

Atmospheric Plasma for medicine and hygiene

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outline



1. An example of “Plasma Medicine” –treatment of chronic wounds
2. An example of “Plasma Hygiene” –for hand washing
3. Interaction of plasma with living tissues

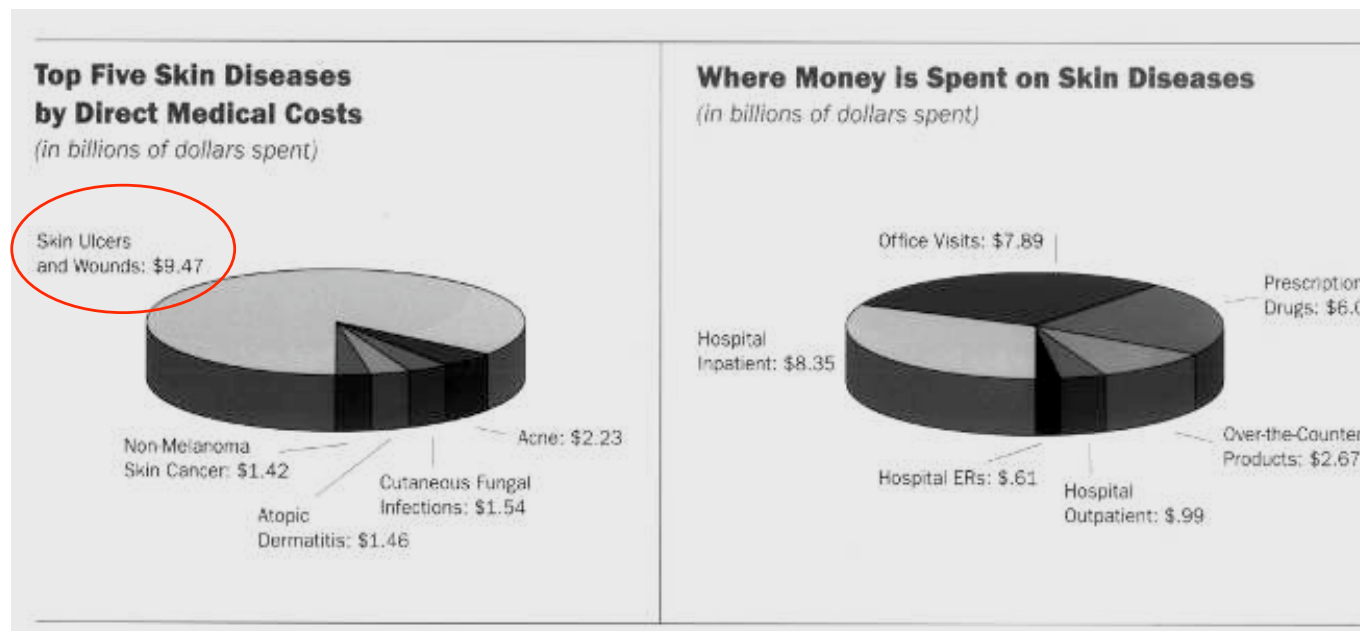
An example of 'Plasma Medicine'

chronic wounds



Chronic wounds are a major burden for the health system

- Prevalence ~ 1-2 % in German Population (> 1.000.000 patients)
- High costs for the community 1-2 % of annual health care budget*
- Venous ulcers require an average of 24 weeks to heal, 15% never heal, recurrence is found once or multiple times in 15-71% of cases** ***



American Academy of Dermatology Report 2005

*Etufugh CN, Phillips TJ. Venous ulcers. *Clin Dermatol* 2007; **25**: 121-30.

**Kurz et al. VEINES Task Force Report, *Int Angiol*. 1999;18(2):83-102.

***Heit et al. Venous thromboembolism epidemiology *Semin Thromb Hemost*. 2002;28(suppl 2):3-13

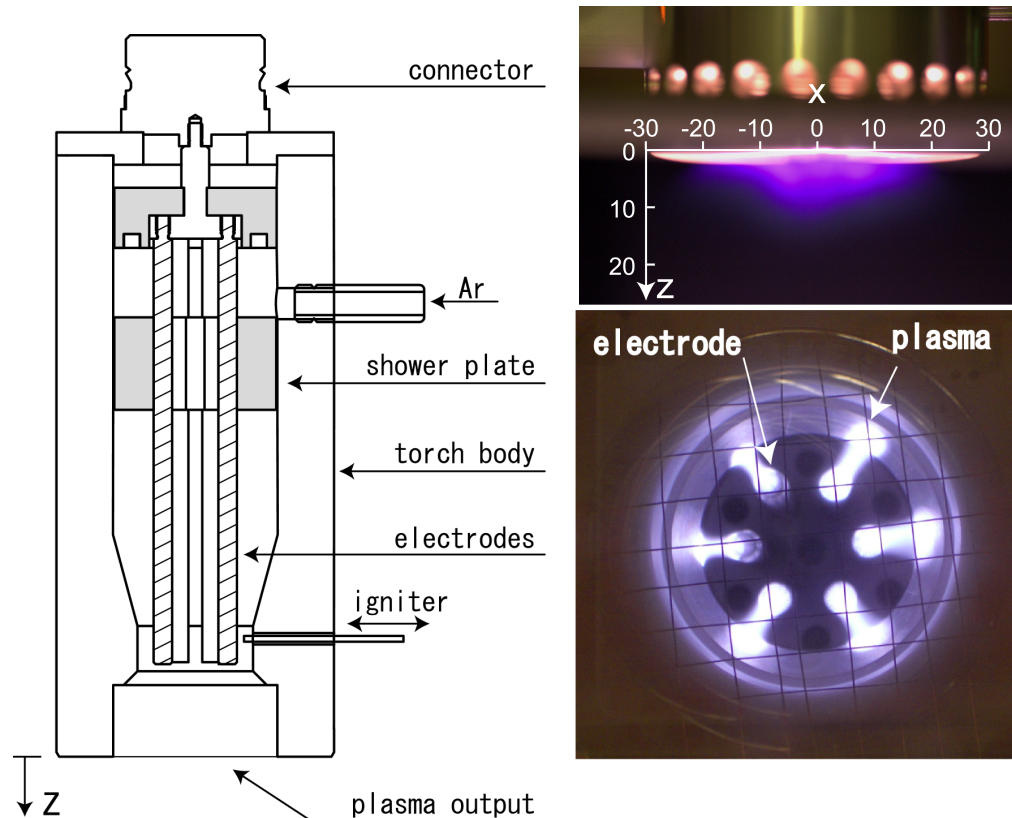
infections and resistance -facts



- „Bacteria can become resistant to antibiotics“ warned Alexander Fleming, when he landed the Nobel prize in Medicine in 1945.
- European Antimicrobial Resistance Surveillance System (EARSS) 2007: Resistance is becoming a larger problem year after year (especially for *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia Coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*)
- Global Health Care Associations consider multi-resistant germs like MRSA as a global threat*
- 19,5 % of all *Staphylococcus aureus* detected in German hospitals are MRSA (EARSS 2008)
- Worrying is the raising resistance against so called reserve drugs within the last 6 years – e.g. Vancomycin (EARSS 2007)
- November 2008 launch of DART (Deutschen Antibiotika-Resistenzstrategie)

*Grundmann H, Aires-de-Sousa M, Boyce J et al. Emergence and resurgence of meticillin-resistant *Staphylococcus aureus* as a public-health threat. *Lancet* 2006; **368**: 874-85.

