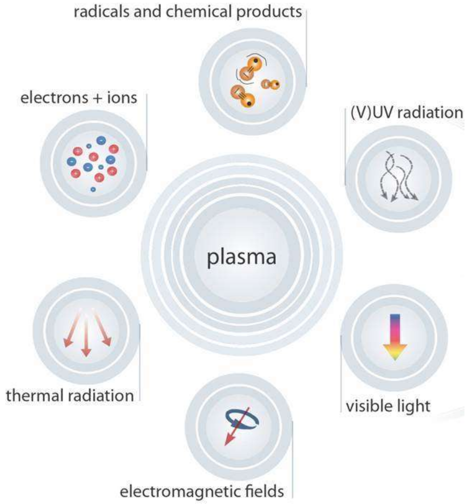
K.-D. Weltmann & Th. von Woedtke, Eur. Phys. J. Appl. Phys. 55 (2011) 13807

Atmospheric pressure plasma generation

1. Ionization and excitation of atoms or molecules of a **gas** (Ar, He, O_2, N_2, air, or mixtures thereof) by supplying (electrical) energy
2. Interaction of ionized atoms/molecules and electrons with other atoms or molecules both in the plasma phase and in neighbouring media (atmospheric air, liquids, surfaces) resulting in **generation of reactive species**
3. Emission of electromagnetic **radiation** (UV/VUV, visible light, IR/heat, electric fields) as additional result of ionization and excitation processes



Atmospheric pressure plasmas



Chemical reactivity:

- Initiation of **chemical reactions at low temperatures** and **without additional catalysts**

Biological effects:

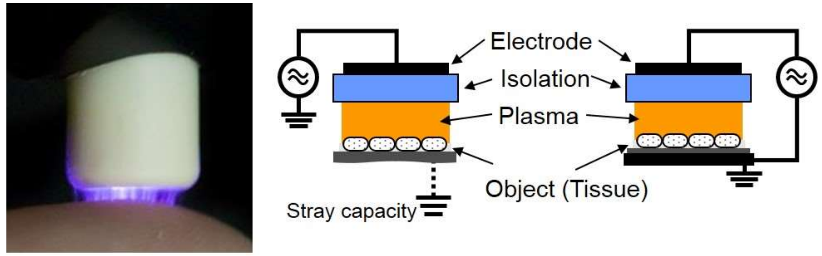
- **Inactivation of** a broad spectrum of **microorganisms** including multidrug resistant ones
- **Stimulation of cell proliferation** and angiogenesis, promotion of tissue regeneration and wound healing
- **Inactivation of cells** by initialization of programmed cell death above all in cancer cells

Atmospheric pressure plasmas

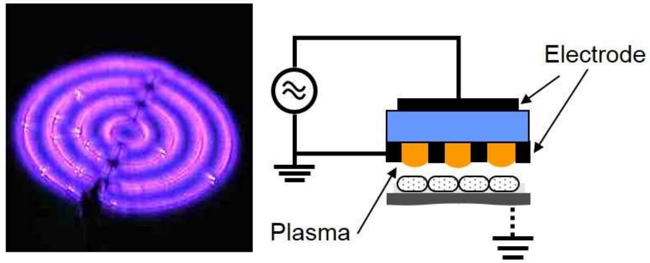
Two basic principles predominatly used in biomedicine

Dielectric barrier discharge (DBD)

Volume dielectric barrier discharge (DBD)

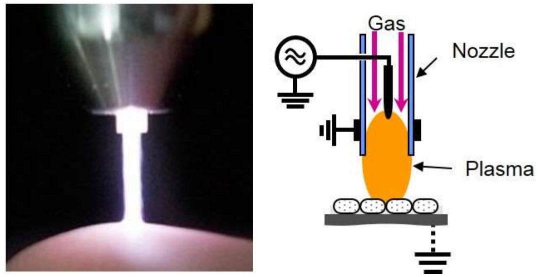


Surface dielectric barrier discharge (DBD)



Jet plasma, Plasmajet

Plasma jet



K.-D. Weltmann, H.-R. Metelmann, Th. von Woedtke, Europhysics News (EPN) 47 No 5-6 (2016) 39-42

Decontamination (Hygiene)

Medicine (Plasma)

Agriculture

Biodecontamination/-sterilization: terms and definitions

Decontamination

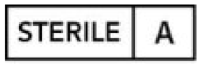
- **Removal of dangerous contaminations**
- **CBNR (Chemical, Biological, Radiological, Nuclear)**
  → includes prions, pyrogens, viruses, chemical contaminations etc.

Disinfection

- *"To put dead or living material in a situation, that it is not longer able to contaminate" (DAB)*
- Practical advise: reduction of micro organisms by at least a factor of 10^5

Sterilization

- *"Sterility is the absence of viable microorganisms."* (Ph. Eur. 5.00/5.1.1.)
- Sterility Assurance Level SAL= 10^{-6} (Ph. Eur. 1997),
- Practical advise: reduction of 6 lg-steps (RKI 1997)



Aseptic/antiseptic

- To keep/inactivate pathogenic microorganisms to prevent infections
- Antiseptic: correlated to lesions
- Aseptic: correlated to objects/products

First investigations with the aim to reduce infections: R. Koch (1881)

Robert Koch (1843–1910)

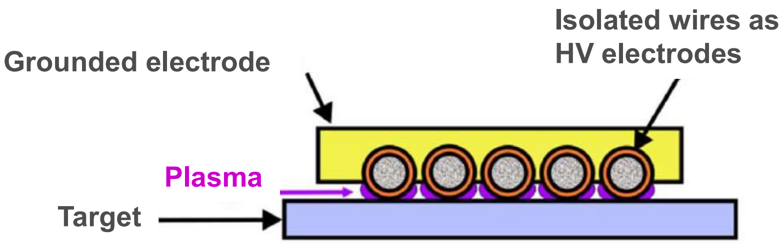
Societal challenge: Nosocomial infections

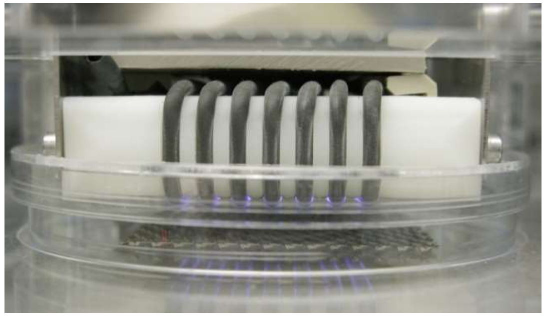
Contaminated surfaces increase cross-transmission:

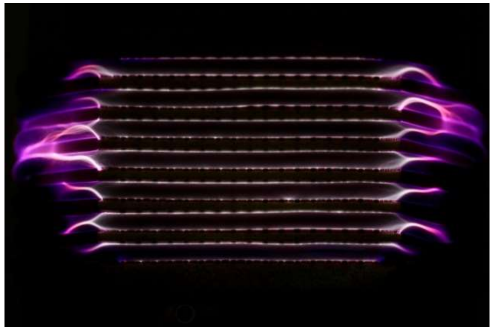
https://commons.wikimedia.org/wiki/File:Contaminated_surfaces_increase_cross-transmission.jpg

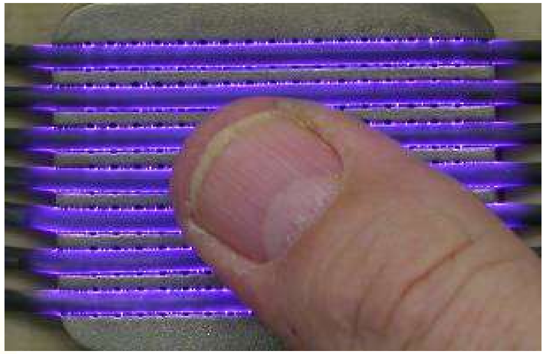
Ideas/prototypes (INP)

Large area treatment: surface-DBD







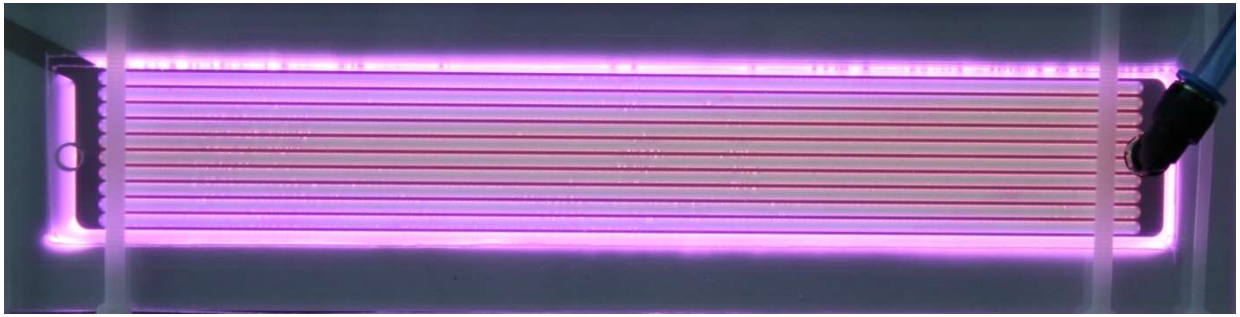


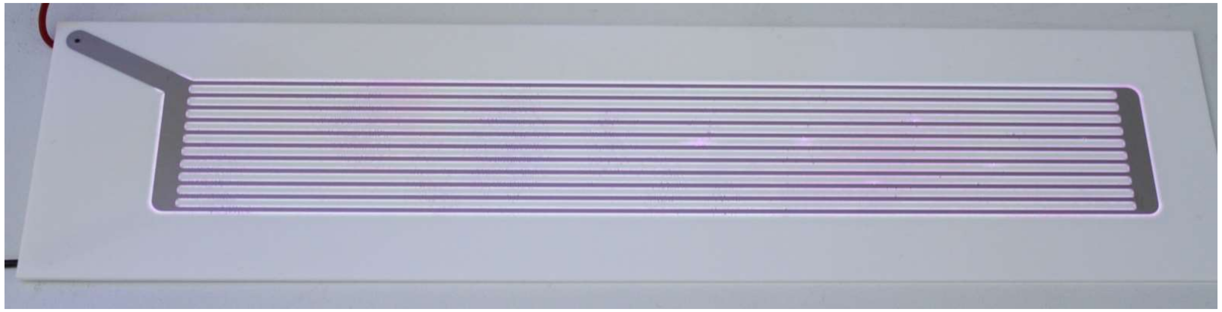
ConPlas: contacted plasma

Weltmann et al., Contrib. Plasma Phys. 49 (2009) 631-640; Weltmann et al., Pure Appl. Chem. 82 (2010) 1223-1237;
Weltmann & von Woedtke, Eur. Phys. J. Appl. Phys. 55 (2011) 13807; Weltmann et al., Contrib. Plasma Phys. 52 (2012) 644-654;
Weltmann et al., IEEE Trans. Plasma Sci. 40 (2012) 2963-2969

Ideas/prototypes, coplanar DBD: CeramTec-Version

➔ large active area treatment : 30mm x 200mm

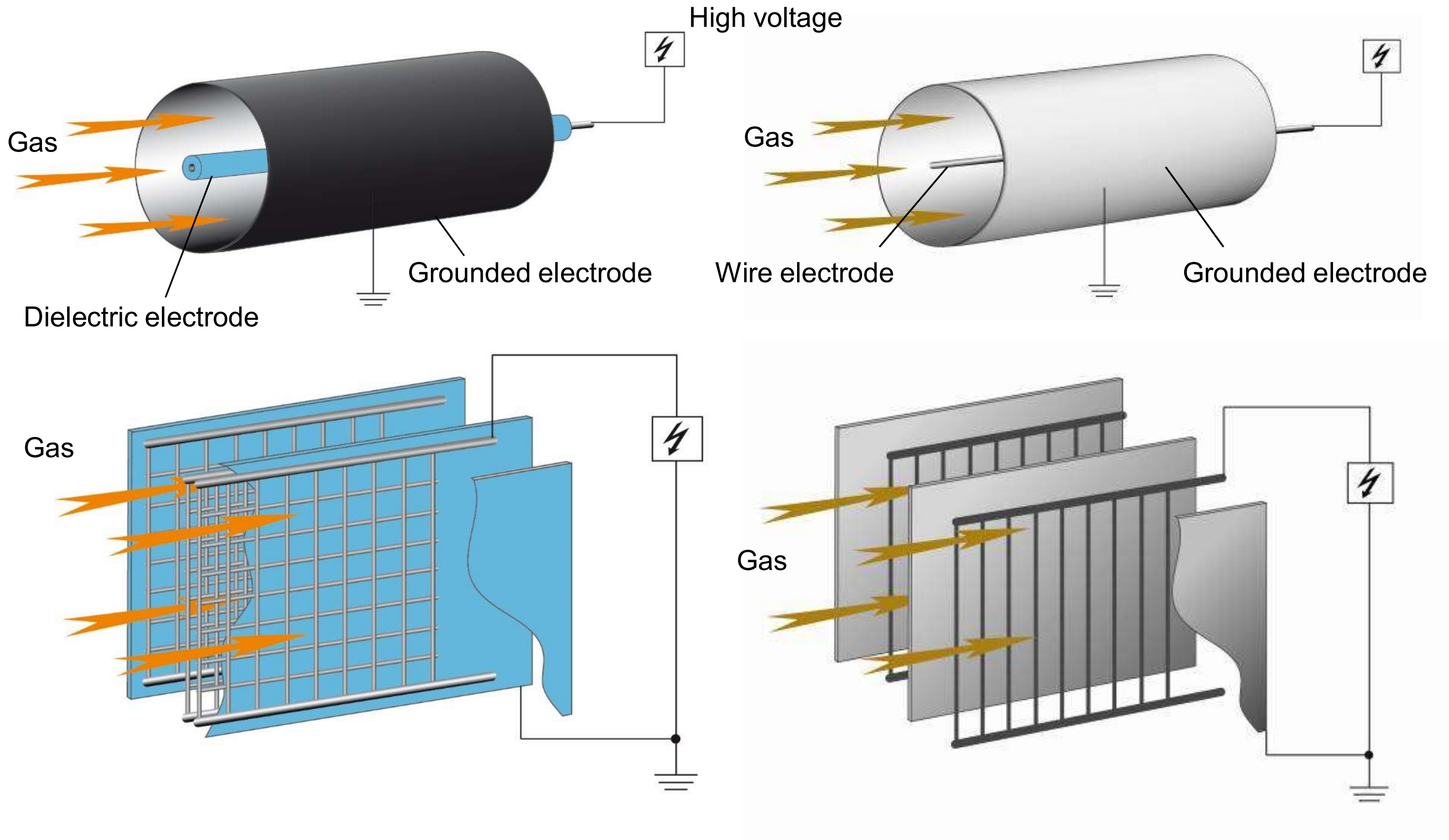




Plasma-based treatment of gas streams

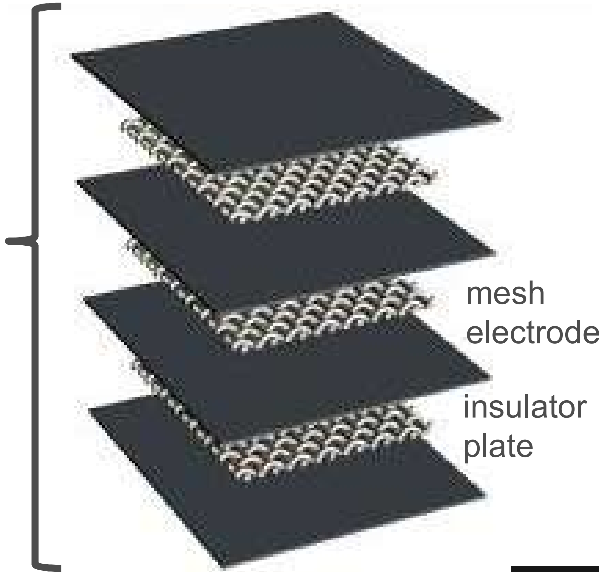
Barrier discharge

Corona discharge



Mobile plasma reactor for gas/air treatment

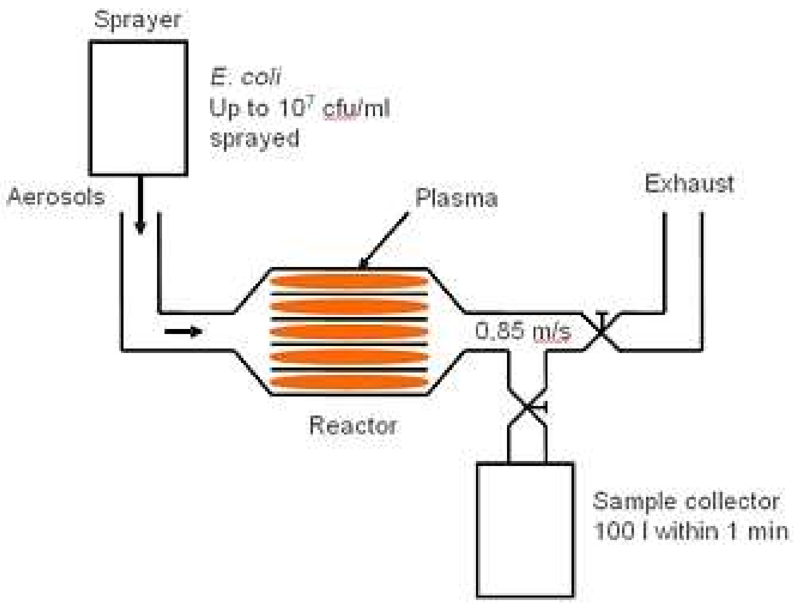
- gas stream up to 1.000 Nm^3/h
- combination with different adsorbents/catalysts
- mobile analytics included

