Development and characterization of an atmospheric plasma source for non-thermal blood coagulation

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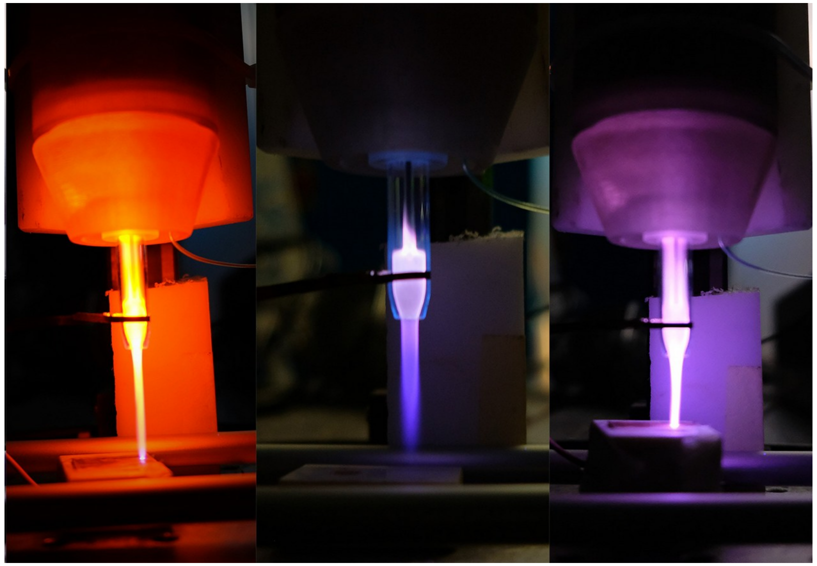
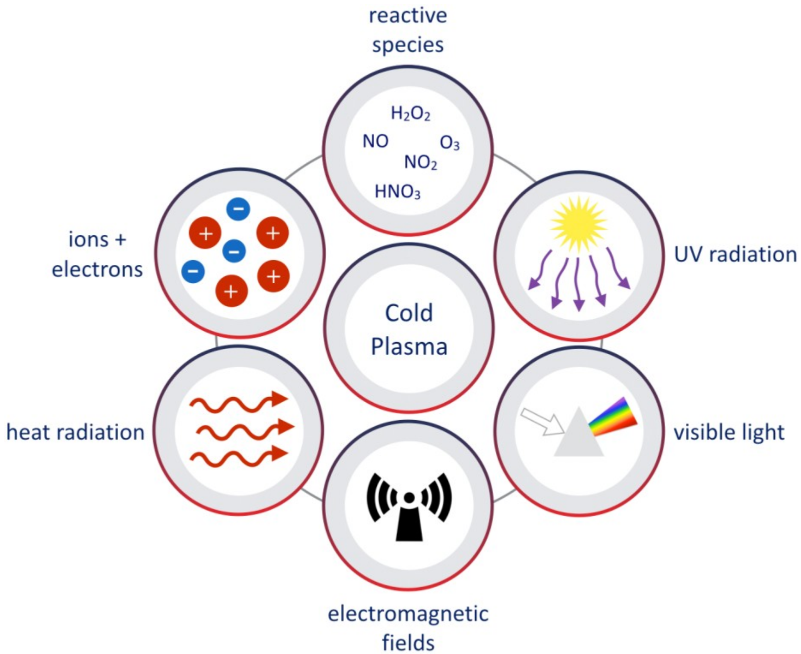
Cold Atmospheric Plasma for Plasma Medicine

Source realized by a specialized research group in *Consorzio RFX Laboratories*, in collaboration with *Università Magna Graecia di Catanzaro*





Plasma applied on biological tissues interacts through:

- <u>Reactive chemical species</u>
- UV radiation
- Electromagnetic field

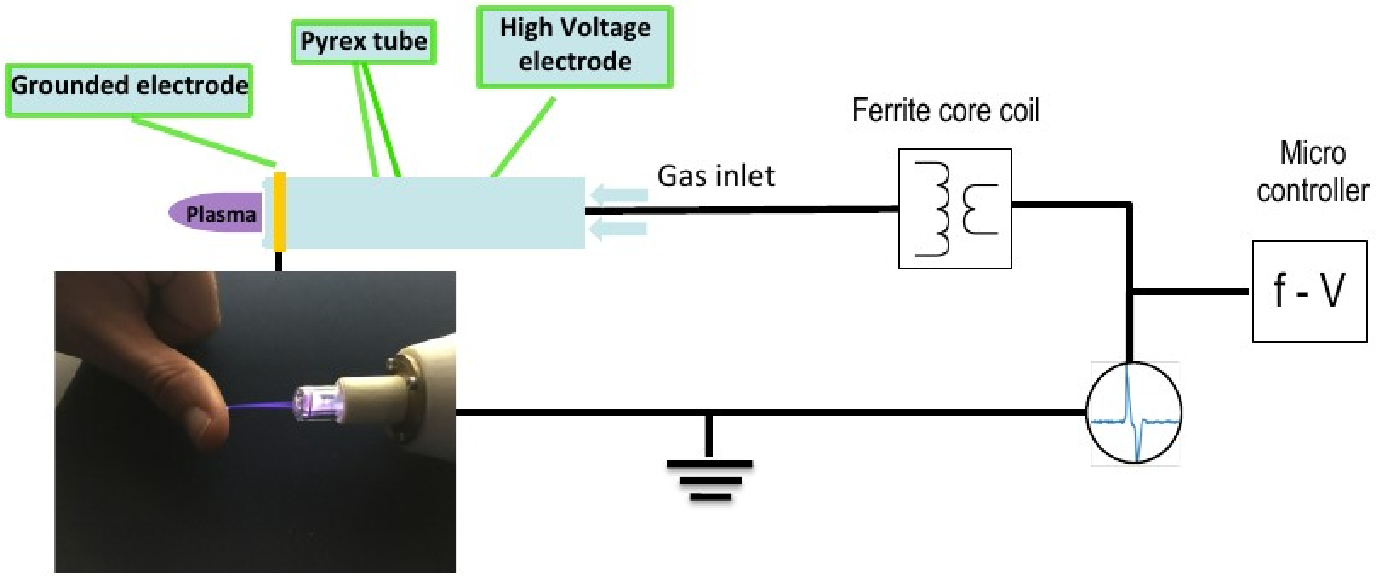
→

Plasma Medicine

- Sterilization and decontamination
- Wound disinfection and healing
- Cancer cell treatment
- Blood coagulation

Plasma Coagulation Controller

Voltage pulse on electrode covered in dielectric =
Dielectric Barrier Discharge



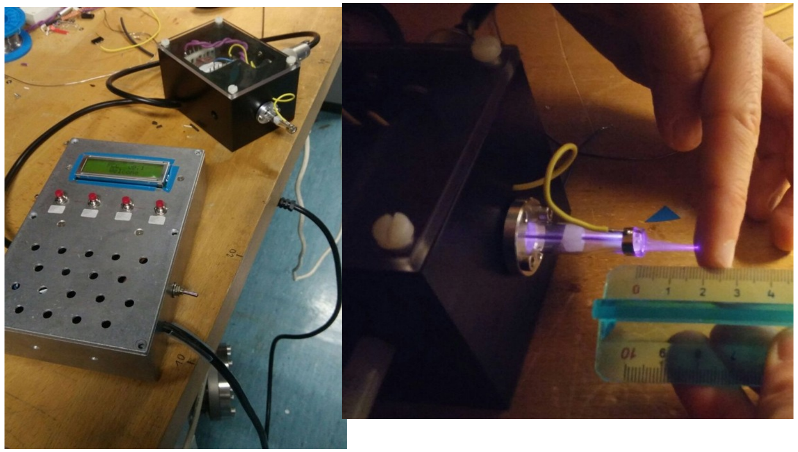
Neutral gas:
- Helium
- Neon
- Argon

Pulse Repetition Rate
1 kHz < f < 40 kHz

- Low current density on target
- Low power deposition on target = low target temperature
- Presence of **Reactive Oxygen Species** and **Reactive Nitrogen Species** = therapeutic effects

PCC development

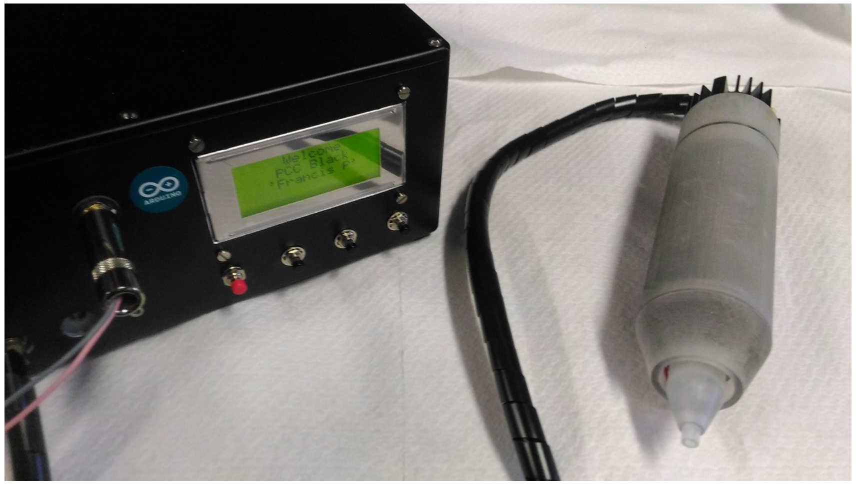
From the first prototype:

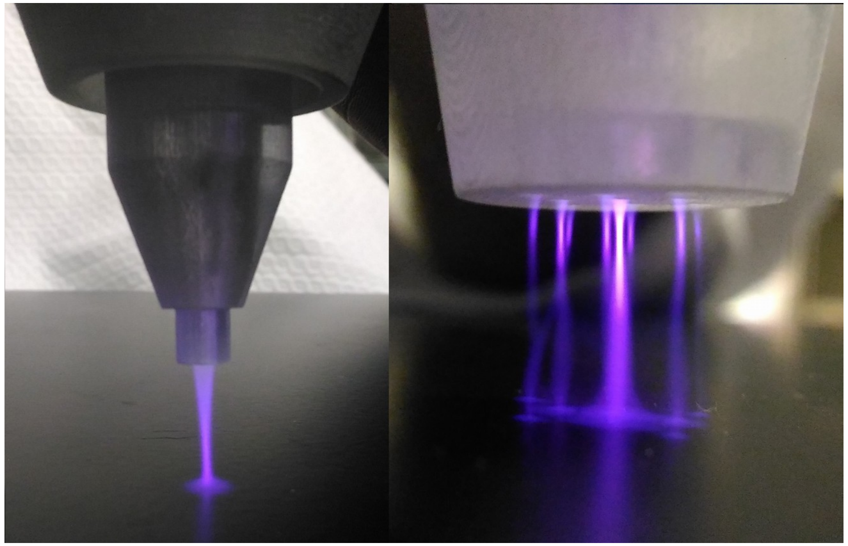


Main improvements:

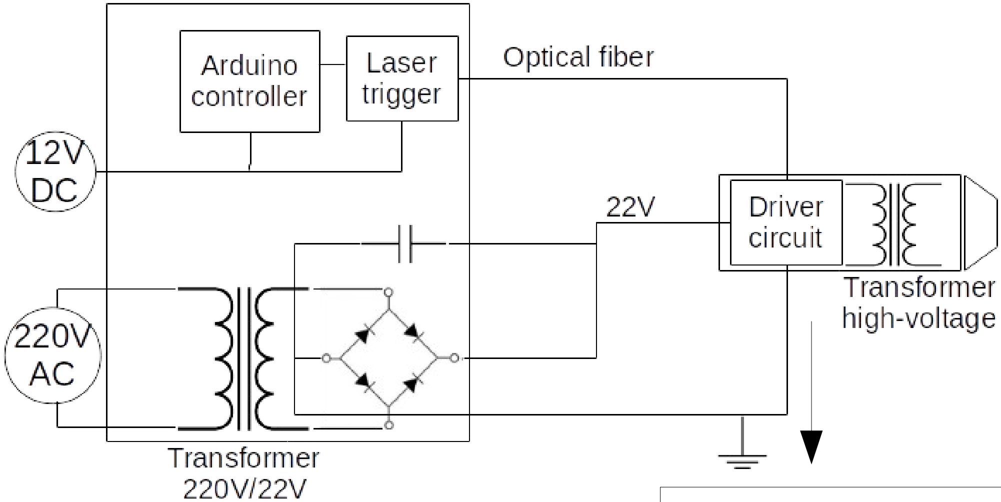
- Higher ionization capabilities
- Resolution of gas diffusion problems
- Removal of high voltage signal reflection
- Different geometry for higher maneuverability
- Possibility of different nozzles

to the third:





