# Plasma Life-Science Applications

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With contributions from partner and colleagues in the network project:

CAMPUS PlasmaMed

INP Greifswald

Leibniz Gemeinschaft

FROM THE IDEA TO THE PROTOTYPE

## First use of the term „plasma": Langmuir (1928)

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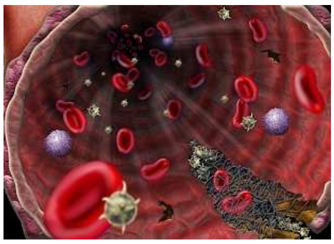
Langmuir's colleague Harold M. Mott-Smith remembers in 1971:

„ ... the discharge acted as a sort of substratum carrying particles of special kinds […] This reminds him of the way blood plasma carries around red and white corpuscles and germs. So he proposed to call our ‚uniform discharge' a ‚plasma'. Of course we all agreed."

H.M. Mott-Smith; Nature, 233, p. 219, (1971)



Credit: Nicole Rager-Fuller, NSF

Irving Langmuir
(1881–1957)
at General Electric
Laboratory (1948)

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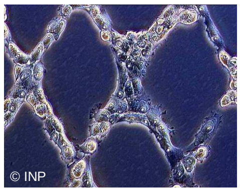
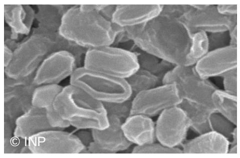
## Plasma for biomedical applications

**Surface modification**
- Biocompatibility
- Antifouling
- Microfluidics
- Cell culture systems




**Bio-Decontamination/Sterilization**
- Inactivation of pathogens and microorganisms on sensitive products (disinfection, sterilization) as well as gases and liquids
- Protection against biological warfare agents



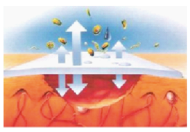

**Plasma Medicine**
- "classical": surgical applications (coagulation or ablation of tissue)
- new: wound and tissue treatment ("plasma can heal")


## Plasma life science

### Biomedical Applications

Surface Modification

Therapeutic Applications



Biological Decontamination

### Plasma Sources

## Surface modification for biomedical applications

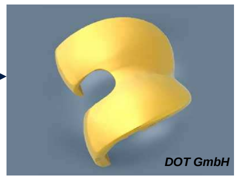
### Implants
- bone implants (joints, teeth)
- tendons and ligaments
- vascular grafts
- stents
- heart valves

### Therapy devices
- catheters
- dialysis devices
- pacemakers

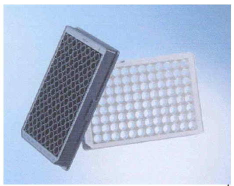
### Disposables
- cell culture dishes
- DNA chips
- biosensors
- high throughput screening systems

Plasma in use

Vacuum Plasma Spraying of titanium



Corrosion protection by PVD


Functionalized titer plates

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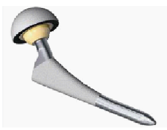
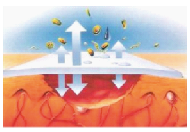
## Plasma life science

Biomedical Applications

| Surface Modification | Therapeutic Applications | Biological Decontamination |
|---|---|---|
|  |  |  |

Plasma Sources

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## Decontamination / Sterilization: some definitions

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

Robert Koch
(1843-1910)

**Antimicrobial Treatment (R. Koch, 1881):**
- Inactivation of microorganisms with the aim to reduce/avoid infections

***Disinfection:***
- *to put dead or living material in a situation, that it is no longer able to contaminate*
- Practical advise: reduction of infective micro organisms including viruses

***Sterilization:***
- *„Sterility is the absence of viable micro organisms."* (Ph. Eur., USP)
- Sterility Assurance Level SAL= $10^{-6}$: not more than one viable micro-organism in one million sterilized items of the final product

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## Sterilisation/decontamination procedures

***Standard and reference procedures***
- Steam sterilisation (heating in an autoclave): 121℃, 2 bar, 15 min
- Dry heat sterilisation : ≥ 160℃, ≥ 2 h

***Alternatives for heat sensitive products***
- Ionising radiation sterilisation (gamma radiation – radioisotopic source, electron beam – electron accelerator): 25 kGy
- Gas sterilisation (ethylene oxide)

- LTSF - Low-temperature steam/formaldehyde
- Chemical wet sterilisation (glutaraldehyde, peracetic acid, hydrogen peroxide)
- VHP - Vapor-phase hydrogen peroxide: hydrogen peroxide, peracetic acid
- UV irradiation (254 nm)

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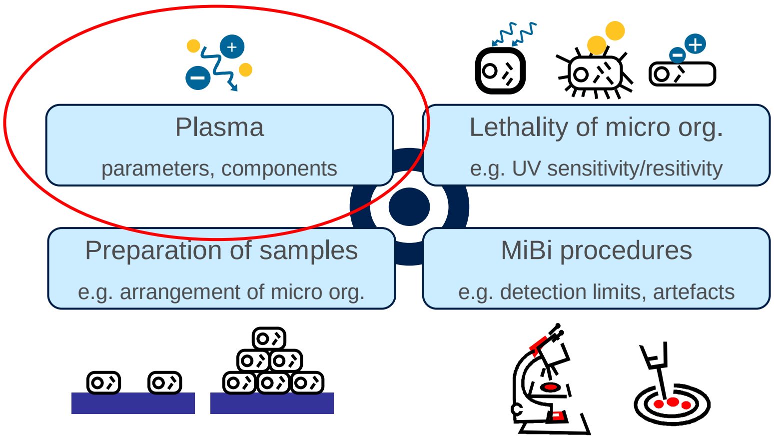
## Specific antimicrobial effects of plasmas

Antimicrobial effect of plasmas

- proven in many experiments with different plasma sources
- but effects very specific

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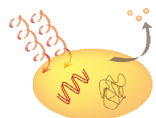
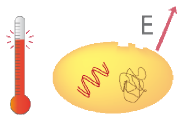
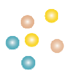
## Biologically active components of plasmas

**(V)UV-radiation**
- damage of DNA
- cell wall damage by photo-induced erosion

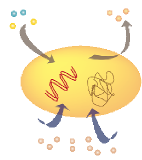


**Global Effects**
- Temperature → surface heating
- Electric Fields → electroporation

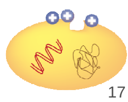


**Radicals and Chemical products**
- cell wall damage by reactive etching (O, $O_2$*)
- DNA damage by oxidation
- oxidation of proteins (O)
- oxidation of lipid bilayers (fatty acids) (OH)
- $O_3$ → cell respiration
- natural signal stimulation (NO)



**Charged particles (ions)**
- electrostatic pressure by accumulating charge carriers on membrane charge → lysis of cells



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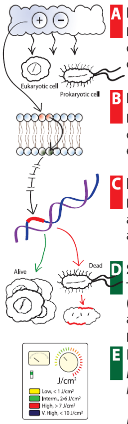
# Plasma-cell interactions: various hypotheses




**A Plasma ions play key role**
Role of positive and negative ions is related to catalysis of peroxidation processes in presence of reactive oxygen species.

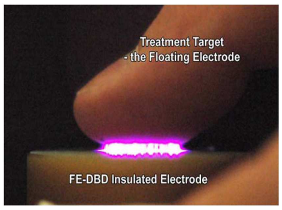
**B Primary target is cell membrane**
Peroxidation of phospholipids and polysaccharides is catalyzed by charged species. Water is required and effect of surrounding medium is important.

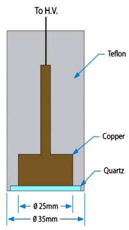
**C Intracellular biochemistry**
Lipid layer peroxidation leads to intracellular pathway activation (i.e. malondialdehyde, MDA formation) which alters DNA structure.

**D Selectivity**
Tissue sterilization without visible or microscopic (histological) damage; selective development of apoptosis in cancer cells; difference in metabolism of peroxidation products; etc.

**E Effect of dose**
*Low doses*: sterilization, blood coagulation.
*Intermediate doses*: cell proliferation, growth factor release, apoptosis in cancers, etc.
*High doses*: normal cell death.
*Very high doses*: necrosis.

**Figure 1.** Summary of key findings on plasma interaction with biological organisms.




*D. Dobrynin, G. Fridman, G. Friedman, A. Fridman, Physical and biological mechnaisms of direct plasma interaction with living tissue. New J. Phys 11 (2009) 115020*

*G. Fridman et al., Plasma Chem. Plasma Process. 26 (2006) 425*

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# Low-pressure plasma

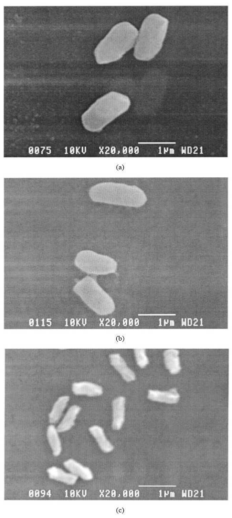


Fig. 9. SEM photographs showing (a) untreated spores, (b) spores inactivated under 0.7% added $O_2$ (same conditions as in Fig. 5), and (c) spores exposed to a 40-min treatment under 10% added $O_2$ (same conditions as in Fig. 5) but not necessarily all inactivated although much eroded.