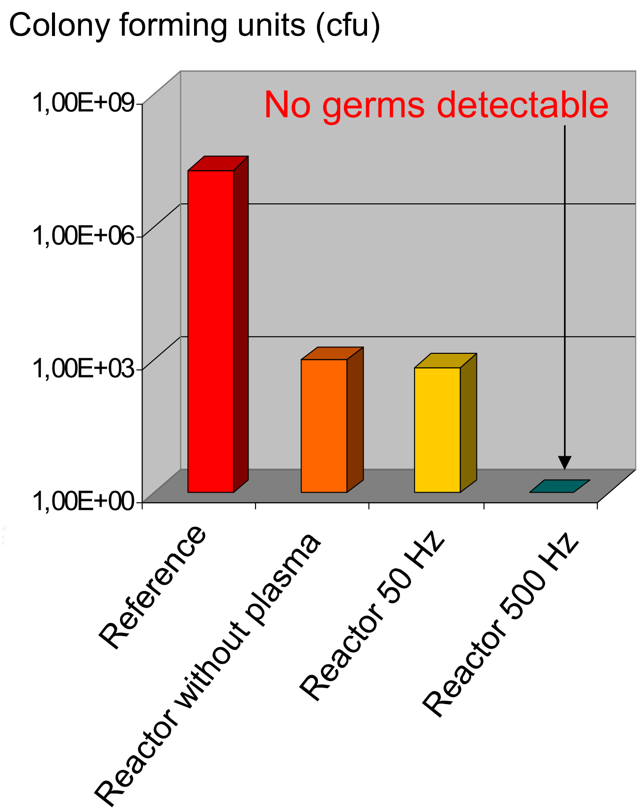


Baltic Sea Region
Programme 2007–2013

Biological decontamination by means of aerosols

Elimination of coli bacteria with DBD stack reactor:





S. Müller, R.-J. Zahn; INP Greifswald

Societal challenge: Water pollution

Drugs on tap

John Naish

1st May 2009

Tweet 8+1 0 Like 52

Taking a pill for a headache may seem like the most natural thing in the world, but prescription drugs are forcing their way into every corner of our lives and environment, says John Naish

> "Big marketing budgets pay dividends when one drug in four sold by pharmacists is a painkiller"

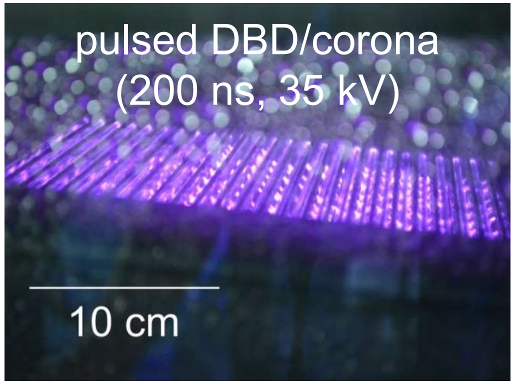
This article was updated on 16th October 2009, following a notification of an inaccuracy.

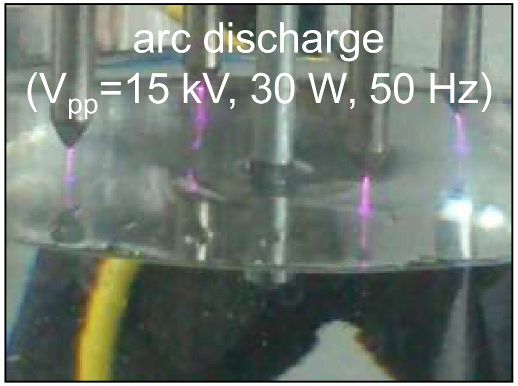
Britain has a serious and unnecessary drug habit, but the implications of our pill-for-every-ill culture go far beyond the adverse effects on human health. The complex chemicals in modern pharmaceuticals, as well as the manufacturing processes involved, leave a massive industrial footprint on the natural world that is largely ignored by both science and government.

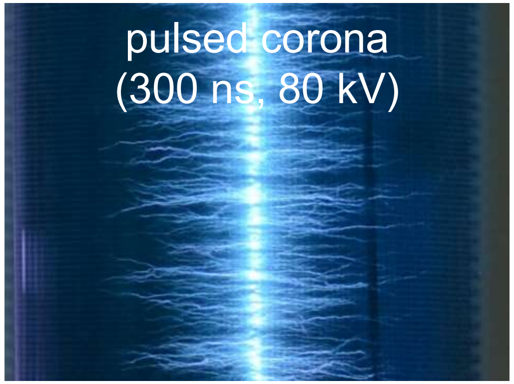
www.theecologist.org/trial_investigations/268166/drugs_on_tap.html

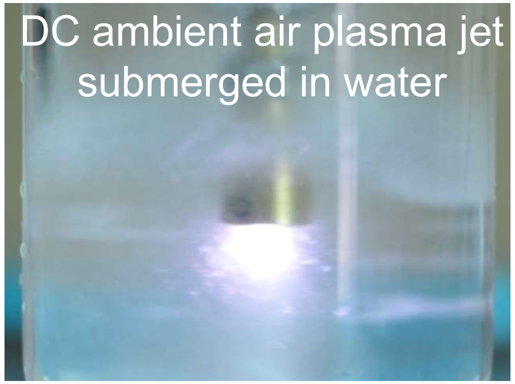
Discharges Close to, Above or in Water

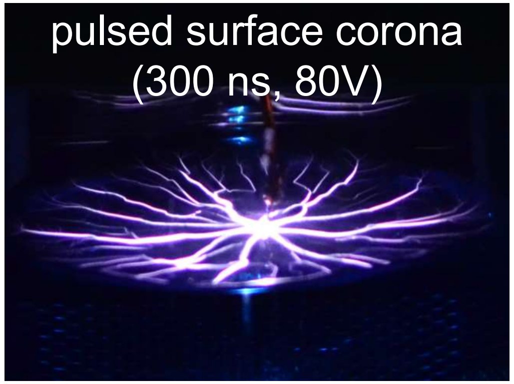
High voltages (AC, pulsed DC) are applied to dedicated electrode geometries to provide intense electric fields and/or ‘cold‘ physical plasmas:

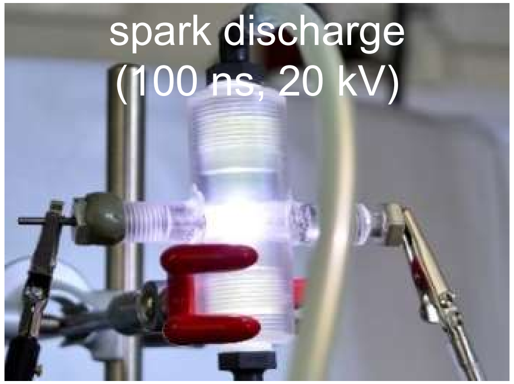






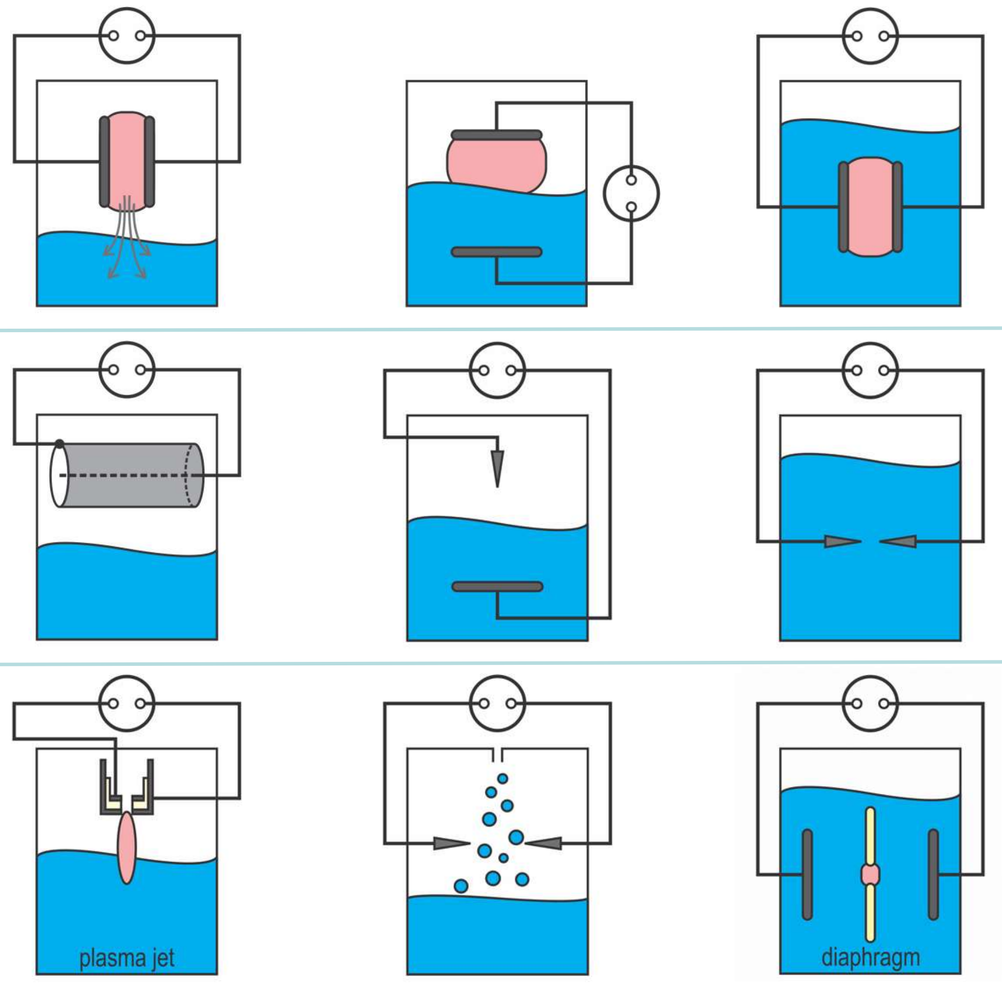






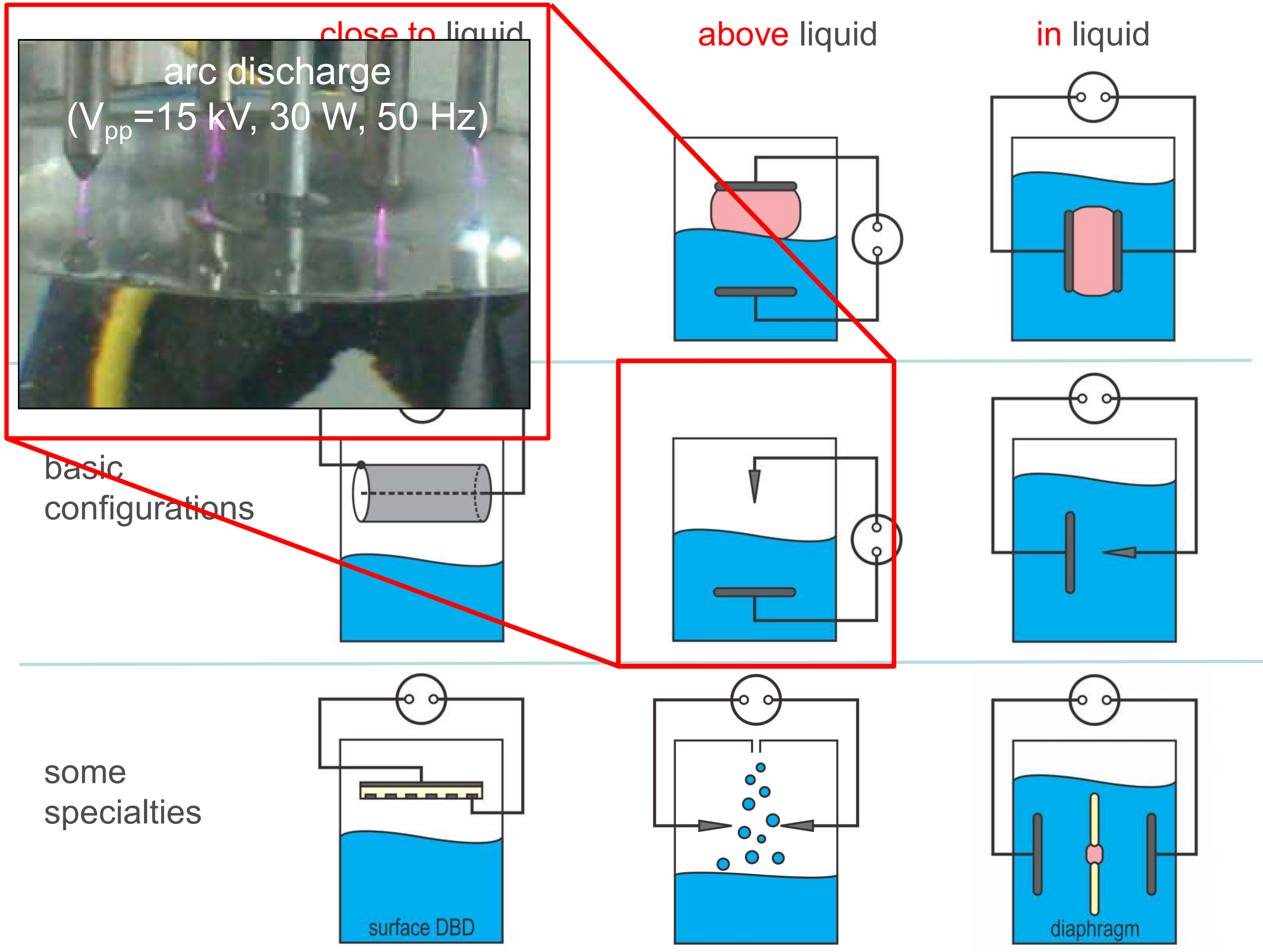
Electrical Discharges with and in Liquids

	close to liquid	above liquid	in liquid
principles			
some basic configurations			
some variations			



P.J. Bruggeman et al., "Plasma-liquid interactions: a review and roadmap," Plasma Sources Sci. Technol. 25 (2016) 053002.