Electric characterization

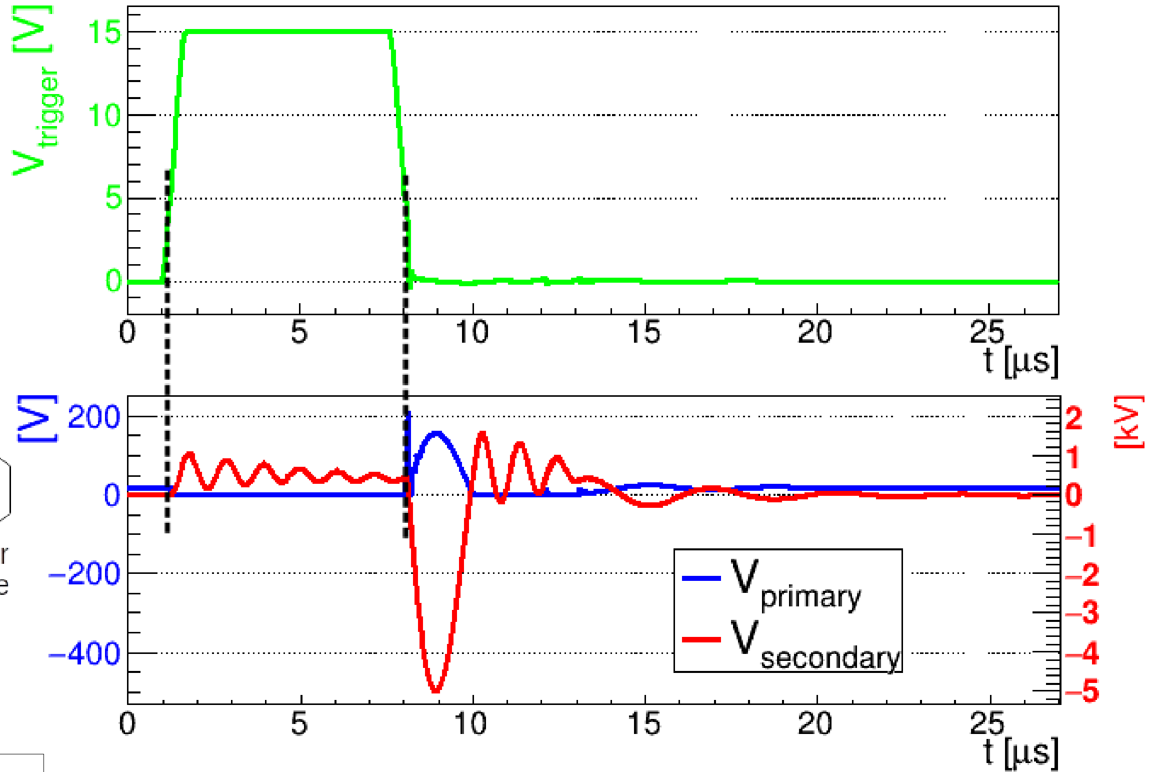


Head module

Plasma formation

Controller module

Discharge trigger



Electric characterization

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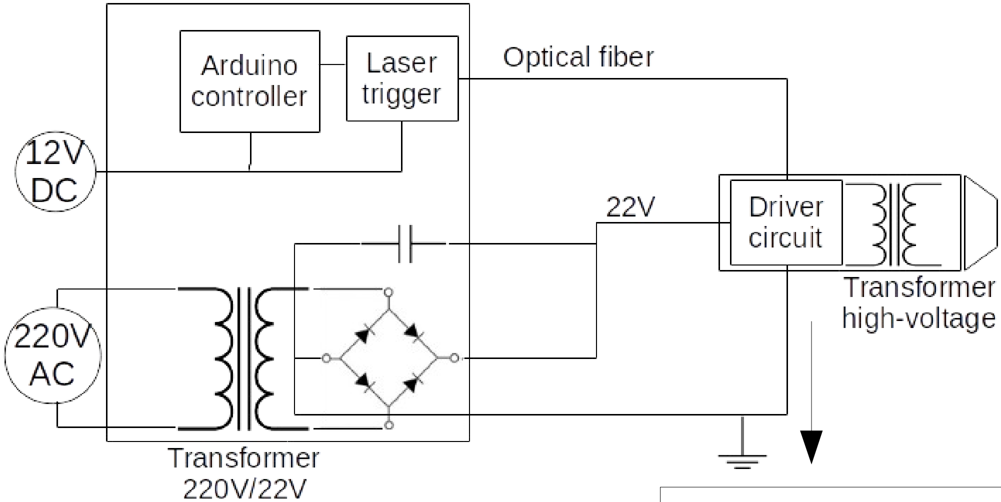

Controller module

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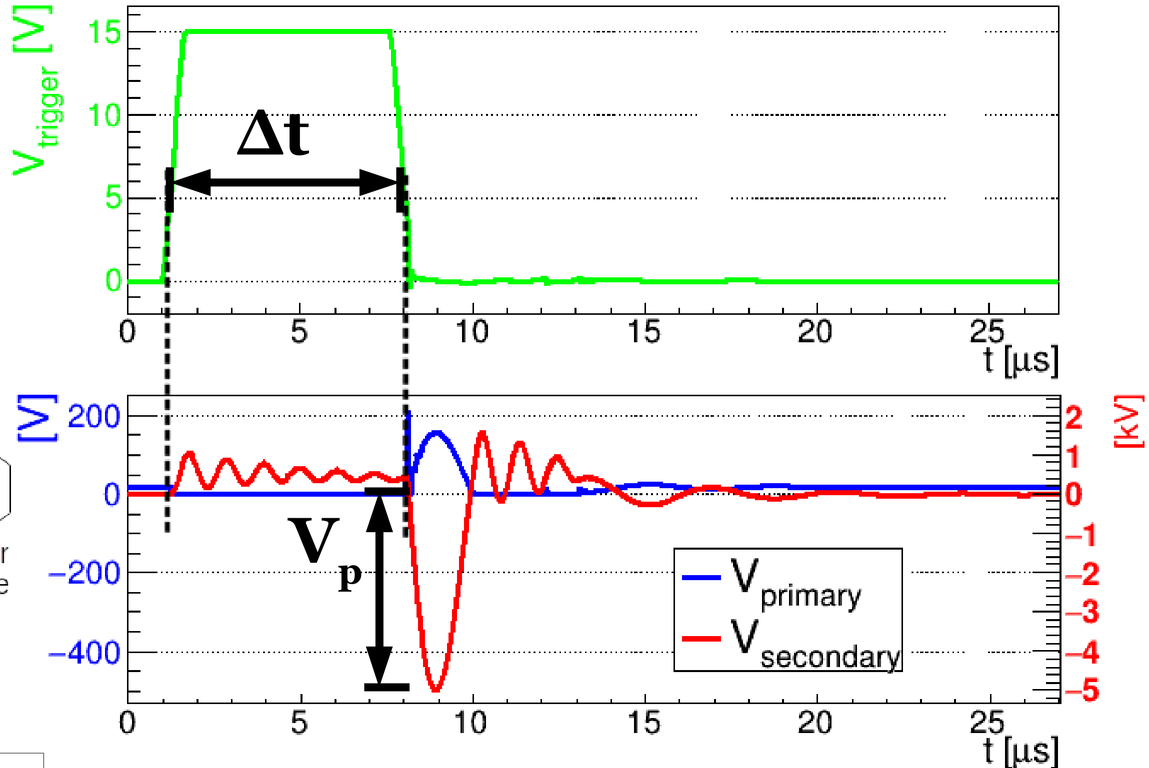
Plasma formation



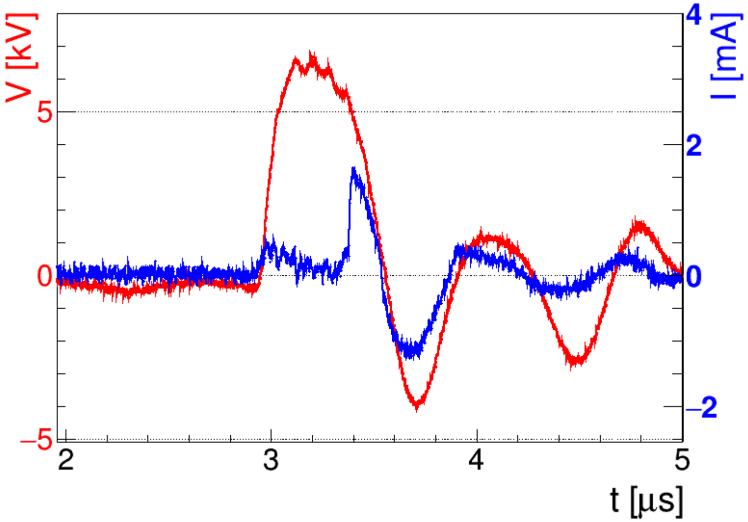
$$V_p \propto \Delta t$$

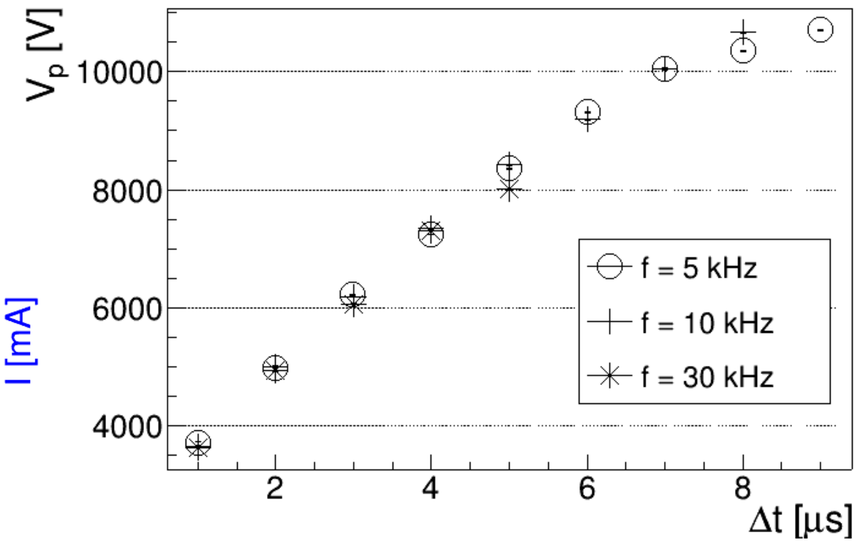
Electric characterization

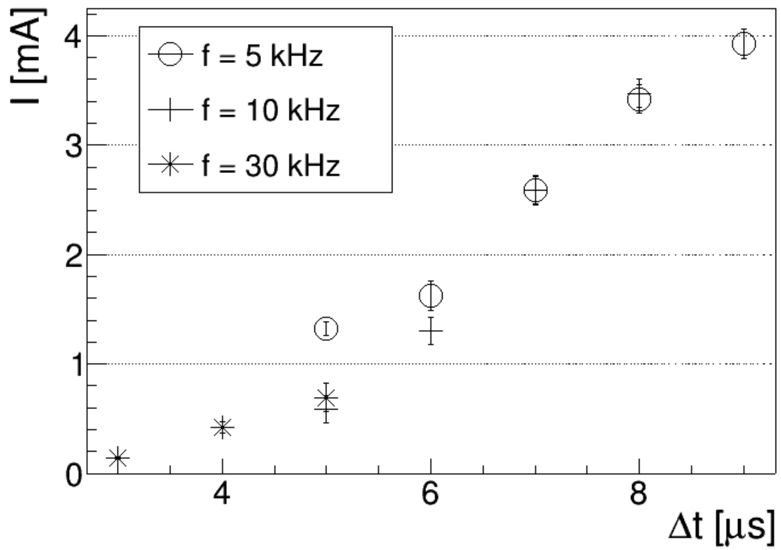
Voltage and current measurements

Measurements of:

- Voltage pulse amplitude
- Current flowing in a copper target at 1cm from the nozzle







Voltage

Linearity $4 < V_p < 10$ kV

V_p independent from f

Pulse width ≈ 1 µs

Current

Always < 10 mA

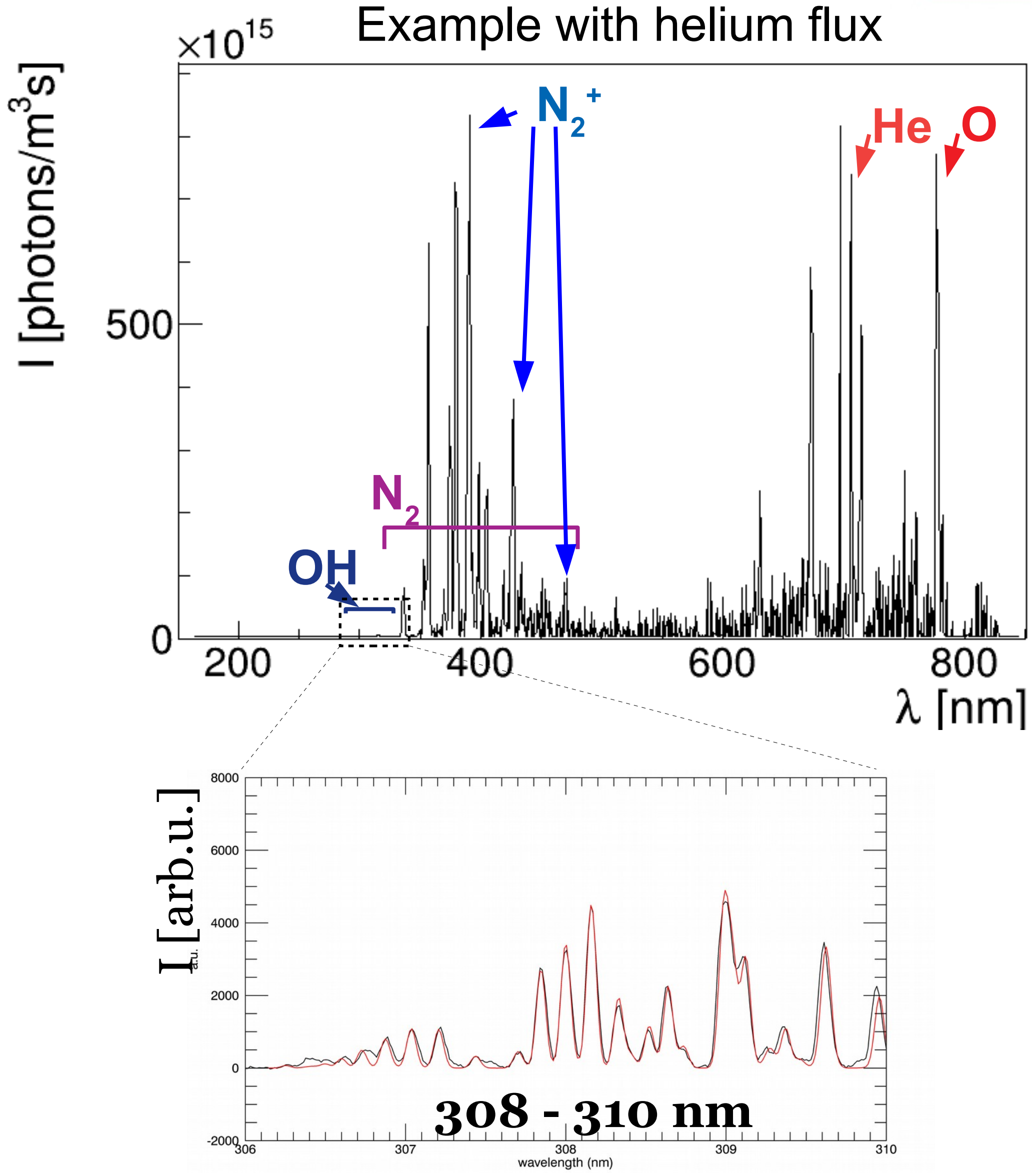
Optical Emission Spectroscopy

Spectrometer range 150-850 nm

Emission spectrum of Helium, Neon, Argon or mixed flux.

