iDORA, un système de mesure des faisceaux à très haut débit de dose

Yannick Arnoud (MdC UGA), Ludovic Léau-Mercier (IR CNRS CDD, SATT)
LPSC Grenoble

RESEARCH ARTICLE | RADIATION TOXICITY

Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

Vincent Favaudon[1,2,*], Laura Caplier[3,†], Virginie Monceau[4,5,‡], Frédéric Pouzoulet[1,2,§], Mano ...
+ See all authors and affiliations

Science Translational Medicine 16 Jul 2014:
Vol. 6, Issue 245, pp. 245ra93
DOI: 10.1126/scitranslmed.3008973

Free Access

Issue	Med Sci (Paris) Volume 31, Number 2, Février 2015
Page(s)	121 - 123
Section	Nouvelles
DOI	https://doi.org/10.1051/medsci/20153102002
Published online	04 March 2015

Med Sci (Paris) 2015 ; 31 : 121–123

La radiothérapie FLASH pour épargner les tissus sains

The radiotherapy FLASH to save healthy tissues

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Radiotherapy & Oncology

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FIRST IN HUMAN | VOLUME 139, P18-22, OCTOBER 01, 2019

Treatment of a first patient with FLASH-radiotherapy

Jean Bourhis • Wendy Jeanneret Sozzi • Patrik Gonçalves Jorge • ... Jean-François Germond • Raphaël Moeckli [1] • Marie-Catherine Vozenin [1] • Show all authors • Show footnotes

Published: July 11, 2019 • DOI: https://doi.org/10.1016/j.radonc.2019.06.019 • Check for updates

Abstract

Background

When compared to conventional radiotherapy (RT) in pre-clinical studies, FLASH-RT was shown to reproducibly spare normal tissues, while preserving the anti-tumor activity. This marked increase of the differential effect between normal tissues and tumors prompted its clinical translation. In this context, we present here the treatment of a first patient with FLASH-RT.

Material & methods

A 75-year-old patient presented with a multiresistant CD30+ T-cell cutaneous lymphoma disseminated throughout the whole skin surface. Localized skin RT has been previously used over 110 times for various ulcerative and/or painful cutaneous lesions progressing despite systemic treatments. However, the tolerance of these RT was generally poor, and it was hypothesized that FLASH-RT could offer an equivalent tumor control probability, while being less toxic for the skin. This treatment was given to a 3.5-cm diameter skin tumor with a 5.6-MeV linac specifically designed for FLASH-RT. The prescribed dose to the PTV was 15 Gy, in 90 ms. Redundant dosimetric measurements were performed with GafChromic films and alanine, to check the consistency between the prescribed and the delivered doses.

High dose-per-pulse electron beam dosimetry: Usability and dose-rate independence of EBT3 Gafchromic films

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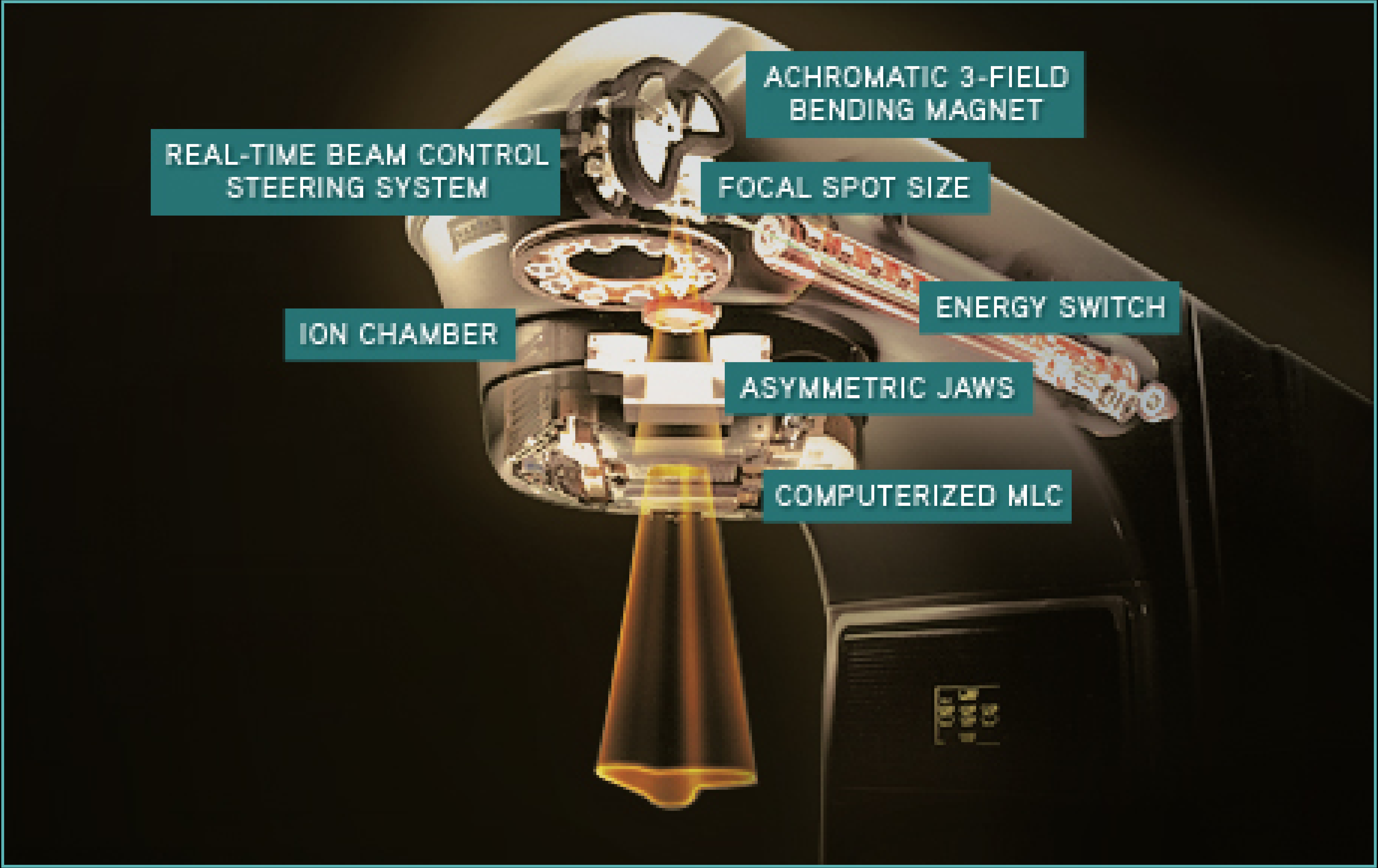
(Received 24 June 2016; revised 2 December 2016; accepted for publication 7 December 2016; published 13 February 2017)

1. INTRODUCTION

Preclinical studies have shown that irradiations using a high dose-per-pulse electron beam with a high dose rate can increase the differential response between normal and tumor tissue compared to radiotherapy delivered with conventional dose rates (of a few Gy/min).[1] Extremely fast irradiations may also improve motion management issues, since the treatment could be delivered to the patient more rapidly than the timeframe of physiological motions.[2,3] These investigations raised the challenge of performing reliable dosimetry in unusual irradiation conditions, such as those produced by a prototype high dose-per-pulse linac recently installed in our department. Ionization chambers, which are in general the instruments of choice for reference dosimetry, cannot be used directly because of strong saturation effects induced by the intense beam of the prototype linac, which cannot be corrected in a satisfactory way by existing saturation models.[4–6] In this work, we examined the usability of Gafchromic EBT3 films for reference dosimetry in high dose rates/dose-per-


ACHROMATIC 3-FIELD
BENDING MAGNET
REAL-TIME BEAM CONTROL
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ION CHAMBER
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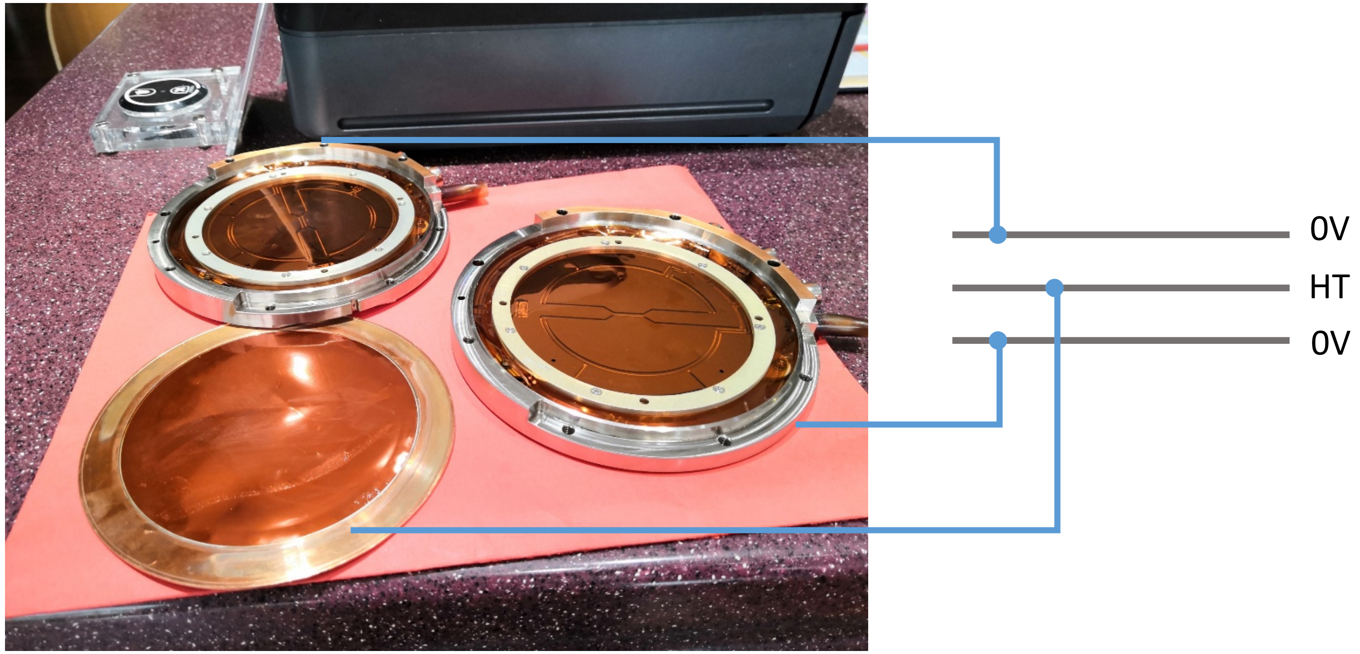
COMPUTERIZED MLC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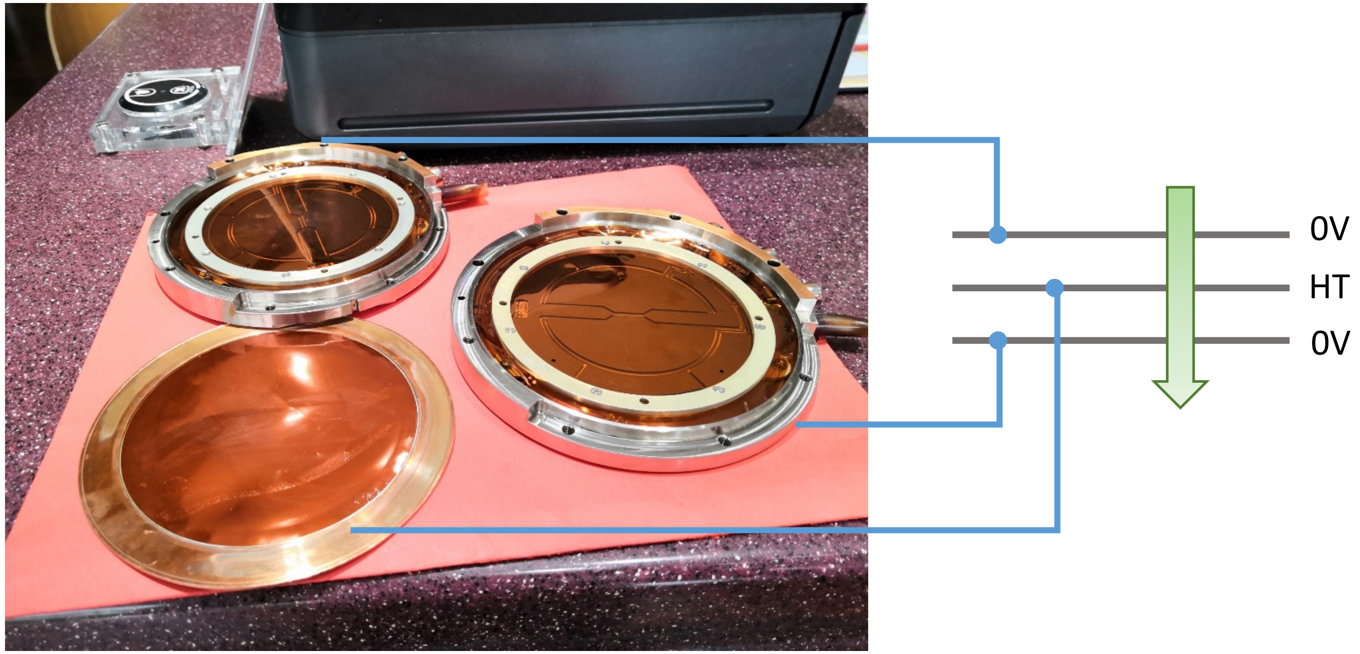