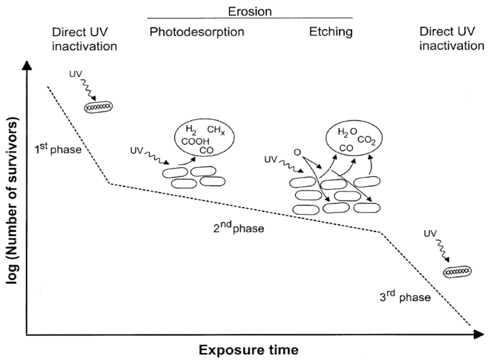


Fig. 1. Schematic illustration of the three-phase survival curve characterizing plasma sterilization, showing the mechanisms predominantly acting in each phase.

**UV radiation**

**+**

**Erosion caused by reactive species**

**Low-pressure afterglow plasma, 915 MHz/2.45 GHz, 100-200 W, $N_2$-$O_2$ gas mixtures; spores dried on a polystyrene surface**

*Philip et al., IEEE Trans. Plasma Sci. 30 (2002) 1429*



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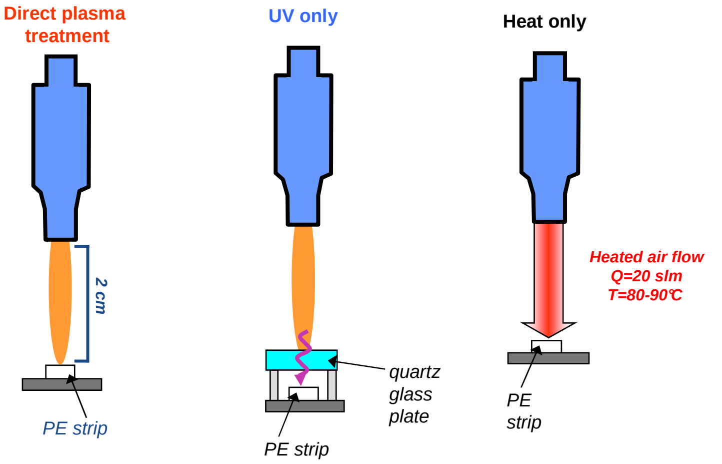
## Atmospheric-pressure plasma

### Atmospheric pressure RF Argon Plasma jet
(27 MHz, 10…60 W)

*Bacillus atrophaeus* spores, dried on PE strips; Separation of plasma compounds by quartz window or hot gas flow




*R. Brandenburg, J. Ehlbeck, M. Stieber, Th. von Woedtke, J. Zeymer, O. Schlüter, K.-D. Weltmann, Contrib. Plasma Phys. 47 (2007) 72-79*



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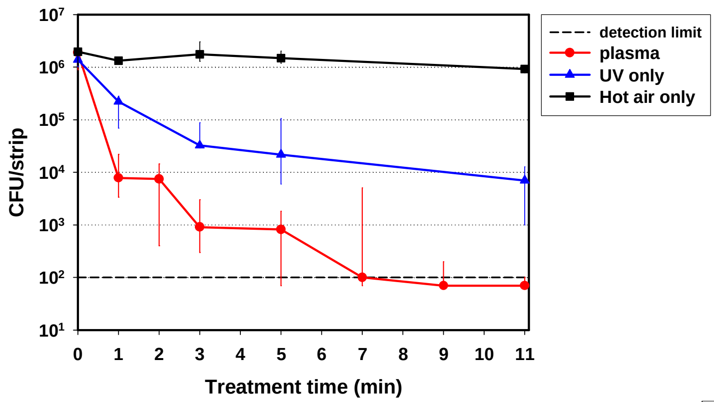


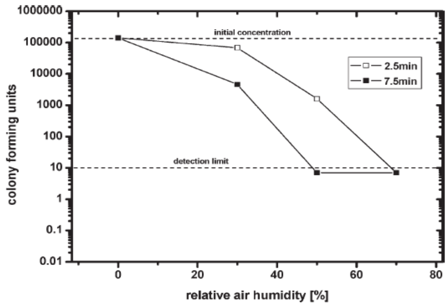

(Median, error bars: Min./Max.; je n=5)

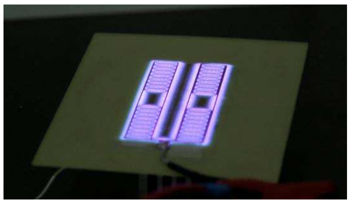
*R. Brandenburg, J. Ehlbeck, M. Stieber, Th. von Woedtke, J. Zeymer, O. Schlüter, K.-D. Weltmann, Contrib. Plasma Phys. 47 (2007) 72-79*

## Influence of humidity

### Indirect surface DBD on air: influence of humidity

***B. Atrophaeus*** **spores dried on PE strips**



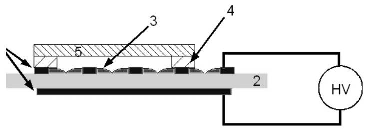



*Figure 6.* Remaining colony forming units (cfu) per strip in dependence of the relative air humidity for 2.5 and 7.5 min plasma treatment time at 250 ms plasma-on time, detection limit is 10 cfu, values below detection limit are set to 7.

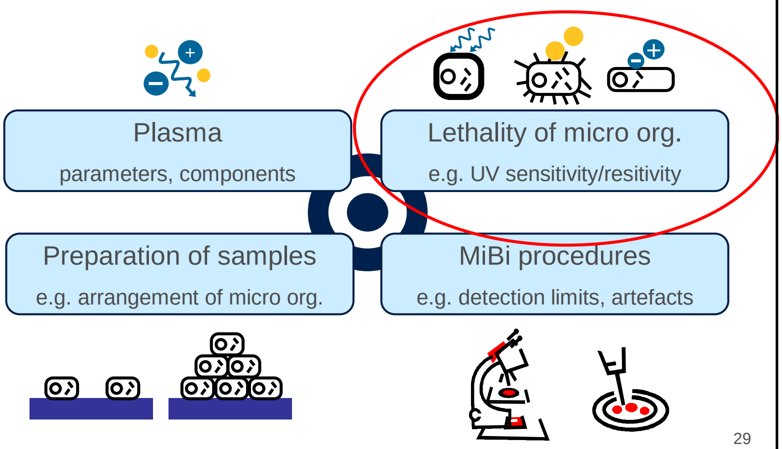
*M. Hähnel, Th. von Woedtke, K.-D. Weltmann, Plasma Process. Polym. 7 (2009) 244-249*



## Specific antimicrobial effects of plasmas

Antimicrobial effect of plasmas

- proven in many experiments with different plasma sources
- but effects very specific



## Specific antimicrobial effects of plasmas

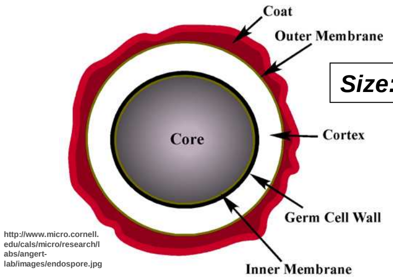
⇨ **Quantification of sterilisation effects**

# Resistance of microorganisms

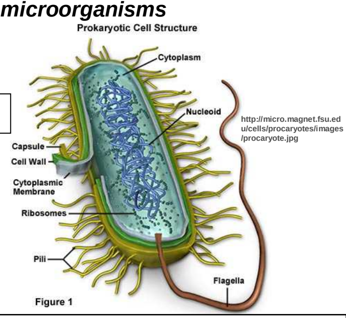
Quantifiable effectivity of an antimicrobial process depends on **nature** and **resistance** of the microorganisms used.