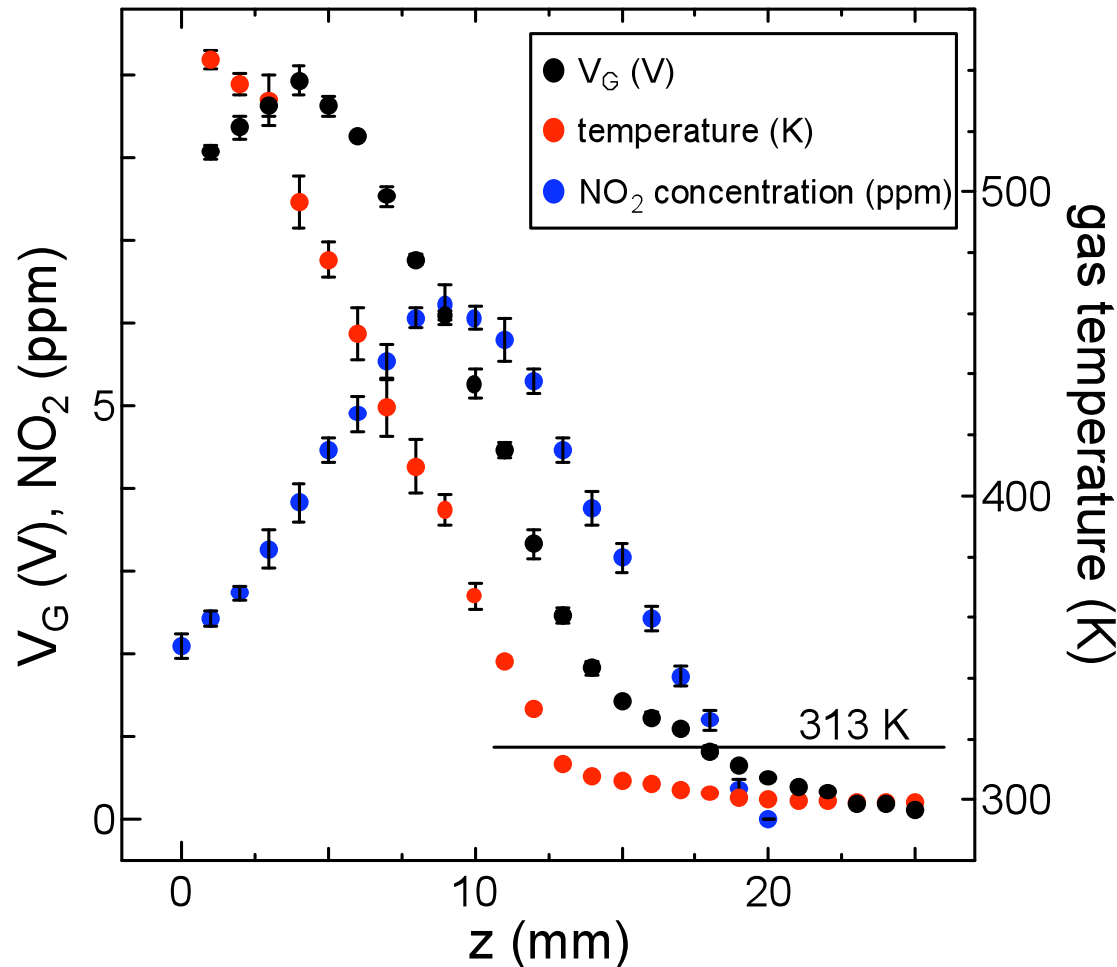
plasma torch



- microwave (2.45 GHz, 86 W)
- Ar (2.2 slm)
- torch body is cooled by air flow

The plasma torch consists of 6 stainless steel electrodes placed inside an aluminium cylinder of 135 mm in length. The centers of the 6 electrodes, whose surfaces are serrated, are distributed equally at a distance of 6 mm from the inner surface of the cylinder. 6 small plasmas are produced between each of the electrode's tips and the inner surface of the cylinder as shown in the figure.

plasma characteristics

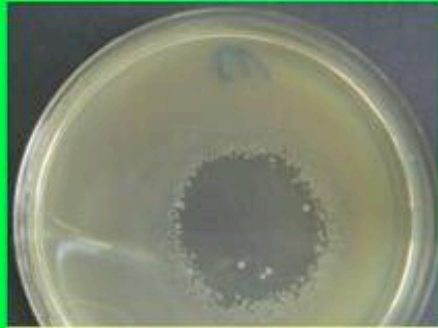


In the vicinity of the torch, the gas temperature is relatively high. However, just after the opening of the torch ($z = 3$ mm) until $z = 13$ mm, the gas temperature decreases drastically. As z increases further, the temperature decreases more gradually.

From the measurement of the NO_2 concentration profile, at $z = 9$ mm there is a maximum (6.2 ppm). This indicates that the flow from the torch has a contact with the ambient air around this position and the gas is cooled drastically.

In order to determine how the plasma is distributed below the torch, the floating potential of the mesh grid is measured ($20 \text{ M}\Omega$ between the grid and ground). The potential also decreases as z increases, almost in the same way as the gas temperature.