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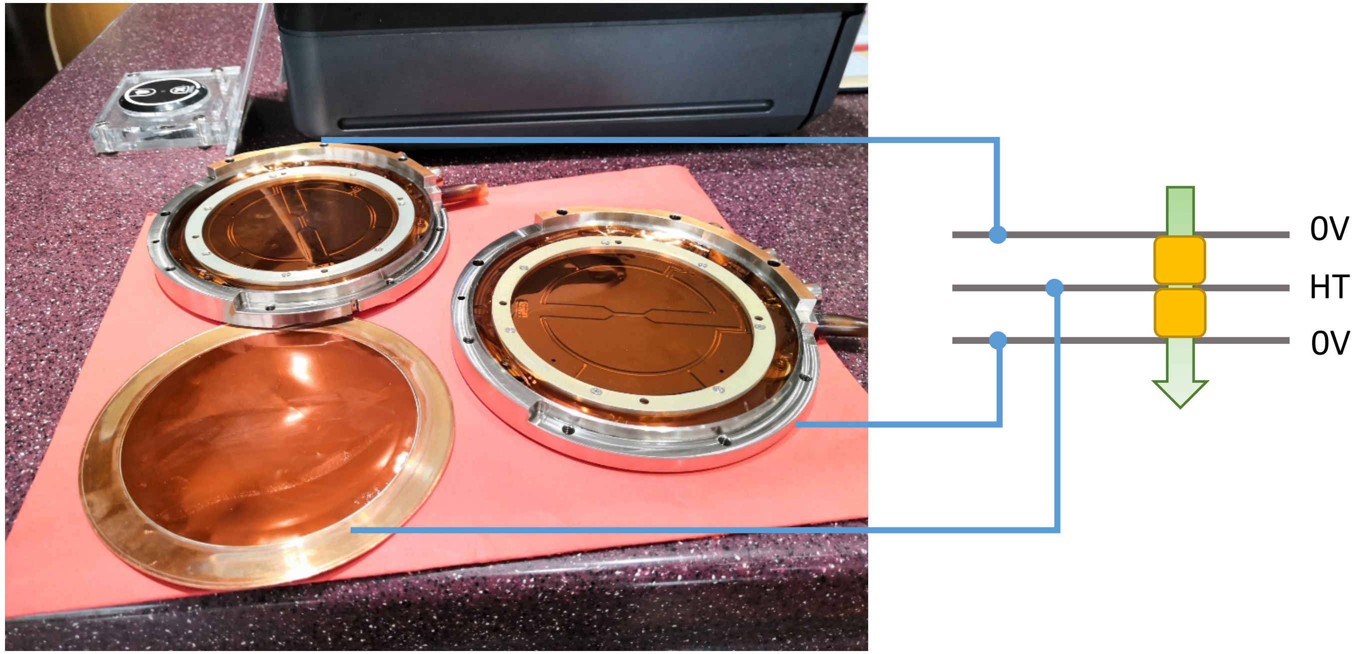
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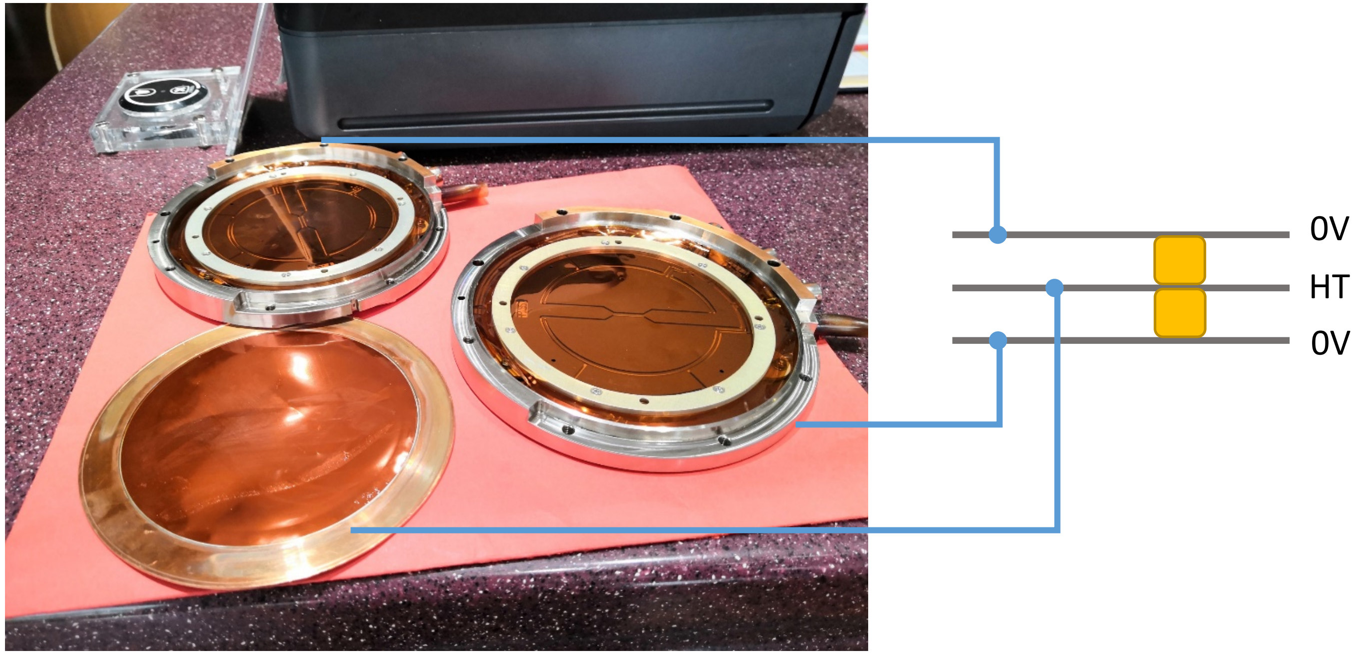