Electrical Discharges with and in Liquids



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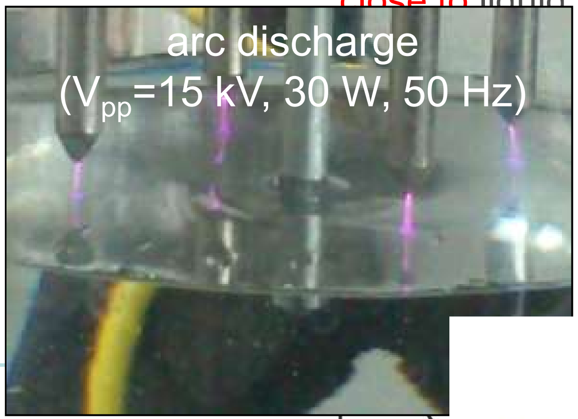
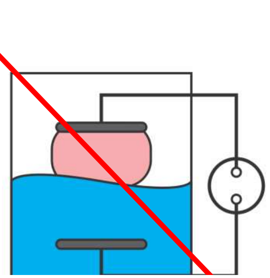
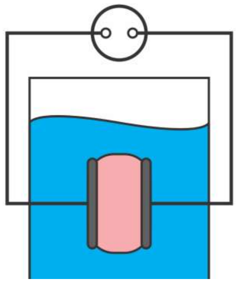
close to liquid



above liquid

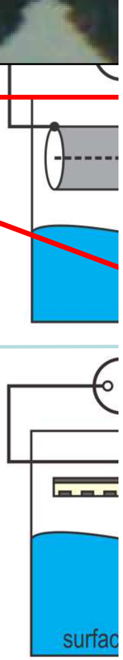


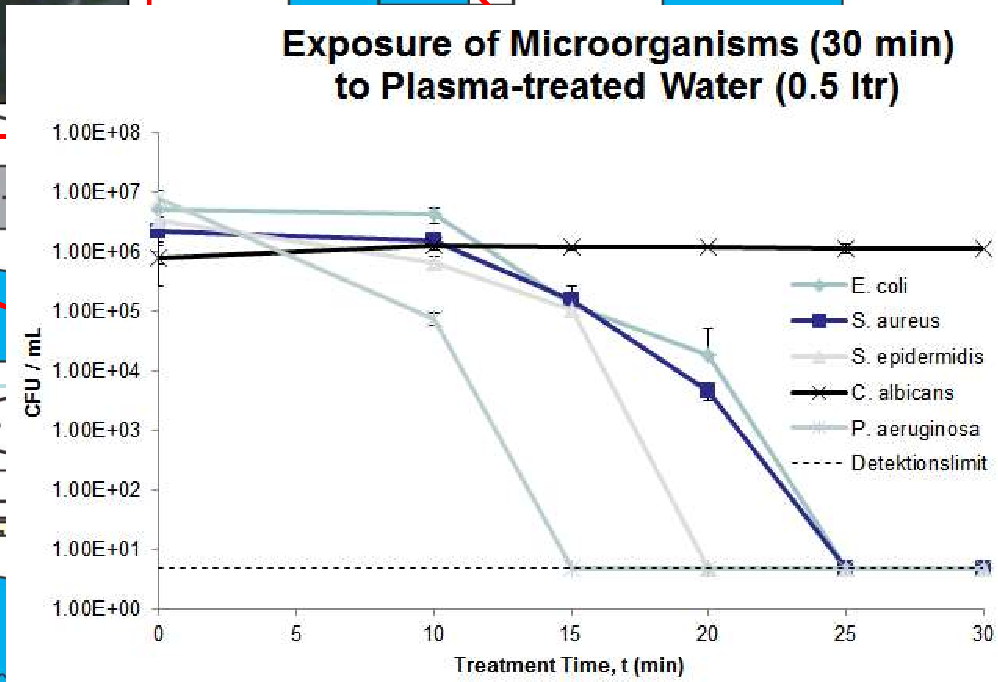
in liquid



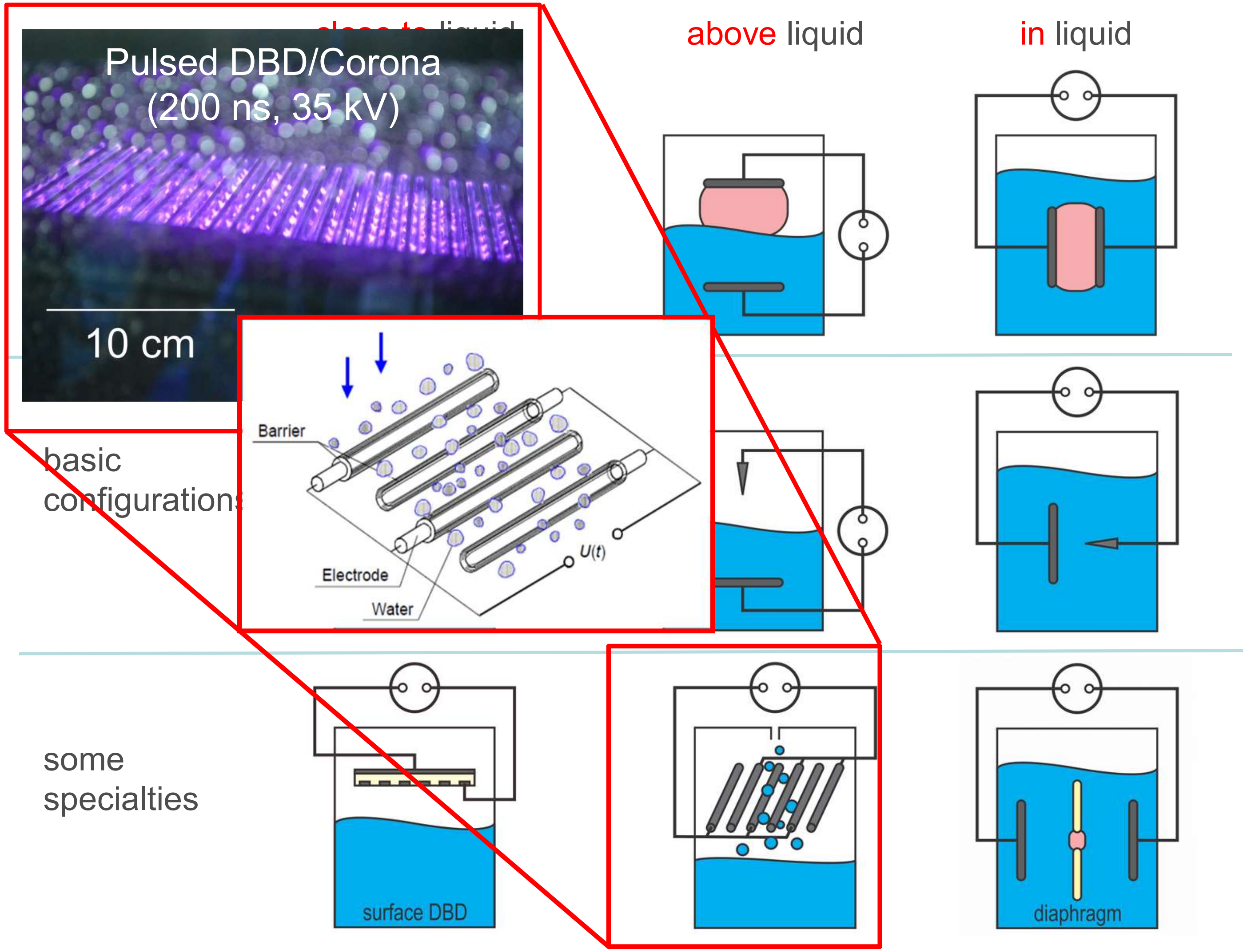
basic configurations

some specialties





Electrical Discharges with and in Liquids



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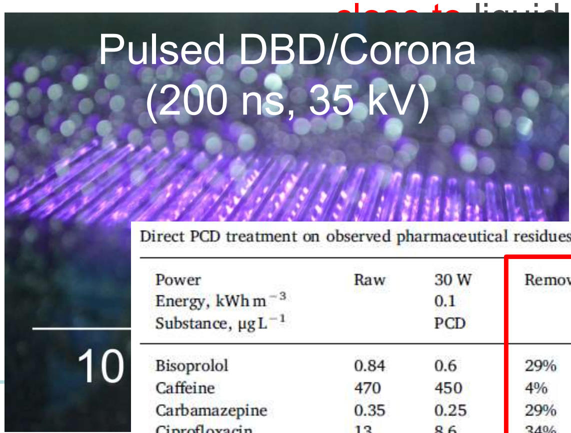
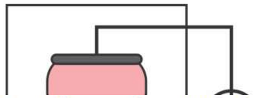
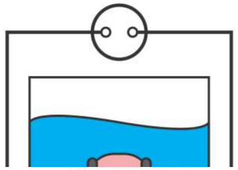


above liquid



in liquid



10

basic
config

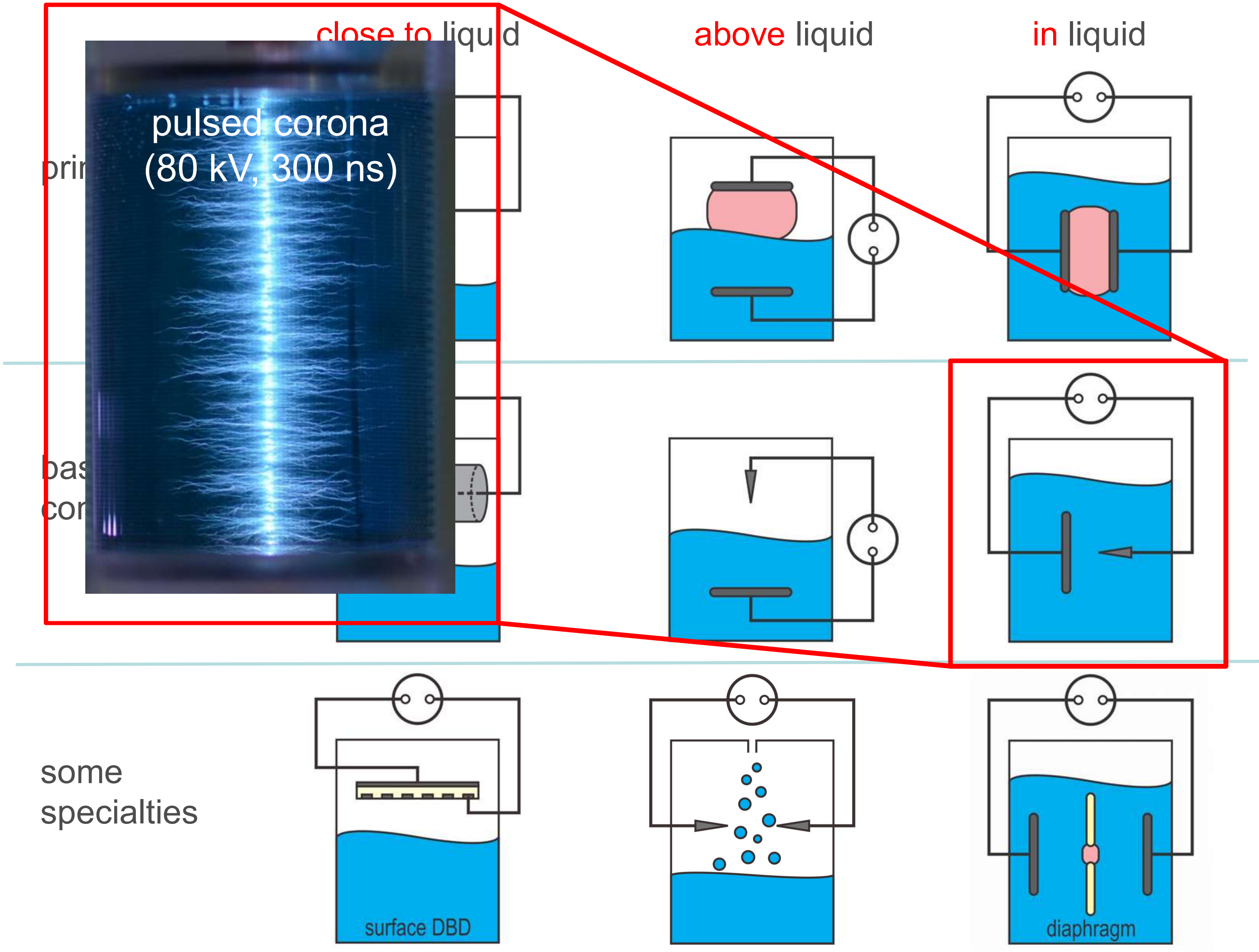
some
specia

Direct PCD treatment on observed pharmaceutical residues in hospital wastewater Batch 2, complete removal of pollutants (100%) manifests concentrations reduced below LQ.

Power Energy, kWh m^{-3} Substance, μg L^{-1}	Raw	30 W 0.1 PCD	Removal	30 W 0.5 PCD	Removal	30 W 1.0 PCD	Removal	250 W 0.5 PCD	Removal	250 W 1.0 PCD	Removal
Bisoprolol	0.84	0.6	29%	0.17	80%	< 0.10	100%	0.5	40%	0.35	58%
Caffeine	470	450	4%	420	11%	380	19%	480	−2%	480	−2%
Carbamazepine	0.35	0.25	29%	< 0.05	100%	< 0.05	100%	0.21	40%	0.088	75%
Ciprofloxacin	13	8.6	34%	4.1	68%	0.85	93%	7.2	45%	5.4	58%
Citalopram	0.23	0.17	26%	< 0.10	100%	< 0.10	100%	0.14	39%	< 0.10	100%
Diclofenac	0.6	0.42	30%	< 0.05	100%	< 0.05	100%	0.26	57%	0.083	86%
Doxycycline	2	1.2	40%	< 0.20	100%	< 0.20	100%	0.81	60%	0.32	84%
Enalapril	0.31	0.26	16%	0.23	26%	0.19	39%	0.27	13%	0.25	19%
Entacapone	1.1	0.26	76%	< 0.10	100%	< 0.10	100%	0.18	84%	< 0.10	100%
Estriol	0.91	1.1	−21%	< 0.05	100%	< 0.05	100%	0.49	46%	0.2	78%
Estrone	0.1	0.065	35%	< 0.05	100%	< 0.05	100%	< 0.050	100%	< 0.05	100%
Furosemide	11	4.7	57%	< 0.50	100%	< 0.50	100%	2.6	76%	< 0.50	100%
Hydrochlorothiazide	4.2	4.8	−14%	4	5%	2.2	48%	5.4	−29%	4.3	−2%
Hydrocortisone	0.45	0.33	27%	0.43	4%	0.35	22%	0.37	18%	0.37	18%
Ibuprofen	28	34	−21%	24	14%	14	50%	43	−54%	26	7%
Metoprolol	0.37	0.33	11%	0.18	51%	< 0.05	100%	0.33	11%	0.26	30%
Metronidazole	8.9	6.6	26%	7.8	12%	7.3	18%	8.1	9%	8.4	6%
Naproxen	1.1	0.78	29%	< 0.10	100%	< 0.10	100%	0.69	37%	0.5	55%
Ofloxacin	16	11	31%	2.2	86%	< 0.50	100%	9.4	41%	5.7	64%
Paracetamol	580	420	28%	70	88%	63	89%	260	55%	130	78%
Propranolol	0.21	0.1	52%	< 0.10	100%	< 0.10	100%	< 0.10	100%	< 0.10	100%
Sulfamethoxazole	5.8	2.7	53%	< 0.10	100%	< 0.10	100%	0.25	96%	< 0.10	100%
Tetracycline	1.6	0.83	48%	0.15	91%	0.14	91%	0.59	63%	0.23	86%
Trimethoprim	1.2	0.92	23%	0.061	95%	< 0.01	100%	0.73	39%	0.31	74%

P. Ajo, S. Preis, T. Vornamo. M. Mänttäri, M. Kallioninen, M. Lohi-Kultanen, " Hospital wastewater treatment with pilot-scale pulsed corona discharge for removal of pharmaceutical residues," J. Environ. Chem. Eng. 6 (2018) 1569-1577.

Electrical Discharges with and in Liquids



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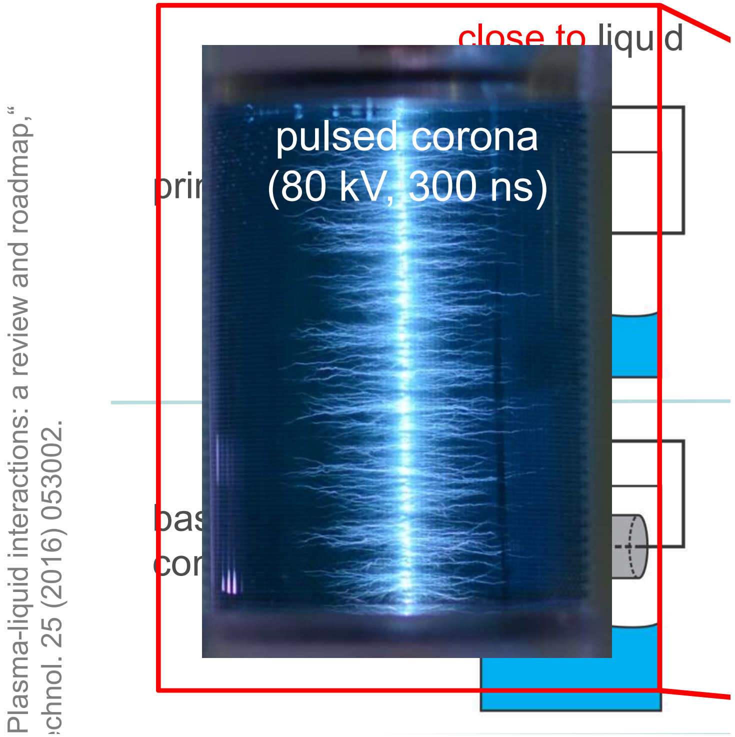
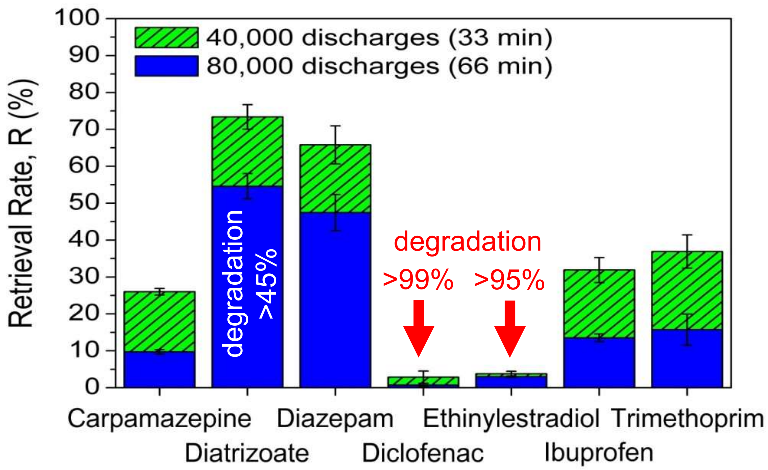
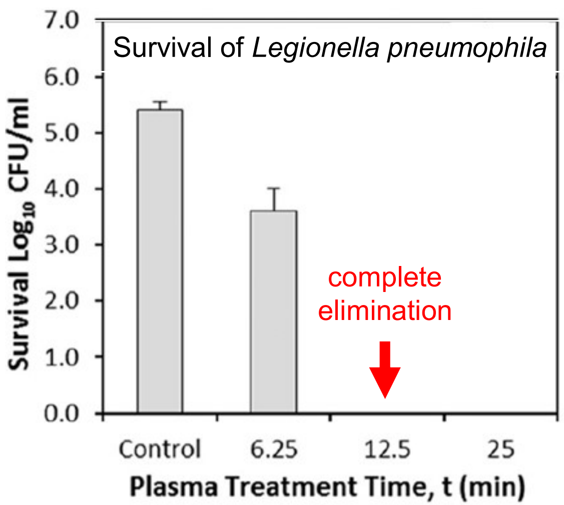




R. Banaschik, P. Lukes, H. Jablonowski, M.U. Hammer, K.-D. Weltmann, J. Kolb, "Potential of pulsed corona discharges generated in water for the degradation of persistent pharmaceutical residues," Water Research 84 (2015) 127-135.