⇨ **Use of test microorganisms with maximum resistance against the process to be examined.**

***Bacterial spores vs. vegetative microorganisms***




*Size: 0.1-1 µm*




| *High resistance against external factors: Bioindicators for sterilization control* | *Different resistance against external factors: heat, UV, chemicals, plasma components, …* |
| --- | --- |

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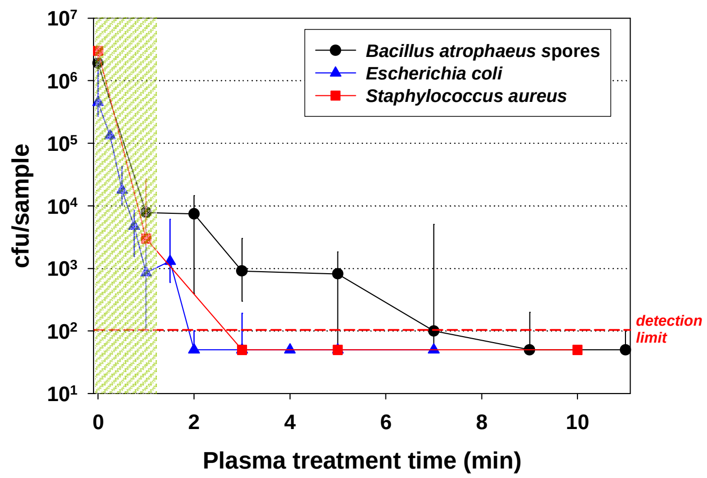
## Microorganism resistance

**Rf-driven Plasma Jet, 20 W, Argon 20 slm**

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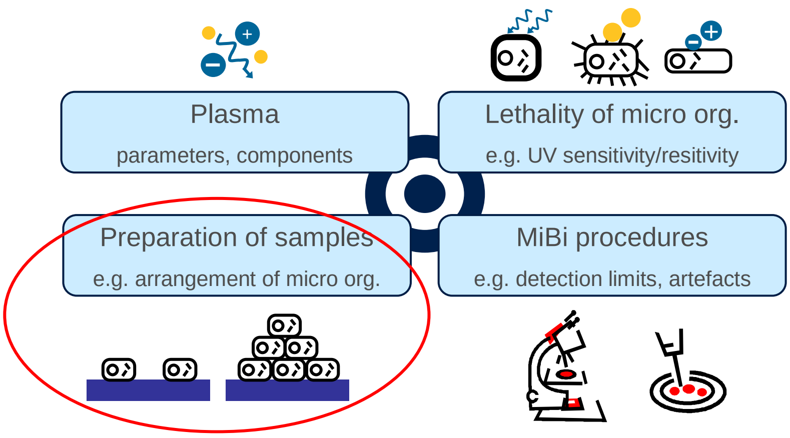
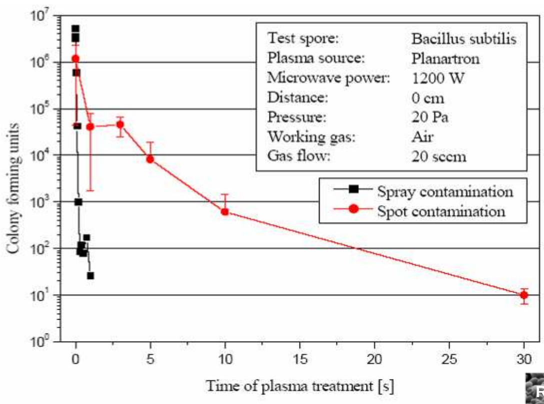
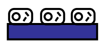





## Bacterial load

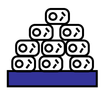



- Spray: 2 $10^4$ MO/cm$^2$

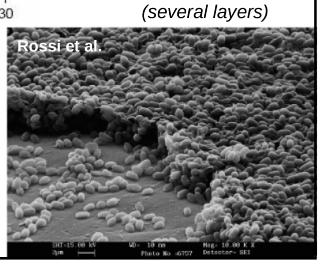


*... more or less single spores on surface*

- Spot: 1.4 $10^7$ MO/cm$^2$



*... stacked spores (several layers)*




- Identical plasma treatment leads to different lethal effects!

*F. Rossi et al., Plasma Process. Polym. 3 (2006) 431; J. Wunderlich et al. ISPC 2003*

# Substrate material

**Low-pressure glow-discharge oxygen RF plasma, 27.12 MHz, 300 W, continuous and pulse mode (5 s on, 25 s off) performance; forced-air cooled discharge vessel; *B. subtilis* spores dried on glass and Al-foil**

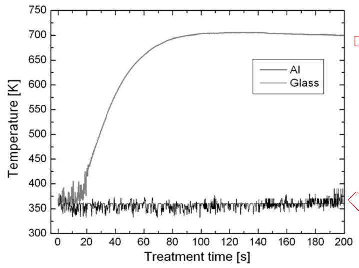



**Figure 4.** The sample temperature of the Al substrate (upper curve) and the glass substrate (lower curve) in continuum mode.

Different substrate heating caused by surface recombination of O-atoms

Combined effects of temperature and O-based atom-by-atom etching of bacteria

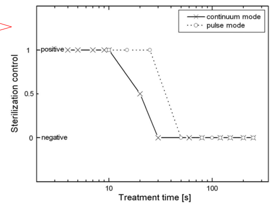



**Figure 5.** The sterilization of *B. subtilis* spores on the aluminium sample holder in continuum and pulse mode.

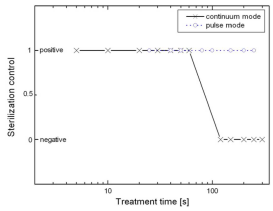



**Figure 6.** The sterilization of *B. subtilis* spores on the glass sample holder in continuum and pulse mode.

*Cvelbar et al., J. Phys. D: Appl. Phys. 39 (2006) 3487*

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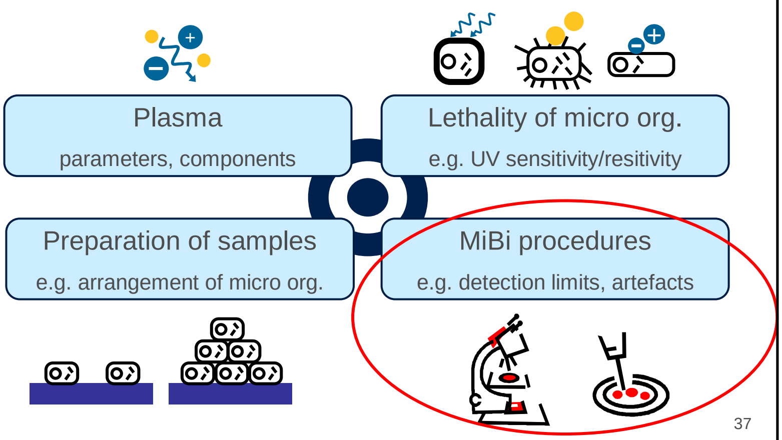

## Plasma “sterilisation“

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**What does it mean: sterility/sterilisation?**

**Ph. Eur. [USP, JP]:**
**„Sterility is the absence of viable micro-organisms.“**

**Sterility Assurance Level - SAL**

**$10^{-6}$**

denotes a probability
of not more than one viable micro-organism
in $1 \times 10^6$ sterilised items

**Problem: Proof of sterility assurance**

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## Microbiological tests

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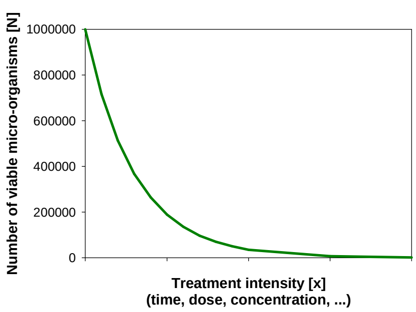
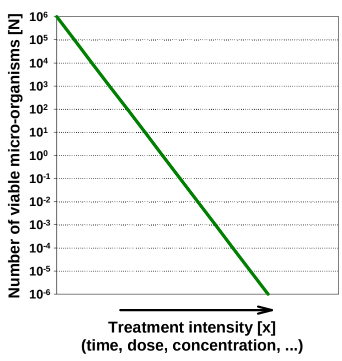
**Exponential microorganism inactivation kinetics**




**general assumption!**

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# Direct cell counting (spread-plate method)

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... applied if viable micro organisms present on all test objects

Detection limit:

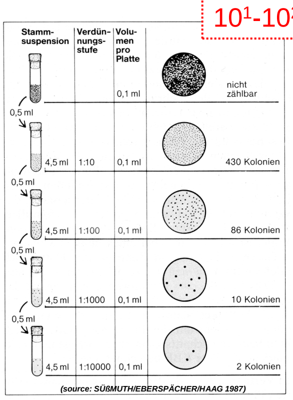
$10^1$-$10^2$ CFU/obj.

***Treated test objects***

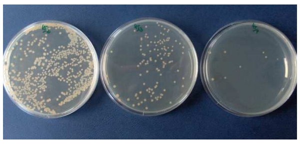

Agitation in 10 ml 0.9 % NaCl

Dilution series with 100 µl aliqout

Spread on culture medium (agar) and incubation




(source: SÜßMUTH/EBERSPÄCHER/HAAG 1987)



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# Membrane filtration

CAMPUS PlasmaMed

... applied when less than a few hundred viable micro organisms on test object expected

Detection limit:

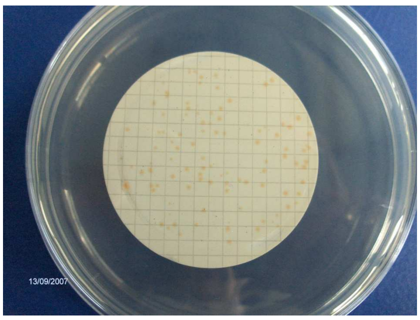
1 cfu/obj.