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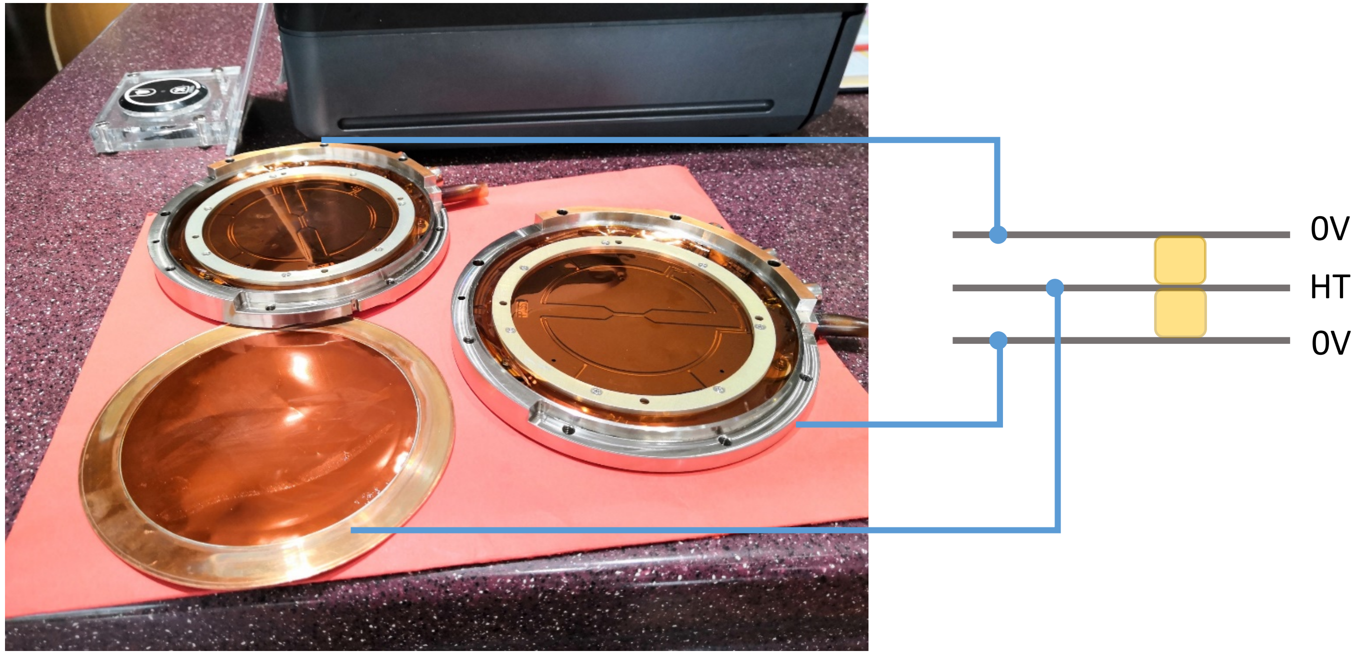
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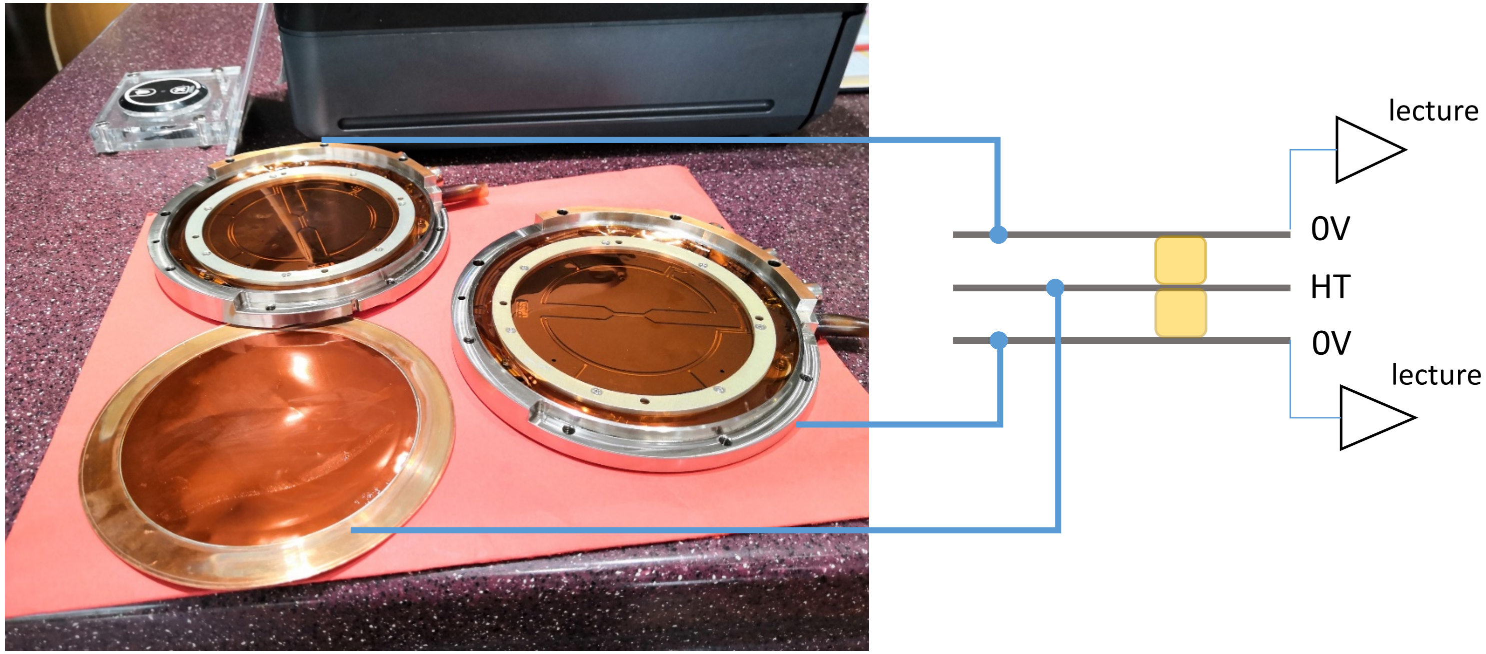
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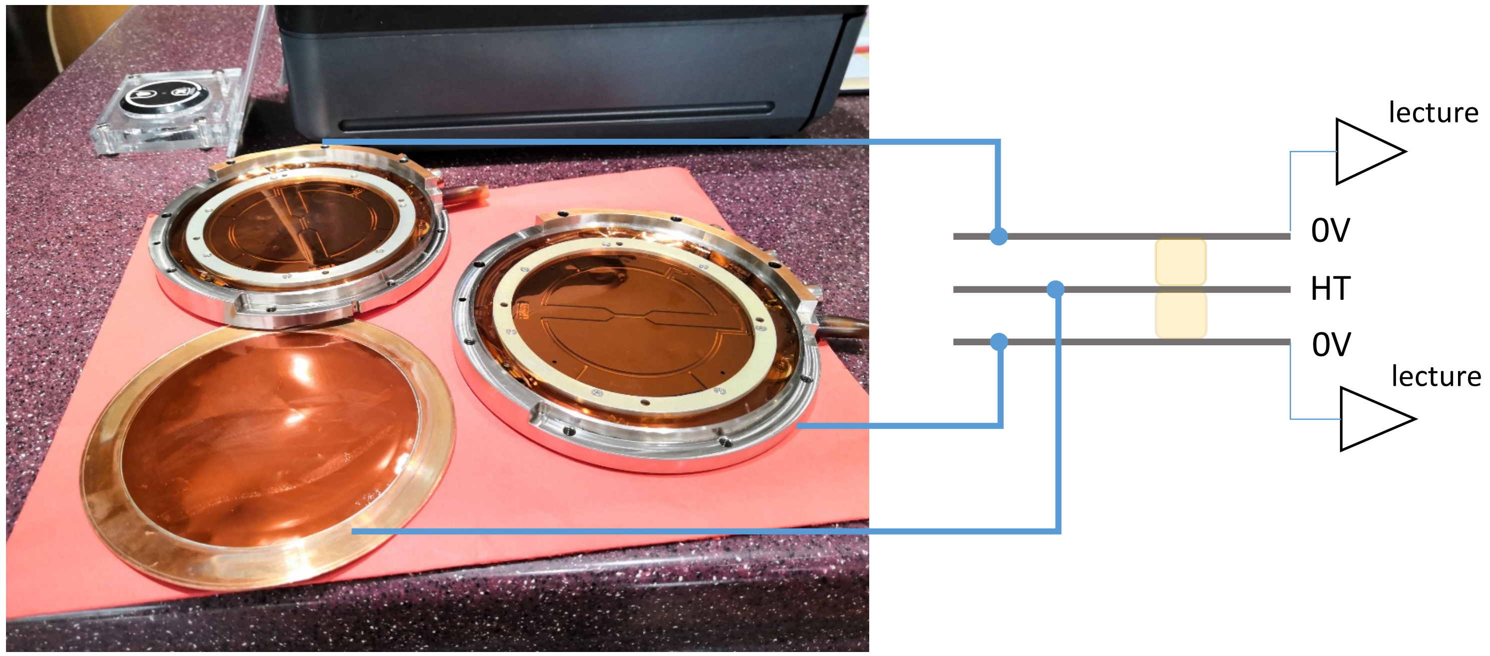
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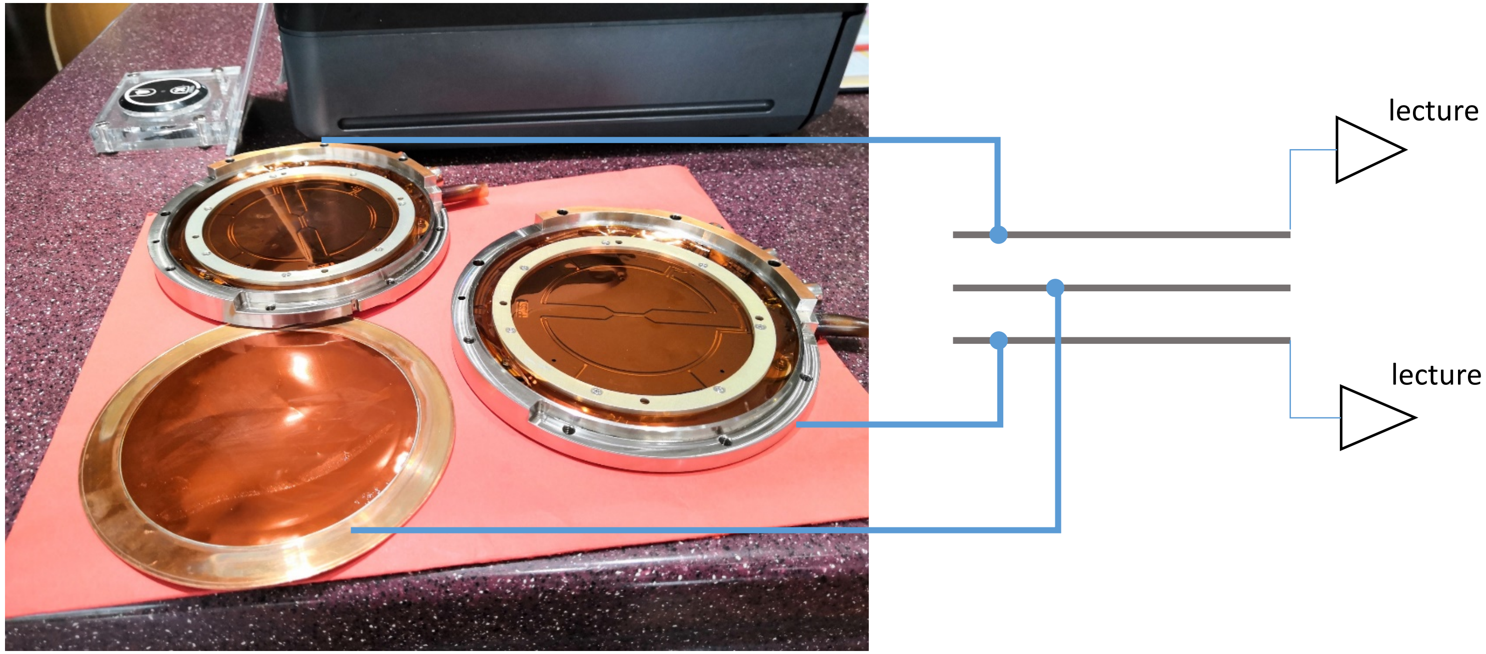
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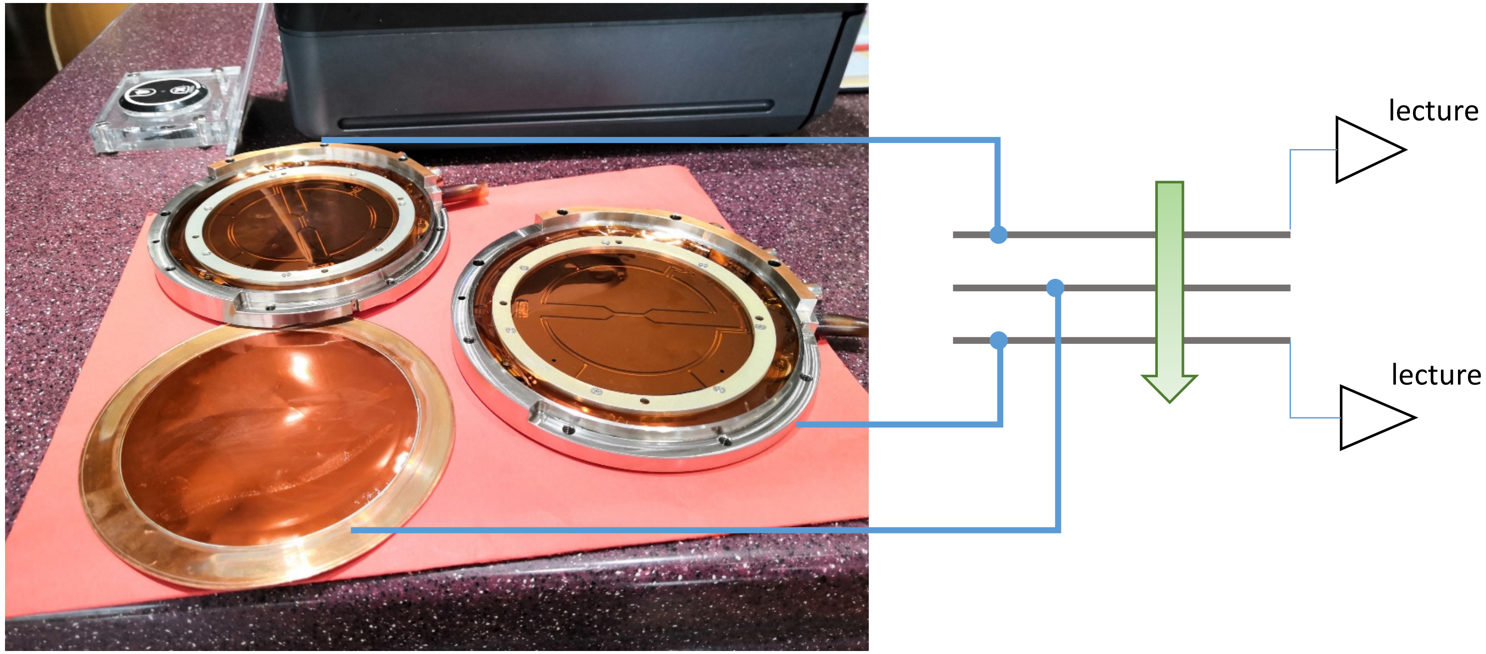
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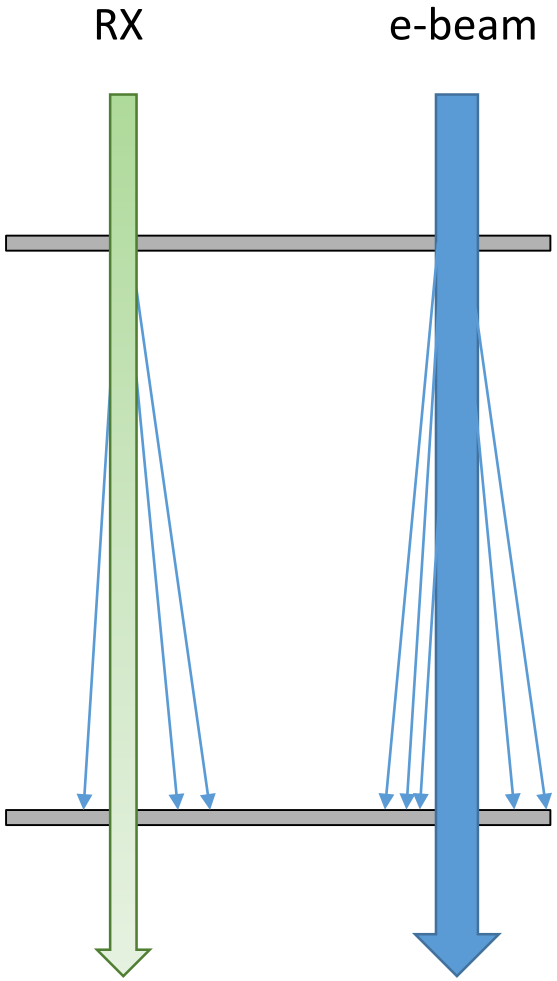
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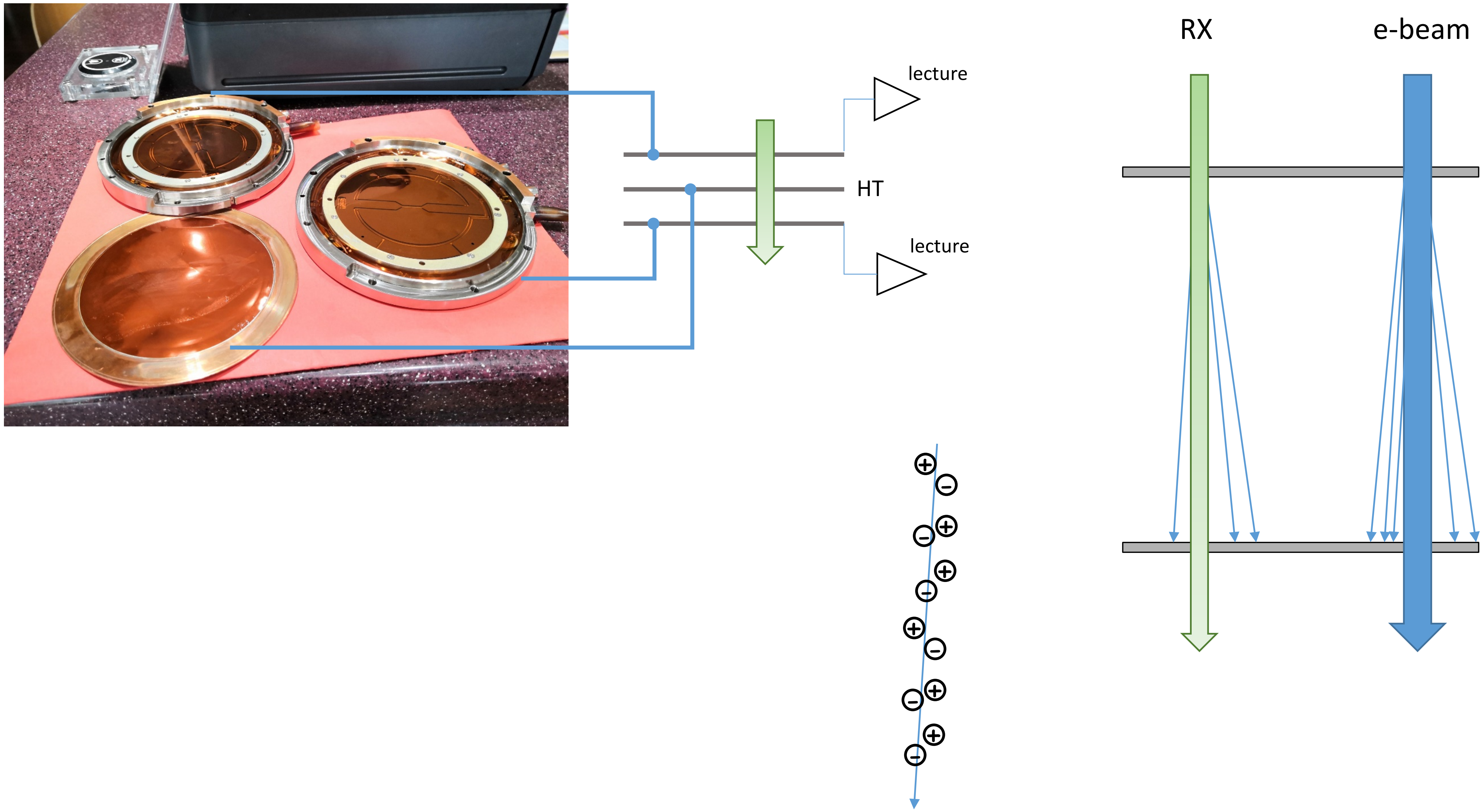
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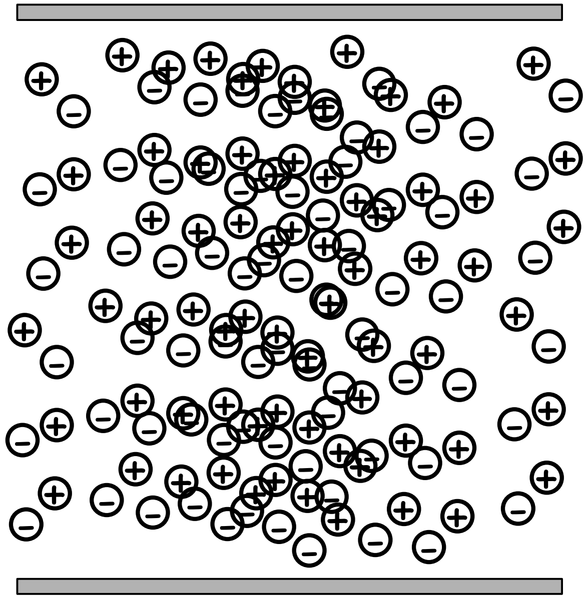