efficiency of plasma –Phase I study



Escherichia coli

present on
healthy persons

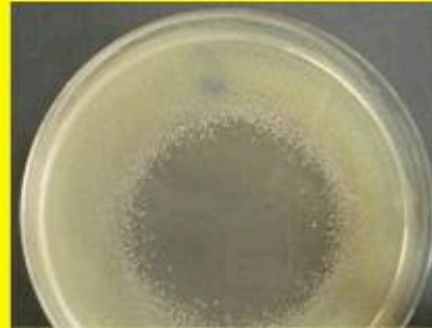


Enterococcus faecalis



Group A streptococcus

facultative pathogenic, occasional resistance



*methicillin-resistant
Staphylococcus aureus*



*vancomycin-resistant
Enterococcus faecium*

facultative pathogenic, seldom present on healthy skin



*Pseudomonas
aeruginosa*



Burkholderia cepacia

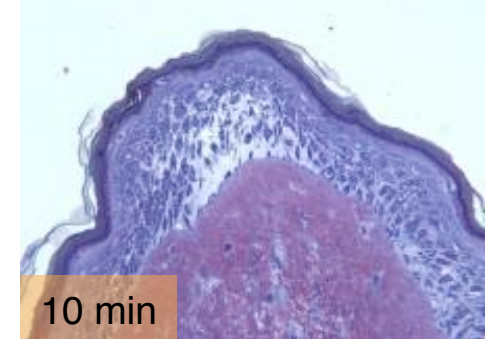
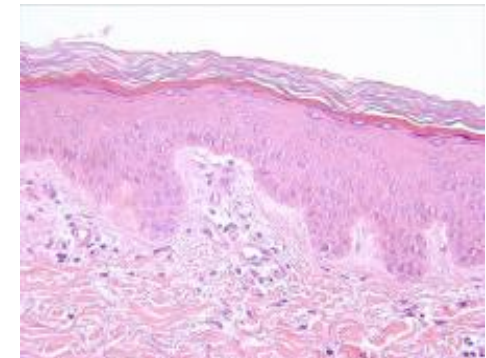
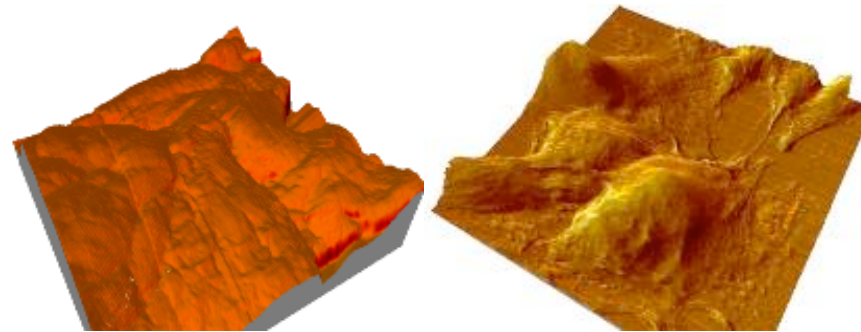


Bacillus cereus

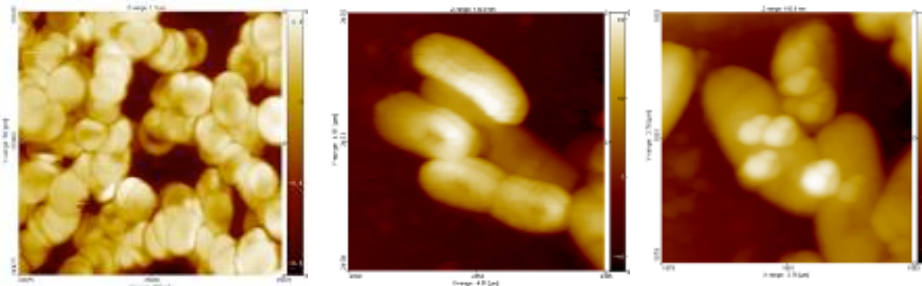
safety of plasma –Phase I study



Numerous tests to find dosages and to check harmlessness of the plasma treatment:
e.g. histologies, blood tests, microscopic images, AFM, cell assays...



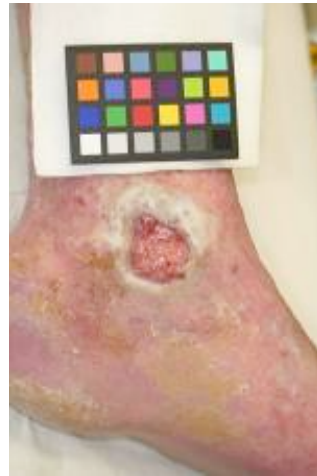
Further investigations with fibroblasts, keratinocytes, cell cultures, essays to check toxicity, mutagenicity, and antibodies