***Treated test objects***


Agitation in 10 ml 0.9 % NaCl

Membrane filtration

Filter on culture medium (agar) and incubation

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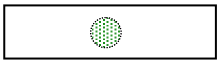
## Fraction negative method

... applied if test objects both with and without viable micro organisms expected



***Treated test objects***


Incubation in nutrient solution (broth)

turbidity of broth gives evidence for microbial growth

Detection limit:

$10^{-1}$ ... $10^{-2}$ cfu/obj.

$$m = - \ln(n_0/n)$$

m ... mean number of survivors per test object

$n_0$ ... number of test objects without viable micro organisms

n ... number of identically treated test objects n



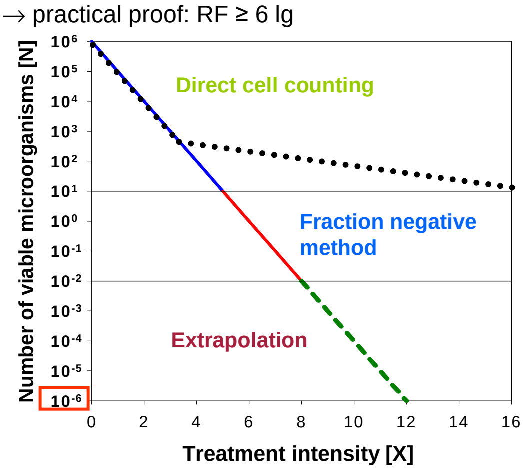
## Plasma-“Sterilisation“

⇨ **Limits:**

„Sterility is the absence of viable microorganisms.“

→ Sterility Assurance Level SAL= $10^{-6}$ (Ph. Eur.)

→ practical proof: RF ≥ 6 lg

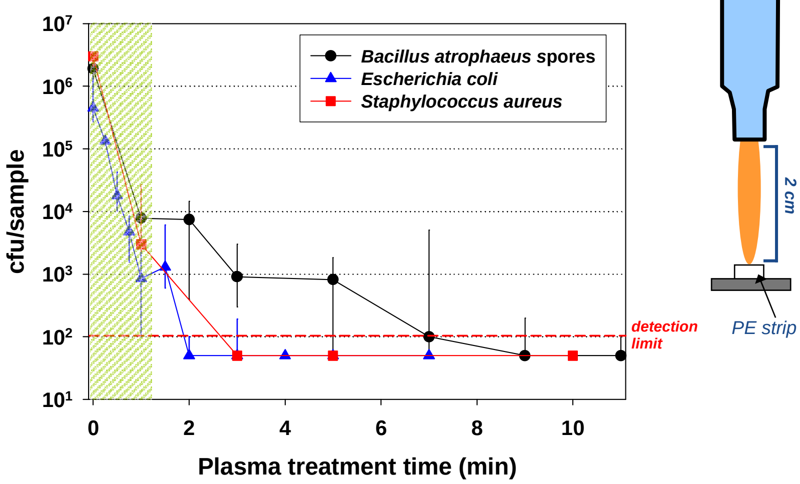



**Ideal:**
linear inactivation kinetics
↓
continuous effectivity

**Real:**
discontinuous effectivity

## Real inactivation kinetics

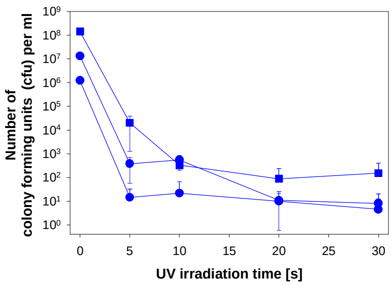
Rf-driven Plasma Jet, 20 W, Argon 20 slm





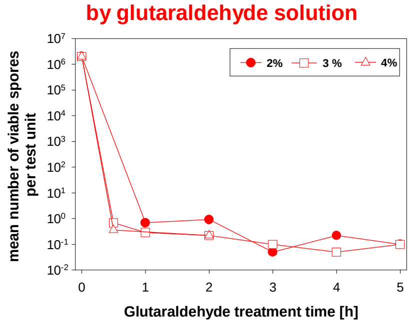

## Other non-thermal treatments

UV irradiation of *B. atrophaeus* spore suspensuions




Direct cell counting
mean ± SD
n=10 per data point

Treatment of *B. atrophaeus* spore strips by glutaraldehyde solution




Fraction negative method
m = - ln ($n_0$/n)
n=20 per data point


*von Woedtke & Jülich, Pharmazie 56 (2001) 561*
*von Woedtke et al., Biosens. Bioelectron. 17 (2002) 373*
*von Woedtke et al., J. Hosp. Infect. 55 (2003) 204*

## Theory of antimicrobial activity

### Heat-based processes

- *global excited energy* ***state***
- lethal changes of micro-organism structures resulting from a **constant and ubiquitous activity**
  **⇒ inactivation kinetics independent from number of targets → extrapolation possible**

### Non-thermal processes

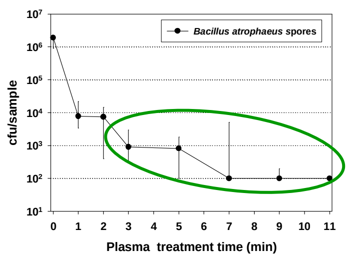
- *discrete energy quanta* or *reactive molecules*
- lethal changes of micro-organism structures resulting from „**hits**“ **at** susceptible **target structures**
  **⇒ inactivation kinetics strongly dependent from number of targets → extrapolation problematic**



## Resulting practical demands for plasma „sterilization“

Proof of antimicrobial efficacy
on the highest experimentally accessible level

- use of most resistant test micro-organisms
- documentation of inactivation kinetics over ~ 5 log first of all in the range of low contamination rates (down to $10^{-2}$ if possible)




ASP STERRAD 100S

OVER 15 YEARS OF PROVEN PERFORMANCE. The STERRAD® 100S System can single-handedly sterilize heat- and moisture-sensitive devices in 55 minutes. 51 trays can be sterilized with the STERRAD® 100S System in the time it takes to complete 34 trays with VHP or 6 trays with EtO.* Our proven, low temperature hydrogen peroxide gas plasma technology efficiently eliminates the potential hazard of toxic residue, ensuring a safe working environment.

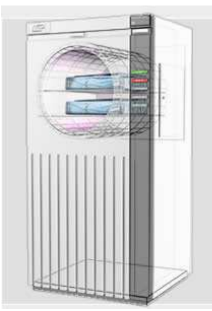




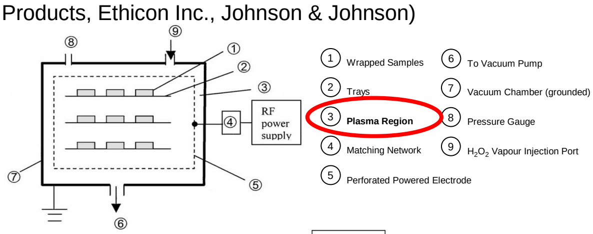
**Commercially available "plasma sterilization":**

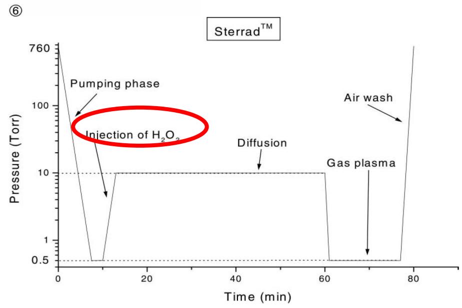
Sterrad® Sterilization Systems

(Advanced Sterilization Products, Ethicon Inc., Johnson & Johnson)



**Sterrad® 100S**




*Lerouge et al., Plasmas and Polymers 6 (2001) 175; Moisan et al., Int. J. Pharm. 226 (2001) 1; http://www.aspjj.com*

## Sterilisation and decontamination using low-pressure plasmas

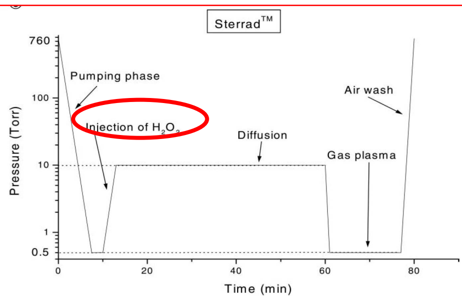
CAMPUS PlasmaMed

**Commercially available "plasma sterilization":**
Sterrad® Sterilization Systems
(Advanced Sterilization Products, Ethicon Inc., Johnson & Johnson)