R. Banaschik, G. Burchhardt, K. Zocher, S. Hammerschmidt, J. F. Kolb, K.-D. Weltmann, "Comparison of Pulsed Corona Plasma and Pulsed Electric Fields for the Decontamination of Water Containing Legionella pneumophila as model organism," Bioelectrochemistry 112 (2016) 83-90.



Medicine (Plasma)

Decontamination
(Hygiene)

Agriculture

Electrosurgery – already in use

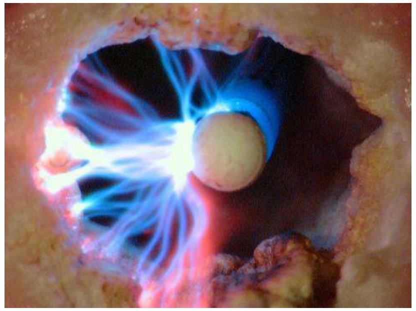
Argon Plasma Coagulation (APC)

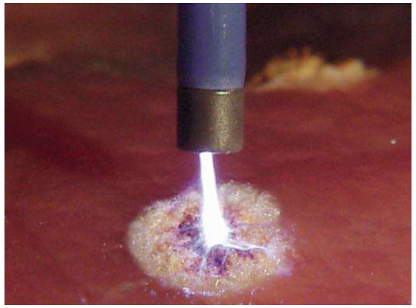
ERBE Elektromedizin GmbH,Tübingen, Germany

Cauterization: tissue destruction, burning

- **hemostatsis**
- **cutting, removal of tissue**

Figure 6: Endoscopic application of APC





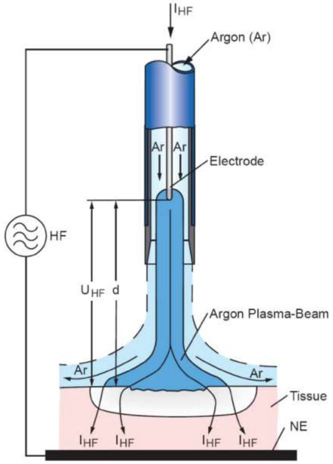


Figure 3: Schematic representation of a typical APC setup. The argon flows through a tube containing the electrode wire. The discharge is ignited by a HF voltage U_{HF} between the wire end and the tissue. After breakdown, HF current I_{HF} flows into the tissue, causing a coagulation effect, and back to the HF generator through the neutral electrode (NE).

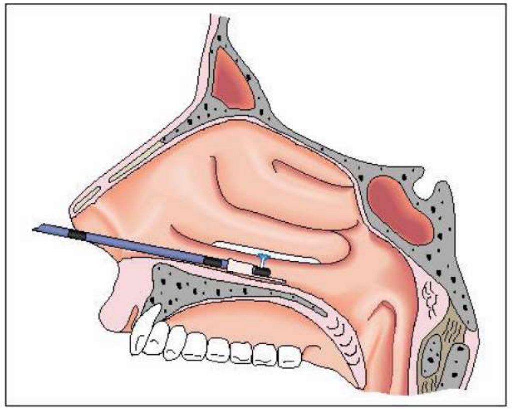


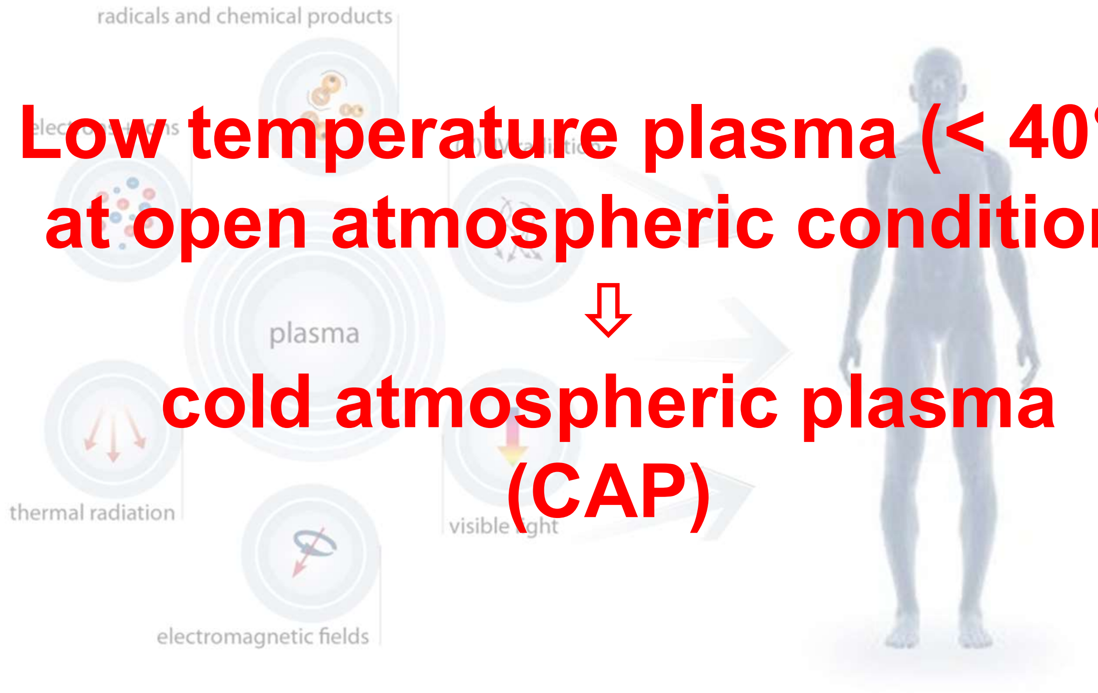
Figure 8: APC in the nasal cavity, where a probe with lateral outlet is used

ERBE

Zenker M, GMS Krankenhaushyg Interdiszip 3 (2008) Doc15; Raiser & Zenker, J. Phys. D: Appl. Phys. 39 (2006) 3520; http://www.erbe-med.com/de/medizintechnik/public/Produkte/Argonplasma-Koagulation--APC-

Plasma medicine

Application of physical plasma directly on or in the human body for therapeutic purposes

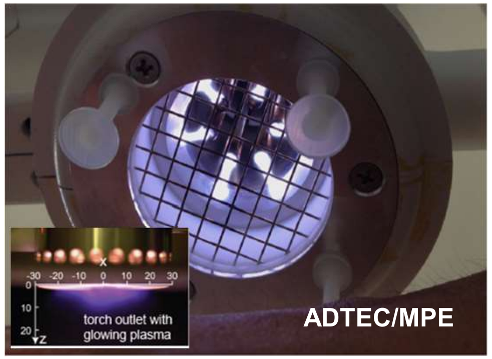


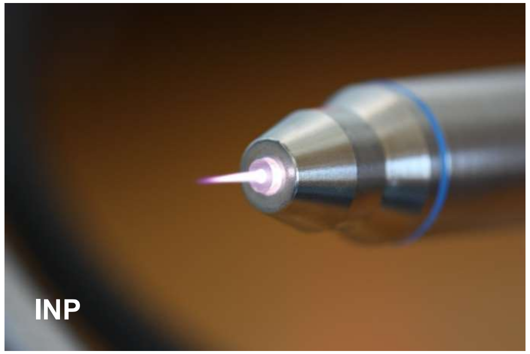
Low temperature plasma (< 40°C) at open atmospheric conditions

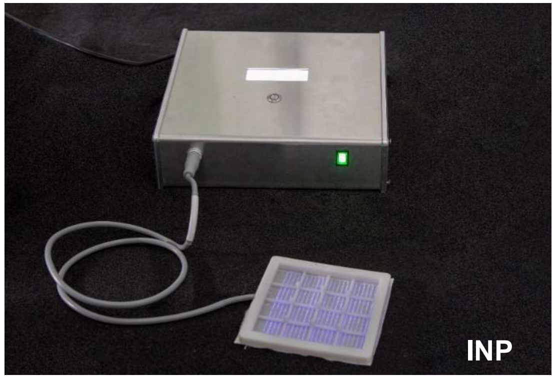
⇩

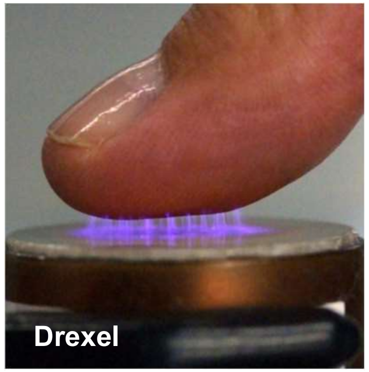
cold atmospheric plasma (CAP)

Atmospheric pressure plasmas for biomedicine



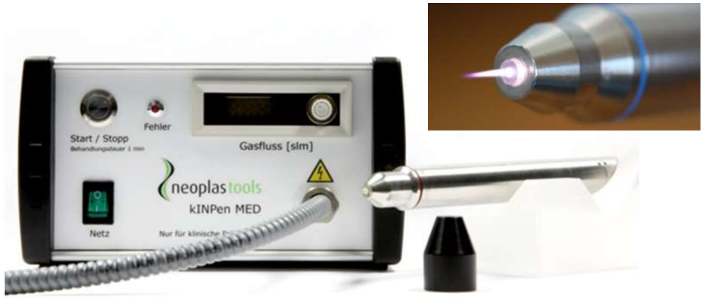






CE certified plasma medical devices

ADTEC Plasma Technlogy Co.Ltd.
http://www.adtecplasma.com/



neoplas tools
medical plasma

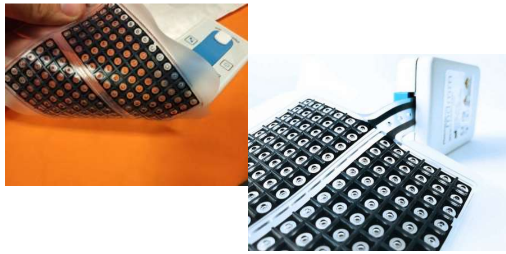
http://www.neoplas-tools.eu

CINOGY
plasma technology for health

http://www.cinogy.de

terraplasma
MEDICAL

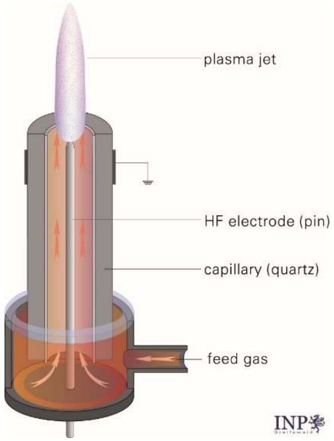
https://www.terraplasma-medical.com/



Certification based on

- ✓ **Clinical research**
- ✓ **Comprehensive physical and biological plasma source characterization**

Atmopheric pressure plasma jet kINPen MED



neoplas tools
medical plasma

CERTIFIED MED CERT ISO 13485

Dimensions:	L = 155 mm, Ø = 20 mm
Weight:	170 g
HF-Voltage:	1.1 MHz; 2…6 kV_{pp}
Gas temp.:	30-50°C
Feed gas:	Argon
Gas flow:	3-5 slm

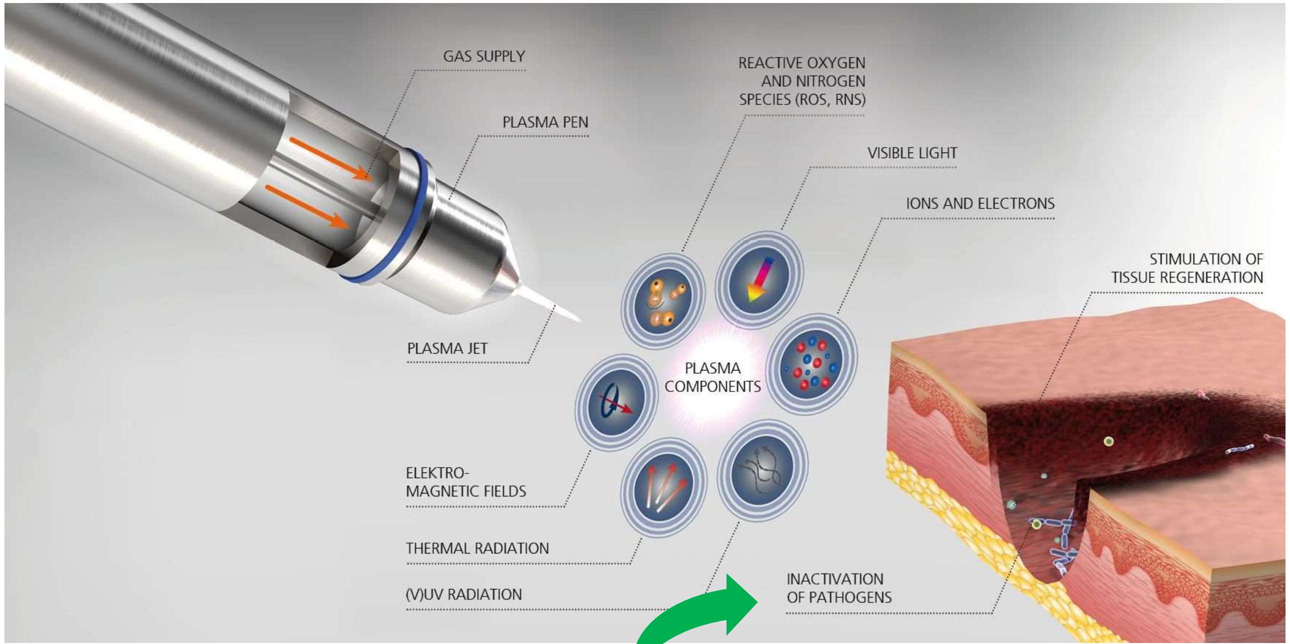
Certified as **medical device class IIa** (June 2013) according to European Council Directive 93/42/EEC

Purpose: Treatment of chronic wounds as well as pathogen-based diseases of skin, skin appandages, extremities and body

K.-D. Weltmann, et al., Contrib. Plasma Phys. 49 (2009) 631-640; S. Reuter et al., J. Phys. D: Appl. Phys. 51 (20189 233001;
S. Bekeschus et al., Clin. Plasma Med. 4 (2016) 19–28
www.neoplas-tools.eu

Plasma medicine: Focus wound healing

Stimulation of cell proliferation and angiogenesis
⇨ Promotion of tissue regeneration



Inactivation of a broad spectrum of microorganisms including multidrug resistant pathogens

INP FROM IDEA TO PROTOTYPE

Clinical plasma medicine: focus on chronic wounds

Case series of kINPen MED in clinical practice

Interims analysis (12/2014 – 04/2016):

Patients: n=61, 20 female, 41 male; age 41-84 years; **"therapied-out", "resistant to therapy"**

Ulcers: 11 venous, 19 ischaemic, 31 mixed-type/others

Comorbidities: 49 (hypertonia, cardiac insufficiency, obesity, diabetes)

Size: 1 – 775 cm^2 (mean 35.8 cm^2)