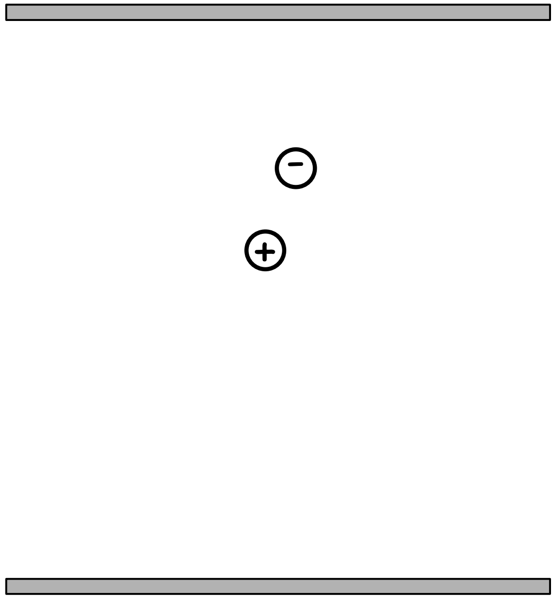

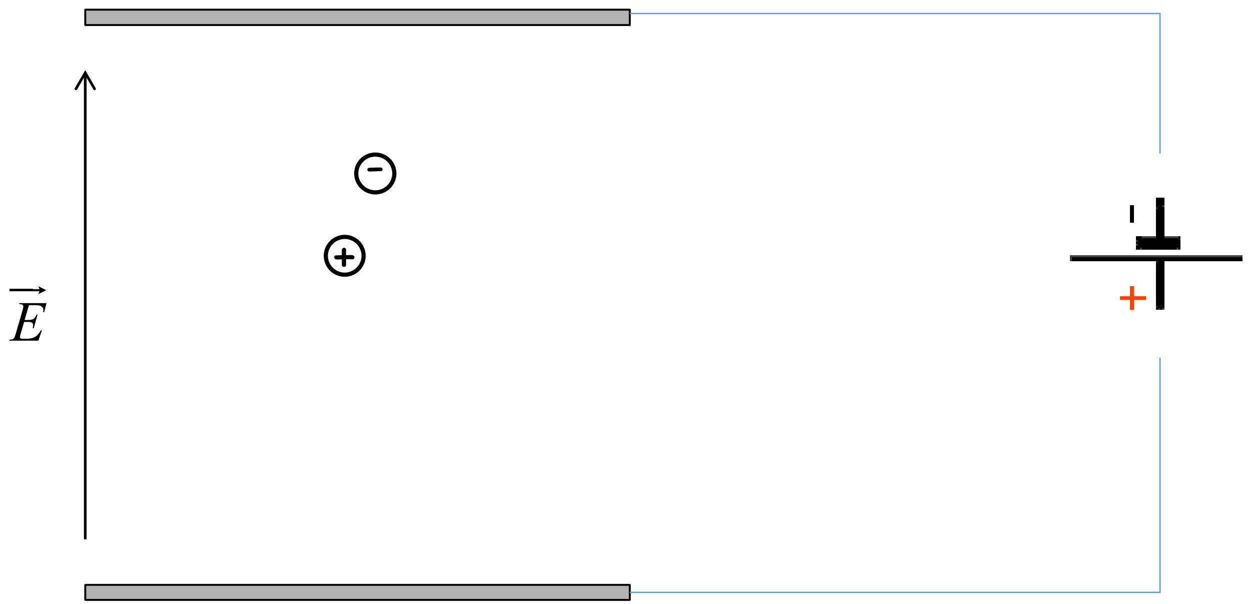
$\vec{E}$
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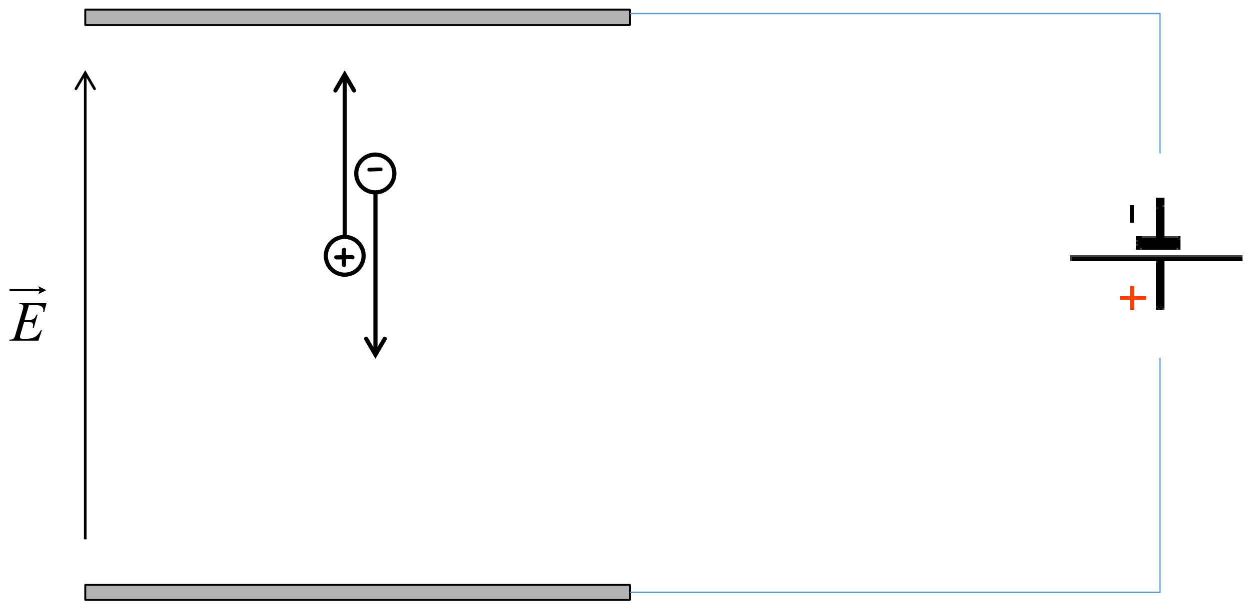
+
-
+