chronic wounds in dermatology



Venous diseases



Arterial diseases



Infections



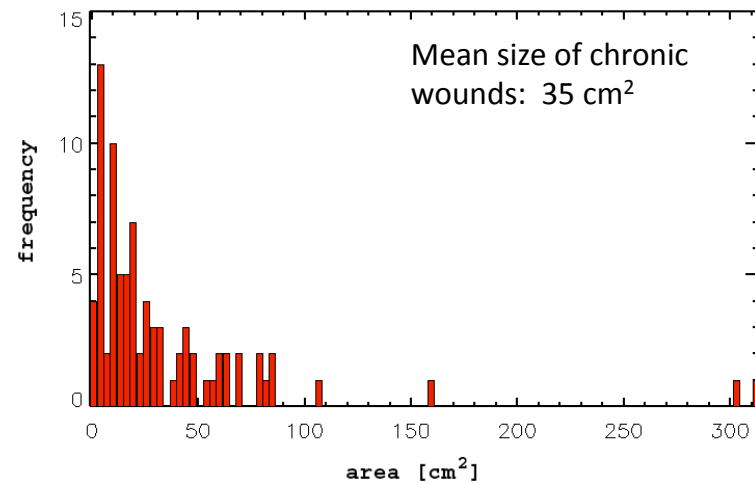
Diabetes mellitus



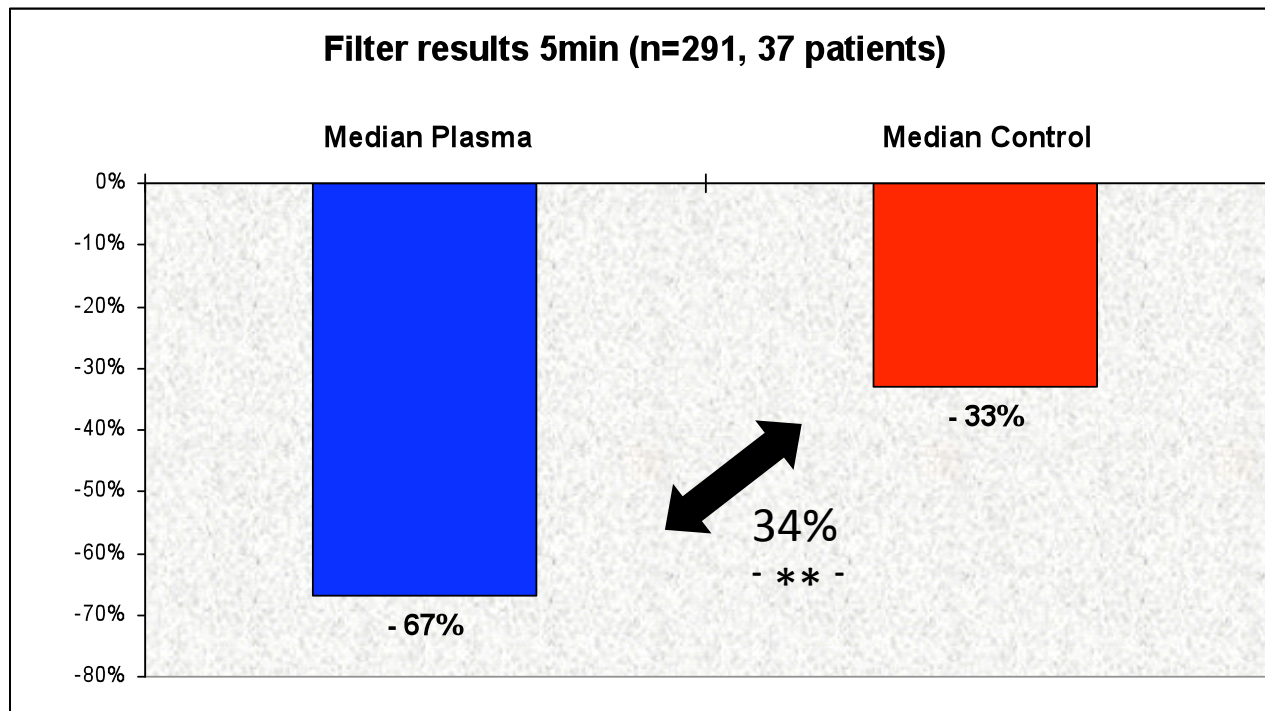
Carcinoma



Pyoderma gangraenosum



results with 5 min treatment

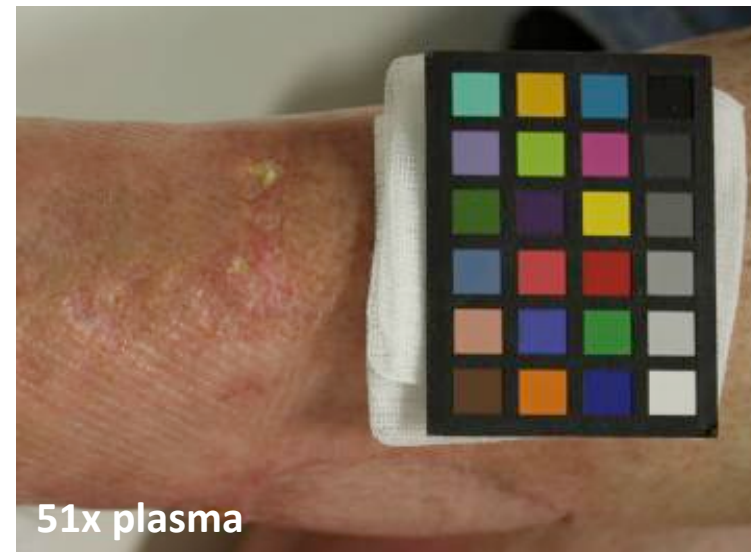
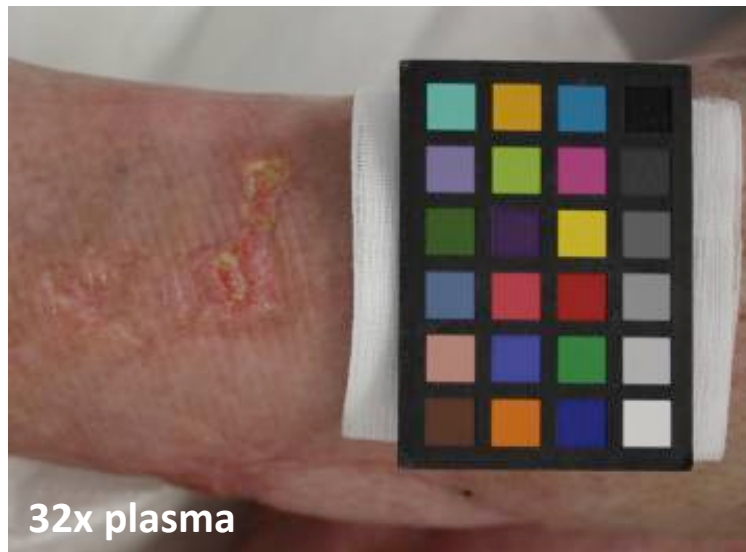
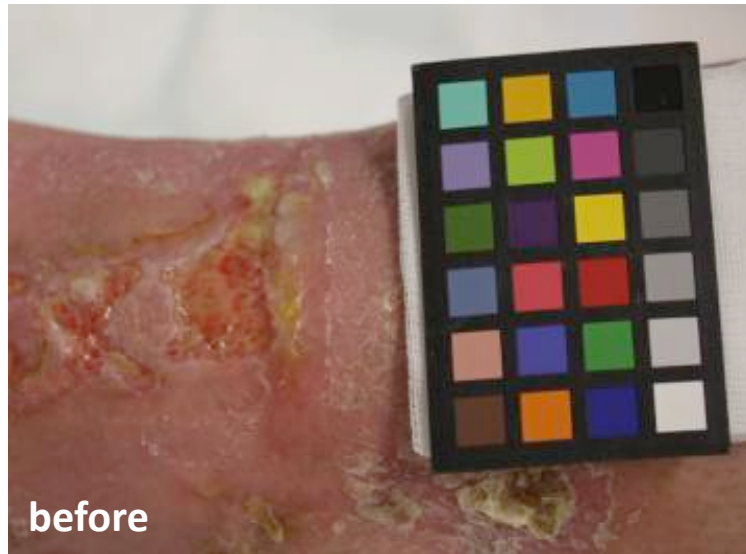


37 patients
291 treatments
5 min treatment time

Primary aetiology of wounds: venous ulcers (47%)

Highly significant ($p < 10^{-6}$) higher germ reduction (34%) in plasma treated area

good result of plasma therapy



insufficient result of plasma therapy



A first prospective randomized controlled trial to decrease bacterial load using cold atmospheric argon plasma on chronic wounds in patients

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Summary

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Background Bacterial colonization of chronic wounds slows healing. Cold atmospheric plasma has been shown *in vitro* to kill a wide range of pathogenic bacteria. **Objectives** To examine the safety and efficiency of cold atmospheric argon plasma to decrease bacterial load as a new medical treatment for chronic wounds.

Patients and methods Thirty-eight chronic infected wounds in 36 patients were treated in a prospective randomized controlled phase II study with 5 min daily cold

An example of 'Plasma Hygiene'

hand washing



Professional Plasma Hygiene



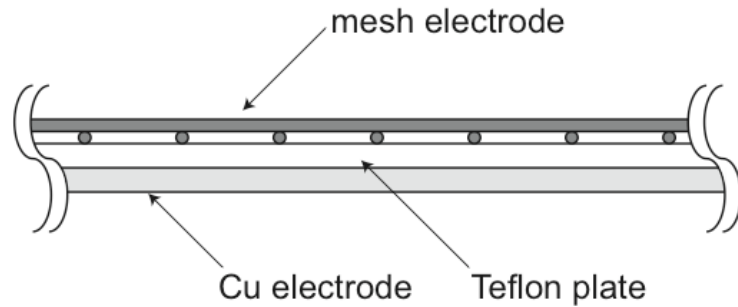
It is well established that frequent hand disinfection with ubiquitously available dispensers would reduce the risk of hospital induced infections substantially –
why then do we have such a serious problem in hospitals?

Hand washing with disinfectants – a tedious task (**minutes**)

If used too often, there are skin **irritations** and **allergies**.