Observed lines:

- **N_2**, **N_2^+** 320-480 nm (1st, 2nd order)
- **OH** 300-310 nm (1st, 2nd order)
- **O** 777 nm
- **He** 706 nm (only with Helium)
- **Ne** 410-780 nm (only with Neon)
- **Ar** 660-850 nm (only with Argon)



Optical Emission Spectroscopy
emission intensity

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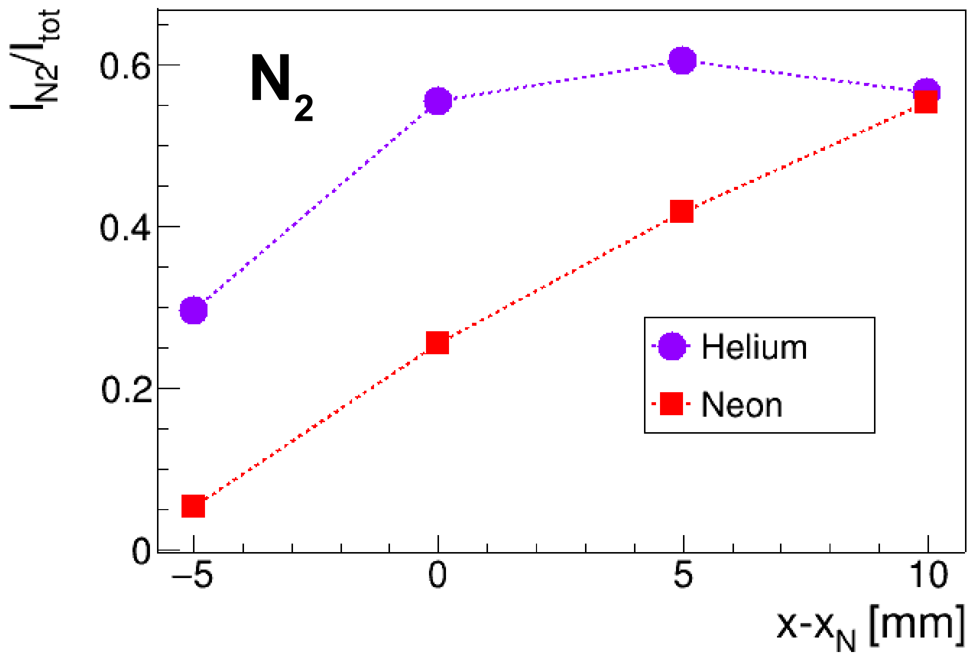

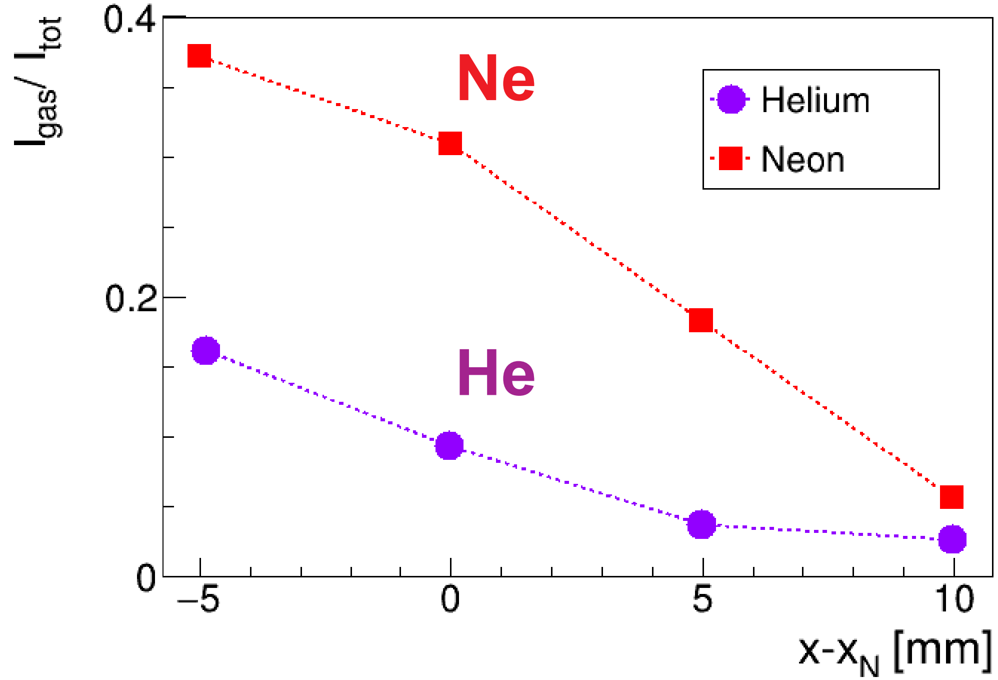

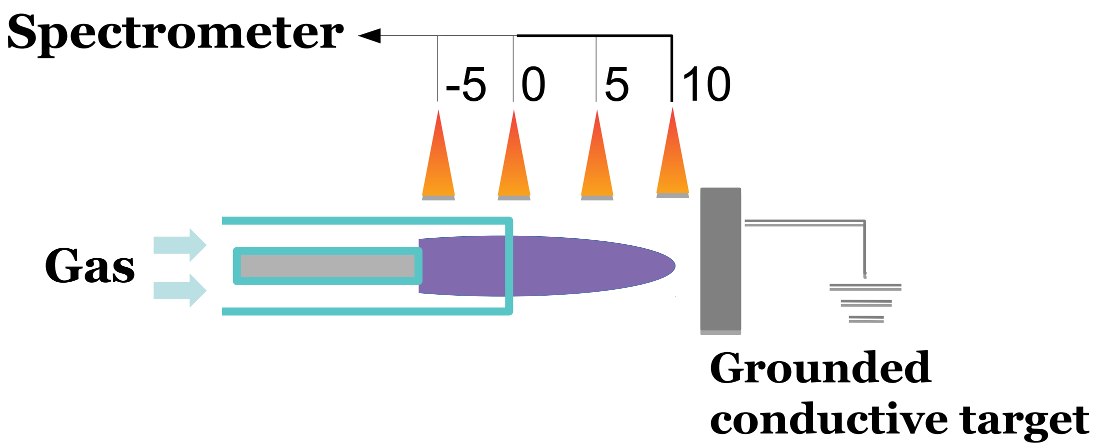

From inside the nozzle to the outside:
- N_2 emission increase
- Gas (He or Ne) emission decrease

Target temperature and power estimate

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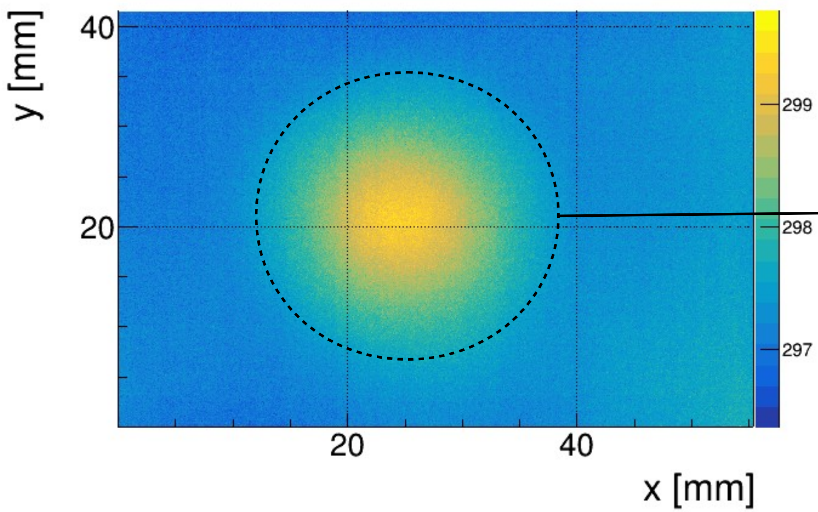
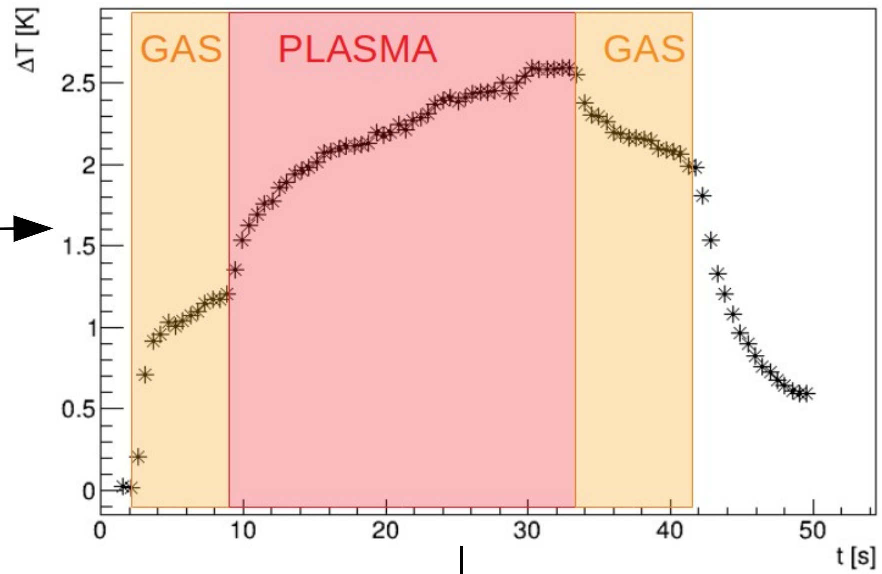
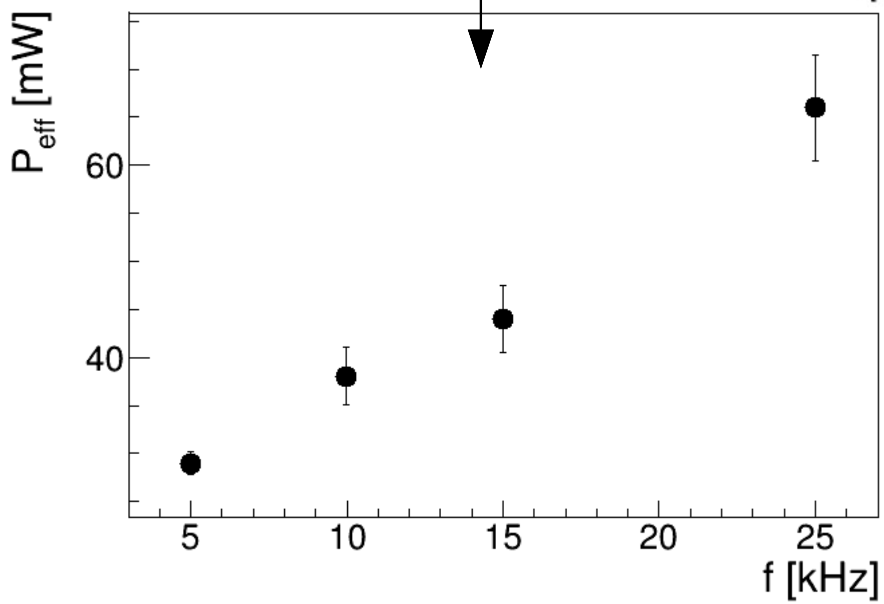