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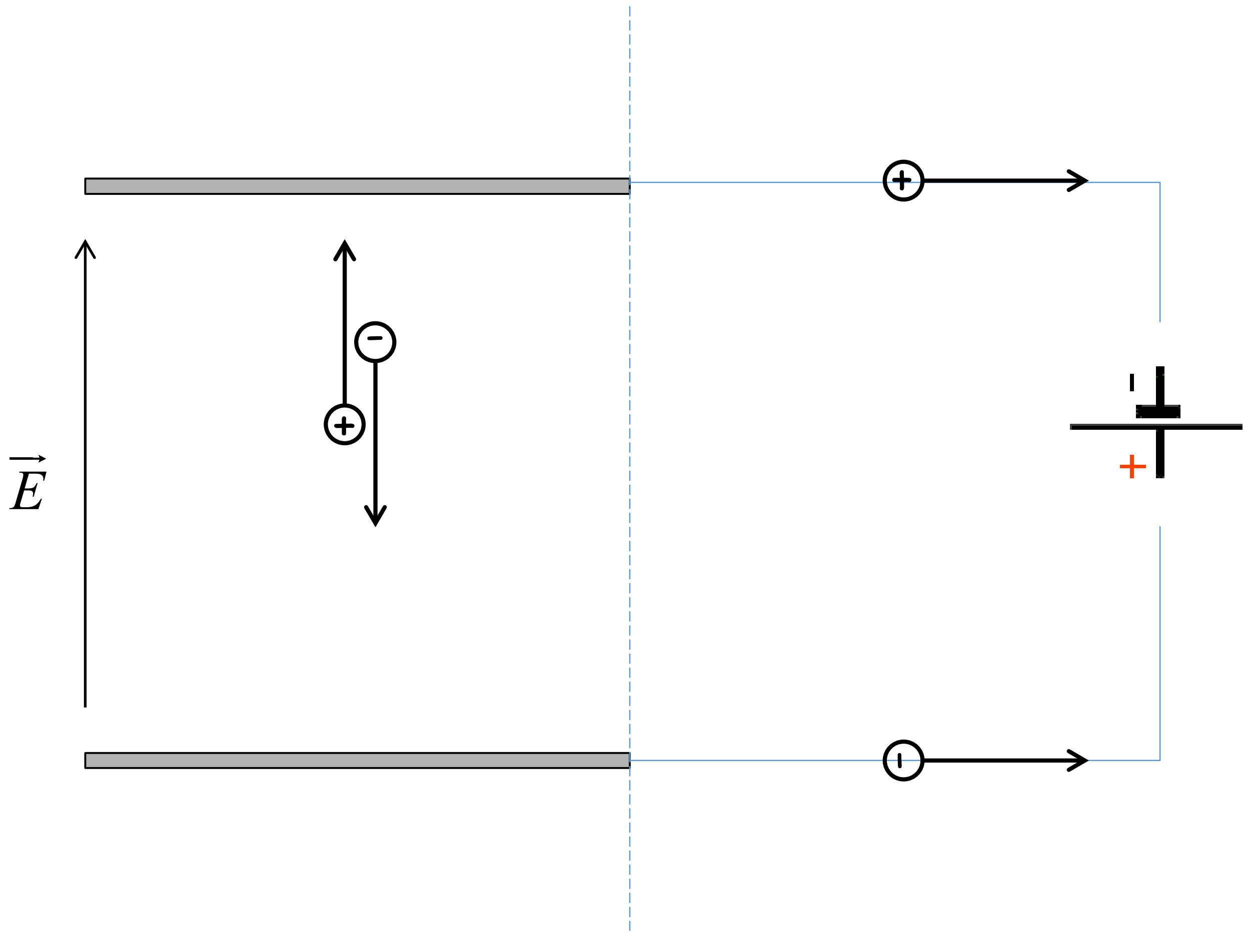
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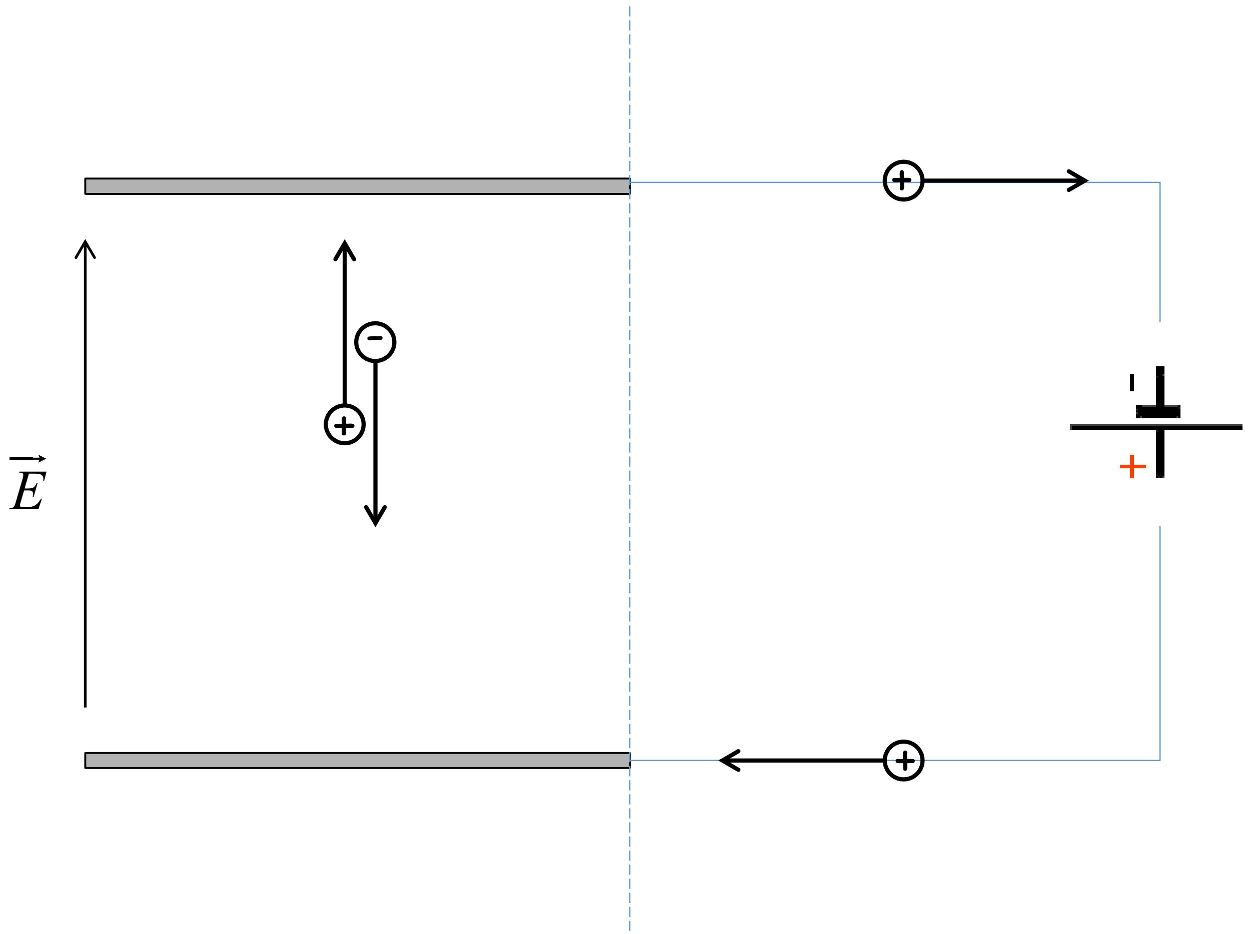

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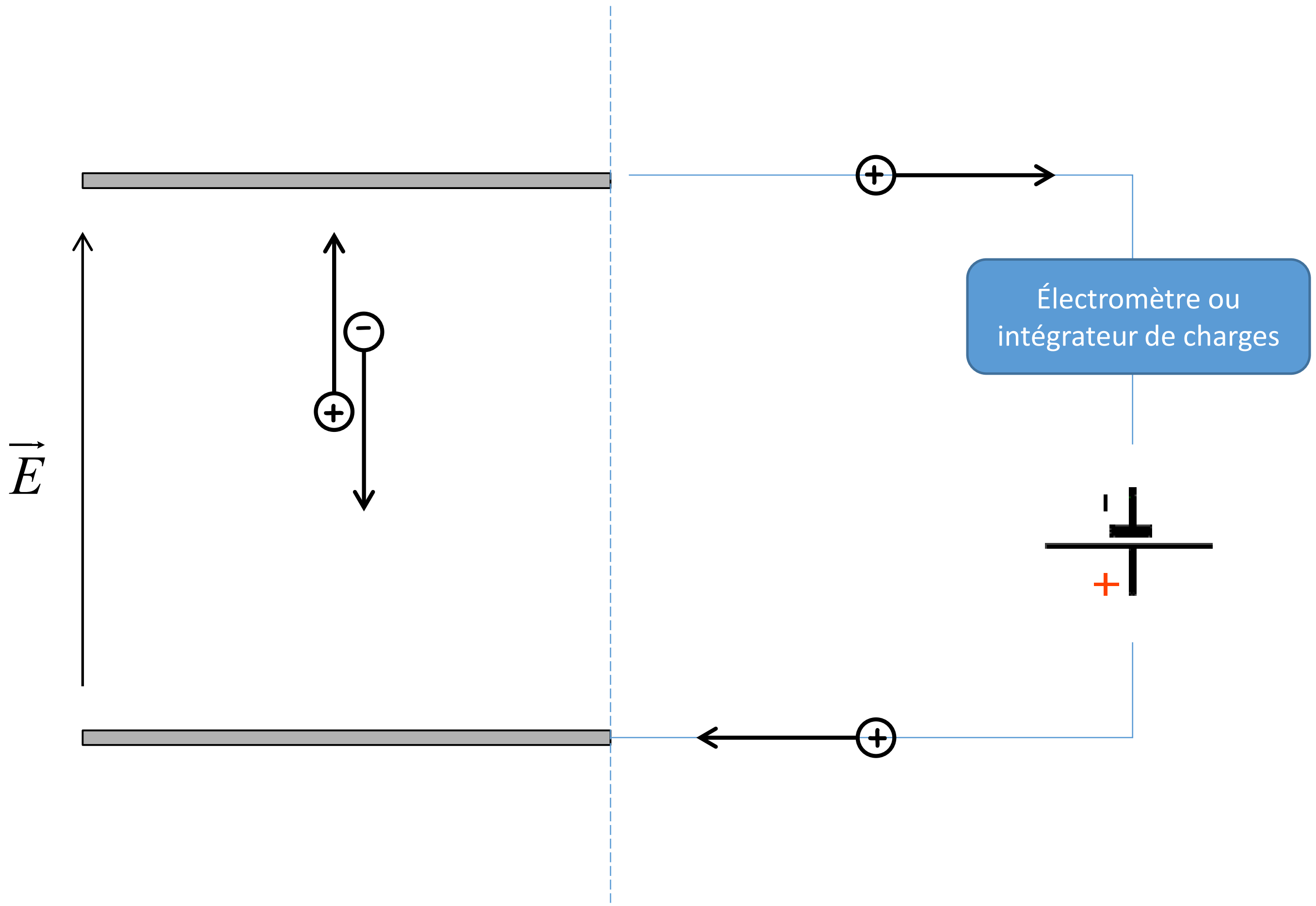


$\vec{E}$
Électromètre ou intégrateur de charges
+

Types of recombinations

- Columnar (or initial) recombination: ion pairs are formed into a column along the track of the ionizing particle → density of pairs is high along the track until pairs diffuse → columnar recombination is most severe for densely ionizing particles (as α) compared to electrons that deposit their energy over a much longer track → independent on the irradiation rate and on *D*
- Volume recombination: due to encounters between ions and/or
rack → since ions slowly
rom independent tracks
rate and with *D*

Type of gas and recombinations

- An e^- created during an ionization can be fixed (attachment) on a neutral atom of the gas → negative ion
- Attachment occurs in electronegative gases (O_2, air, …)
- The drift velocity of an ion is $v_d \approx 1$ cm/s per applied V/cm and for an e^- $v_d \approx 1000$ cm/s per V/cm
- The e^- are quickly cleared out of the ion chamber → little chance to recombine
- On the contrary ions being slowly collected have more chance to recombine
- Recombinations are particularly important for electronegative gases and thus for air

Recombinations in an ion chamber

Definition of a recombination collision rate *R* ($m^{-3}s^{-1}$) and of a recombination coefficient α (m^3s^{-1}) such as:

$$R = -\frac{dn^+}{dt} = -\frac{dn^-}{dt} = \alpha n^+ n^-$$

with n^+ and n^-, the volume densities of charge

electrodes (1)

area *S*) separated by a

from the positive electrode
) and cathode (−) at $x = d$
ble (at first approximation)

u_+) and negative (u_-) ions
are constant

- The ionization rate *q* (number of ionizations per unit of time and volume) is assumed to be constant and uniform