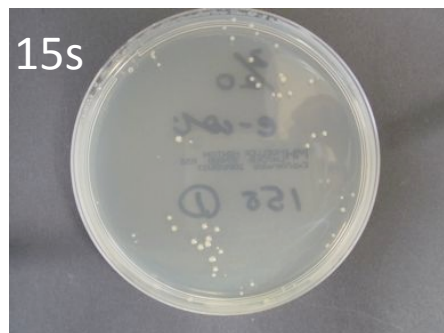
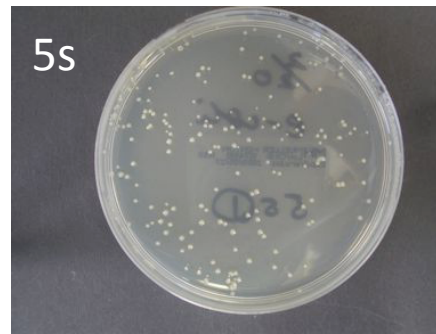
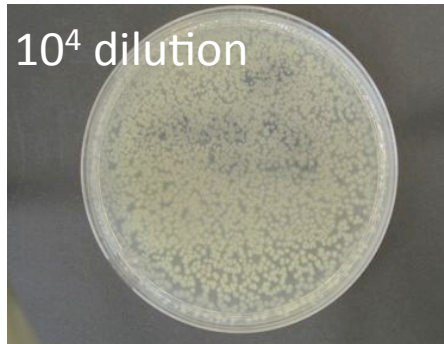


surface micro-discharge electrode

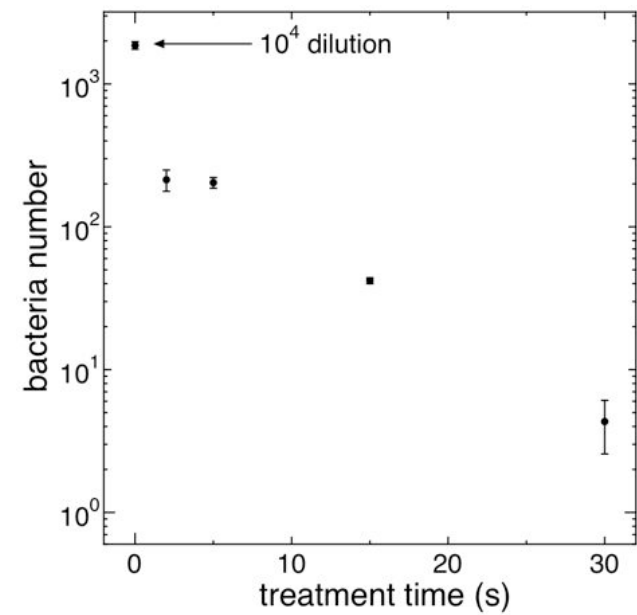


frequency: 12.5 kHz (sinusoidal)
voltage: 15~18 kV_{pp}
power: 0.5 W/cm²
area: ~100 cm² for each

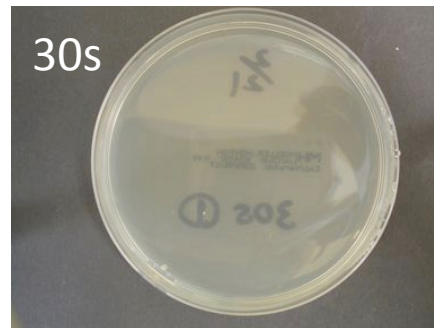
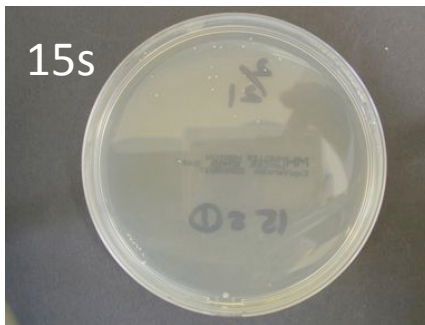
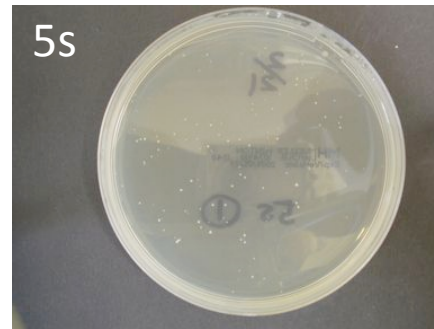
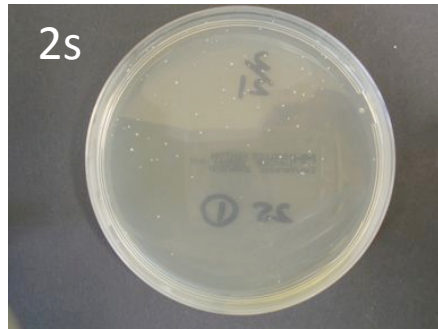
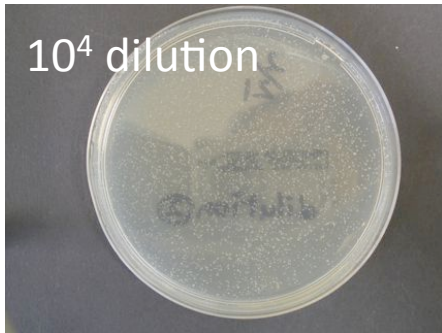
bactericidal property



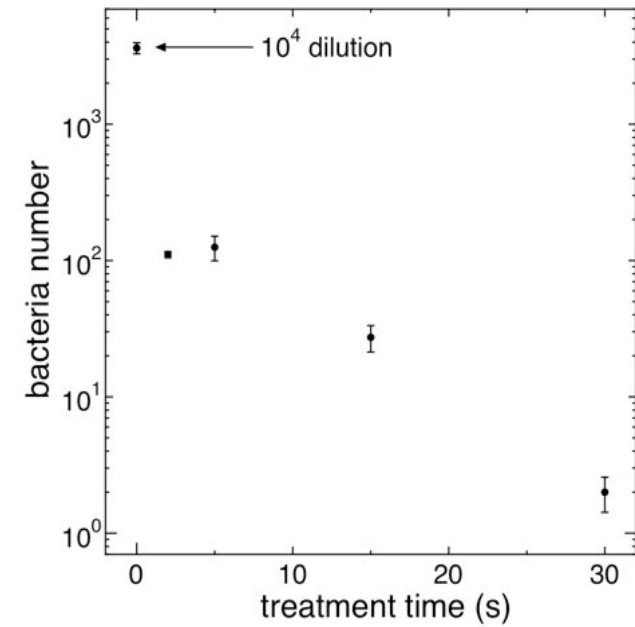
Escherichia coli (g -ve)