Duration: 0.25 – 228 months (mean 24.8 months)

Wound contamination/infection: sensitive: 42, multiresistant: 18

Treatment: kinpen MED, 4.5 slm Ar, 30-60 s/cm^2, additionally to conventional wound care

Number of treatments: 1 - 52 (mean 10); 1 – 5 per week (mean 3)

Healing rate	**96.7 %**
Complete healing	**43.3 % (27 patients)**
Ulcus reduction	**52.5 % (32 patients)**
No effect	**3.2 % (2 patients)**

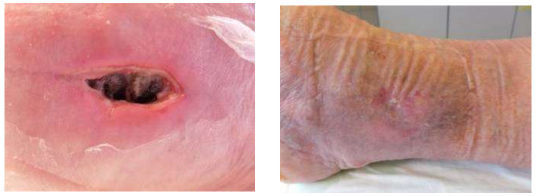
Wound decontamination

Sensitive bacteria	**73.8 % (31/42)**
Multiresistant bacteria	**100 % (18/18)**

Complications **0**

Lower leg of a male patient (63 years old) with chronic wound (peripheral artery disease stage IV) contaminated with *P. aeruginosa*, before (left) and after the end of 34 treatments by kinpen MED over 17 weeks (right)

Male patient (74 years old), ischaemic stump of forefoot, before (left) and after (right) 8 treatments by kinpen MED; complete elimination of MRSA

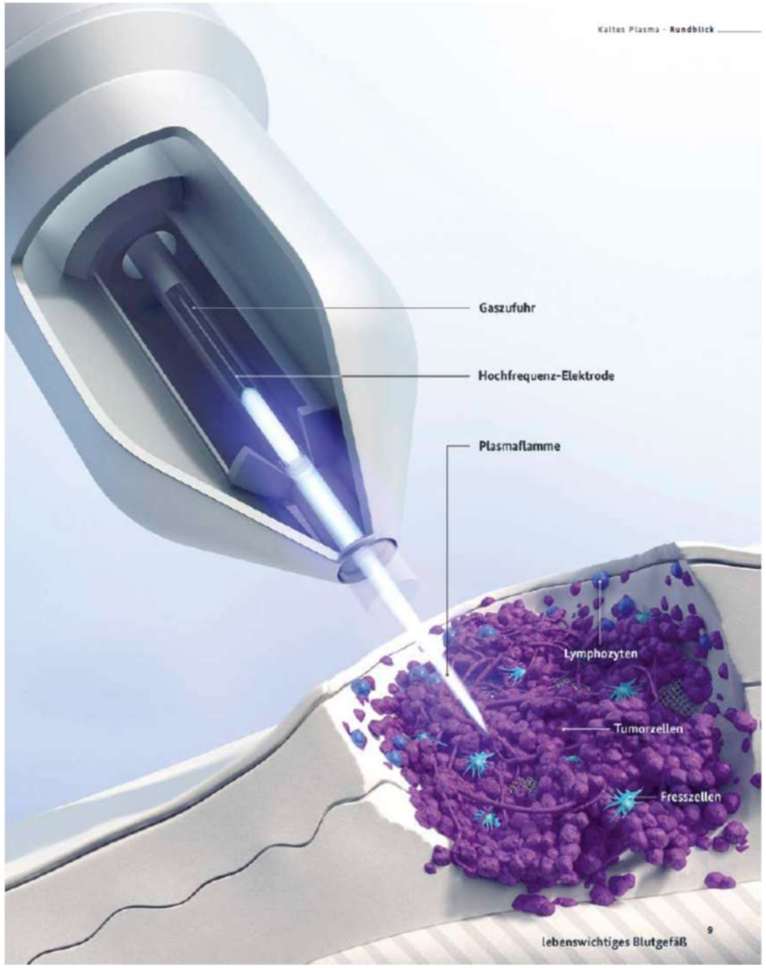


Lower leg of a female patient (64 years old), venous ulcus wound contaminated with sensitive bacteria before (left) and after (right) 8 treatments by kinpen MED

KLINIKUM Altenburger Land
Akademisches Lehrkrankenhaus des Universitätsklinikums Jena
Akademisches Lehrkrankenhaus der Universität Leipzig

B. Schwetlick, 5th German Plasma Medicine Workshop, September 13-14, 2017, Rostock, Germany

Clinical plasma medicine: vision - cancer treatment



Unternehmen Region 2/2016

Inactivation of a broad spectrum of microorganisms including multidrug resistant pathogens

Inactivation of cells by initialization of programmed cell death (apoptosis)

Cancer treatment: clinical plasma application

Antiseptic treatment of infected cancer ulcerations as part of palliative medicine program

12 patients; advanced squamous cell carcinoma of the head and neck, intraoral or extraoral ulcerations beyond reach of standard cancer therapies

- gently removal of biofilm covering with gauze
- repeated kinpen MED scanning over the area of the ulceration, 1 min/cm^2
- 1 cycle: 3 single treatments within 1 week, followed by 1 week intermittence
- 1-9 cycles per patient
- 3-18 Monate clinical follow-up

General results:

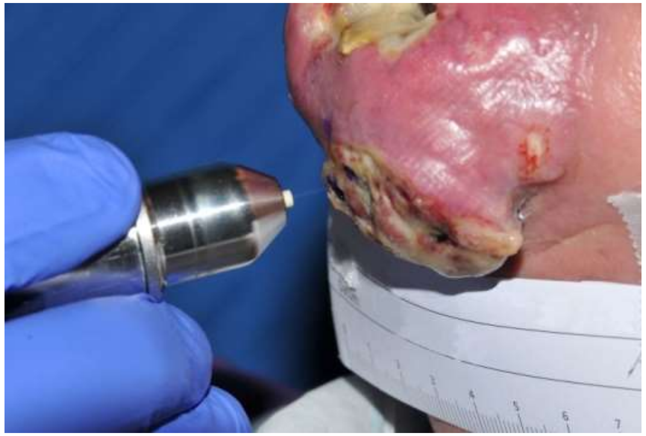
(1) Reduction of microbial load

(2) Reduction of typical fetid odor

(3) Decreased request for pain medication in some cases

(4) Superficial partial remission of tumor

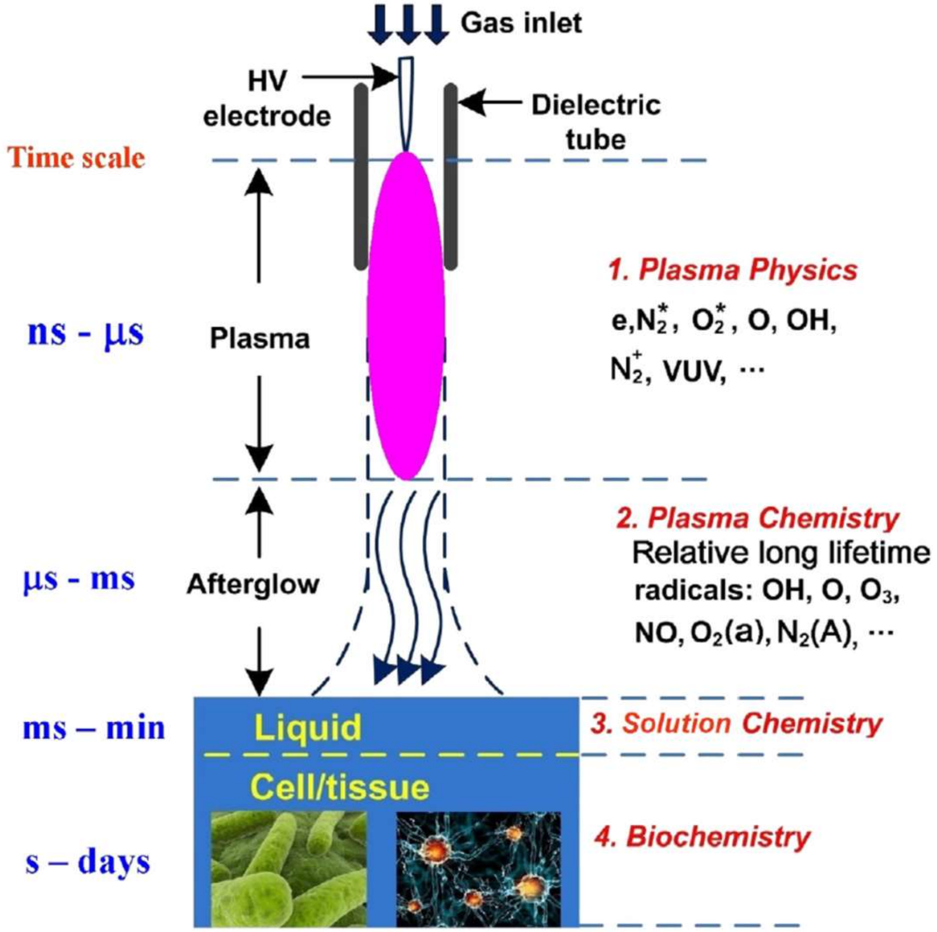
(5) Wound healing of infected ulcerations



Th. von Woedtke & H.-R. Metelmann, Clin. Plasma Med. 2 (2014) 37

H.-R. Metelmann et al., Clin. Plasma Med. 3 (2015) 17-23

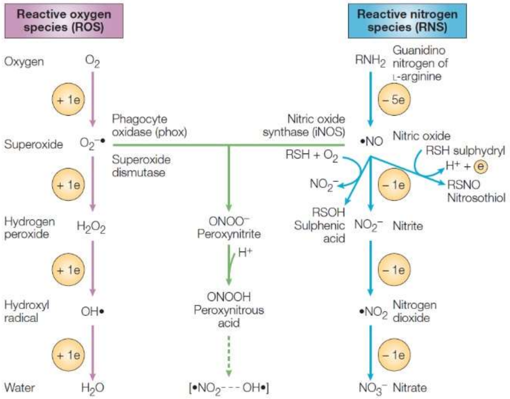
Plasma interaction with biological systems



X. Lu et al., Phys. Rep. 630 (2016) 1-84

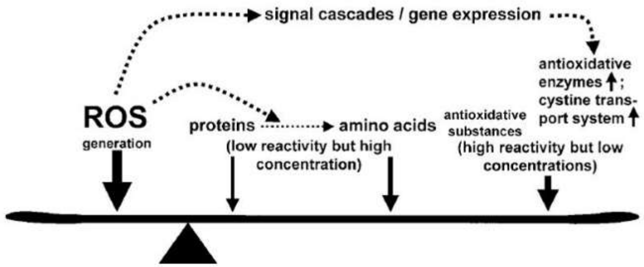
ROS and RNS in cell physiology

Redox-active plasma components are the same as occur in regular physiological and biochemical processes in the body.



Fang, Nat. Rev. Microbiol. 2 (2004) 820-832

Mechanisms of redox homeostasis.
Balance between ROS production and various types of scavengers



W. Dröge, Physiol. Rev. 82 (2002) 47-95

Because its localized and short-term generation by local plasma treatment these substances can be detoxified by processes of regular cell metabolism.

No increased risk of genotoxic effects

Plasma medicine: Risk assessment

No increased risk of genotoxic effects

Evidenced by:

- ***In vitro* standard assays**

Mutation Research/Genetic Toxicology and Environmental Mutagenesis

Investigation of the mutagenic potential of cold atmospheric plasma at bactericidal dosages

Mutation Research/Genetic Toxicology and Environmental Mutagenesis

Risk assessment of a cold argon plasma jet in respect to its mutagenicity

Environmental and Molecular Mutagenesis 58:172–177 (2017)

PLOS ONE

Investigating the Mutagenicity of a Cold Argon-Plasma Jet in an HET-MN Model

Research Article

Investigation of Toxicity and Mutagenicity of Cold Atmospheric Argon Plasma

T. Maisch,[1] A. K. Bosserhoff,[2,3] P. Unger,[1] J. Heider,[1] T. Shimizu,[4,5] J. L. Zimmermann,[4,5] G. E. Morfill,[4,5] M. Landthaler,[1] and S. Karrer[1]*

- **Long-term animal trial**

Environmental and Molecular Mutagenesis 59:268–277 (2018)

Research Article

High Throughput Image Cytometry Micronucleus Assay to Investigate the Presence or Absence of Mutagenic Effects of Cold Physical Plasma

International Journal of *Molecular Sciences*

MDPI

Article

One Year Follow-Up Risk Assessment in SKH-1 Mice and Wounds Treated with an Argon Plasma Jet

Anke Schmidt[1,*], Thomas von Woedtke[1,2], Jan Stenzel[3], Tobias Lindner[3], Stefan Polei[3], Brigitte Vollmar[4] and Sander Bekeschus[1]

- **Clinical experiences and monitoring**

Atmospheric Pressure Plasma Jet Application on Human Oral Mucosa Modulates Tissue Regeneration

Sybille Hasse, Olga Hahn, Stefan Kindler, Thomas von Woedtke, Hans-Robert Metelmann & Kai Masur

Experimental dermatology • Original article

CED Clinical and Experimental Dermatology

Induction of proliferation of basal epidermal keratinocytes by cold atmospheric-pressure plasma

S. Hasse,[1] T. Duong Tran,[1] O. Hahn,[1] S. Kindler,[2] H.-R. Metelmann,[2] T. von Woedtke[3] and K. Masur[1]

Clinical Plasma Medicine

Invited paper

Non-thermal plasma—More than five years of clinical experience

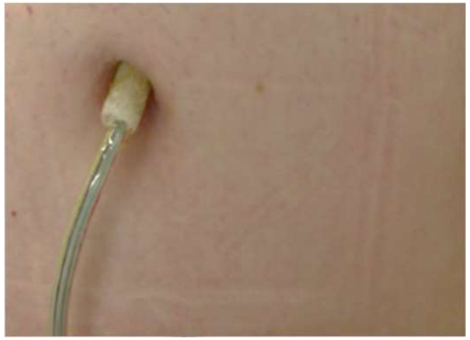
Clinical Plasma Medicine

Invited paper

Scar formation of laser skin lesions after cold atmospheric pressure plasma (CAP) treatment: A clinical long term observation

Plasma treatments in clinical practice

Chronic wounds	Acute wounds	Niche applications e.g. cardiology – Drive-line infection
KLINIKUM Altenburger Land	Universitätsmedizin Greifswald	Klinikum Karlsburg Herz- und Diabeteszentrum



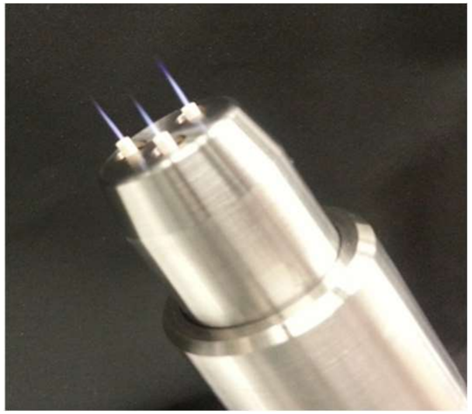
<u>Chronic wounds:</u> Currently, especially in cases where after exhausting all other treatment options, the healing process stagnates

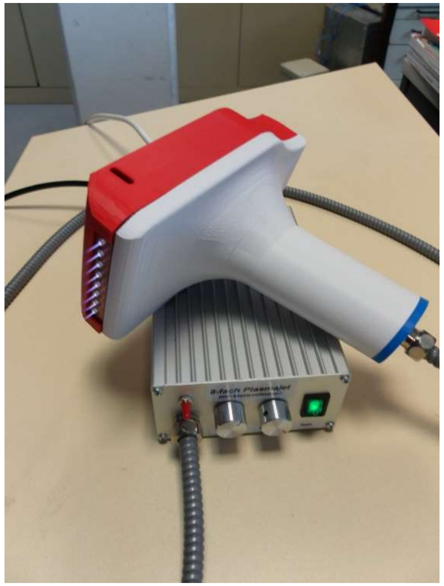
⇨ **success rate > 80 %!**

H. Uhlemann, Klinikum Altenburger Land; H.-R. Metelmann et al., Am. J. Cosmetic Surg. 29 (2012) 52-56; H.-R. Metelmann et al., Clinical Plasma Medicine 1 (2013) 30-35; L. Hilker, Klinikum Karlsburg –Herz- und Diabeteszentrum

Forthcoming ideas/prototypes (INP)