Ion chamber with plane-parallel electrodes (2)

- The quantity of + charges produced between *0* and *x* in the time interval *dt* is equal to the quantity of charges crossing the plane *X = x* in the same time interval → with $n^+(x)$ and $n^-(x)$ the bulk densities of charges at the distance *x* of the anode →

$$qSxdt = n^+(x)Su_+dt$$
$$qS(d-x)dt = n^-(x)Su_-dt$$

$$\Rightarrow \quad n^+(x) = \frac{qx}{u_+} \qquad n^-(x) = \frac{q(d-x)}{u_-}$$

Ion chamber with plane-parallel electrodes (3)

- The recombination rate R' (per unit of surface and time - $m^{-2}s^{-1}$) is:

$$R' = \int_0^d \alpha n^+(x)n^-(x)dx = \frac{\alpha q^2 d^2}{u_- u_+}\int_0^d \frac{x}{d}\left(1-\frac{x}{d}\right)dx = \frac{1}{6}\frac{\alpha q^2 d^3}{u_- u_+}$$

- With *qd*, the number of ionizations per unit of surface and time, we define the collection efficiency of charges *f* as the ratio between Q_{coll}, the collected charge at the electrodes and *Q*, the charge produced in the chamber by a constant radiation field →

$$f = \frac{Q_{coll}}{Q} = 1 - \frac{R'}{qd} = 1 - \frac{1}{6}\frac{\alpha q d^2}{u_- u_+} = 1 - \frac{1}{6}\xi^2$$

Ion chamber with plane-parallel electrodes (4)

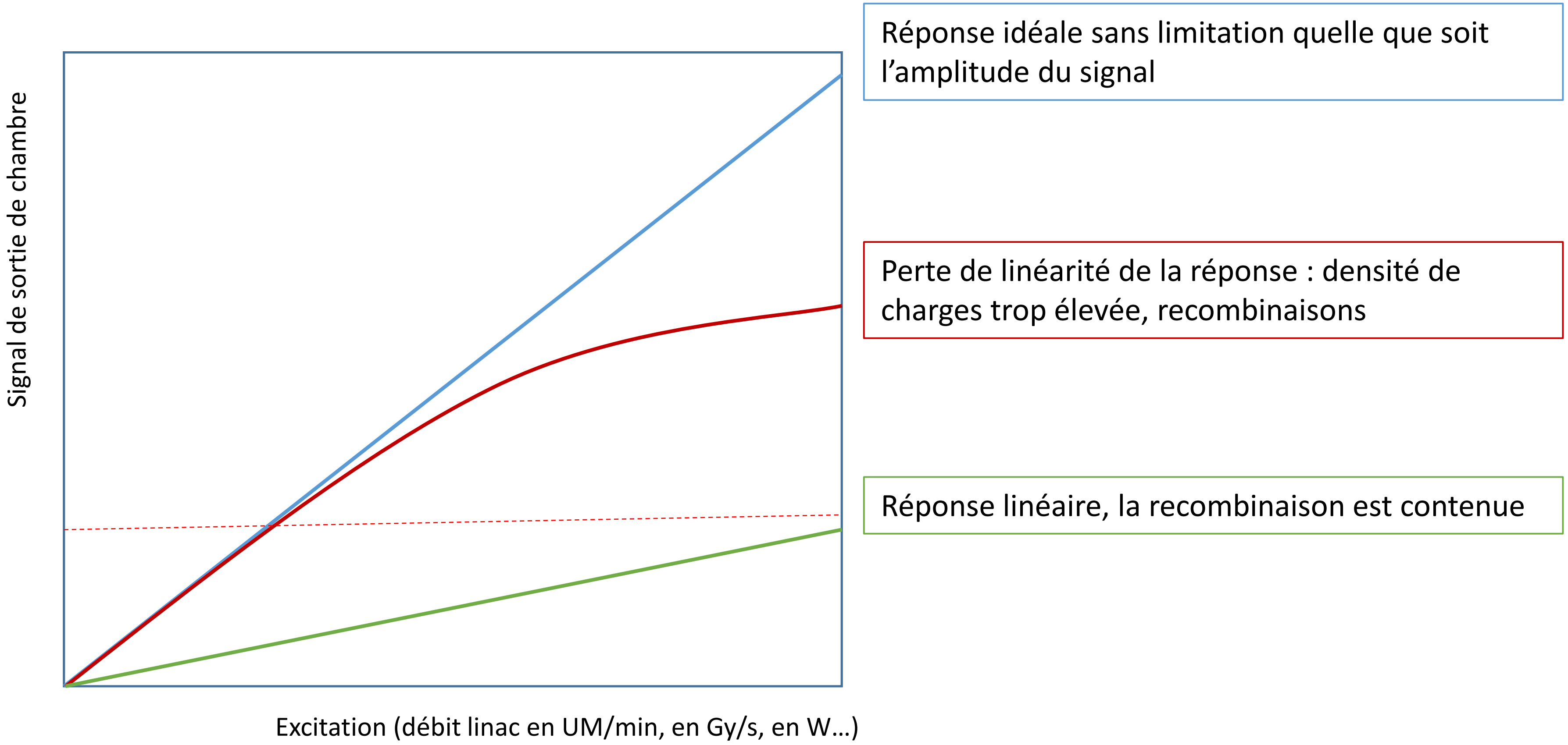
- The drift velocity of a charge *u* is linked to the applied electric field *E* by $u = \mu E$ (with μ, the mobility – $m^2V^{-1}s^{-1}$)
- In this case the applied potential $U_0 = Ed$ →

$$\xi = \sqrt{\frac{\alpha q d^2}{u_- u_+}} = \sqrt{\frac{\alpha}{\mu_+\mu_-}}\frac{d^2\sqrt{q}}{U_0} = m^2\frac{d^2\sqrt{q}}{U_0}$$

with m^2 a constant of the gas (for air NCTP $m^2 = 6.47 \times 10^{-5}$ V^2sm^{-1})

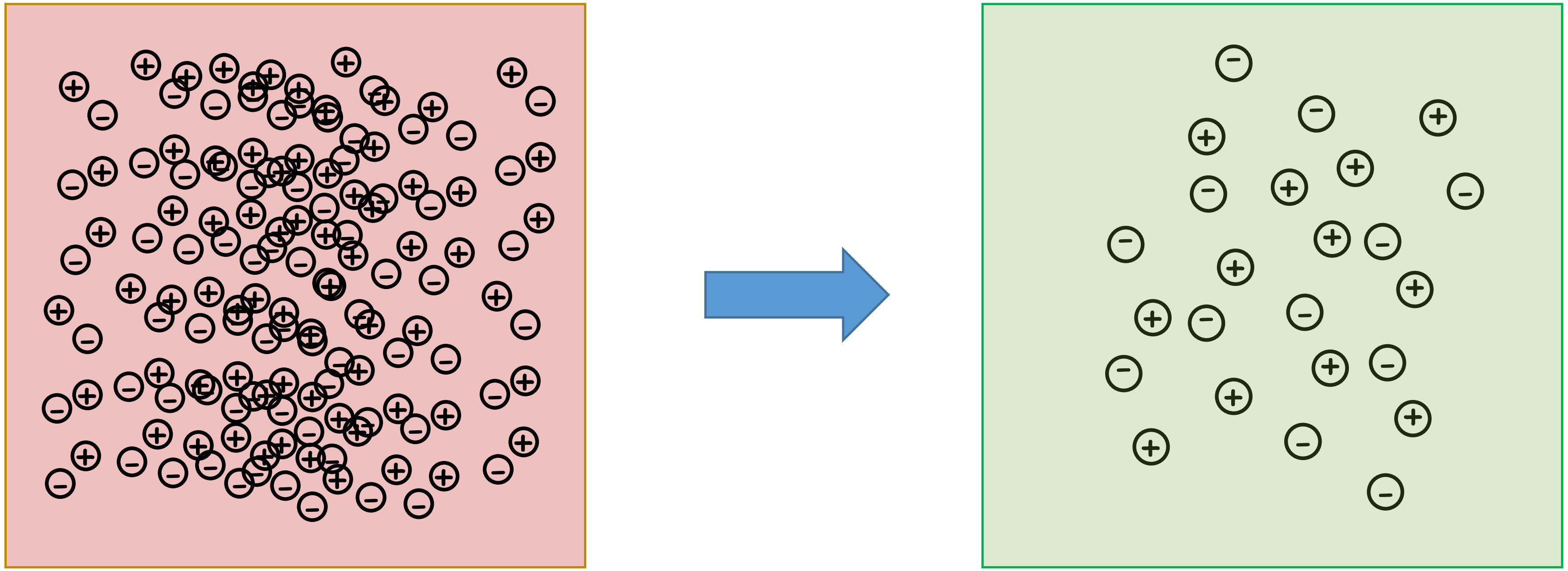
- Calculation accounting for the electric field produced by the space charges (→ non-uniform *E*) gives →

$$f = \frac{1}{1+\frac{1}{6}\xi^2}$$



Objectif : diminuer le taux de recombinaisons ($P_{beam} \times 1000 \rightarrow "ions"/1000$)

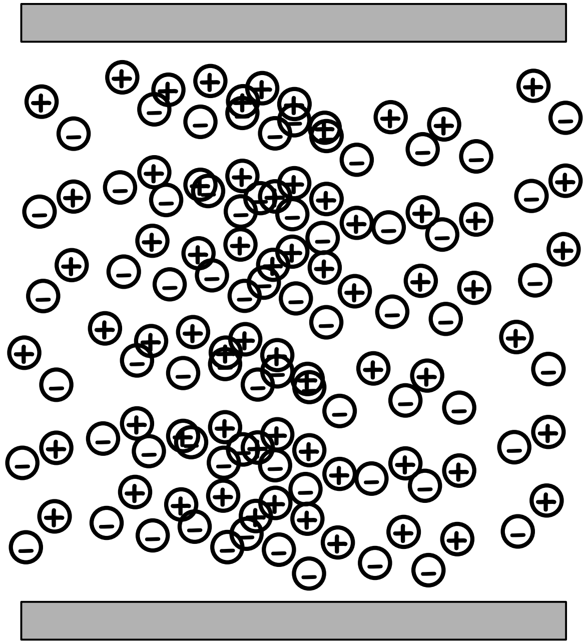
- Réduire le taux d'ionisation (par unité de temps et de volume)
- Diminuer la durée de déplacement des ions (ou augmenter leur vitesse, ou réduire la distance)
- Augmenter la sensibilité de l'électronique d'acquisition



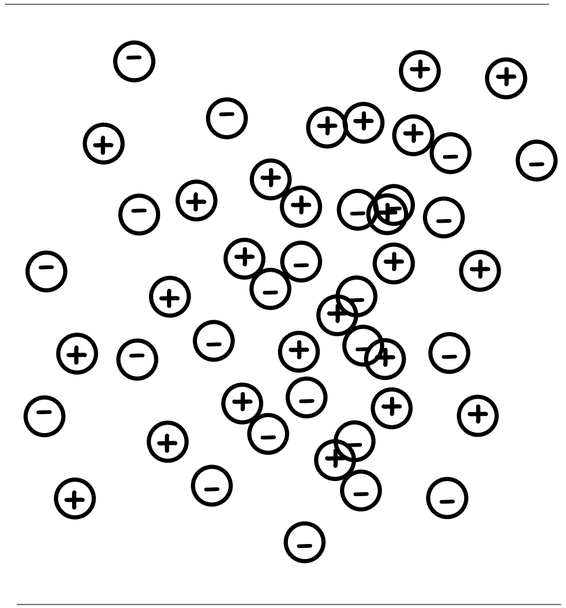
CSDA$_{H2O}$ e- 10 MeV : $4975\ mg/cm^2$