$$\sum_{pixs} \Delta T / N_{pixs}$$



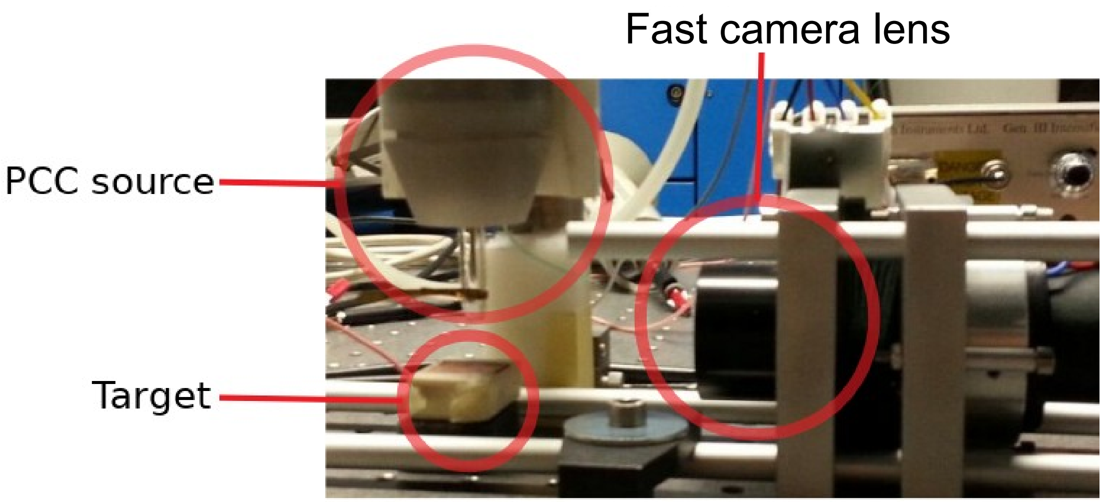


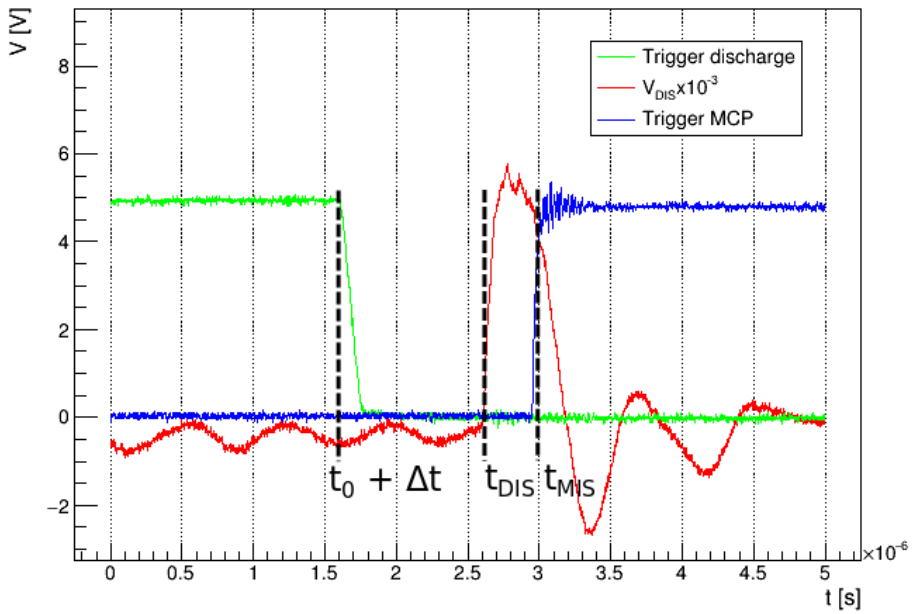
Thermal camera measurements of aluminium target during plasma application with set discharge parameters and source-target distance.

Always $\mathbf{\Delta T_{MAX} < 3\ K}$
for $\Delta t \approx 30$ s

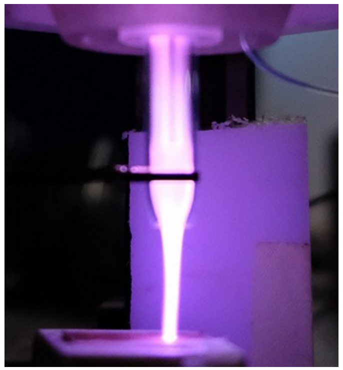
Fast camera measurements

Fast imaging allows us to see plasma formation and propagation.





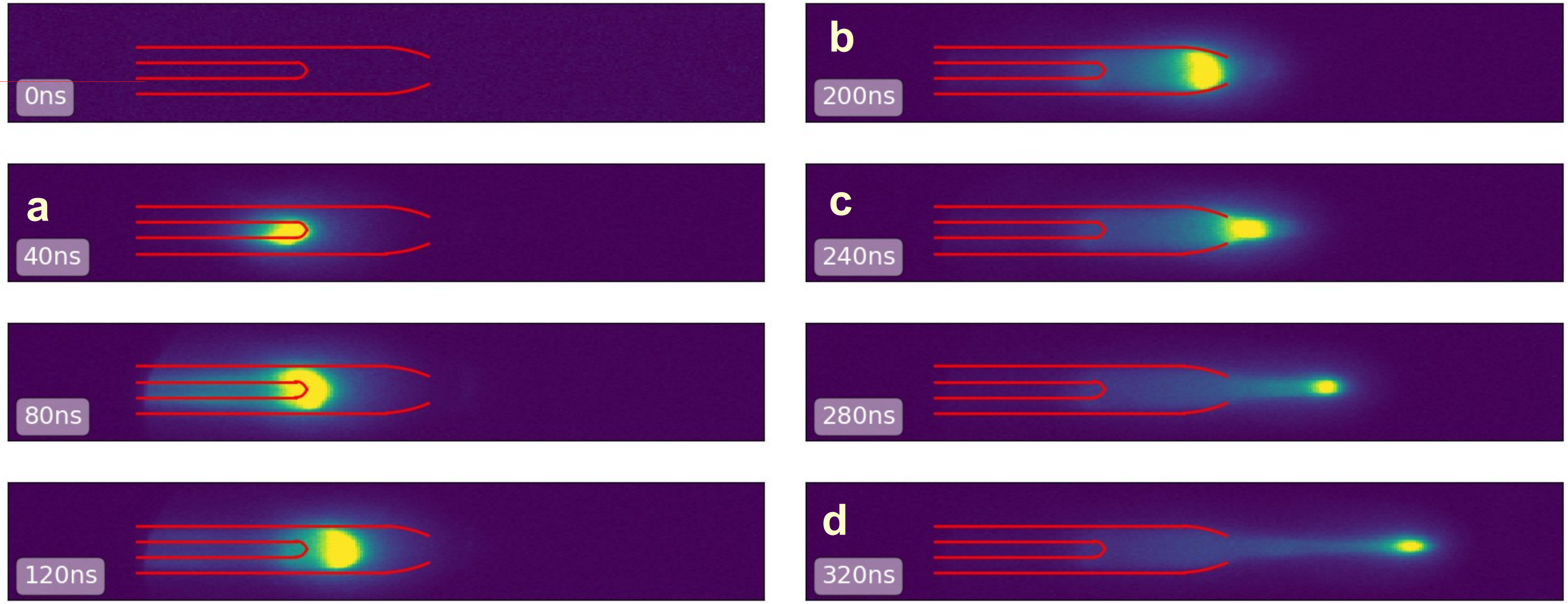
Synchronization between discharge and camera allows us to see the evolution of the discharge.

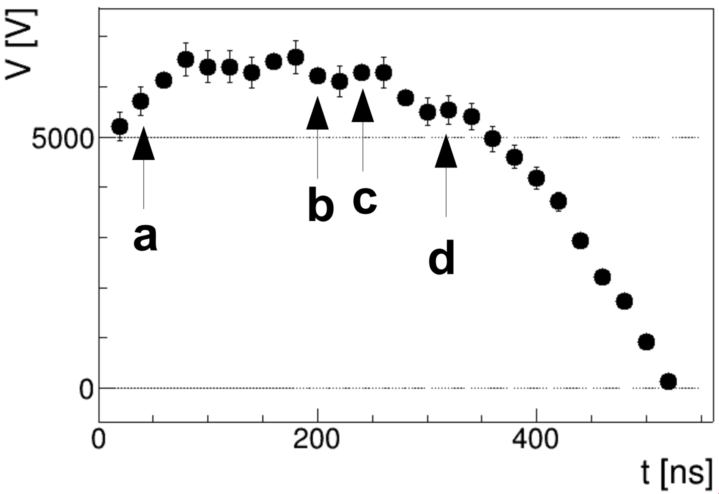


Standard camera
integration time > 10ms

Fast camera
integration time = 15ns

Helium and Neon plasma Bullets





Plasma propagates as ***bullets*** : a ionization front that moves from the electrode to the air outside.

Plasma forms first near the electrode (a), then the ionization continues inside the nozzle covering its entire area (b) and propagates in air with decreasing luminosity (c-d).

Bullet position and velocity

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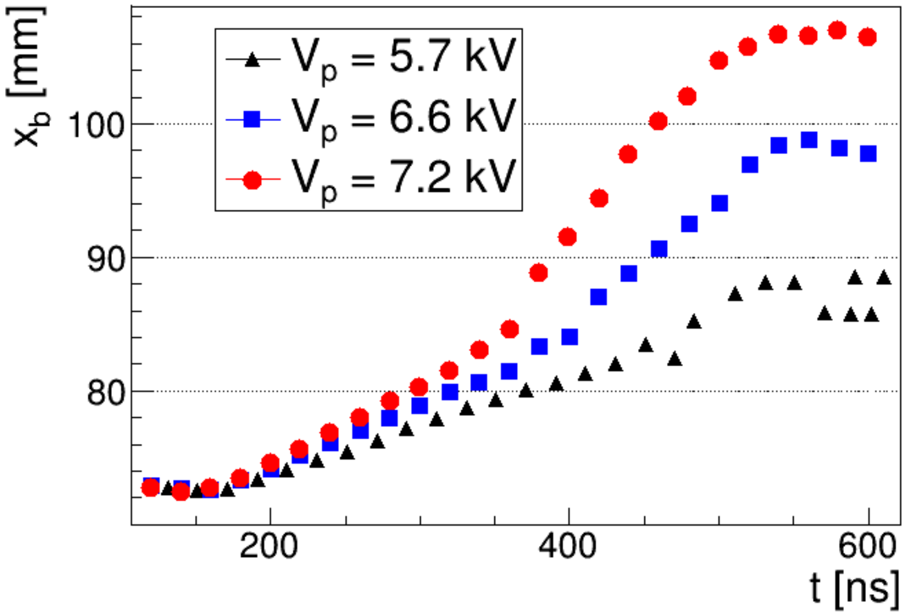
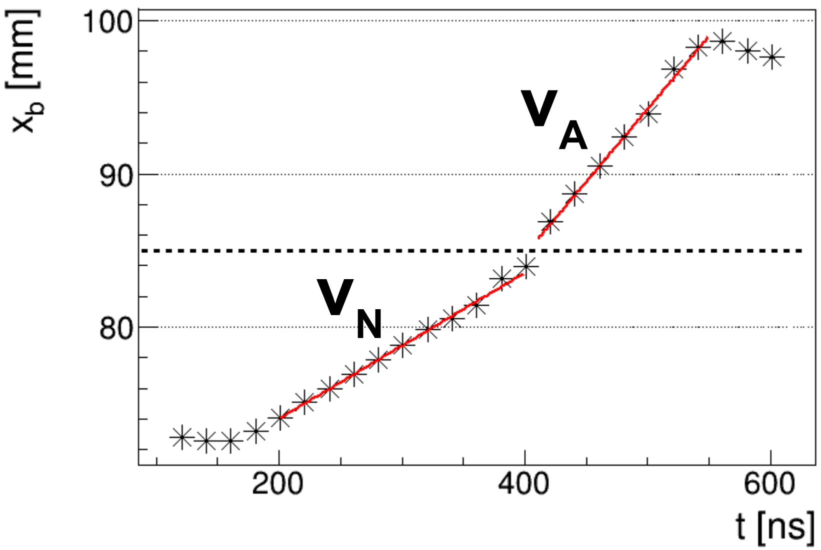


Plasma propagates from the electrode to the air.
Increasing voltage peak amplitude:

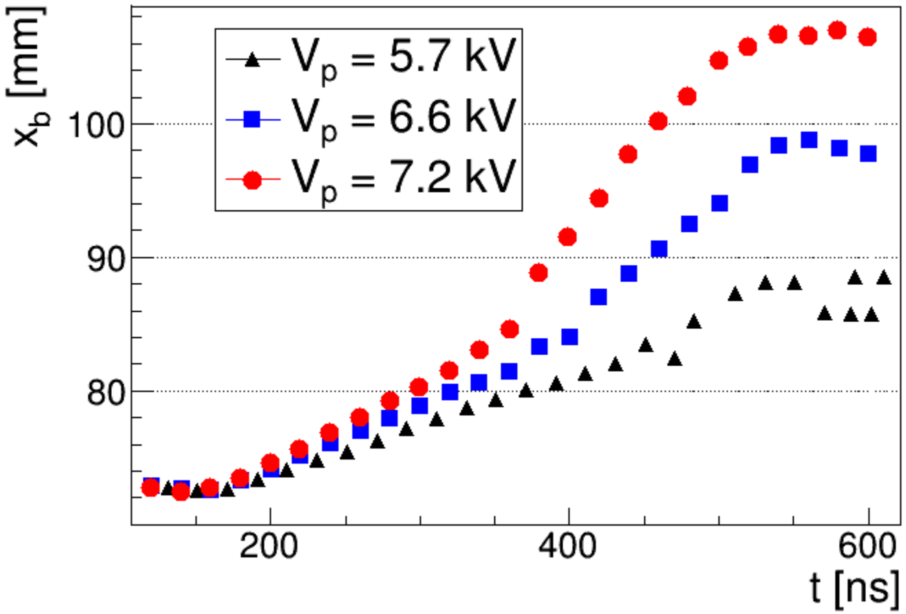
- different distances
- different velocities



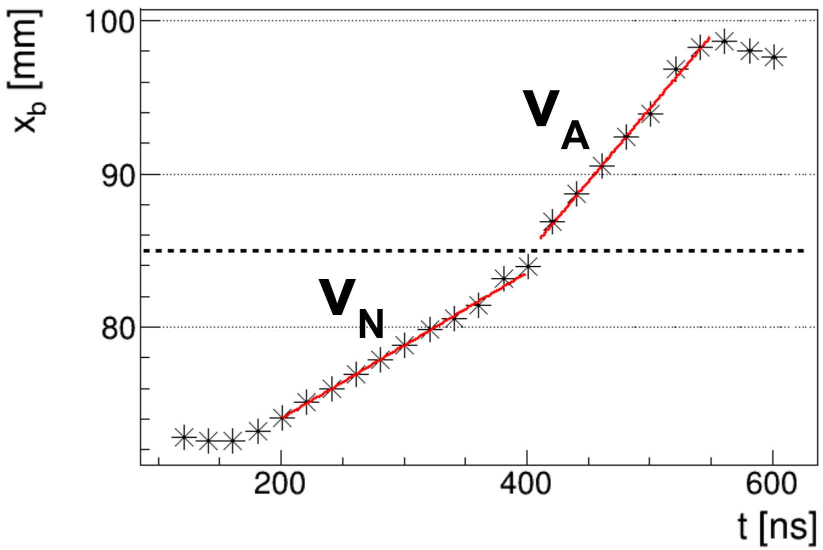
$\mathbf{v_N}$ = velocity inside the nozzle