**Sterrad® 100S**

- **inherent efficacy is above all due to hydrogen peroxide**
- **plasma phase: residue detoxifying process**

*Krebs et al., Int J. Pharm. 160 (1998) 75*




*Lerouge et al., Plasmas and Polymers 6 (2001) 175; Moisan et al., Int. J. Pharm. 226 (2001) 1; http://www.aspjj.com*

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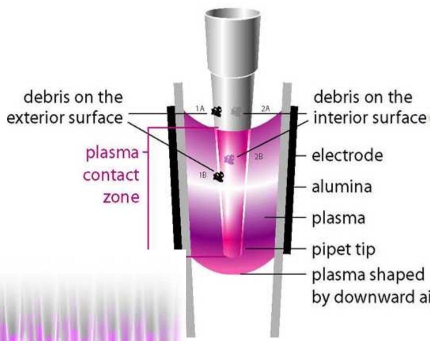
## Sterilisation and decontamination using atmospheric pressure plasmas

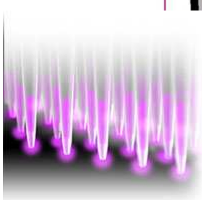
CAMPUS PlasmaMed

***Commercially available atmosperic pressure plasma system:***
**TipCharger™** (Cerionx Inc., Rxton, PA, USA)

- low-temperature ('cold') atmospheric pressure plasma (DBD) used to clean and sterilize pipet tips by removing organic substances from treated surfaces.

TIP CHARGER by CerionX




www.cerionx.com

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## Plasma-“Sterilisation“

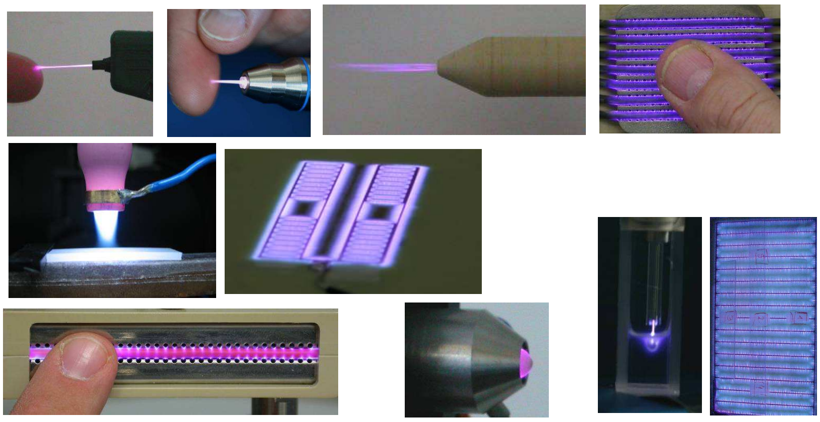
CAMPUS PlasmaMed

⇨ **additional features of atmospheric pressure plasma:**

- contracted plasmas

  ⇨ effects are limited locally

  ⇨ effects can be located exactly



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## Plasma-“Sterilisation“

CAMPUS PlasmaMed

⇨ **Chances of atmospheric pressure plasmas:**

- customisation according to special product characteristics, demands, geometries


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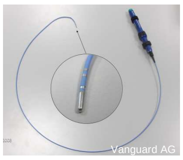
# Plasma technology for biological decontamination

CAMPUS PlasmaMed

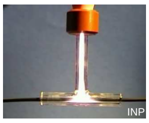
‘Sterilization’ of heat sensitive products

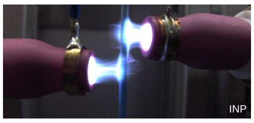
- Medical devices (instruments, implants)
- Pharmaceutical packagings
- Pharmaceutical preparations



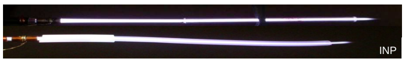










PLASMOSE

endoplas
science for fine lumen plasma

2004: Beginn der Verbundprojekts „PLASMOSE – Plasmagestützte Oberflächenmodifizierung mittels modularer selektiver Plasmaquellen“

GEFÖRDERT VOM Bundesministerium für Bildung und Forschung

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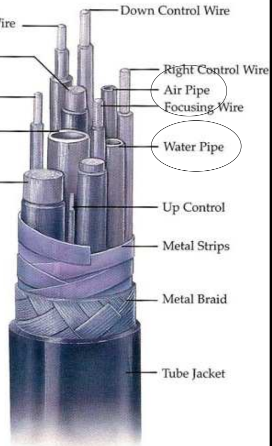
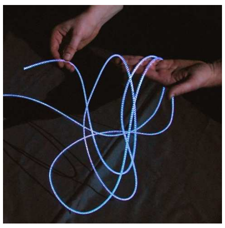
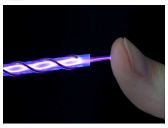
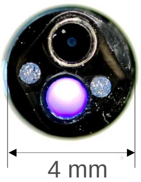
# Endoscopes as medical instruments

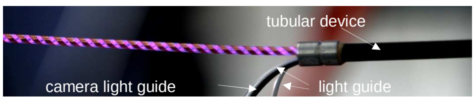
CAMPUS PlasmaMed



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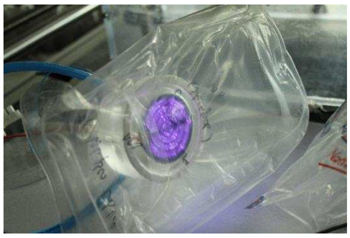
## Plasma inside closed packaging

- Adapted Dielectric Barrier Discharge (DBE)
  Plasma ignited inside of the packaging
- Prooven by FTIR-Gasanalyses within packaging



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## Sterilisation and decontamination using atmospheric pressure plasmas

### ⇨Chances and perspectives:

1. Antimicrobial effectivity of atmospheric pressure plasmas against a broad spectrum of microorganisms was proved in many cases
2. Ubiquitous applicable sterilization procedures based on atmospheric pressure plasma are hardly to realize
3. Several possibilities to integrate atmospheric pressure plasma sources as part of special product and/or process-related master plans of (micro-) biological decontamination, above all for manufaacturing and (re-)processing of medical devices
4. Plasma treatment of liquids expandable:
   - microbiological decontamination
   - Investigation of biological plasma effects
5. Huge potential in the field of *in vivo* antiseptics → **plasma medicine**

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## Plasma life science

Biomedical Applications

| Surface Modification | Therapeutic Applications | Biological Decontamination |
|---|---|---|
|  |  |  |

Plasma Sources

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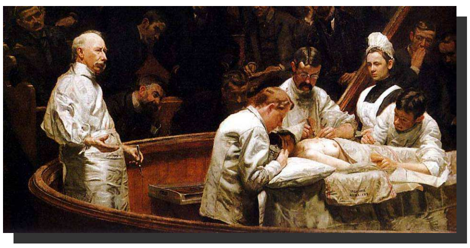
## Plasma medicine

„Recent demonstrations of plasma technology in the treatment of living cells, tissues, and organs are creating a new field at the intersection of plasma science and technology with biology and medicine – *Plasma Medicine*.“

M. Laroussi & A. Fridman, Editorial

Plasma Process. Polym. 5 (2008) 501



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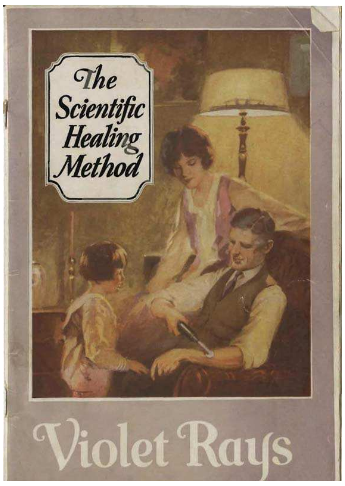
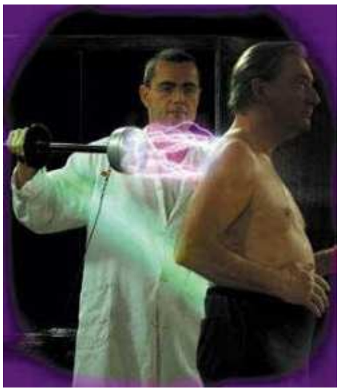
## ‘Violet Rays’ or ‘Violet Wands’ & the Zeileis method

Antique 'quack' medical devices claimed to be useful in electrotherapy




www.electrotherapymuseum.com

The Zeileis method (1912) – HV treatment



1 H. BURGER: The Doctor, the Quack, and the Appetite of the Public for Magic in Medicine,Proceedings of the Royal Society of Medicine, 1.11.1933 [1]
2 Zeileis-Institut, Valentin-Zeileis-Straße 33, A-4713 Gallspac