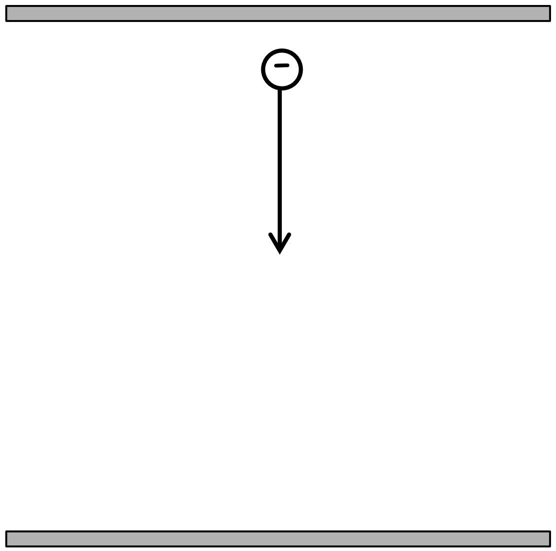
104 mg/cm^2

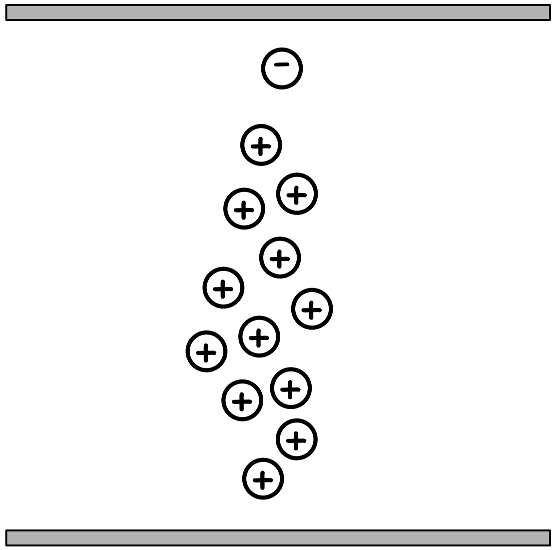
Chambre d'ionisation NACP

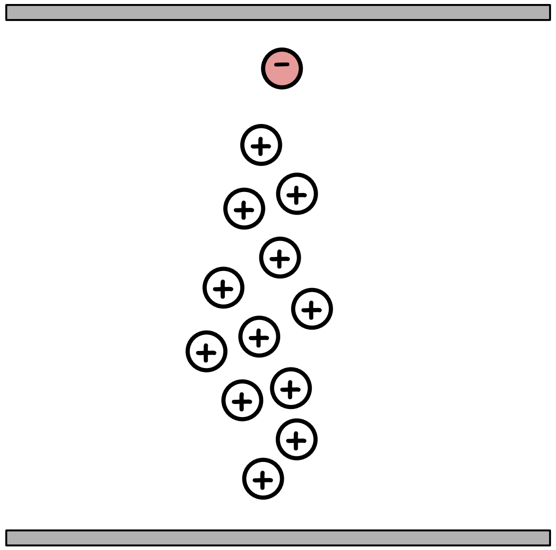


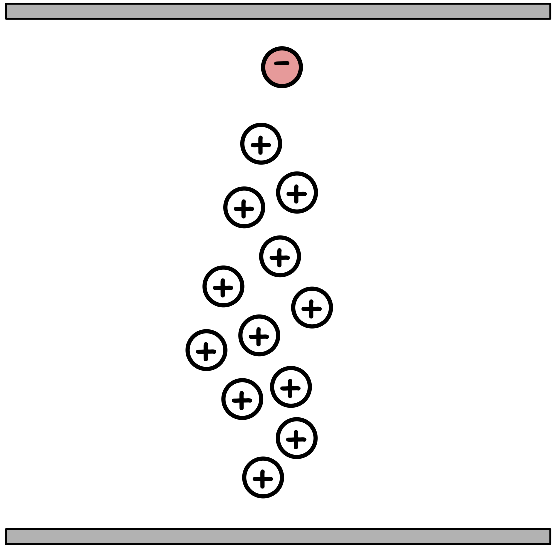
$10\ mg/cm^2$

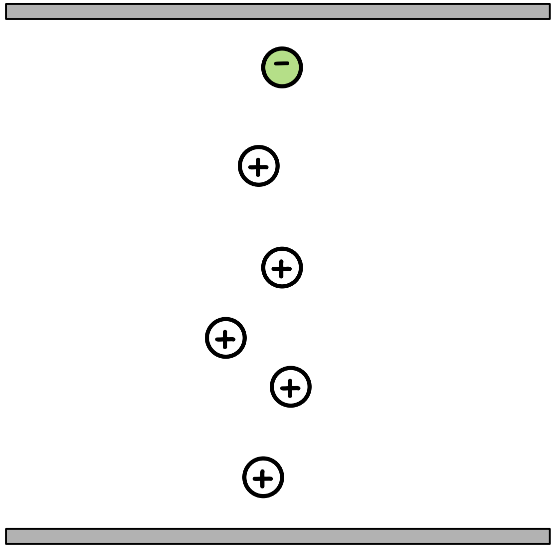


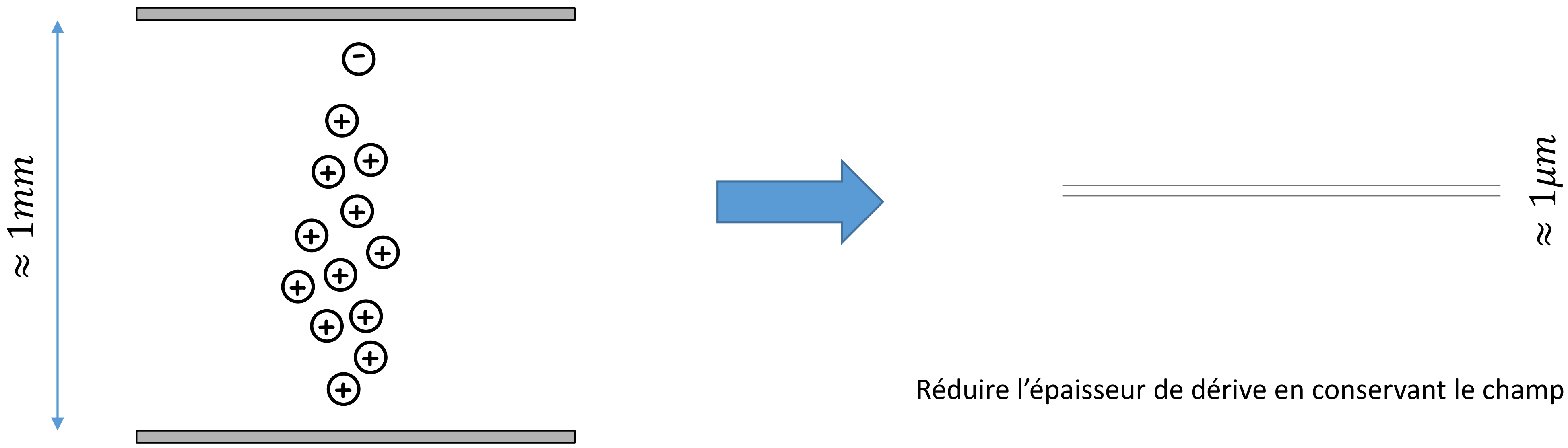












Réduire l'épaisseur de dérive en conservant le champ électrique constant

Rigidité électrique de l'air : 3600 V/mm à 1 atm

Chambre d'ionisation standard : typ. 100 V/mm

Microsystem Technologies 6 (1999) 6–10 © Springer-Verlag 1999

Electric field breakdown at micrometre separations in air and vacuum

J.-M. Torres, R.S. Dhariwal

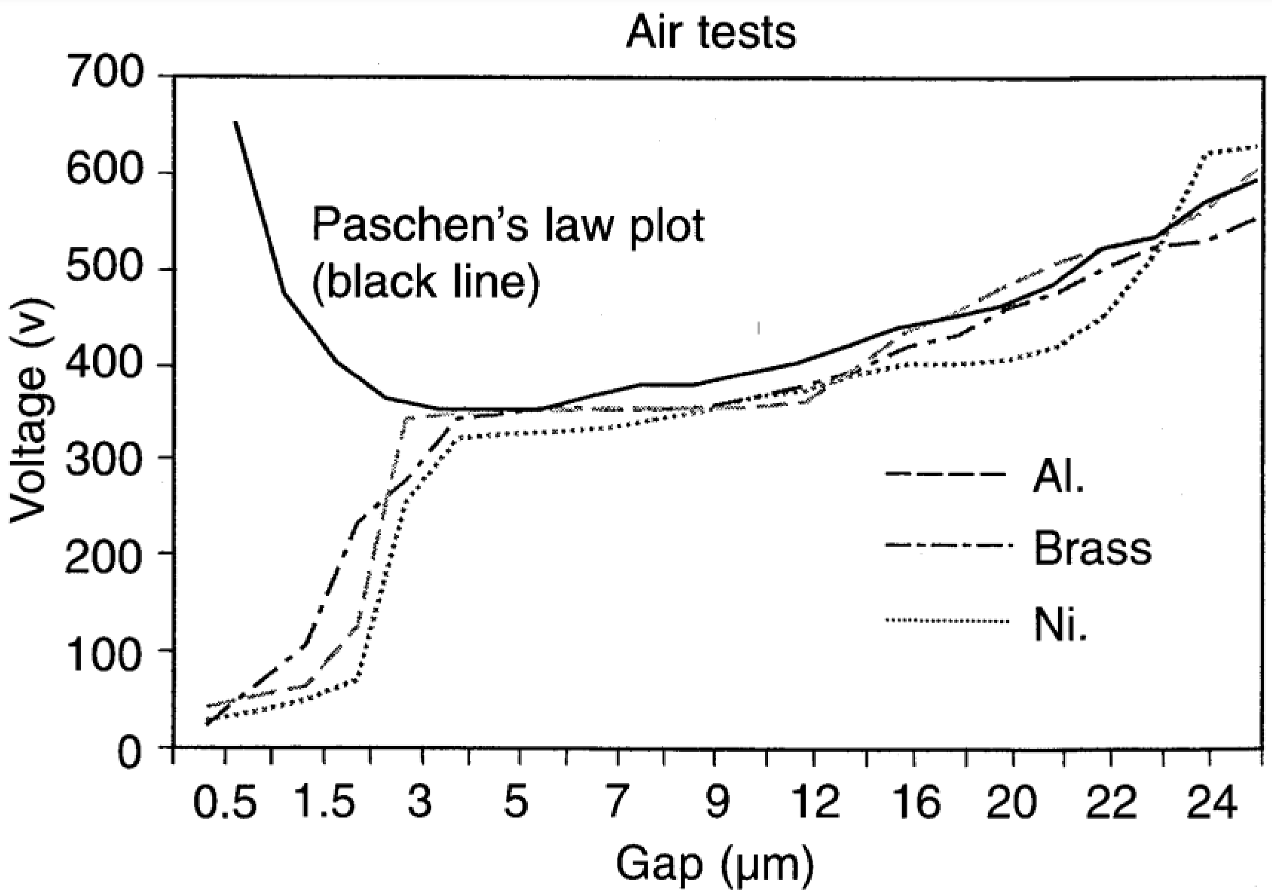


Fig. 3. Breakdown voltage results in air versus gap for three materials

Microsystem Technologies 6 (1999) 6–10

Electric field breakdown at micrometre separations in air and vacuum

J.-M. Torres, R.S. Dhariwal

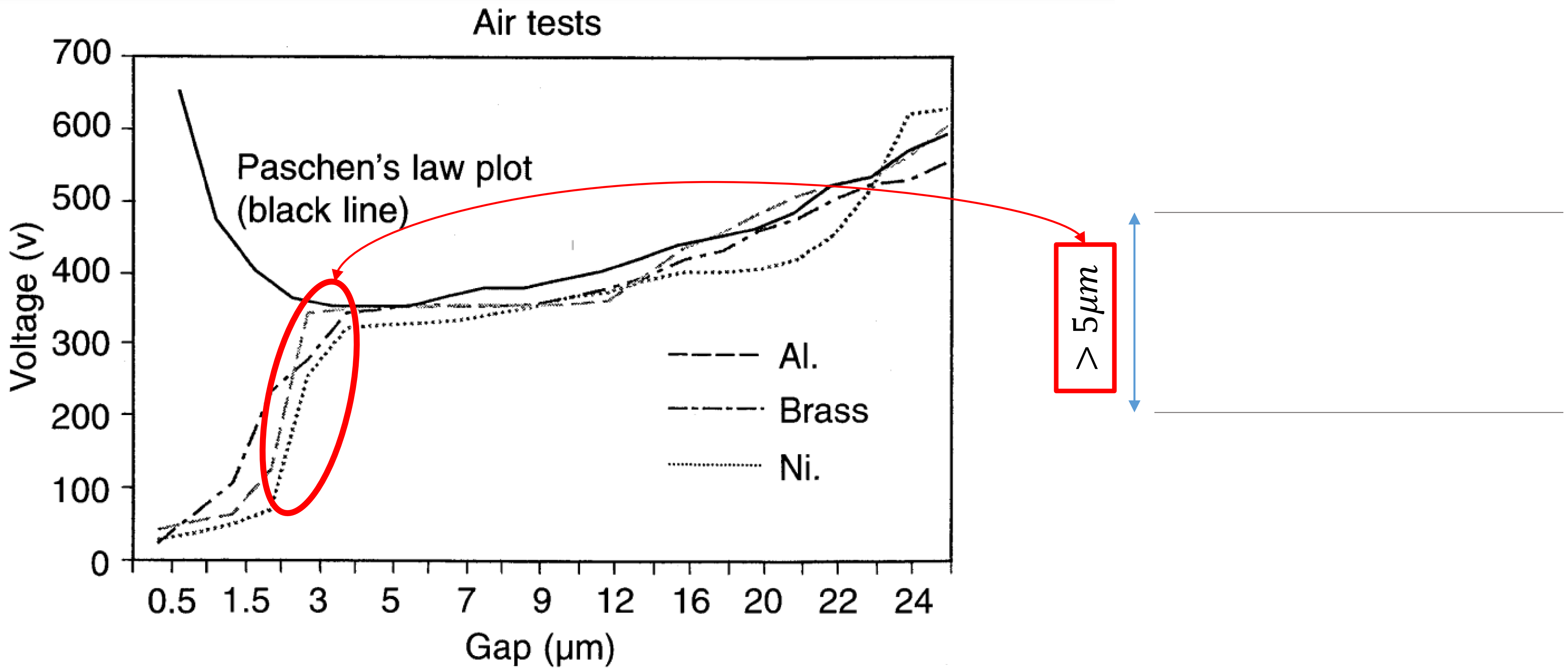
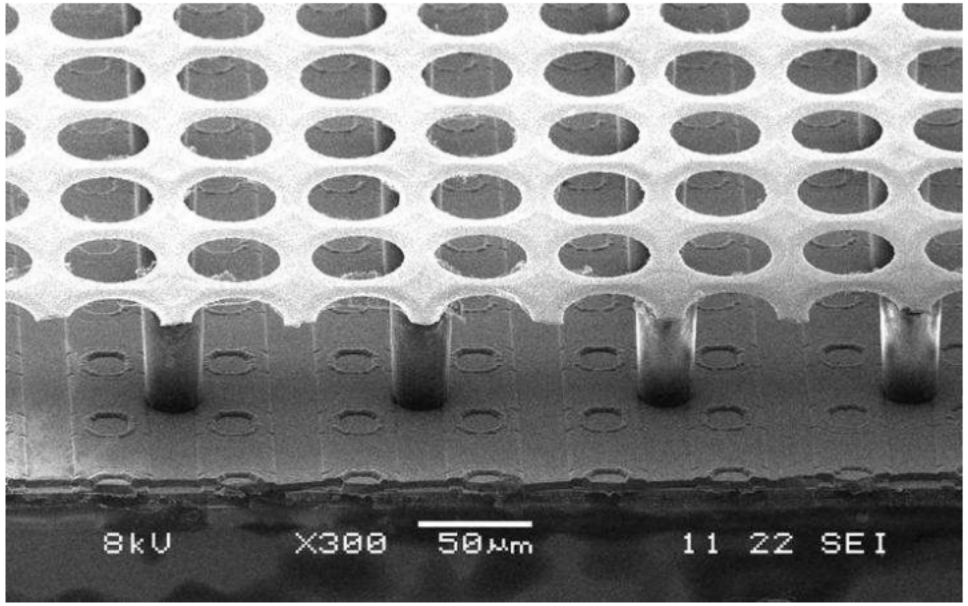


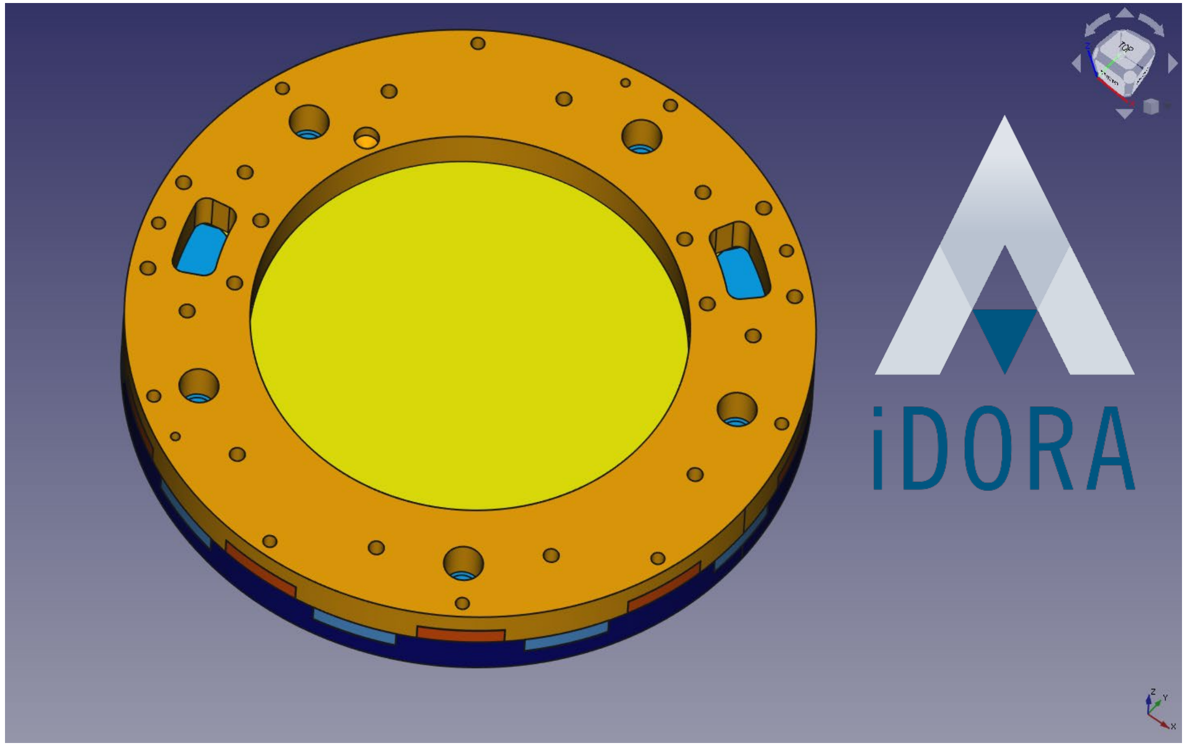
Fig. 3. Breakdown voltage results in air versus gap for three materials