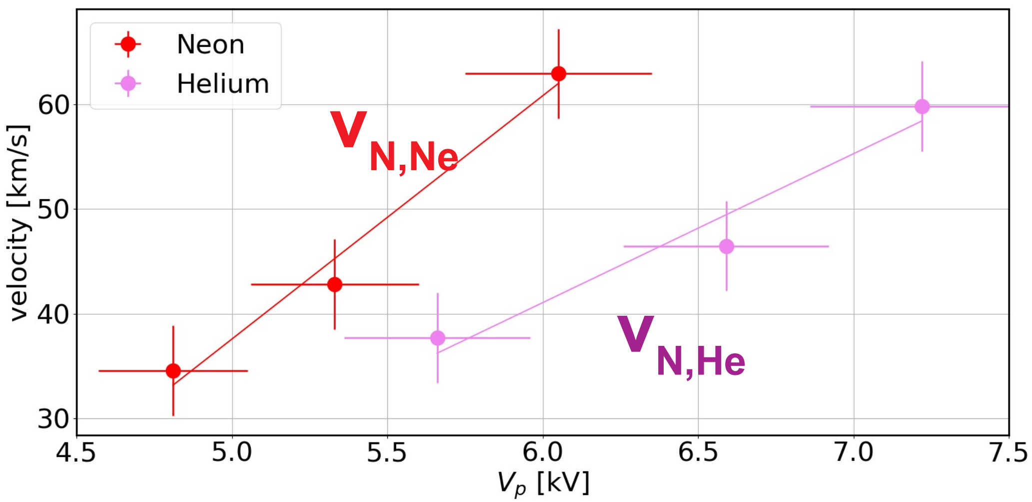
$\mathbf{v_A}$ = velocity in air

Bullet position and velocity



Gas	V_p [kV]	Δx_{MAX} [mm]	v_N [km/s]	v_A [km/s]
Helium	5.7 ± 0.3	16.0 ± 0.8	37.7 ± 3.2	-
	6.6 ± 0.3	26.1 ± 0.5	46.5 ± 4.0	95.2 ± 6.3
	7.2 ± 0.4	34.6 ± 0.5	59.8 ± 4.3	149.5 ± 11.9
Neon	4.8 ± 0.2	18.1 ± 0.9	34.6 ± 3.0	43.2 ± 7.2
	5.3 ± 0.3	22.4 ± 0.8	42.8 ± 4.6	61.2 ± 6.8
	6.1 ± 0.3	26.6 ± 0.9	62.9 ± 5.1	160.3 ± 15.7





Electronic motion equations

Electron energy distribution ***f*** in 6-dim phase space, without magnetic field :

$$\frac{\partial f}{\partial t} + v \cdot \nabla f - \frac{e}{m} E \cdot \nabla_v f = C[f]$$ **Boltzmann eq**

Where ***C[f]*** is given by collisions.

First two moments:

$$\frac{\partial n}{\partial t} + \nabla \Gamma = S$$ **Continuity eq**

$$\Gamma = -\mu E n - \nabla (D n)$$ **Drift diffusion eq**

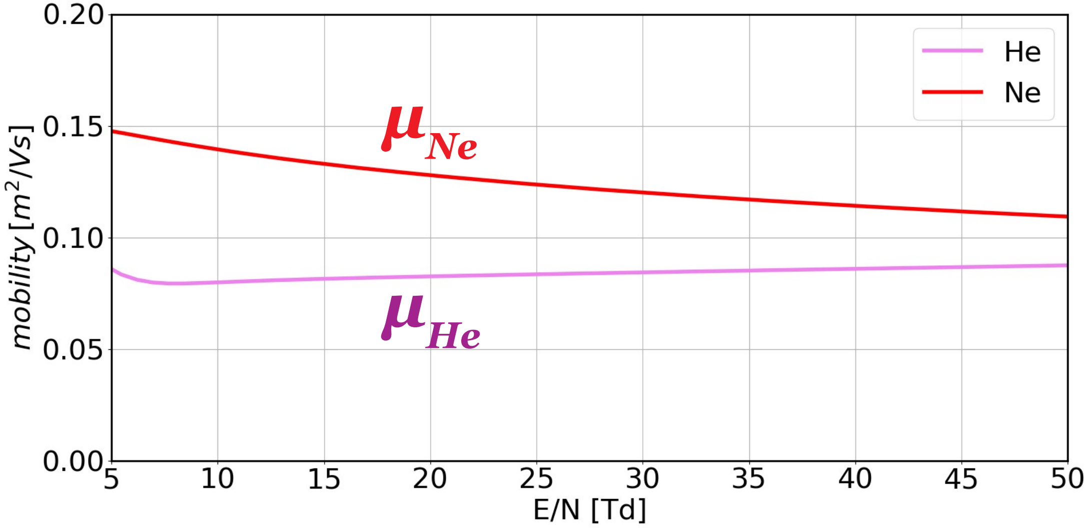
Where:

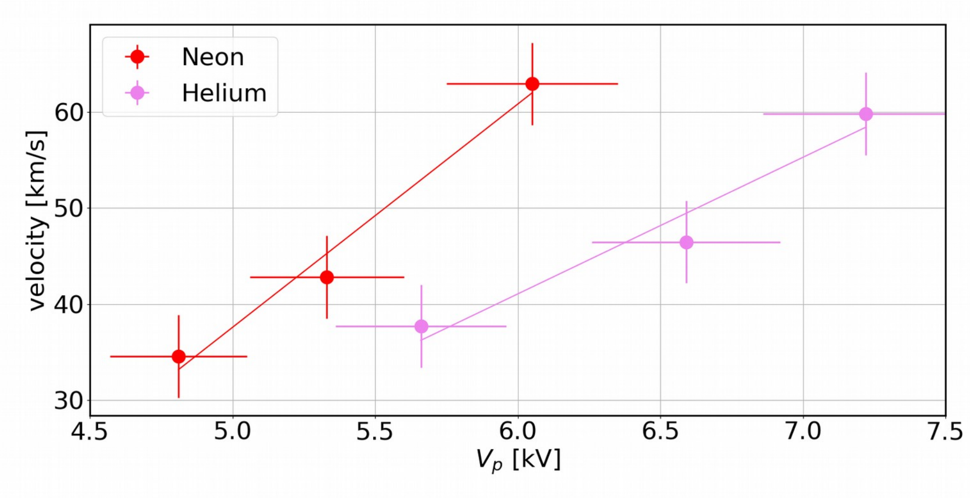
- **n** is the electron density
- **S** is the source term given by reactions
- **Γ** is the electron flux
- **μ** is the electron mobility
- **D** is the electron diffusion coefficient

Electronic parameters

Previous equations can be solved by *Bolsig+*, a Boltzmann Equation solver for plasma with variable composition inside an electric field with variable intensity.

Atmospheric pressure electric fields from **130 V/mm** to **1.3 kV/mm** :





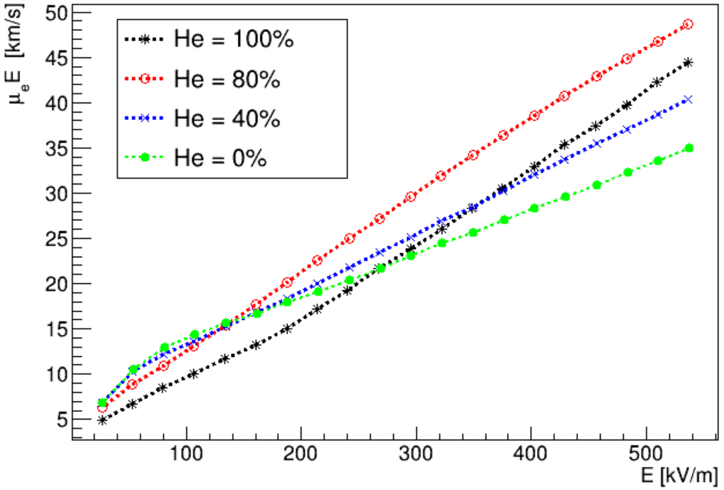
$$\mu_{He} < \mu_{Ne}$$

Bullet velocity related to electron mobility

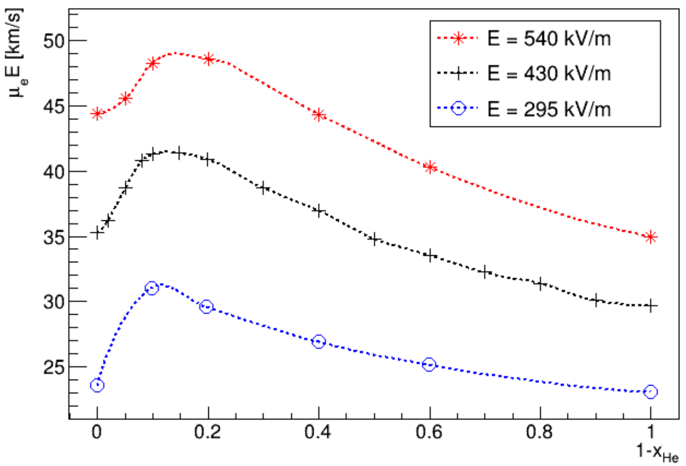
*Submission of article "*On the electrical and optical features of the PCC low temperature atmospheric plasma jet* " at *Plasma*

Drift velocity and bullet velocity

Drift velocity $\mathbf{v_D} = \boldsymbol{\mu_e}\mathbf{E}$

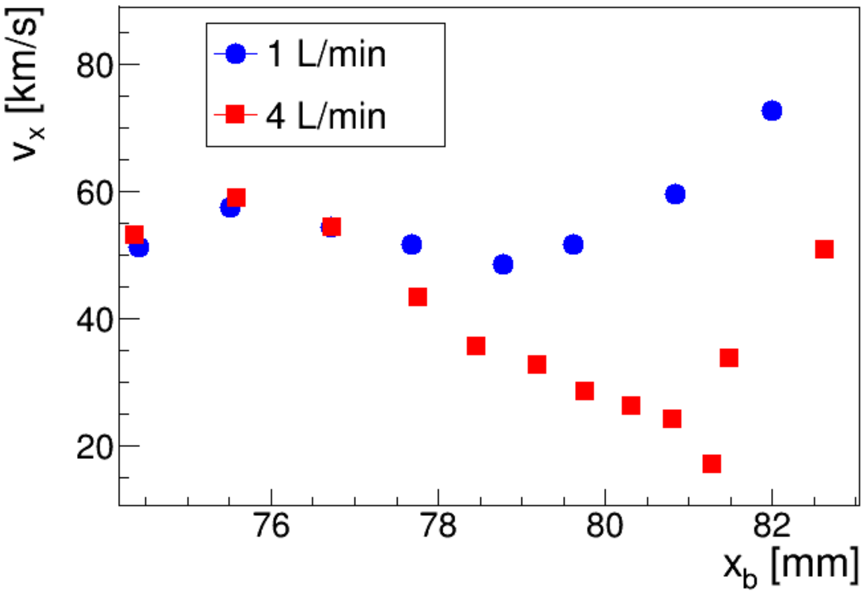


Inside the nozzle, costant gas composition: linearity between **v** and E



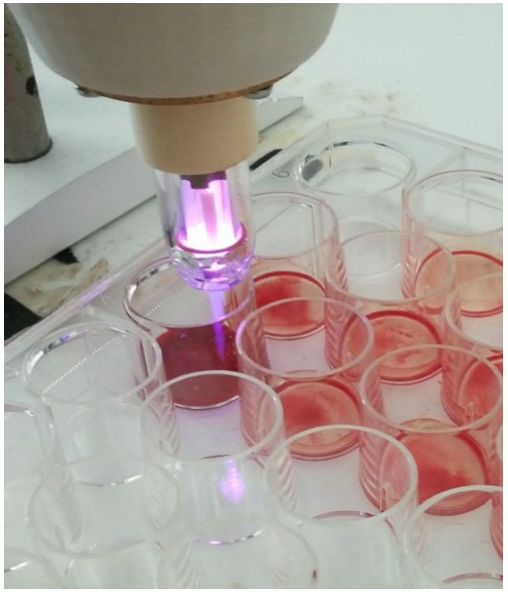
Outside the nozzle: peak in $\mathbf{v_D}$ for increasing $\mathbf{N_2}$ concentration

Bullet velocity decreases while distance from the electrode increases and increases while air concentration increases