## „Conventional“ surgical plasma applications

**Argon Plasma Coagulation (APC)**
ERBE Elektromedizin GmbH,Tübingen, Germany

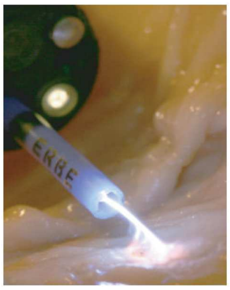
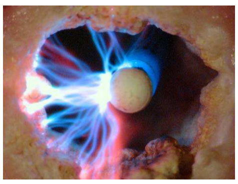



Figure 6: Endoscopic application of APC



*Zenker M, GMS Krankenhaushyg Interdiszip 3 (2008) Doc15; Raiser & Zenker, J. Phys. D: Appl. Phys. 39 (2006) 3520*

**Coblation®** (cold ablation)
ArthroCare Corp., Synnyvale, CA,USA

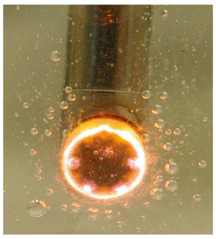
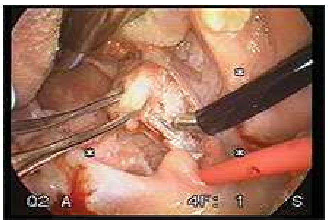


**Fig. 1** Photograph of a planar-electrode-type electrosurgical device operating in isotonic saline solution at 300 volts rms. (Online colour: www.cpp-journal.org).




*Stalder KR, Woloszko J, Contrib Plasma Phys 47 (2007) 64; www.arthrocareent.com/*

## Plasma medicine: step forward

**lethal plasma effects**

**(antimicrobial; surgical)**

**+**

**non-lethal plasma effects**

**Selectivity of plasma treatment**

**Plasma can heal!**

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## Actual Focus: Wound Healing

Chronic wounds

- **4.5 to 5 million people in Germany suffer from chronic wounds**
- i.e. ca. 5% of all stationary patients in hospitals and rehab hospitals
- ⇨ loss quality of life for patients

⇨ health economic problem: > 5 Mrd. € per year in Germany
⇨ increasing problem because of ageing population

e.g. pressure ulcers, venous insufficiency ulcers, **diabetic/neuropathic ulcers**

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## Wound antiseptics

CAMPUS PlasmaMed

# **Chronic wounds** (no healing within 8 weeks)

Frequent cause: **wound infections**

*Staphylococcus aureus, Staphylococcus epidermidis*
*Streptococcus pyrogenes,* MRSA
*Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa*
anaerobians

Conventional therapy: chemical antiseptics

WIRKSTOFFAUSWAHL
Antiseptika im
Kampf mit den Keimen

***expenditure of time, adverse effects***

**!**

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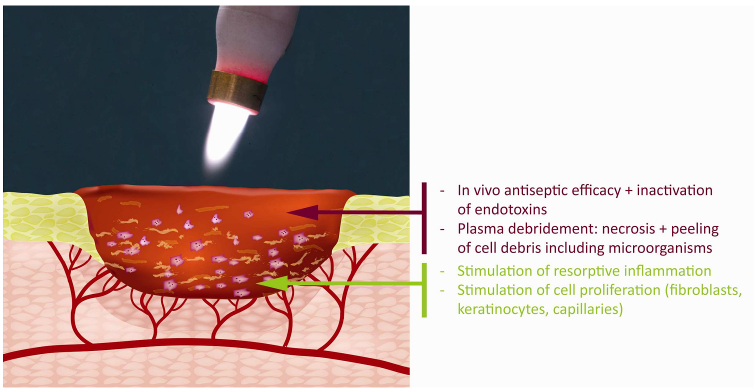
## Plasma Medicine: vision

CAMPUS PlasmaMed

**Superficial cleaning and antiseptics**

**+**

**Stimulation of tissue regeneration in deeper layers**




**Integrated concept of plasma-based wound treatment**

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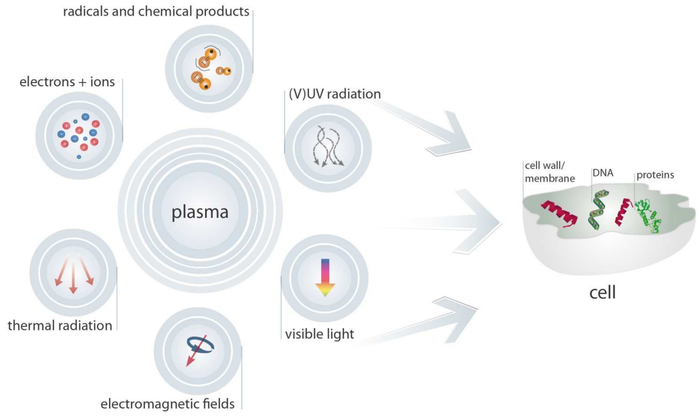
CAMPUS PlasmaMed

## Plasma-cell interactions




PLASMA | GAS PHASE | LIQUID PHASE | CELLS

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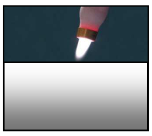
CAMPUS PlasmaMed

## Experimental Plasma Medicine

**Plasma sources**

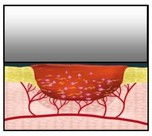


- development
- adaptation
- diagnostics
- optimization, control, monitoring
- experimental applications

in vitro

in vivo

**Biological effects**



- physiological liquids
- cells:
  - microorganisms
  - mammalian cells
- cell and tissue cultures:
  - not contaminated/infected
  - contaminated/infected
- isolated tissues/organs
- organisms:
  - animal experiments
  - clinical investigations

Therapeutic Applications

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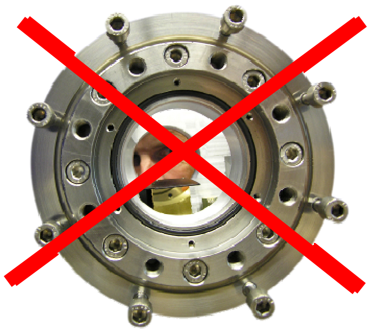
## The bans for new methods in medicine …



**Non-thermal** **Atmospheric Pressure**

**Plasma Sources**



## Basic requirements for therapeutic applications

Plasmas which ...

... operate at atmospheric pressure

- treatment of living objects
- manageability (operation at open atmospheres)

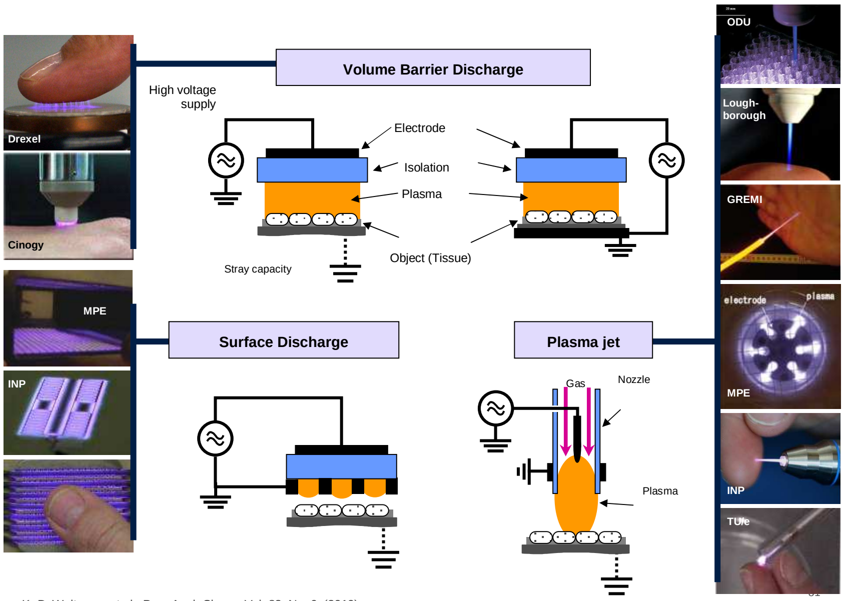
... operate stable

- reproducibility of treatment results
- reliability

... are well characterized

- quantitative knowledge on plasma parameters and “macroscopic” characteristics
- process monitoring
- influence by operation parameters

## Atmospheric pressure plasmas for biomedicine



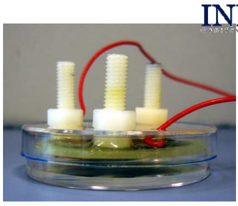

K.-D. Weltmann et al., Pure Appl. Chem., Vol. 82, No. 6, (2010)