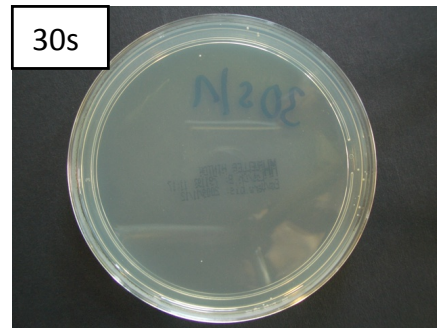
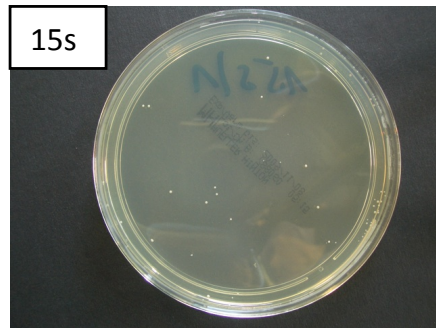
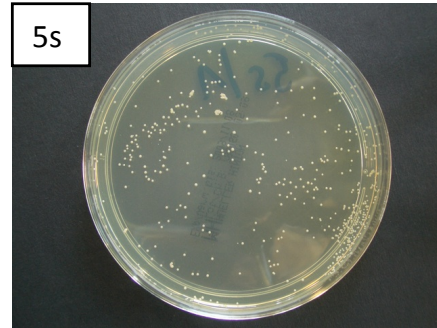
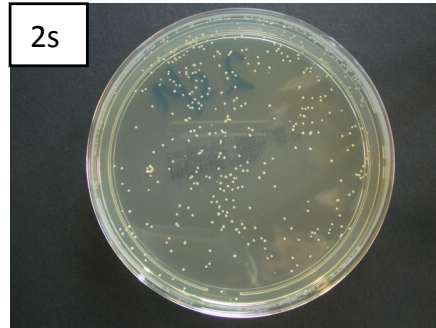
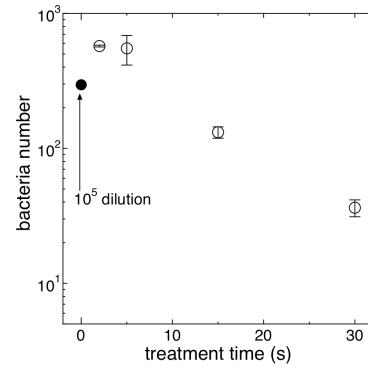
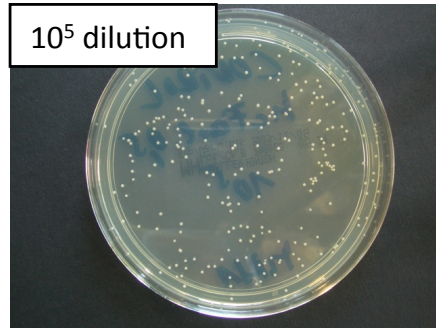
bactericidal property



Enterococcus (g +ve)

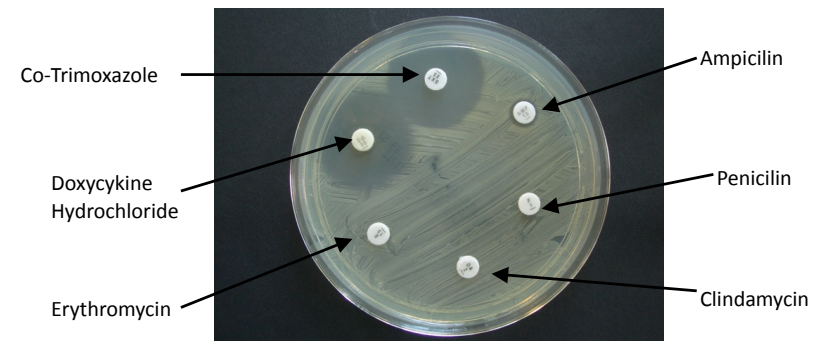
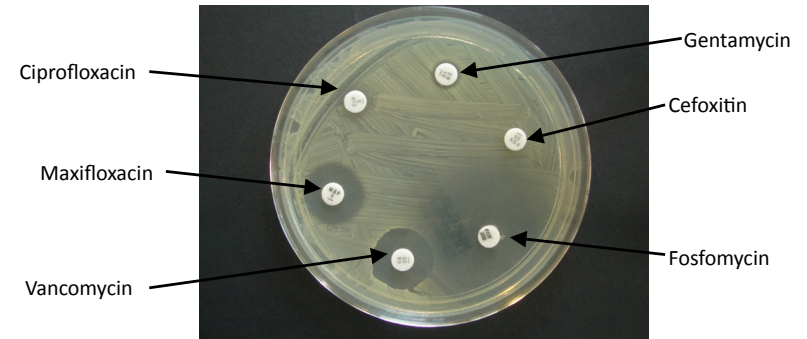