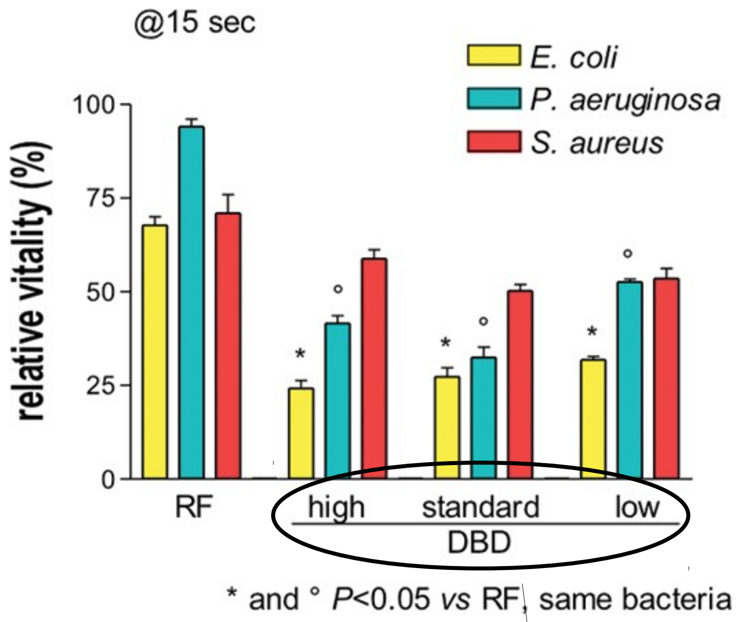


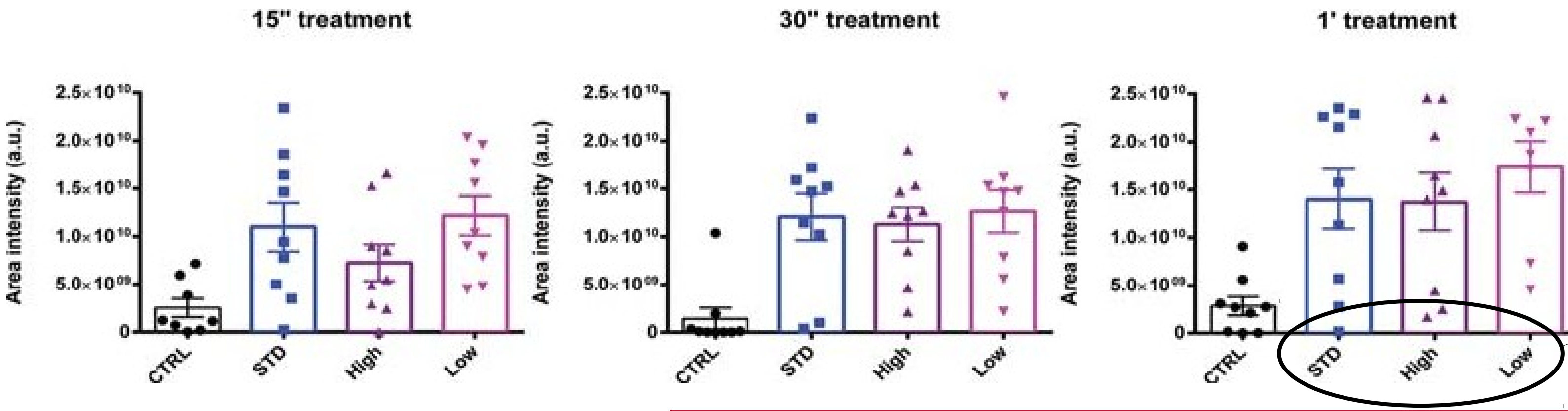
Non thermal blood coagulation

Good results for blood coagulation experiments



Good results for bactericidal experiments





Three different parameters setup

Conclusions and future development

In conclusion in this work was:

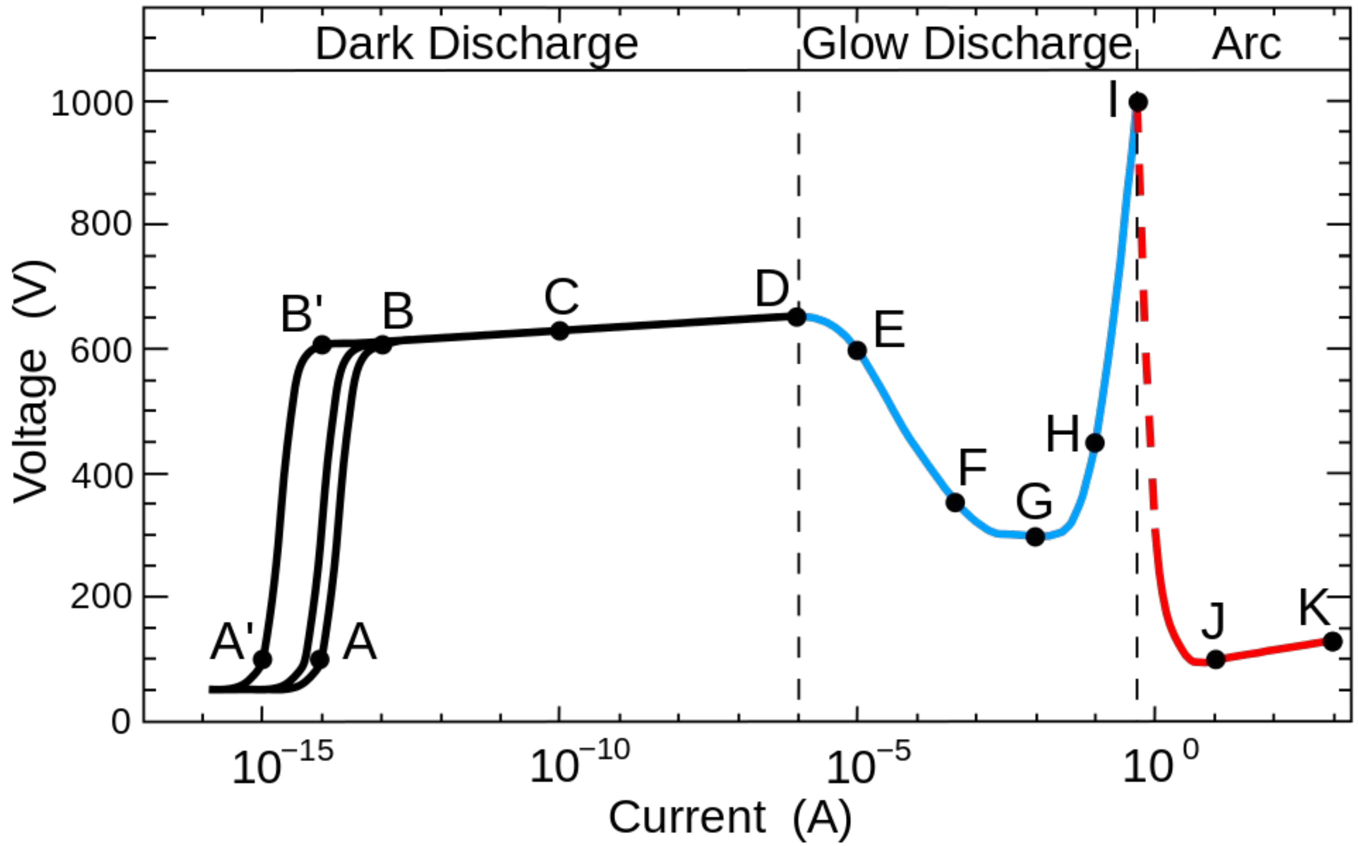
- Developed the new PCC prototype.
- Guaranteed fine control over voltage output and low current intensities.
- Assured the presence of **ROS** and **RNS**, in different concentrations for different positions in plasma.
- Studied plasma propagation dynamics in different conditions: changing voltage peak value, neutral gas, neutral gas flow, distance from a target, typology of target.
- Plasma jet length, bullet velocity, current measurement are compared for Helium and Neon plasma, resulting that bullet velocity is correlated with electron mobility.

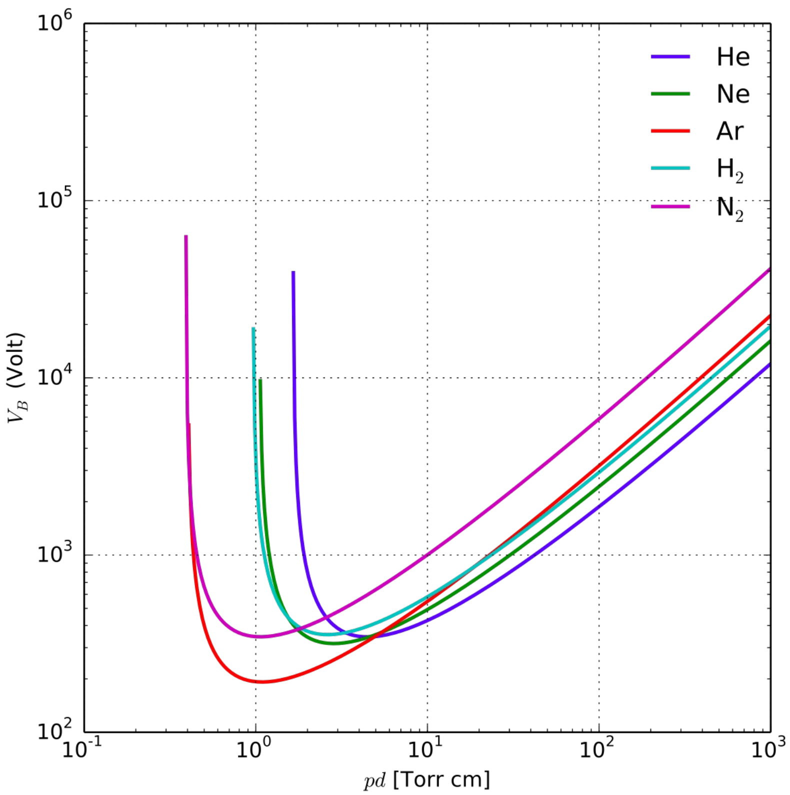
Future development

- Formulation of a model that could explain measurements and observations collected with this work.
- Further measurements, including the evaluation of the electric field around the electrode.
- Start of clinical trials on human patients.

Thank you for your attention

Plasma discharge





F = subnormal glow discharge
G = normal glow discharge
H = abnormal glow discharge

Paschen breakdown curve

Optical Emission Spectroscopy
temperature estimation

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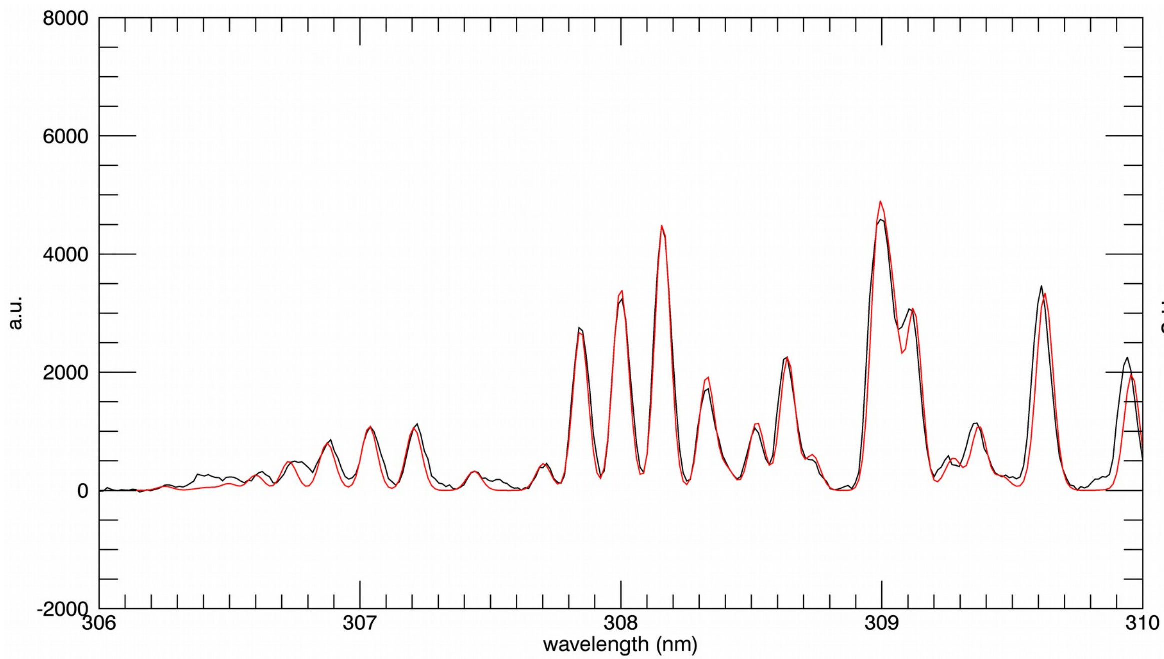
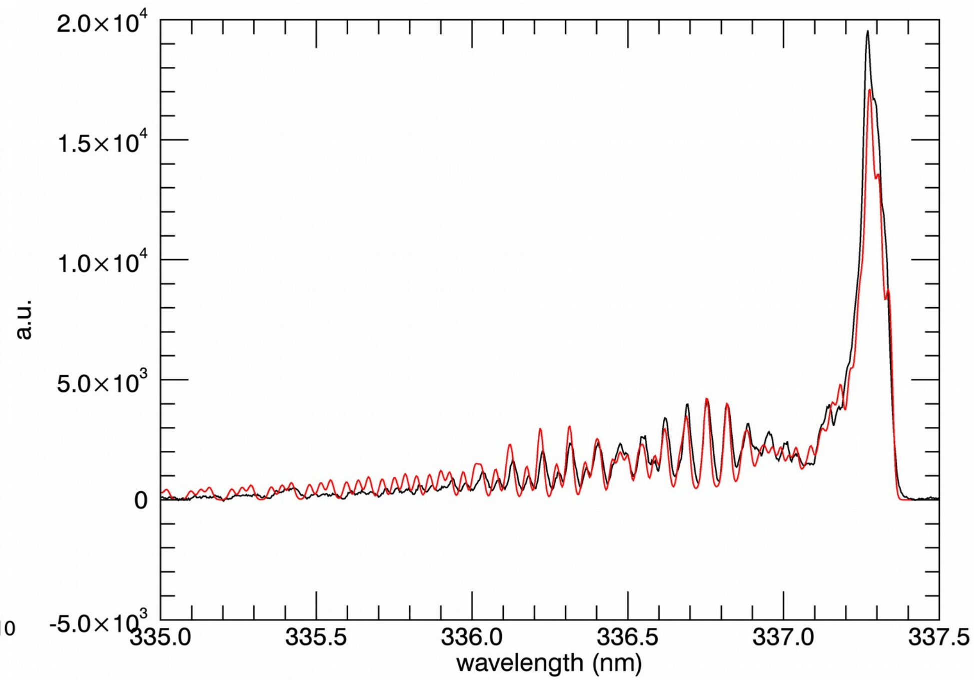
An high resolution spectrometer allows us to observe **OH** and **N_2** rotational bands.