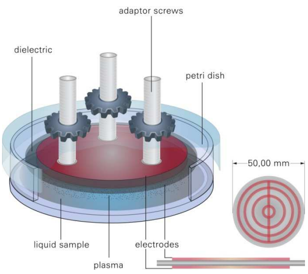
## From kINPen 09 to kINPen MED

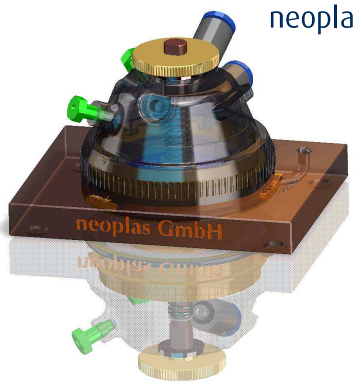
Simple and safe use under consideration of the excisting and known basic plasma properties

- Requirements according to DIN EN 60601-1
- PLL-Electronic for optimal Plasmaignition
- Gas-flow-control, automatic shut down
- Timercontrol to secure a maximum dosage
- Burst-Mode: lower irritation by current and temperature to the surface, lower radiation output
- Distance holder for reproducable treatment

## Adapted device for petri dishes



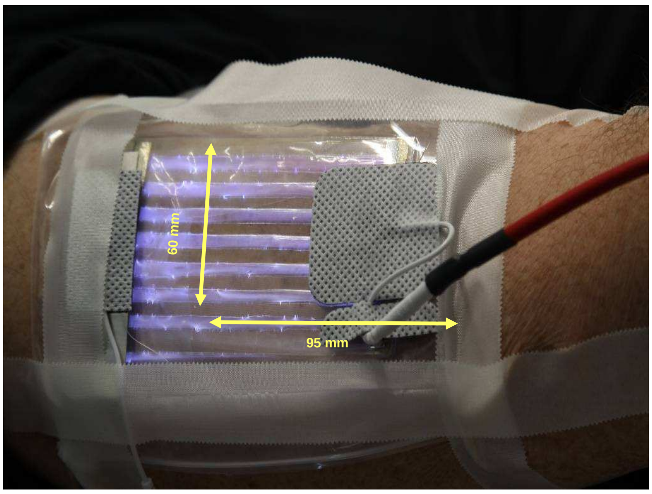



- closed confinement
- variable distance DBD to surface/suspension
- well defined and stable discharge and treatment parameters possible

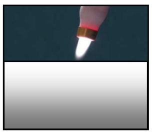


## Flexible discharge arrangement



## Experimental Plasma Medicine

**Plasma sources**

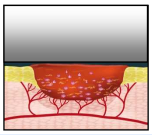


- development
- adaptation
- diagnostics
- optimization, control, monitoring
- experimental applications

in vitro

in vivo

**Biological effects**



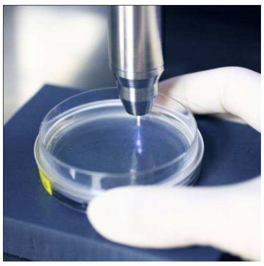
- physiological liquids
- cells:
  - microorganisms
  - mammalian cells
- cell and tissue cultures:
  - not contaminated/infected
  - contaminated/infected
- isolated tissues/organs
- organisms:
  - animal experiments
  - clinical investigations

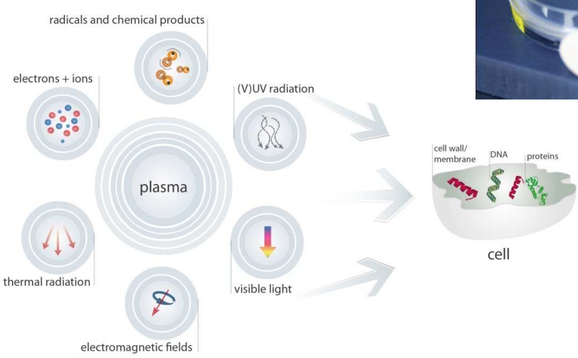
Therapeutic Applications



## *In-vitro* characterization of plasma-cell interactions

- General estimation of biological effectivity
- Estimation of therapeutic options
- Estimation of possible risk factors
- Insights into reaction mechanisms



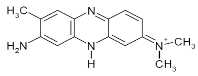


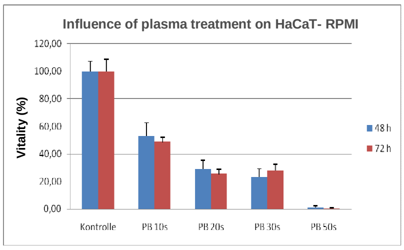
## Cells in suspension → cytotoxicity

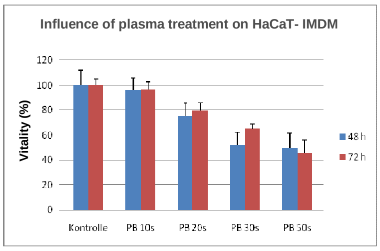
CAMPUS PlasmaMed

**Keratinocytes (HaCaT) in suspension, different media; kINPen (Ar 3.8 slm); seeding after plasma treatment**

Neutral red uptake (NRU) assay 48 and 72 h after plasma treatment
(uptake of the dye into lysosomes of vital cells → dyed cells = living cells)




**Cytotoxic effects dependent on plasma treatment time and on cell culture medium**

RPMI – Rosewell Park Memorial Institute,
IMDM – Iscoves Modivied Dulbeccos Media (more glucose, buffer, pyruvate)

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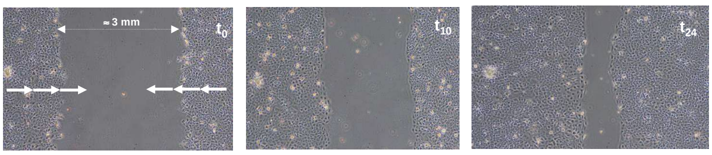
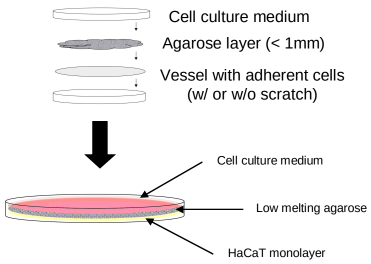
## Adherent 2D cell cultures → scratch assay

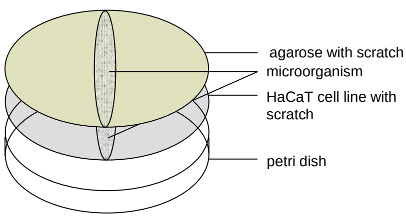
CAMPUS PlasmaMed

***Scratch assay***: mechanical scratching of a 2D keratinocyte (HaCaT); detection of time-dependent scratch-width reduction




Modified scratch assay

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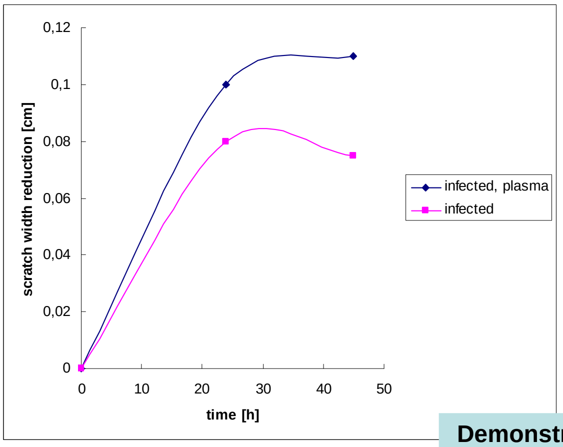
*K. Wende, K. Landsberg, U. Lindequist, K.-D.. Weltmann, Th. von Woedtke, IEEE Trans. Plasma Sci. 38 (2010) 2479 - 2485*

## Adherent 2D cell cultures → scratch assay

**2D keratinocytes (HaCaT) culture (RPMI), co-cultivated with *S. epidermidis*;**
**40 s APPJ (Ar gas)**

***Modified scratch assay***: protection of cells by agarose overlay




**Demonstration of selective antiseptic plasma treatment**

*K. Wende, K. Landsberg, U. Lindequist, K.-D.. Weltmann, Th. von Woedtke, IEEE Trans. Plasma Sci. 38 (2010) 2479 - 2485*

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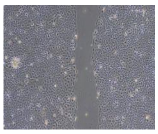
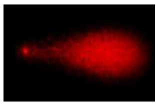
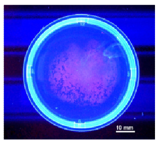
## Key results Plasma Vitro

PlasmaVitro

- Stimulation of cell regeneration by atmospheric pressure plasma treatment
- No substantial structural changes of intracellular proteins (charge influenced)
- Dose dependent, but reversible influences on cell DNA
- Dose dependent emergence/generation of ROS in cells
- Important influence of cell culture medium on in vitro results