Large area treatment: Multijet

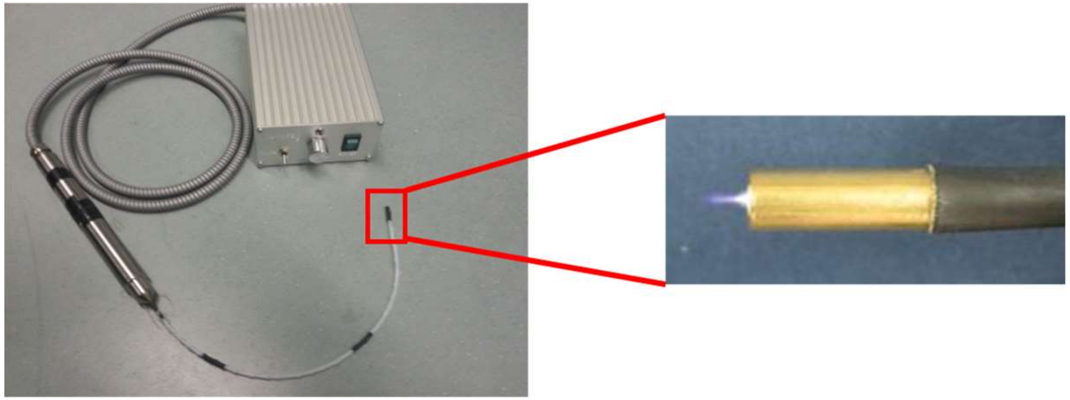




„8er“

Forthcoming ideas/prototypes (INP): Treatment of cavities

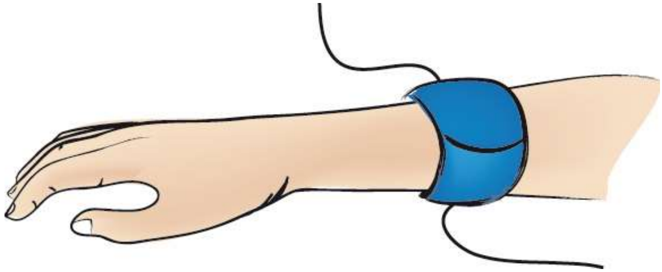
Prototype of a cold atmospheric Ar-plasma jet device intended for dental applications based on KINPen technology

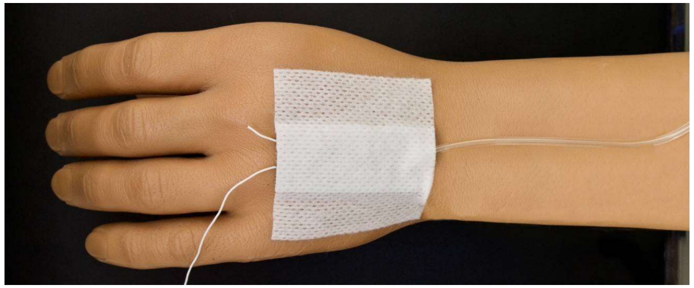


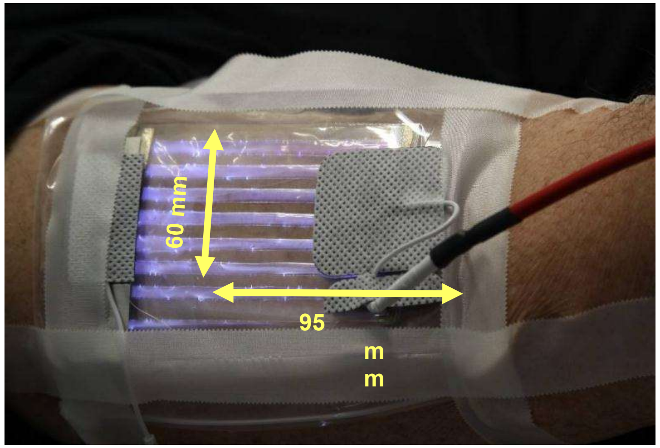
Prototype of a flexible catheter-like cold atmospheric Ar-plasma jet device based on kINPen technology

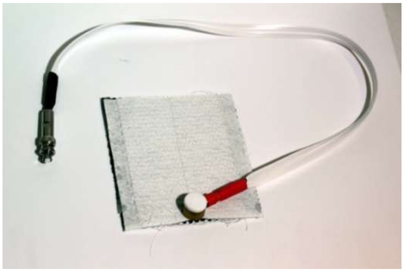
K.-D. Weltmann & Th. von Woedtke, et al., Plasma Phys. Contr. Fusion, submitted

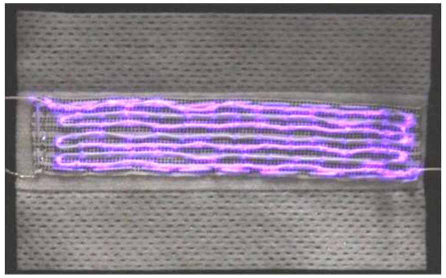
Large area treatments: Flexible surface-DBD







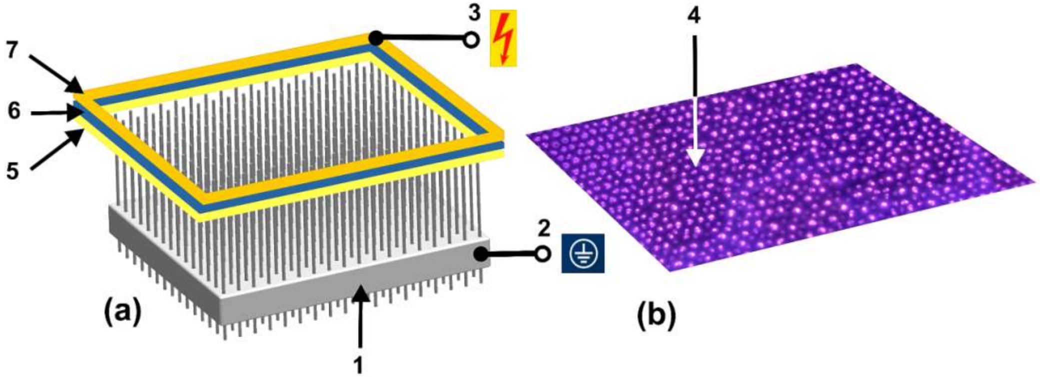


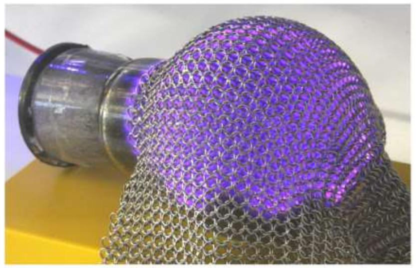


Weltmann et al., Contrib. Plasma Phys. 49 (2009) 631-640; Weltmann et al., Pure Appl. Chem. 82 (2010) 1223-1237; Weltmann & von Woedtke, Eur. Phys. J. Appl. Phys. 55 (2011) 13807; Weltmann et al., Contrib. Plasma Phys. 52 (2012) 644-654; Weltmann et al., IEEE Trans. Plasma Sci. 40 (2012) 2963-2969

Forthcoming ideas/prototypes (INP)

Flexible discharge arrangement (others)





(c)

(d)

Self sterilizing gloves
ond/or -surfaces

Like „coat of mail“ –
„knight‘s armour“…

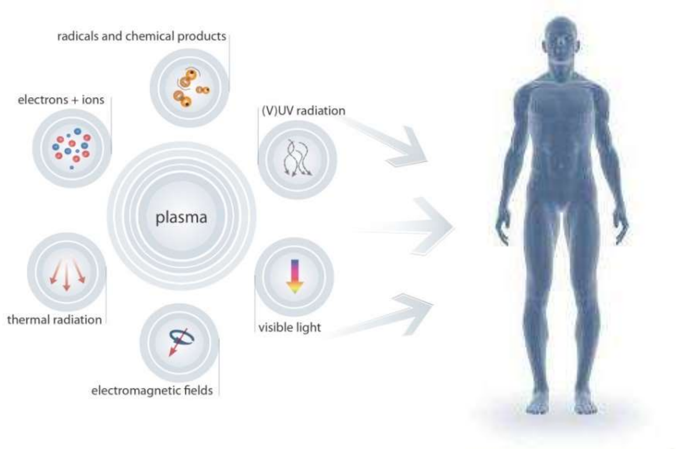
MRS Spring Meeting, San Francisco 2012

Arbeitskreis Atmosphärendruck-Plasmaquellen, Berlin, 2013

gloves

Plasma medicine: summary

1. Active components are generated locally and only for the required duration of the application on-site primarily by a physical process.
2. Biologically active plasma components are the same as occur in regular physiological and biochemical processes.
3. Because of effective cellular redox control, the risk of cold atmospheric plasma application is low, assessable and manageable. Actually, there are no indications for genotoxic effects.
4. Cold atmospheric plasma application for wound healing is clinical reality, yet.



Agriculture

Medicine (Plasma)

Decontamination (Hygiene)

Societal challenge: Food contamination

Contaminated Food Causes More Than 3,000 Death Each Year

Bloomberg View | By the Editors

Posted: 10/13/2012 10:46 am EDT | Updated: 10/13/2012 10:47 am EDT

499 Like | 225 Share | 60 Tweet | 0 LinkedIn | 521 Comment

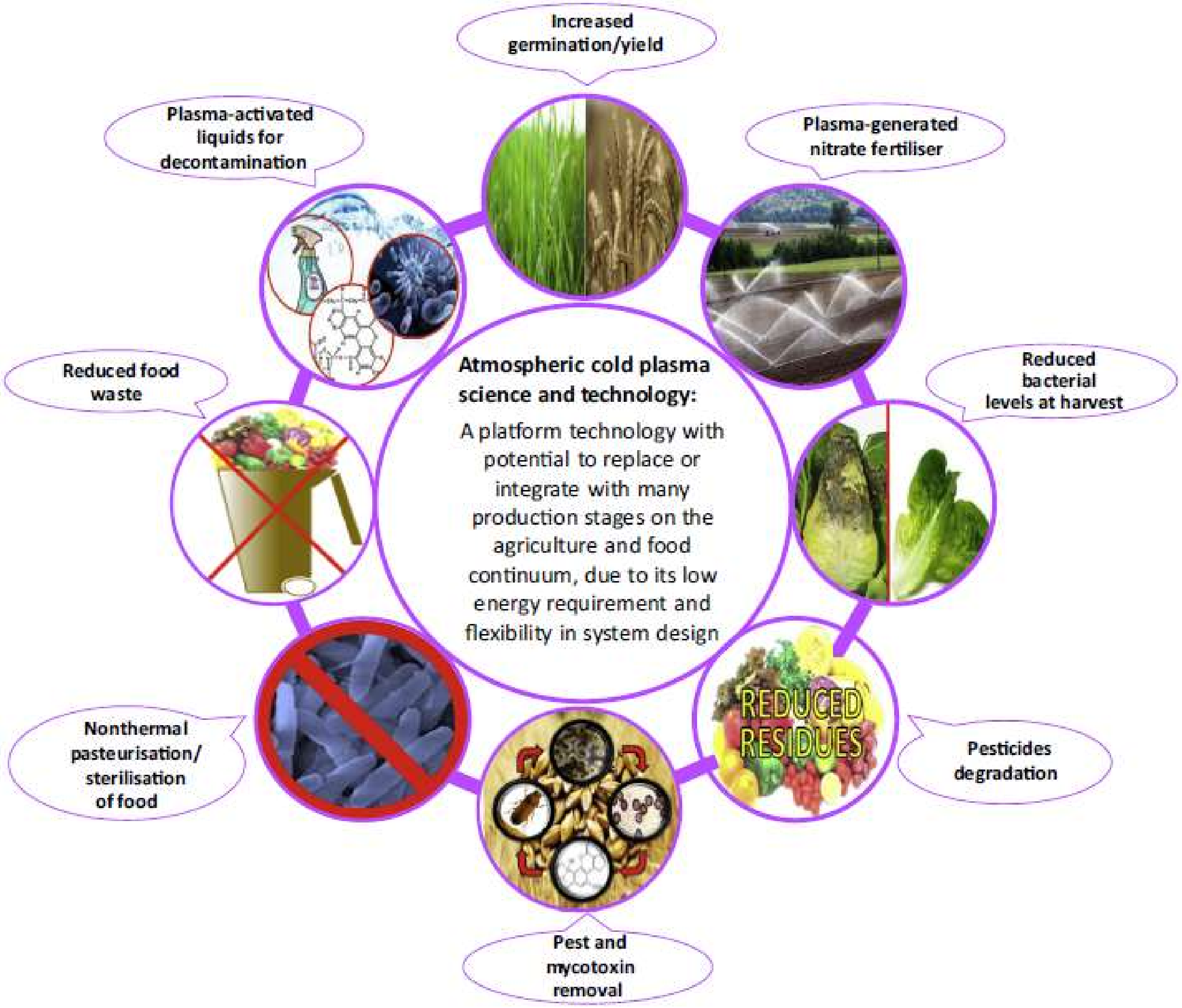
Bloomberg View

Contaminated food sickens 48 million Americans, resulting in more than 3,000 deaths and more than 100,000 hospitalizations each year. That's right: 3,000 deaths.

Hard as this is to believe, it's easy to see how we got here. It starts with the neglect of the Food and Drug Administration, the agency created to ensure the quality of much of the U.S. food supply, which has been starved of funds for decades. Congress gives the FDA about $1 billion a year for overseeing the bulk of the $1.2 trillion food industry. That's enough to pay for about 1,100 inspectors, who manage to check only 6 percent of domestic food producers and 0.4 percent of importers each year.

www.huffingtonpost.com/2012/10/13/contaminated-food-deaths_n_1962313.html

Plasma agriculture



P. Bourke, D. Ziuzina, D. Boehm, P.J. Cullen, K. Keener, "**The Potential of Cold Plasma for Safe and Sustainable Food Production**," Trends in Biotechnology 1580 (2018)

N. Puac, M. Gherardi, M. Shiratani, "**Plasma agriculture: A rapidly emerging field**," Plasma Process. Polym. 15 (2018)

M. Ito, J.-S. Oh, T. Ohta, M. Shiratani, M. Hori, "**Current status and future prospects of acricultural applications using atmospheric-pressure plasma technologies**," Plasma Process. Polym. 15 (2018)

N.N. Misra, O. Schlüter, P.J. Cullen (Eds.), ***Cold plasma in food and agriculture: fundamentals and applications***, Academic Press, (2016).

M. Ito, T. Ohta, M. Hori, "**Plasma agriculture**," J. Korean Physical Soc. 60 (2012)

Food value chain - Challenges

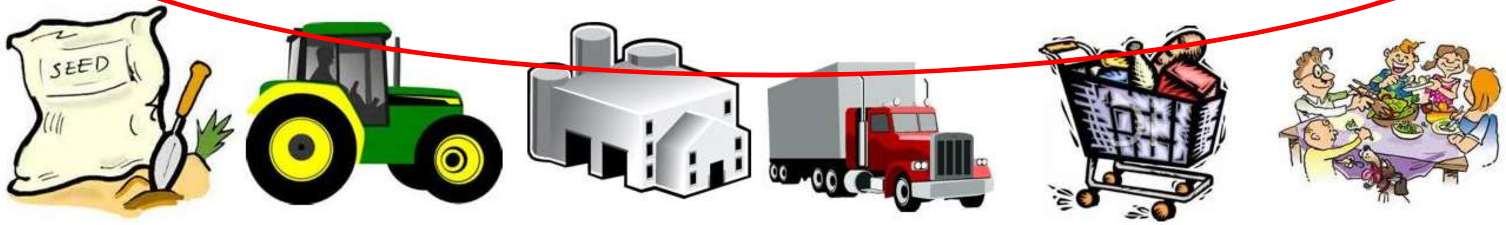
Plasma decontamination

- Germination & growth
- Spoilage
- Sustainabilitly
- Environmental impact

- Refinement
- Extraction
- Packaging
- Preservation

- Shelf life
- Appearance

- Safety
- Quallity
- Price



Input → Farm → Processing → Distribution → Retail → Consumer

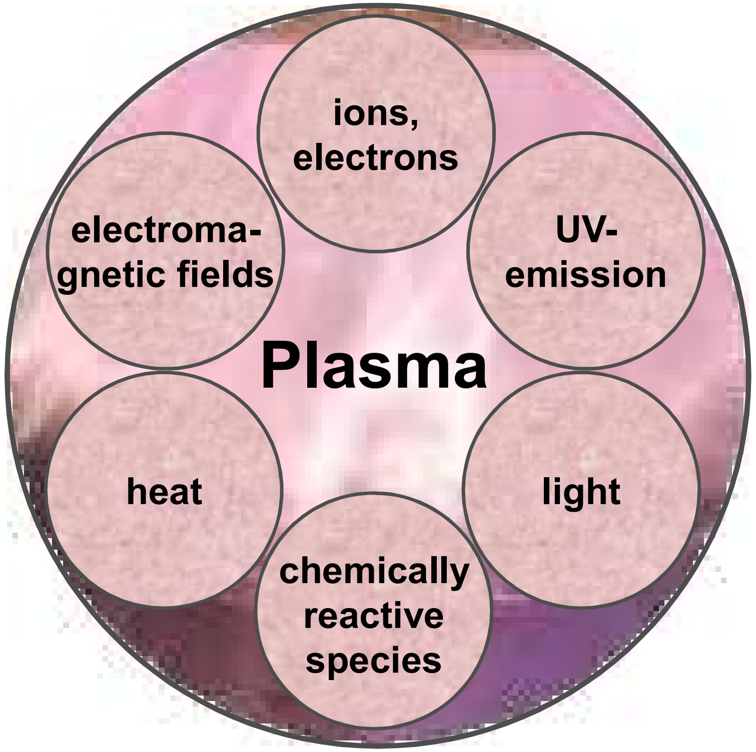
Input	Farm	Processing	Distribution	Retail	Consumer
Seeds Pesticides Agbiotech Traits Fertilizers	Farmers Ranchers Fishermen	Aggregators Processors Manufacturers Beverages	Distributors Importers Exporters	Retailers Supermarkets Restaurants	Consumers