bactericidal property



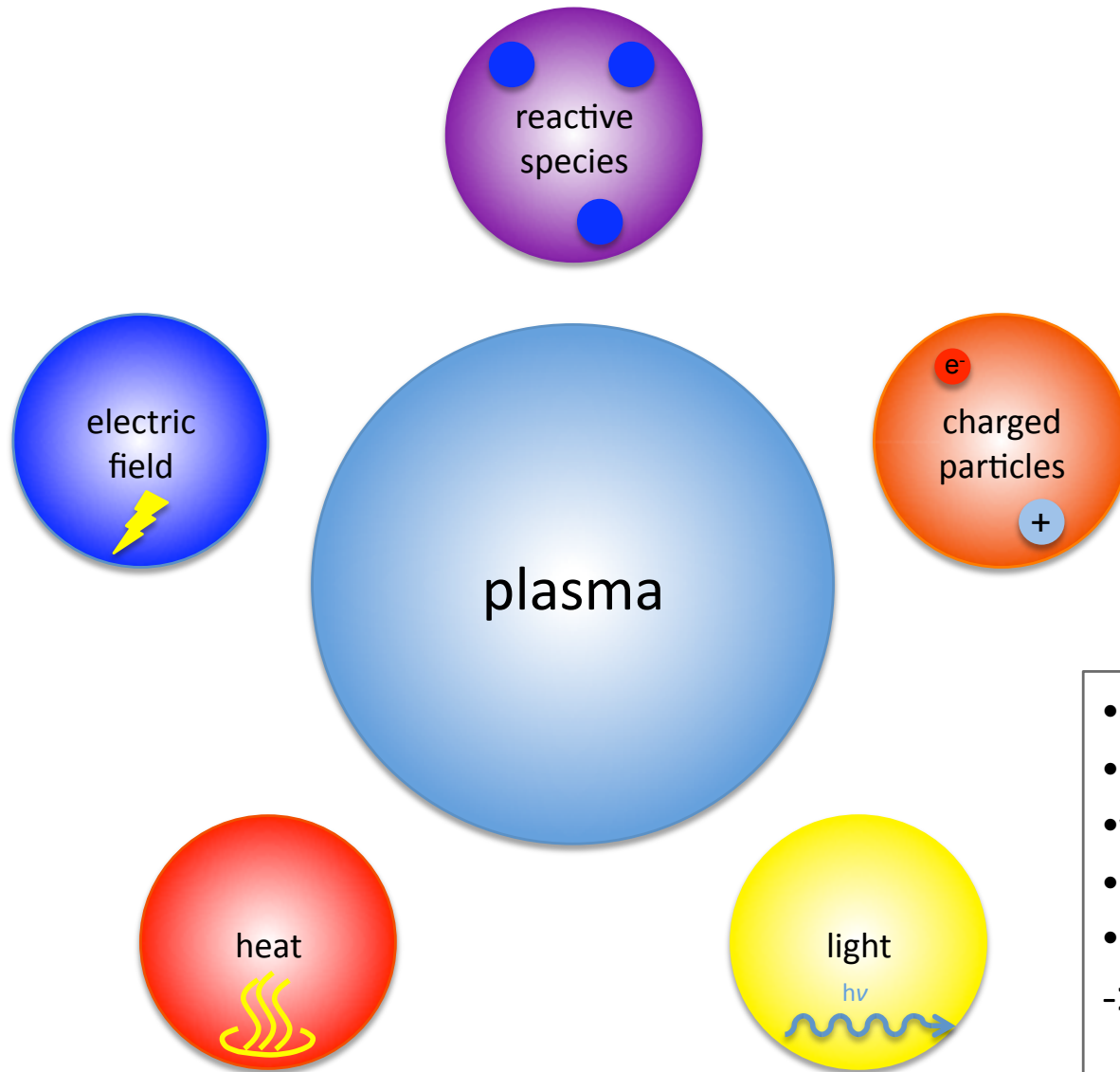
MRSA

drug resistance



Transport from plasma to tissues

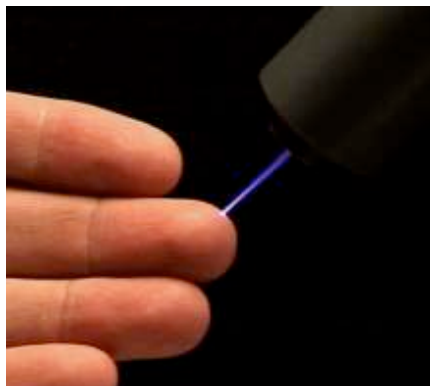
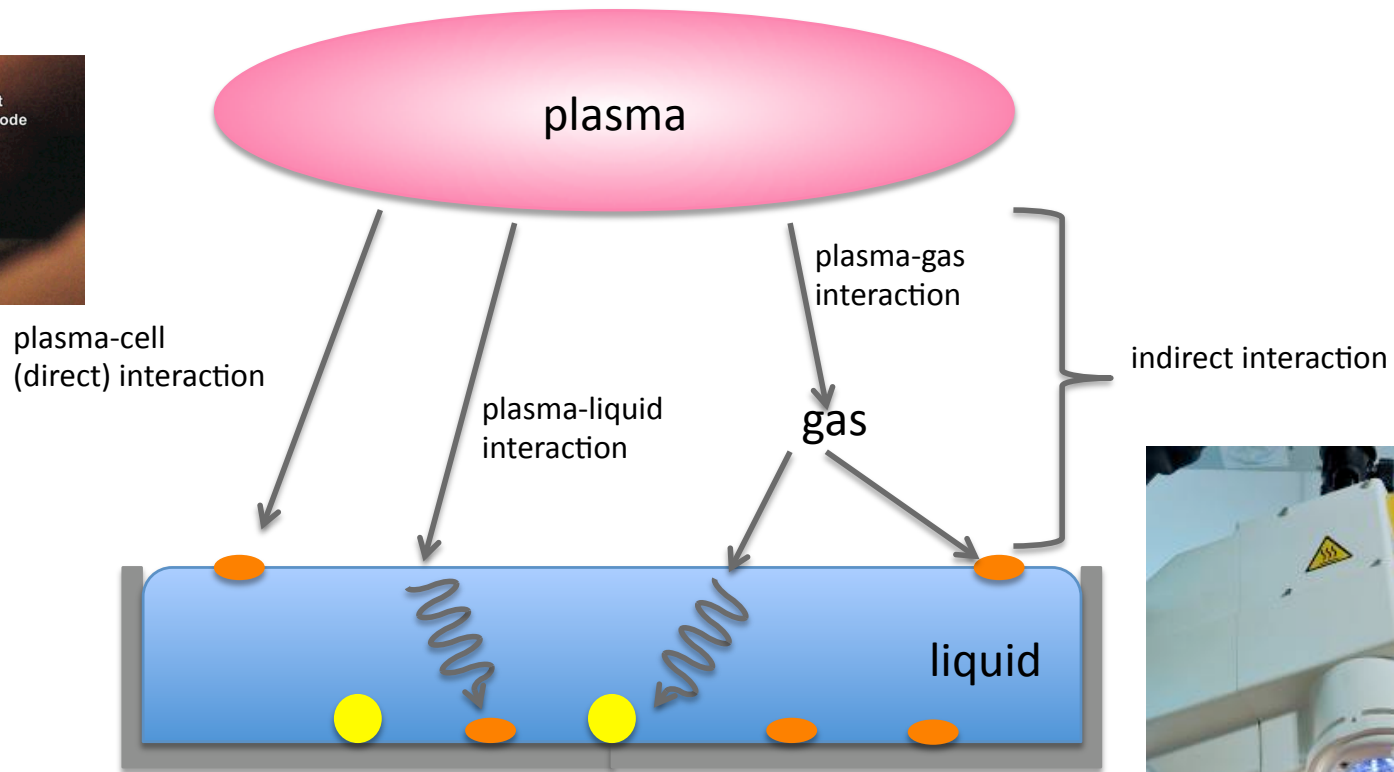
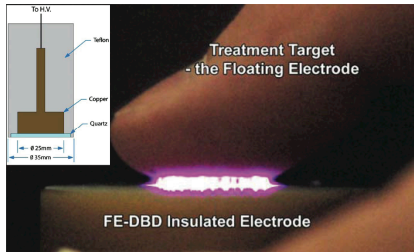
plasma treatment



All components react together.

- contact-free treatment
 - rough surface reachable
 - waste-free treatment
 - bactericidal, fungicidal, virucidal
 - physical-therapy
- > resistance and allergic reactions are less feasible