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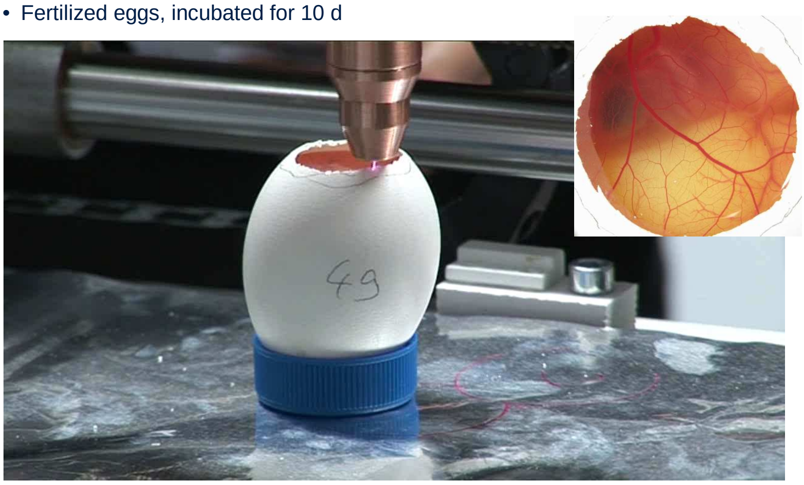
## Living tissue – irritation potential

HET-CAM: Hens‘s Egg Test – Chorioallantoic Membrane
- Standard test for eye and skin irritating potential of chemicals
- Fertilized eggs, incubated for 10 d

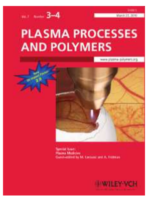



*C. Bender et al., Plasma Process. Polym. 7 (2010) 318–326*



## Key results Plasma Cure

- Proof of tissue compatibility of plasma treatment in antiseptically effective doses
- Inactivation of bacteria without irritation of the surrounding cells/tissue
- Antiseptic plasma effect on human skin comparable to conventional antiseptics
- No influence on skin barrier function as well as on the antioxidative potential of the skin


A. Hammann et al., Skin Pharmacol. Physiol. 23 (2010) 328-332

C. Bender et al., Plasma Process. Polym. 7 (2010) 318–326

## Key results Plasma Derm

PlasmaDerm

- Antimicrobial effect on bacteria, fungi and parasites shown
- Safety of application proven e.g. no skin irritation, no influence on skin barrier function, no desiccation, no change of skin pH-value, no other visible side effects
- Successful treatment of athlet‘s foot (Tinea pedis)
- Successful single treatment of inflammatory skin diseases e.g. psoriasis, acne, lichen ruber

Acne vulgaris

Before and 72 h after APPJ treatment (3x15 s)

Lichen ruber planus

Before and 48 h after APPJ treatment (3x15 s)

G. Daeschlein et al., Plasma Process. Polym. 7 (2010) 224-230
G. Daeschlein et al, IEEE Trans. Plasma Sci. 38 (2010) 2969-2973
G. Daeschlein et al., IEEE Trans. Plasma Sci. 39 (2011) 815-821

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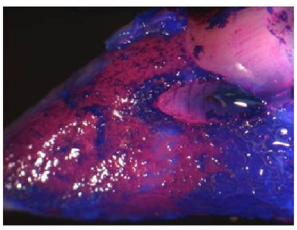
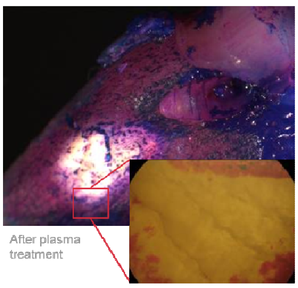
## Key results Plasma Dent

PlasmaDent

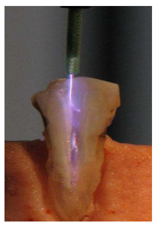
- Successful treatment of teeth root channel *in vitro*
- Inactivation of biofilms on teeth and on dental implants
- Improved cell adhesion on implant surfaces
- Successful decontamination and coating of dental prosthesis



Before plasma treatment



After plasma treatment



Th. Kocher et al., Greifswald University

I. Koban et al., GMS Krankenhaushyg Interdiszip. 2009;4(2):Doc09.
I. Koban et al., New J. Phys. 12 (2010) 073039
I. Koban et al., Plasma Process. Polym, submitted

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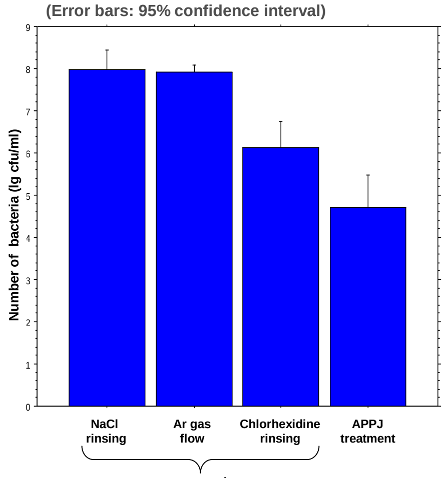
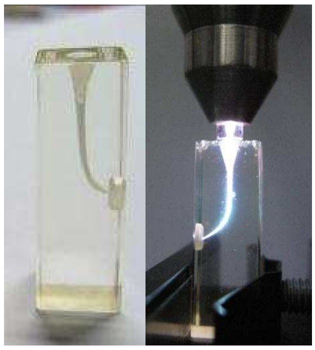
## Highlight Plasma Dent (example)
## Endodontics – reduction of *E. feacalis*

PlasmaDent

*Enterococcus faecalis* inactivation
**(Error bars: 95% confidence interval)**



Root canal model

- Chlorhexidine (standard): 2 log (after 5 min. treatment)
- APPJ (kINPen): 3…4 log (after 1 min. treatment)

Th. Kocher et al., Greifswald University

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## Example
## German shepherd dog with chronic wound

PlasmaCure

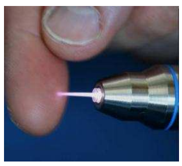
Persisting 4 years

Plasma + Polihexanide

'Harras', 9 years

After 6.5 weeks

After 11 weeks



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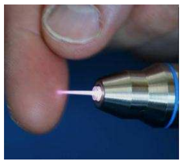
## Example
## Labrador with chronic wound

Plasma + Polihexanide

‚Astor, 12 years

2010-12-08

2011-01-10



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## Outlook – „Plasma goes into hospital“

### Clinical needs

Indications (examples)
- chronic inflammatory diseases
- acute infections
- auto immune diseases

In vitro tests
- susceptibility
- toxicity
- selectivity

Clinical tests
- susceptibility
- compatibility
- long-term effects

### Practical needs

For the patient
- no fear
- no pain
- no delay

For the doctor
- simple („one doctor – one knob“)
- robust (mm not µm)
- small (ambulant treatment)

effectivity

safety

**TISSUE TOLERABLE PLASMA - TTP**

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## Summary: chances & risks

CAMPUS PlasmaMed

▪**Chances of Tissue Tolerable Plasma:**

1. Prevention and treatment of diseases (chronic wounds, skin and mucosal infectious diseases, localized tumors, keloid formation, promotion of angiogenesis, tissue ablation, hemostasis)
2. Inhibition of biofilm formation by surface treatment and by direct action on biofilms
3. Promotion of incorporation of implants into viable tissue by changing the surface (hydrophobicity, plasma steered application of antimicrobial active layers with drug delivery function)
4. Promotion of improved penetration of topically applied drugs with therapeutic outcome
5. Improved cleaning performance in the treatment process of medical devices by surface modification.

▪**Risks of plasma medicine**:

- A few physical, more technological and administrative
- Generation of false expectations (ahead of time)
- Basic scientific understanding is lacking or inadequate
- Costs for implementation into practice (approval of medical devices, health insurance companies, …)

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## Summary: statement

CAMPUS PlasmaMed

The field is new,

with huge chances,

with significant research potential,

is broad enough to promote co-operations

is an opportunity for plasma technology.

INTERNATIONAL SOCIETY FOR•PLASMA•MEDICINE

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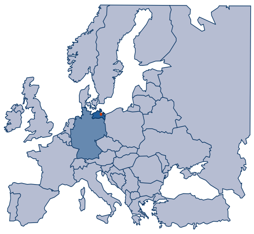
## Contact

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CAMPUS PlasmaMed

www.campus-plasmamed.de

This study was realized within the joint research project "Campus PlasmaMed" supported by the *German Federal Ministry of Education and Research* (grants no. 13N9779 and 13N11188).

SPITZENFORSCHUNG & INNOVATION IN DEN NEUEN LÄNDERN

GEFÖRDERT VOM Bundesministerium für Bildung und Forschung

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