Procedures of decontamination of food in Germany

procedure/treat-ment	disadvantage	e.g. product
nothing	foodborne disease	egg
water	humid environment	salad
chemical	residues	drinking water, apples, citrus fruits
temperature/hot steam	quality of products strongly impaired	fish, preserves
high pressure	only without air inclusions, high costs	ham
UV/Pulsed Light	heating of the product, shading, high costs	tomatoes
PEF (high-intensity pulsed electric field)	reduced product quality, high costs	juices
Y-radiation	very high costs, hazardous substances (TRGS - Technical Rule for Hazardous Substances)	spices

Searching for alternative technologies:
- ozone
- electron beam
  bacteriophages ("biological weapon")
- Innovative Plasma
- Combination of different conventional and new procedures

Potential of plasma for agriculture

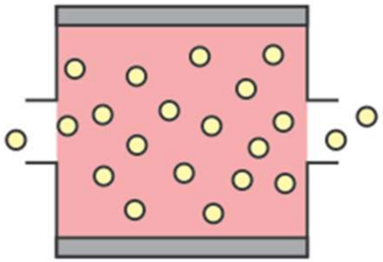


Cold Atmospheric Pressure Plasma:
by electrical means provided transient reactive gas

- **No chemicals**
  - Short-lived reactive species regenerated from ambient air or water
  - Transient interaction of plasma-induced chemistry for minutes up to days
  - No toxic or environmental harmful residues
- **On-demand treatment:**
  - Only electricity needed;
    no other supplies
  - Autonomy for farmers and producers
- **Possible Applications:**
  - Elimination of harmful microorganisms
  - Degradation of chemical compounds
  - Stimulation and protection of plant biology
  - Improvement of food processing

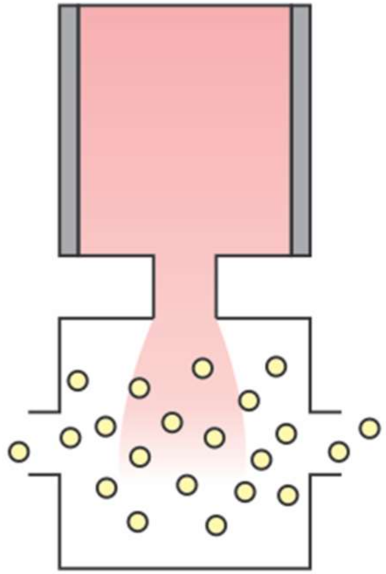
Plasma-treatment concepts

Direct plasma-exposure



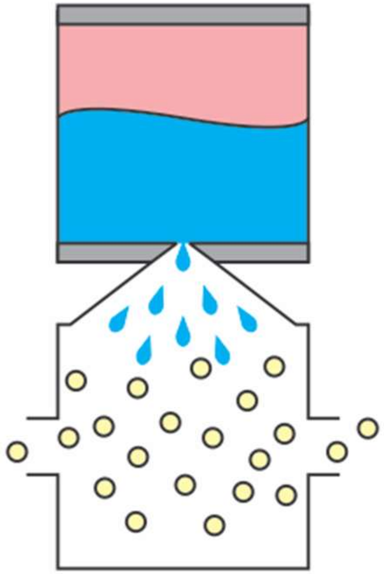
- Microbial inactivation
- Pest control
- Surface modification (hydrophilization)
- Improved germination

Exposure to plasma-treated air



- Preservation, storage
- Improved germination?
- Improved growth?

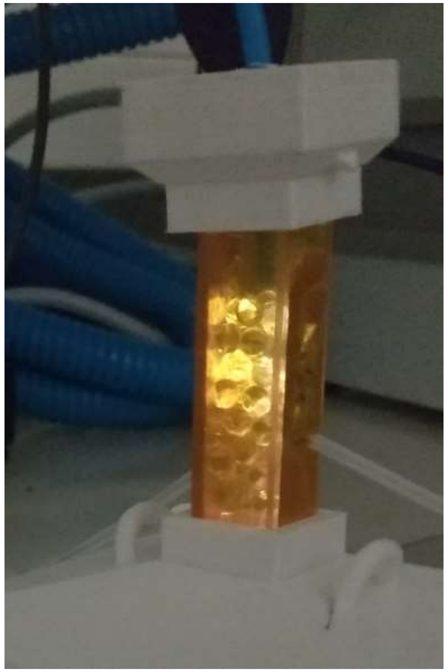
Exposure to plasma-treated water



- Microbial inactivation
- Edging
- Improved germination, growth
- Sustaining soil health

Plasma-treatment concepts

Direct
Plasma-Exposure



• packed bed reactor
(• gliding arc reactor)
(• DBD reactor)

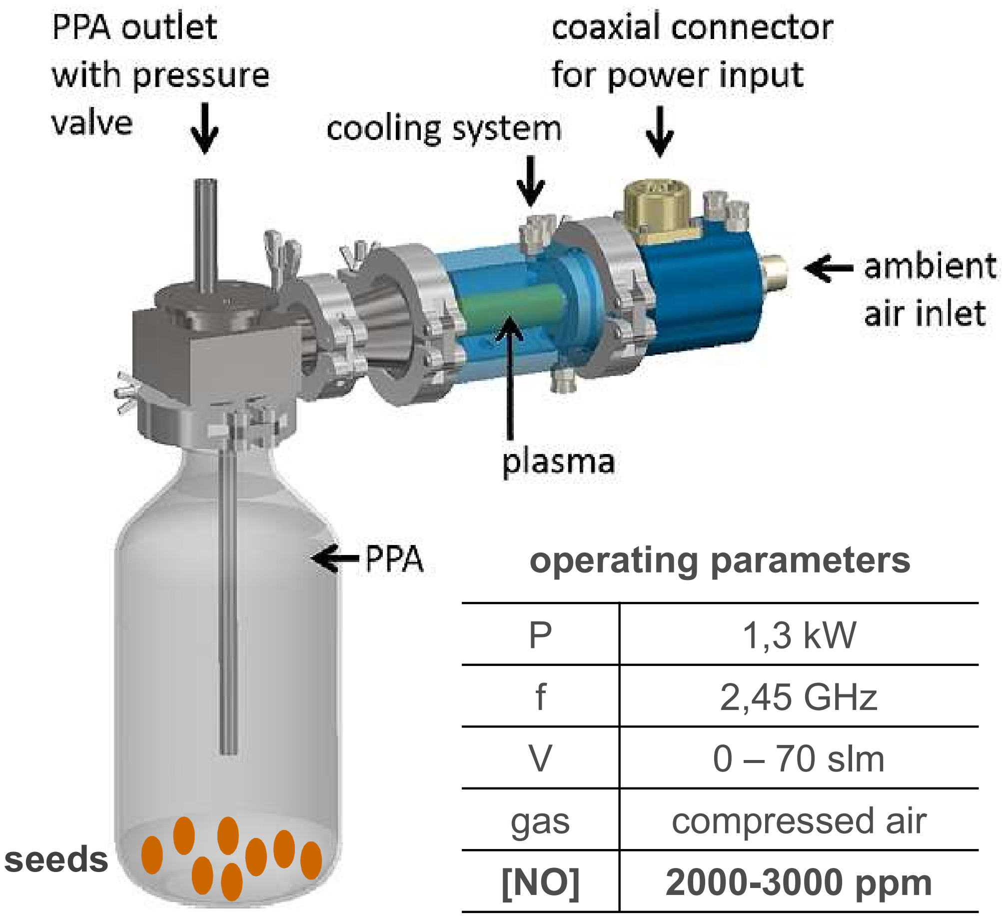
Exposure to Plasma-
treated Air

• plasma processed air
(• ozonation)

Exposure to
Plasma-treated Water

• plasma processed water
• pin-to-liquid discharge

Plasma treated air (PTA)



operating parameters

P	1,3 kW
f	2,45 GHz
V	0 – 70 slm
gas	compressed air
[NO]	**2000-3000 ppm**

Plasmatorch: PLexc®

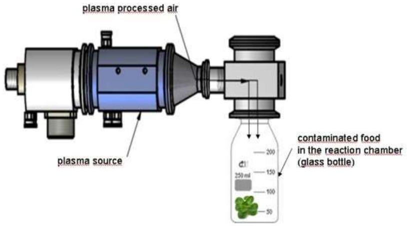
A: microwave torch, **B**: cooling system,,
C: gas inlet, **D**: microwave power input,
E: gas feed, **F**: **PPA reaction chamber**

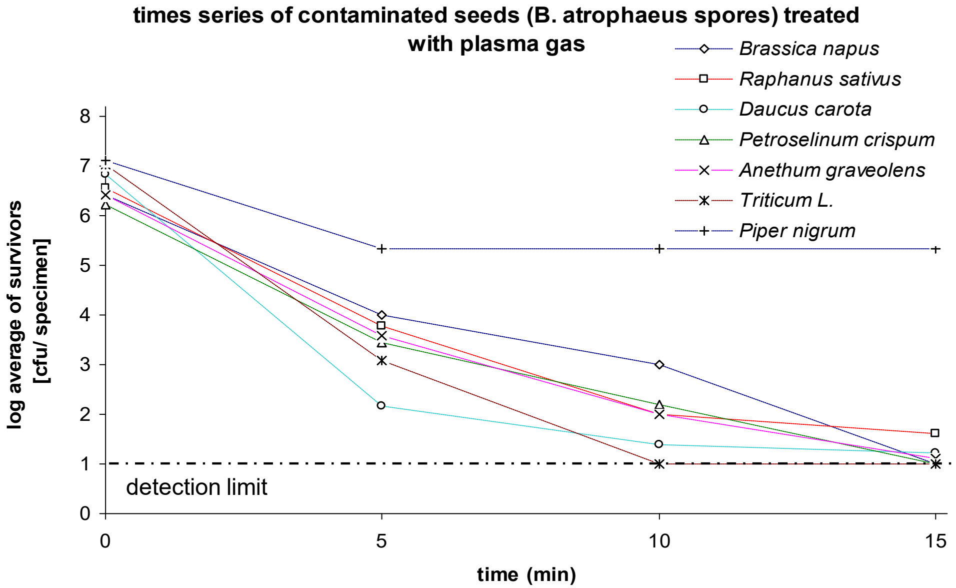
U. Schnabel, M. Andrasch, K.-D. Weltmann, J. Ehlbeck, Inactivation of Vegetative Microorganisms and Bacillus atrophaeus Endospores by Reactive Nitrogen Species (RNS), Plasma Processes and Polymers **11** (2014) 110.

PPA: Seed decontamination

Treatment of *B. atrophaeus* spores on seeds by PLexc® processed air

- *B. atrophaeus* spore reduction on seeds: 2 to 6 log cfu reductions in 15 min
- temperature of 22 °C maximum





Reduction factors:

Rapeseed – 5,41 $\log_{10}$

Radish – 4,95 $\log_{10}$

Carot – 5,63 $\log_{10}$

Parsley – 5,23 $\log_{10}$

Dill – 5,3 $\log_{10}$

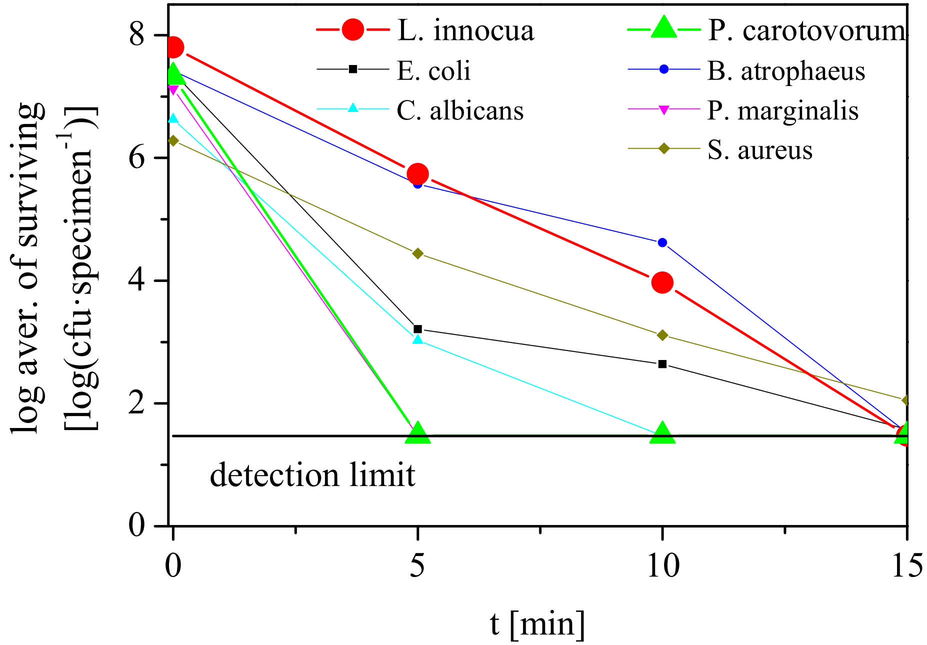
Wheat – 6,02 $\log_{10}$

Pepper – 1,77 $\log_{10}$

U. Schnabel et al., Plasma Process. Polym. 9 (2012) 569-575; U. Schnabel et al., J. Agricult. Sci. Appl. 1 (2012) 99-105

Selected activities – INP, Food decontamination

Microwave torch PLexc®:



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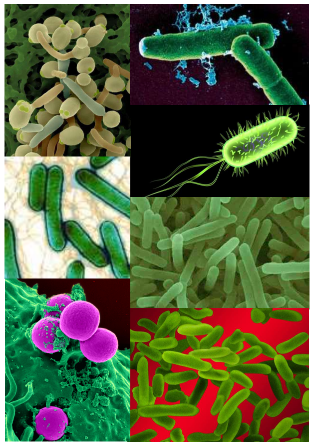


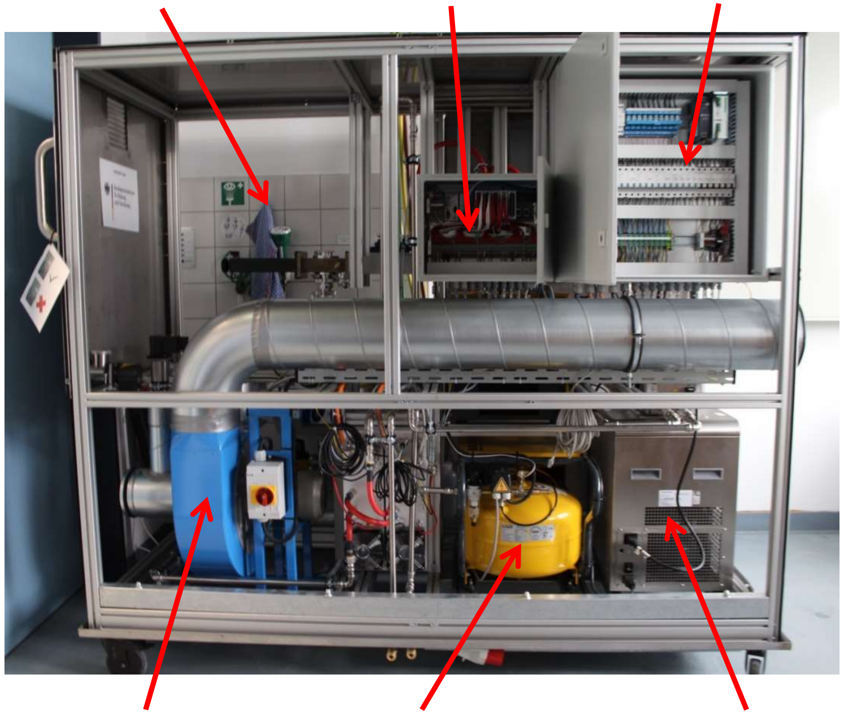
inactivation kinetics of microorganisms on apples as a result of treatment with Plexc® processed air.