interaction of plasma with living tissues



cell membrane permeabilisation and reactive species transport

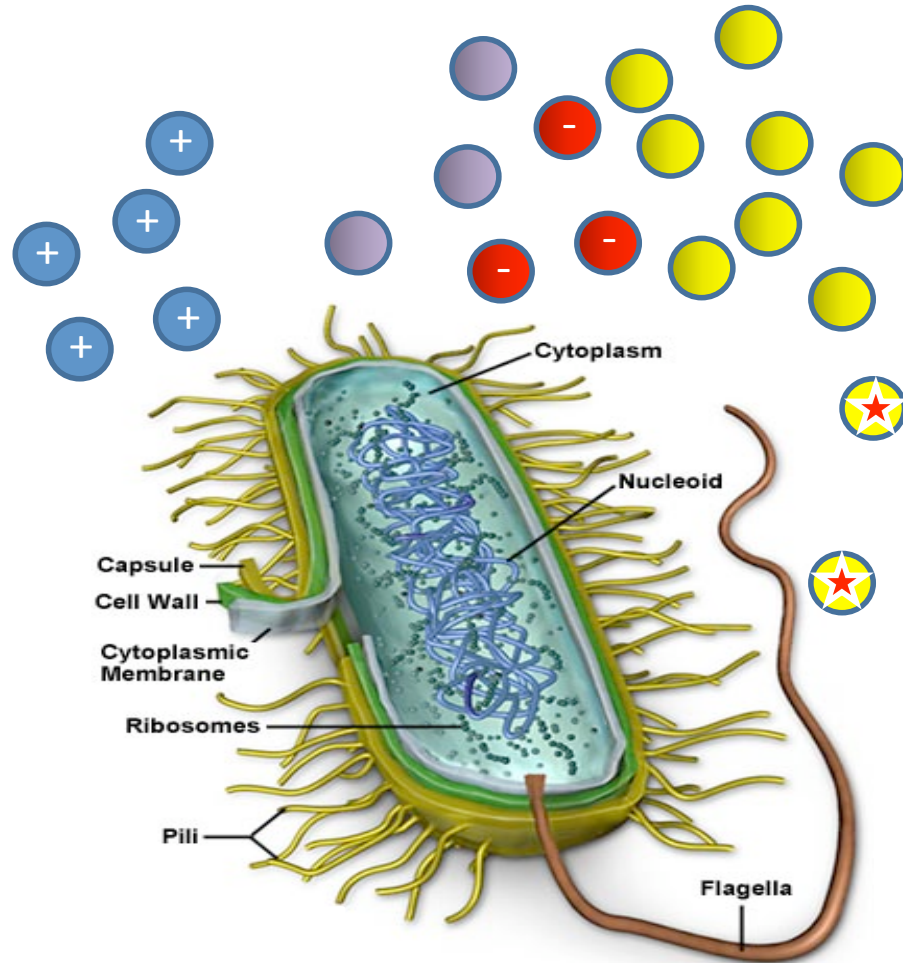


cell permeabilisation



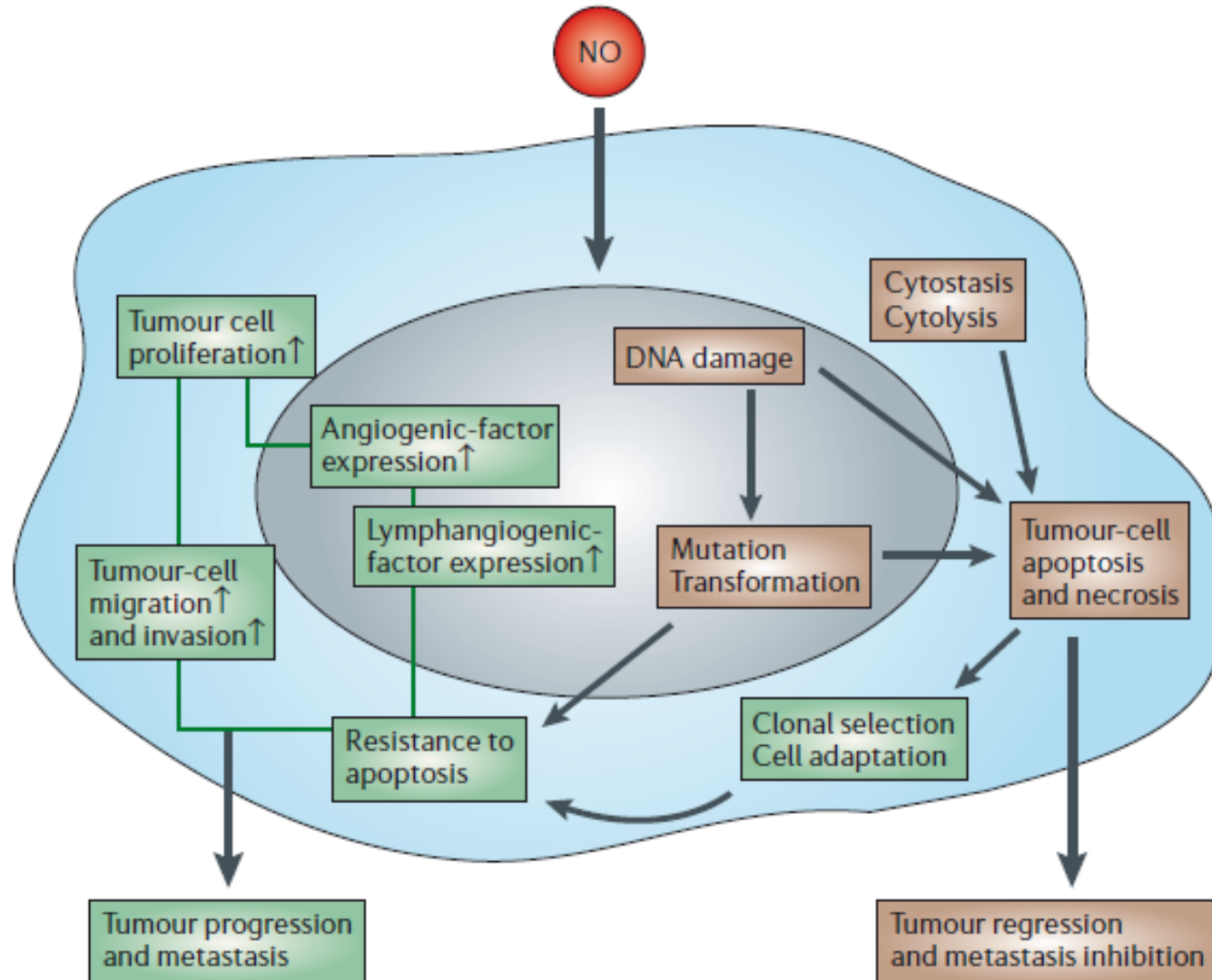
Unique Plasma Features

- Electron-ion recombination can make the bacteria cell wall permeable (up to 5 nm).
- Non-equilibrium chemistry produces many **reactive O, H and N species**, e.g. NO, NO₂, •OH, O₂⁻ and H₂O₂, which can then penetrate
- **Bacterial DNA in the cytoplasm** is directly accessible to the reactive species.



<http://micro.magnet.fsu.edu/cells/bacteriacell.html>

NO signalling in tumour cells



After D.Fukumura et al., 2006

summary



Understanding the **physics** of cold atmospheric plasmas

Understanding the **chemistry** of cold atmospheric plasmas

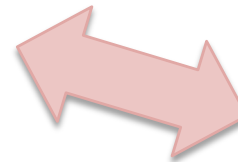
Understanding the **transport** from cold atmospheric plasmas

Understanding **plasma-cell/protein interaction through gas/liquid**

Designing **plasmas for hygiene**

Designing **plasmas for medicine**

are necessary.



plasma physics
engineering
plasma chemistry
fluid dynamics

biology
microbiology
cell biology
medicine

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