Through a simulation of the rotational spectrum of the molecule it is possible to estimate its rotational temperature, which is approximately the temperature of the molecule itself. → $\mathbf{T_{rot} \approx T_{ion}}$

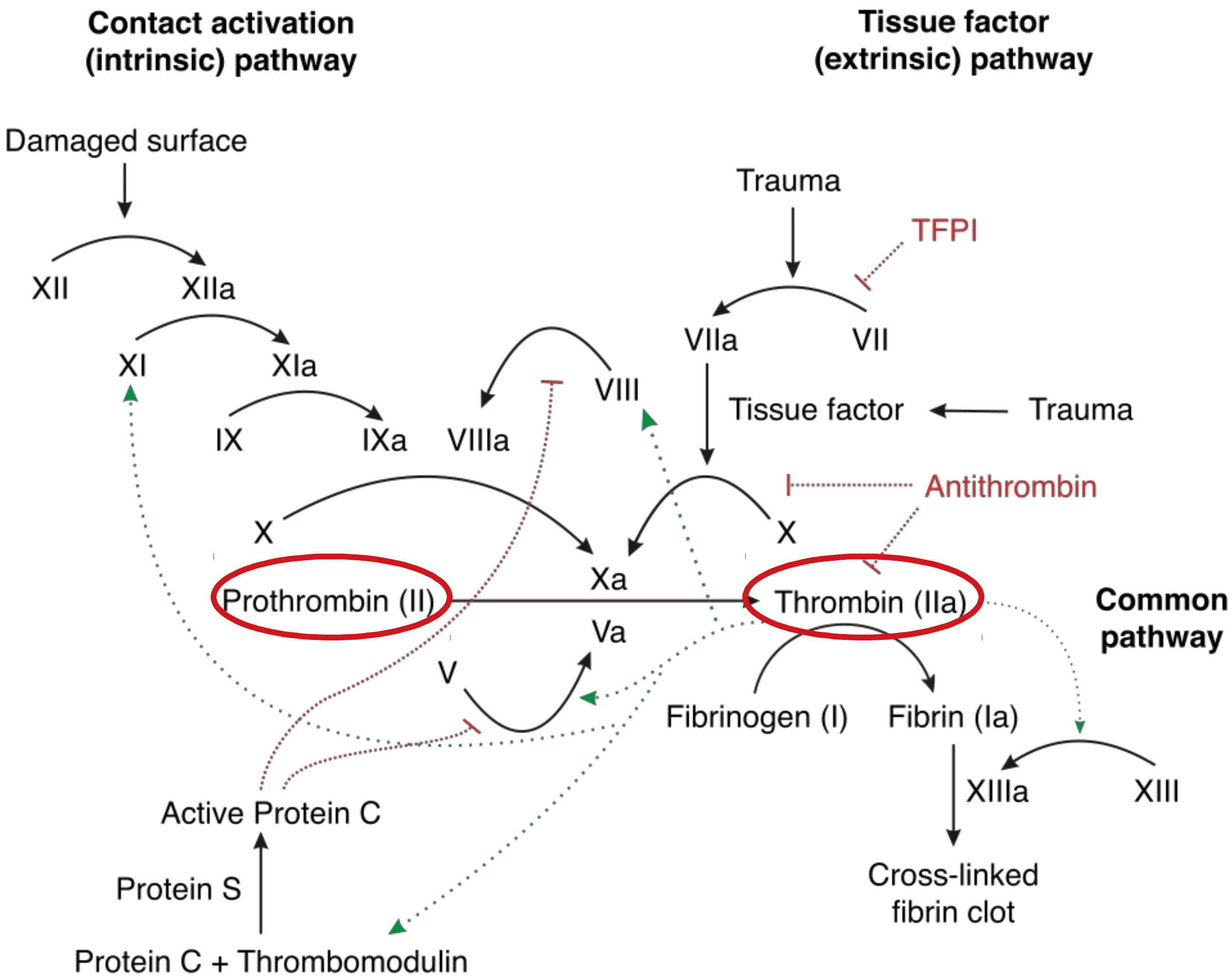


$\mathbf{T_{rot,\,OH} = 352 \pm 38}$



$\mathbf{T_{rot,\,N_2} = 321 \pm 41}$

Non thermal blood coagulation

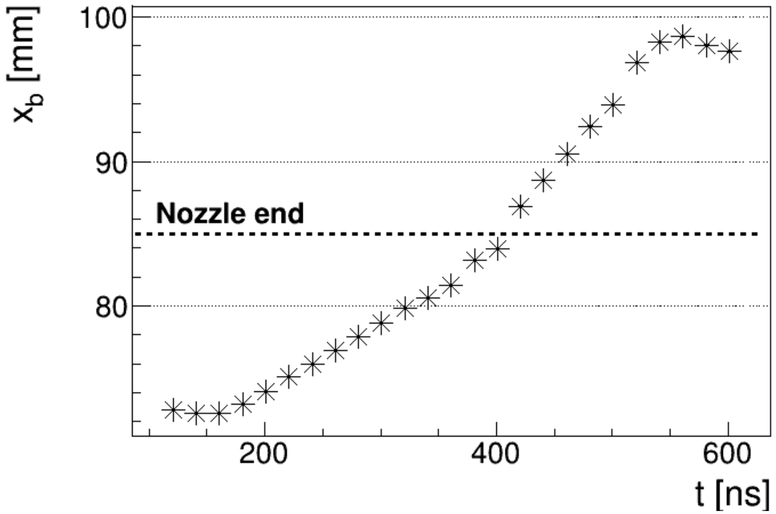


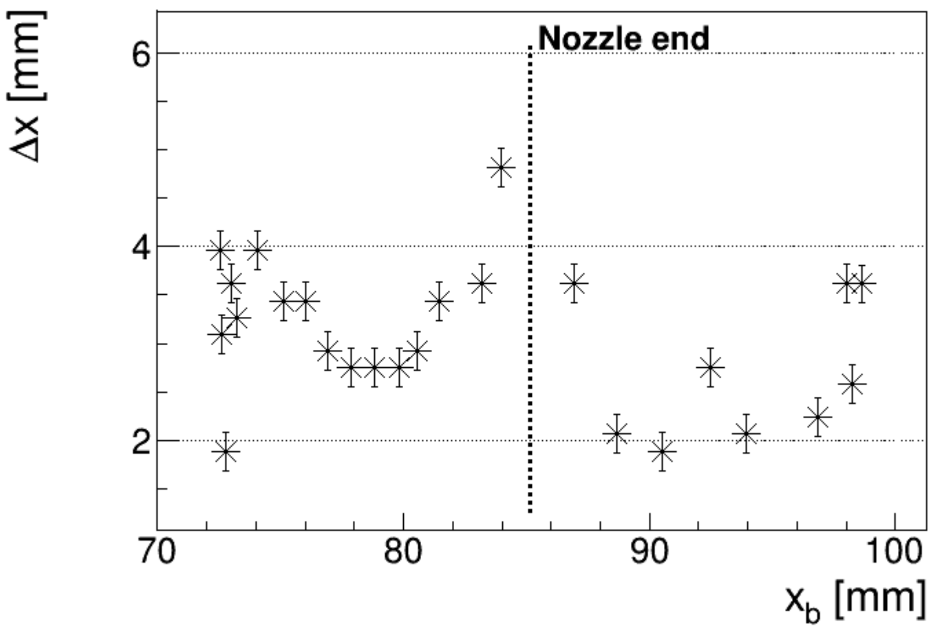
Two pathways, many tissue factors and proteins involved. PCC improves *Prothtrombin* and *Thrombin* production.

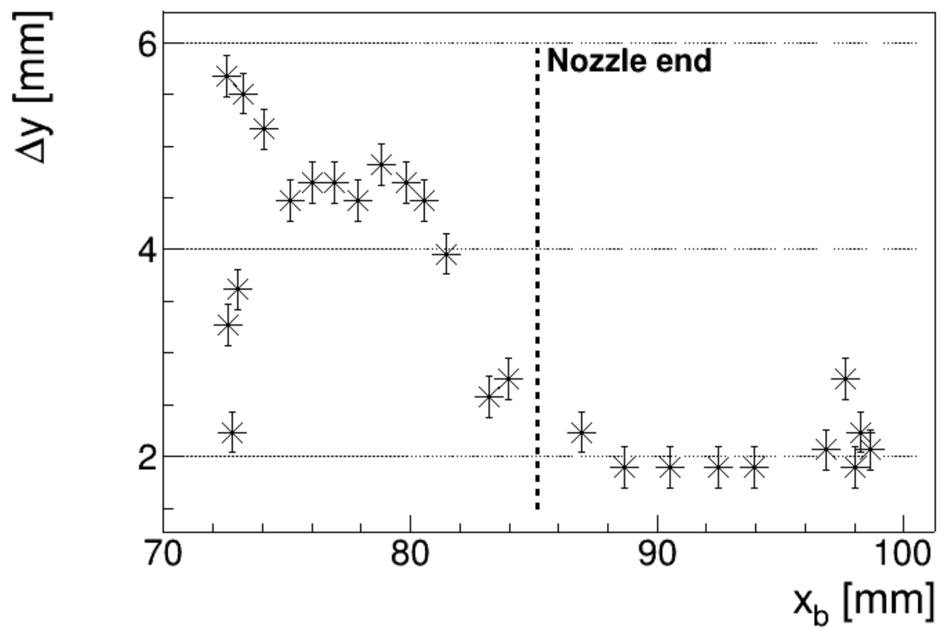
Bullet position and dimensions

The bullet propagates from the electrode to the end of the nozzle (velocity $\mathbf{v}_N$> 40 km/s) with constant diameters.

When the bullet meets the air it speeds up ($\mathbf{v}_A$> 80 km/s) and propagates with lower diameters until it stops.



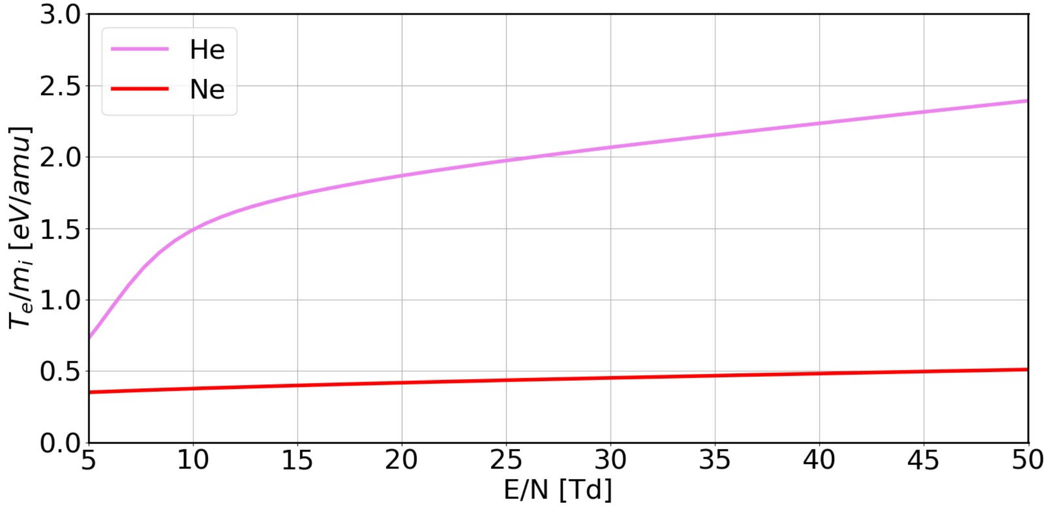


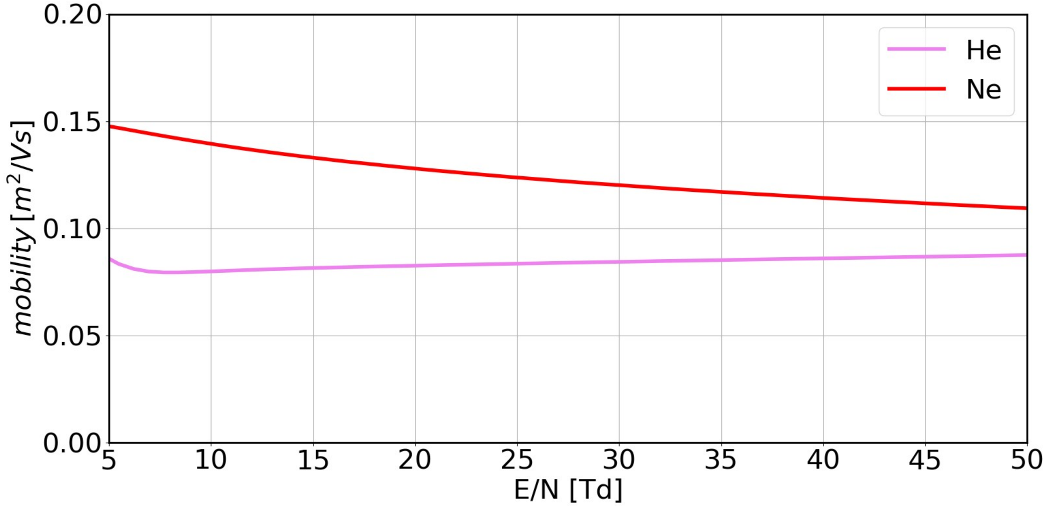


Electronic parameters

Previous equations can be solved by *Bolsig+*, a Boltzmann Equation solver for plasma with variable composition inside an electric field with variable intensity.