Schnabel U, Niquet R, Krohmann U, Polak M, Schlüter O, Weltmann K-D, Ehlbeck J, 2012. Journal of Agricultural Science and Application 1, 100-106.

Schnabel U, Niquet R, Schlüter O, Gniffke H, Ehlbeck J, 2014. Journal of Food Processing and Preservation, online published (DOI:10.1111/jfpp.12273).

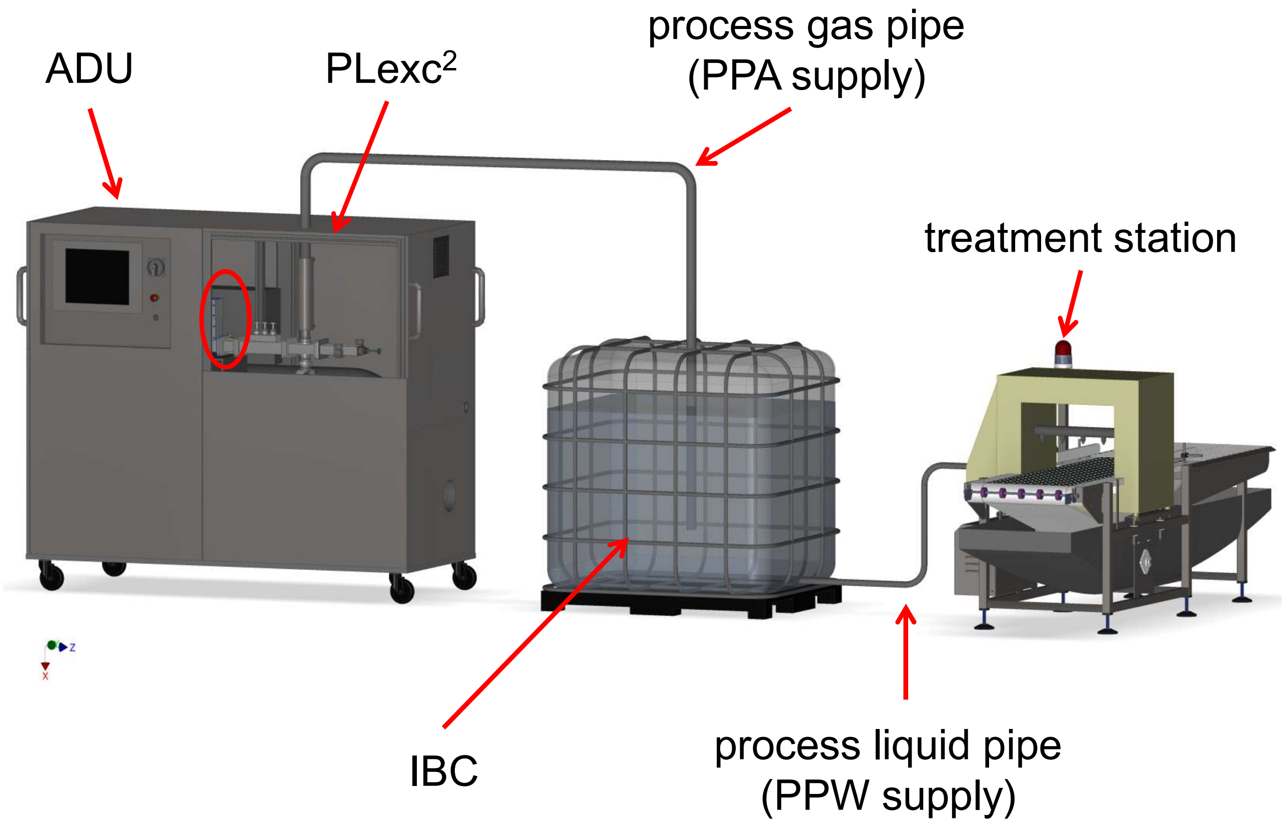
Auxiliary Decontamination Unit - ADU

complete integration of PPA generation



mobile stand alone disinfection system

PPW concept for pilot plant operation

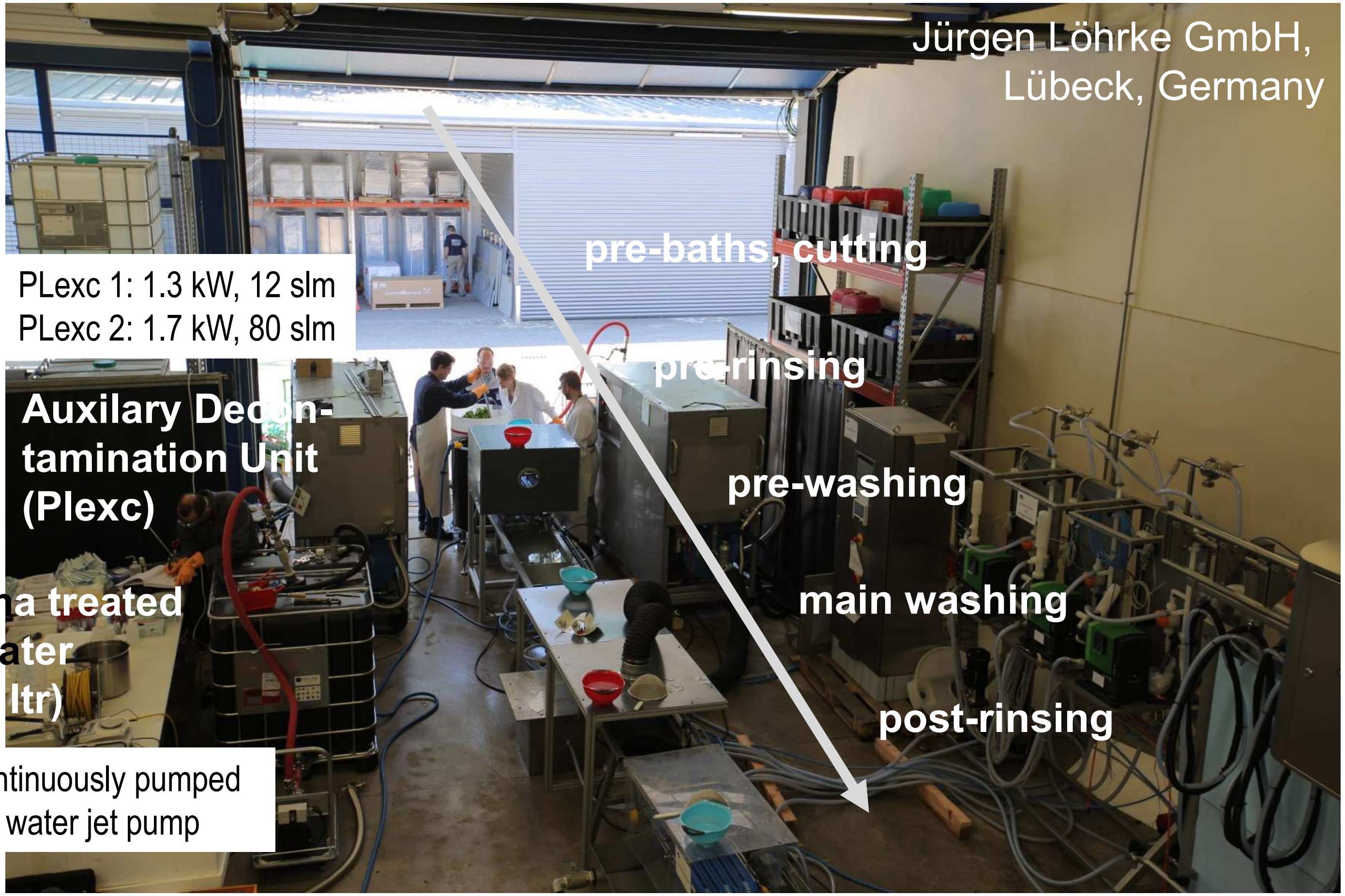


ADU = auxiliary decontamination unit
PLexc = self-igniting microwave plasma source
PLexc^2 = PLexc with additional plasma stage
PPA = plasma processed air
PPW = plasma processed water
IBC = intermediate bulk container

Sanitation of Fresh-cut Lettuce by PPW - Upscaling

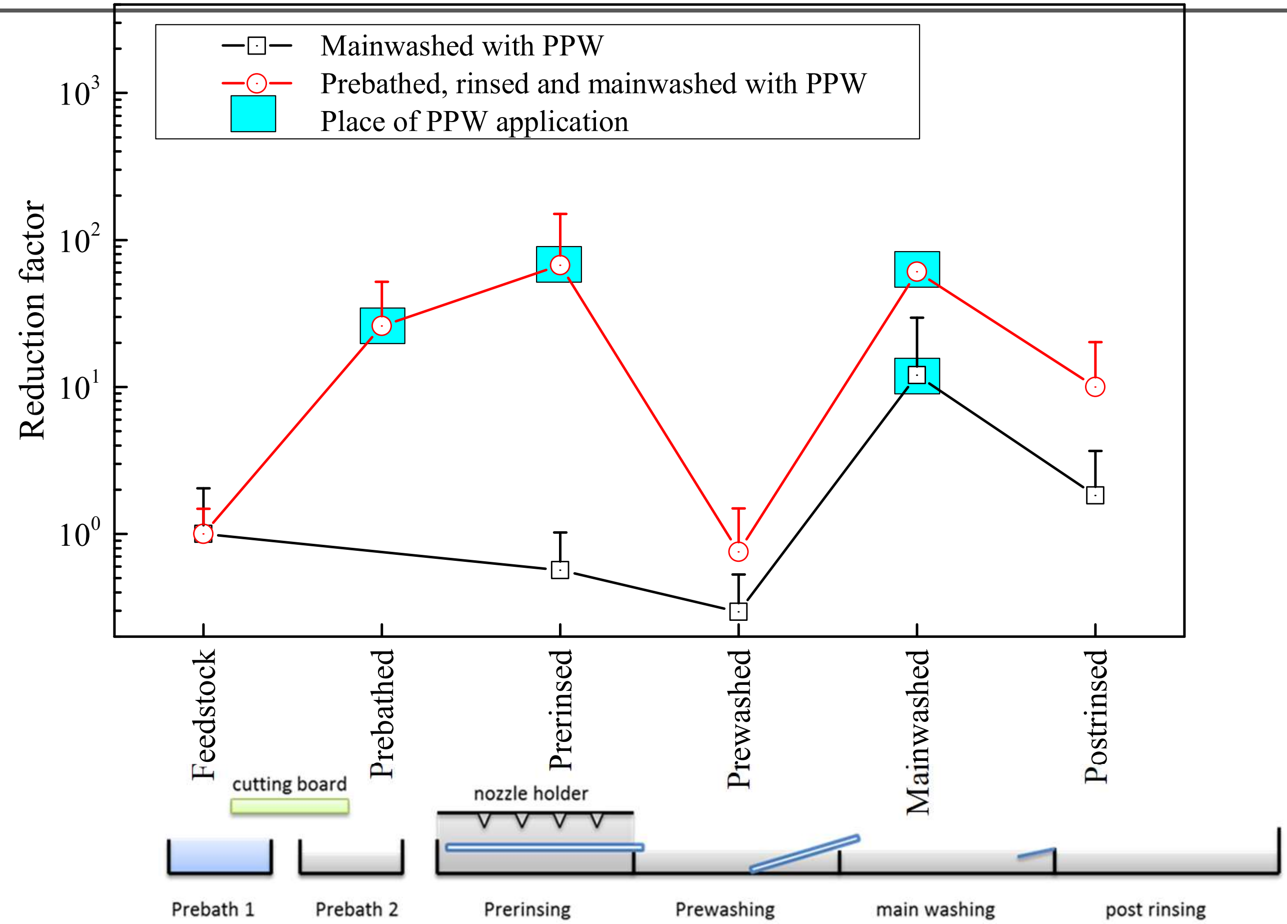
U. Schnabel, M. Andrasch, J. Stachowiak, Ch. Weit, Th. Weihe, Ch. Schmidt, P. Muranyi, O. Schlüter, J. Ehlbeck, "Sanitation of fresh-cut endive lettuce by plasma processed tap water (PPtW) – Up-scaling to industrial level," Innovative Food Science and Technology in print.

Sanitation of Fresh-cut Lettuce by PPW - Upscaling



U. Schnabel, M. Andrasch, J. Stachowiak, Ch. Weit, Th. Weihe, Ch. Schmidt, P. Muranyi, O. Schlüter, J. Ehlbeck, "Sanitation of fresh-cut endive lettuce by plasma processed tap water (PPtW) – Up-scaling to industrial level," Innovative Food Science and Technology in print.

Microbiological results of pilot plant trial



→ inactivation of up to 2 log steps for fresh-cut salad possible
→ clear limit for pilot plant trials: no controlled room temperature, no hygienic management

Conclusions (Agriculture)

- NO-dominated plasmas provide efficient means for the indirect treatment of seeds with plasma treated air (PPA)
- In addition to an effective decontamination can Reactive Nitrogen Species effectively stimulate biochemical responses resulting in an increased stimulation of germination (and growth) for suitable treatment parameters
- For seeds of already high germination rates are atmospheric pressure plasmas a potential replacement for chemical treatments

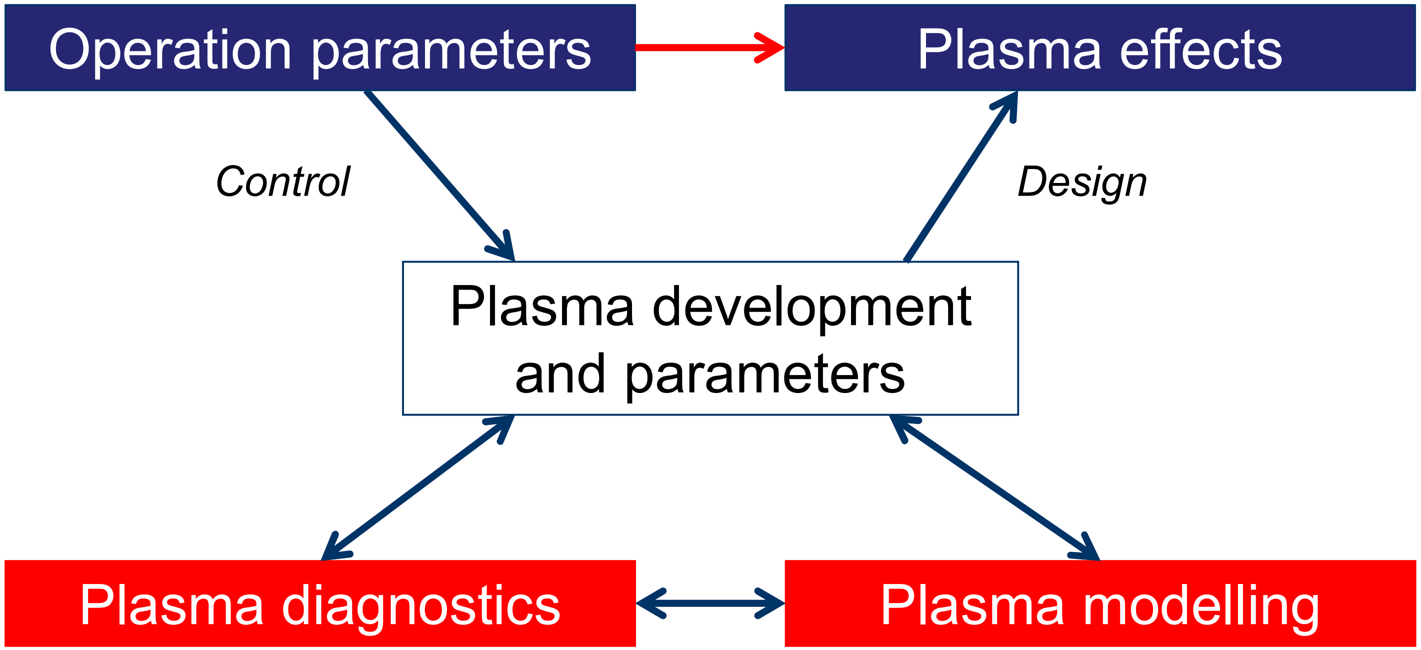
Summary

There is no life science today without PLASMA Physical Applications

- Innovative and promising application fields: hygiene (decontamination), agriculture, medicine
- Gentle and effective treatment of different materials and surfaces: radiation and heat sensitive materials and devices; seed, food and food products; living tissue
- Customization according to special product and process characteristics, demands, geometries
- On-demand treatment: electricity and – in some cases – gas supply needed; no other supplies, e.g. chemicals

Requirements for technological breakthrough

Reliable plasma sources are the key issue for the development of new technologies and applications, but need to be **fully characterized**.



K.-D. Weltmann & Th. von Woedtke, et al., Plasma Phys. Control. Fusion 59 (2017) 014031

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