Helium and neon plasma at atmospheric pressure, electric fields from **130 V/mm** to **1.3 kV/mm** :





$$\left(\frac{T_e}{m}\right)_{He} > \left(\frac{T_e}{m}\right)_{Ne}$$ → **Bullet velocity not related to ion wave propagation**

$$\mu_{He} < \mu_{Ne}$$

Bullet velocity related to electron mobility

Current measurements

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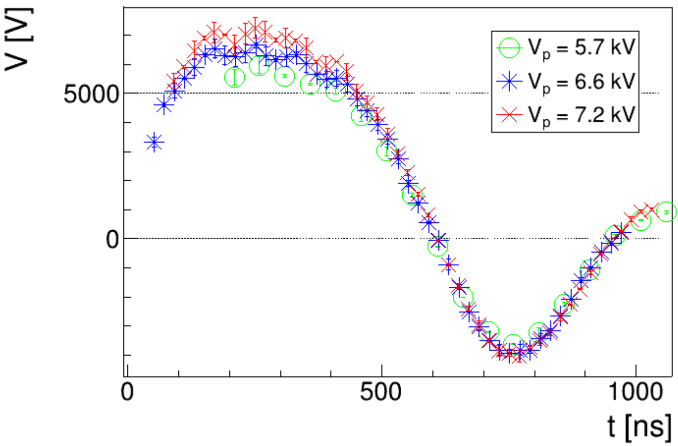
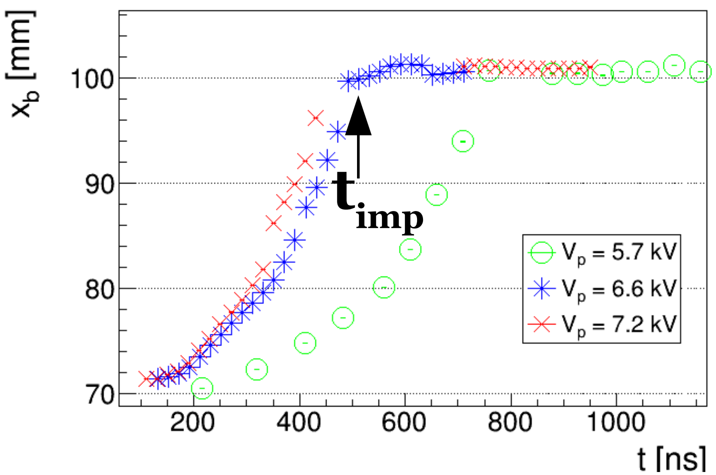
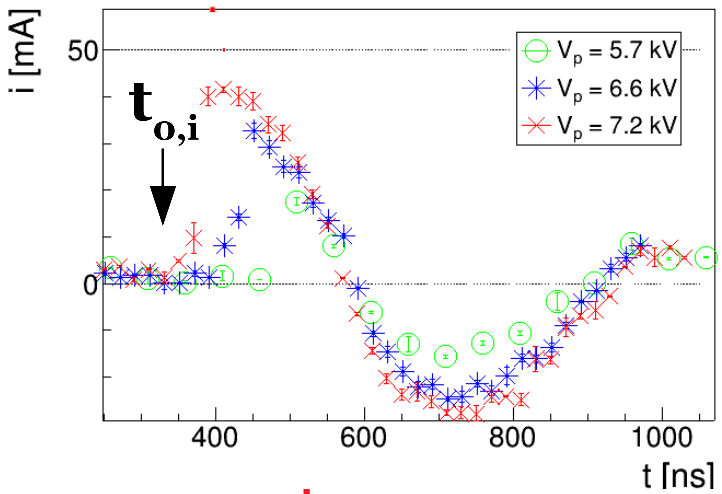
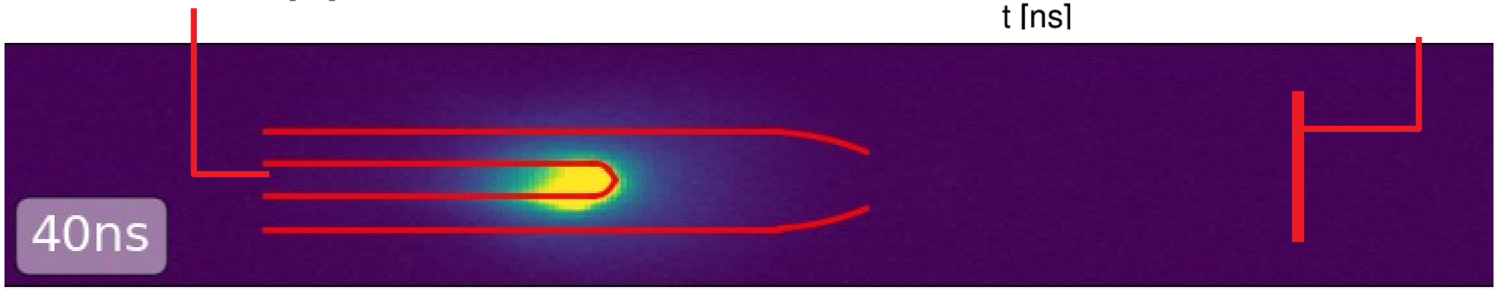
With a conductive target in front of the electrode: synchronization between voltage, fast camera and current measurements.









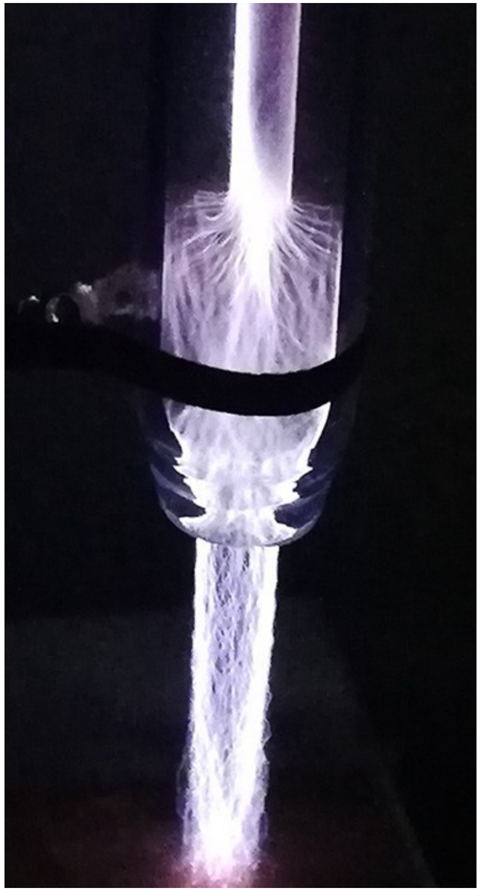
Current is measured
before bullet impact

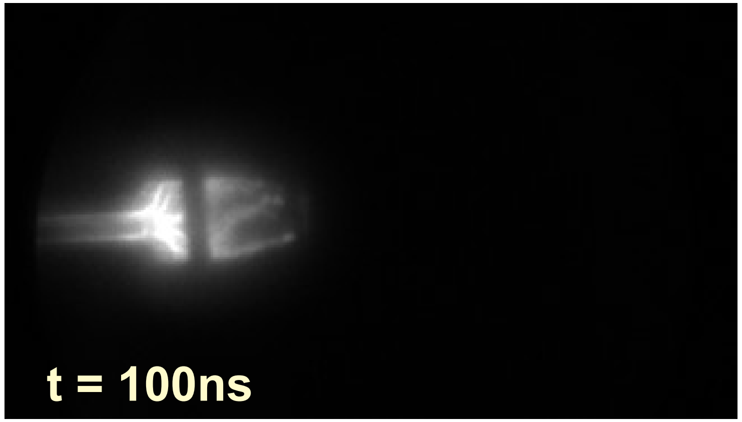
$t_{o,i} < t_{imp}$

Argon plasma

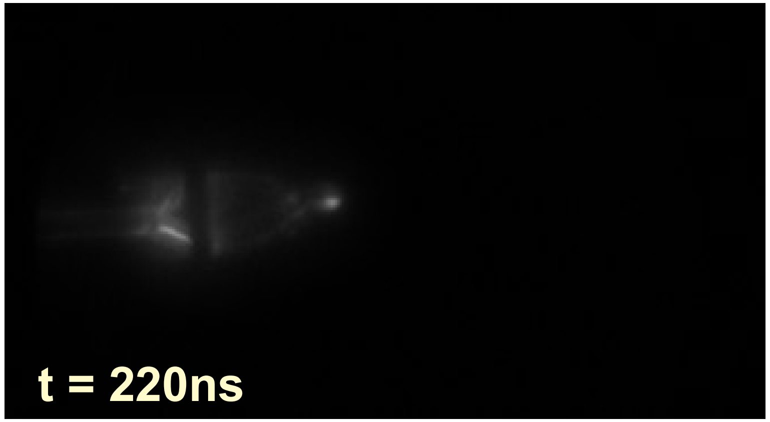
Argon plasma is hard to produce, a conductive grounded ring around the nozzle helps the process.

Once ionized, Argon produces filaments instead of bullets.





Argon filaments goes from the electrode to the end of the nozzle.



After a certain time there are tiny round shaped plasma formations going out from the nozzle.

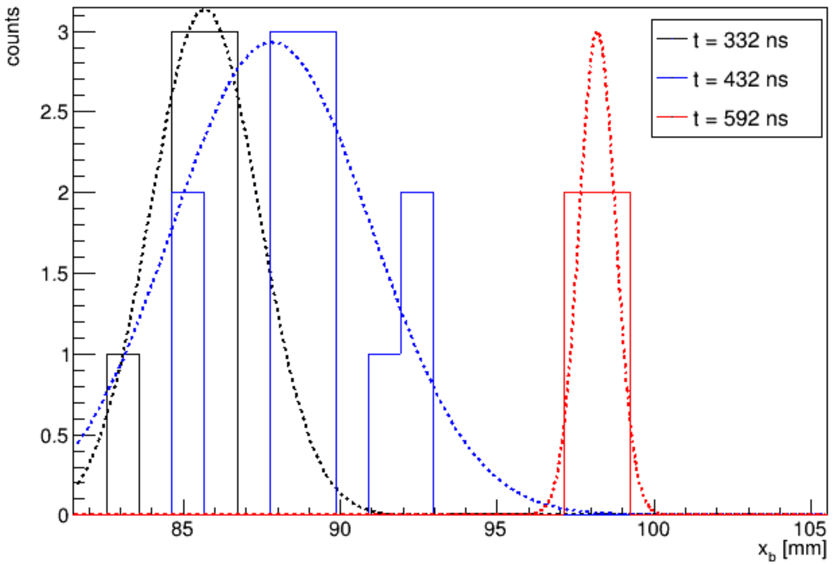
Is possible to study those formations as plasma bullets

Argon plasma
propagation

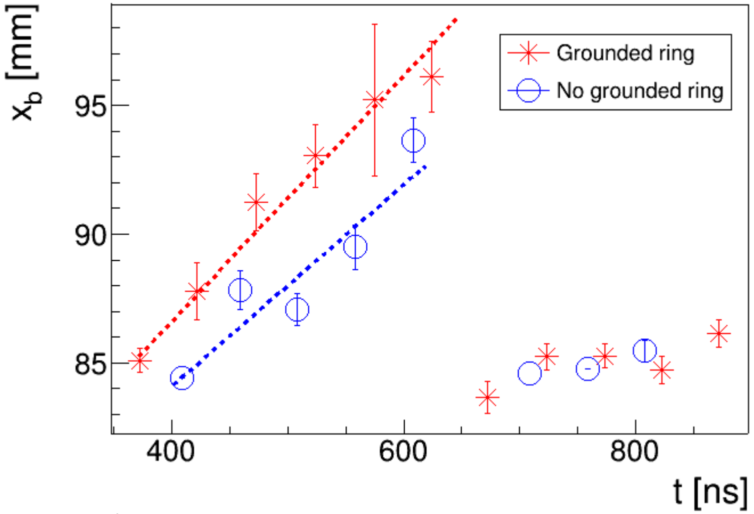
For each time, histogram for:

- **positions**
- **dimensions**

and are evaluated *average values*

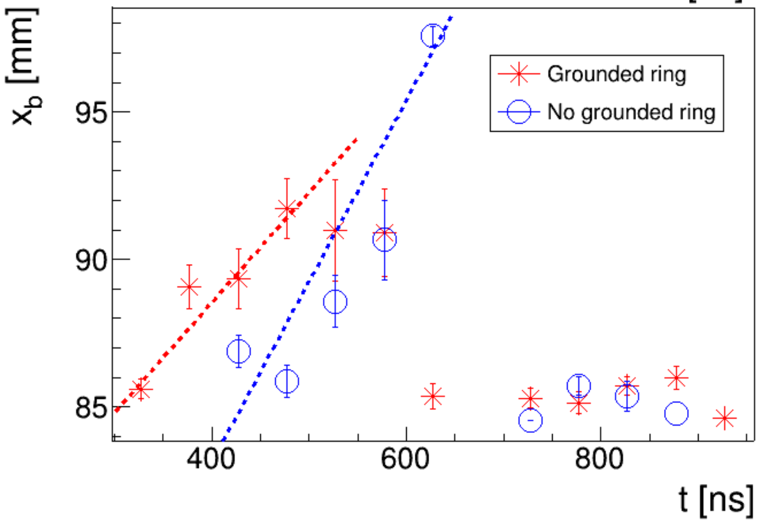


There is an average barycenter motion



Without target

$\mathbf{v_A = 47.9 \pm 4.9}$ **km/s**



With target

$\mathbf{v_A = 61.2 \pm 2.8}$ **km/s**