$5\ \mu m$ entre électrodes, c'est petit, plus petit qu'une chambre Micromégas…

Immunité au bruit (CEM) $\rightarrow$ adaptations de process de microélectronique

dépôts plasma



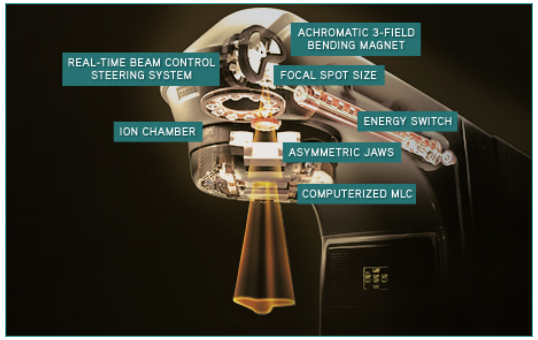
Ionisation très faible : sur 5 µm, on s'attend à en moyenne à 0,015 ions créés
Proba d'avoir au moins une ionisation : 1,5 %

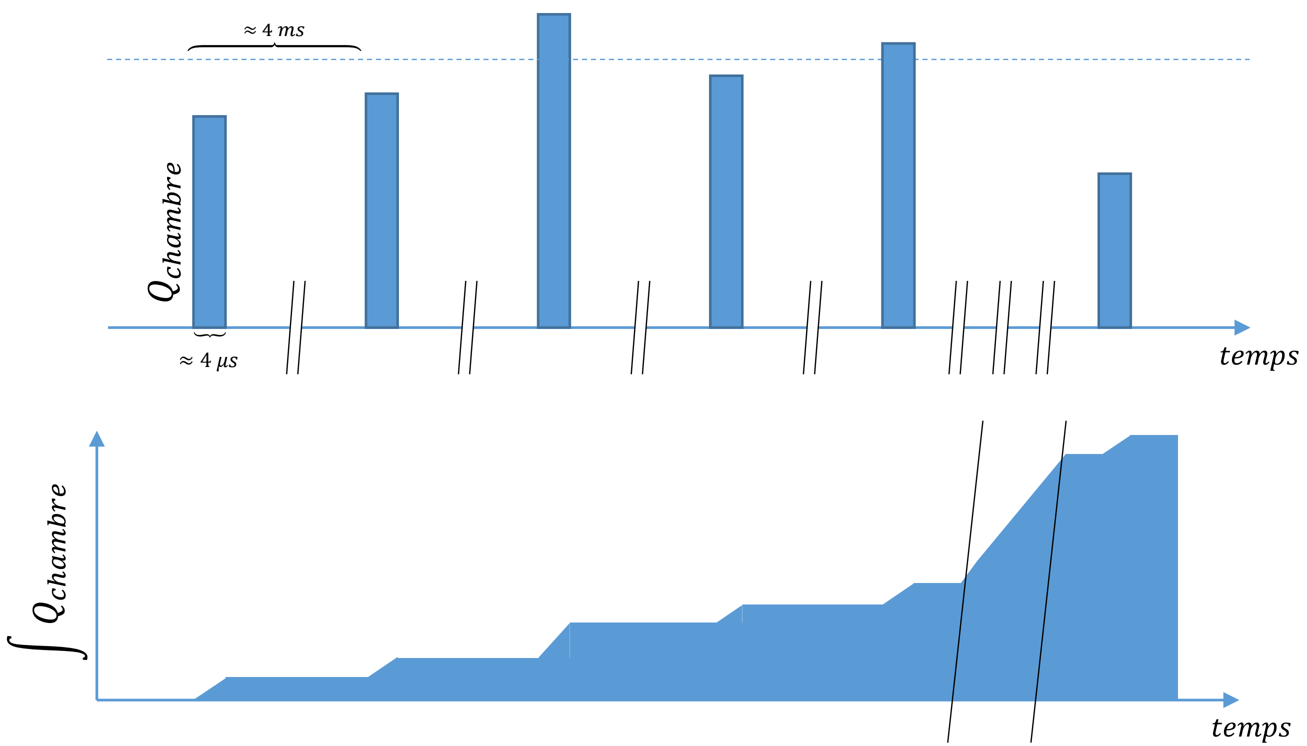
Chambre standard d'épaisseur 2 mm : 100% des particules ionisantes génèrent en moyenne 7 ionisations.

Réduction d'un facteur 500 des ionisations
De plus, le parcours des ions est réduit d'un facteur 400 : la collecte est plus rapide

La chambre reste bien **en deçà de la saturation** ↔ l'électronique d'acquisition doit être très sensible et peu bruitée.

Structure temporelle des impulsions délivrées par un Linac





La puissance des impulsions du faisceau est contrôlée par un système de contre réaction : chambre moniteur

La somme des charges de la chambre moniteur doit correspondre à la dose planifiée pour le traitement

Développement d’une chambre moniteur sous accord de non divulgation (financement SATT)

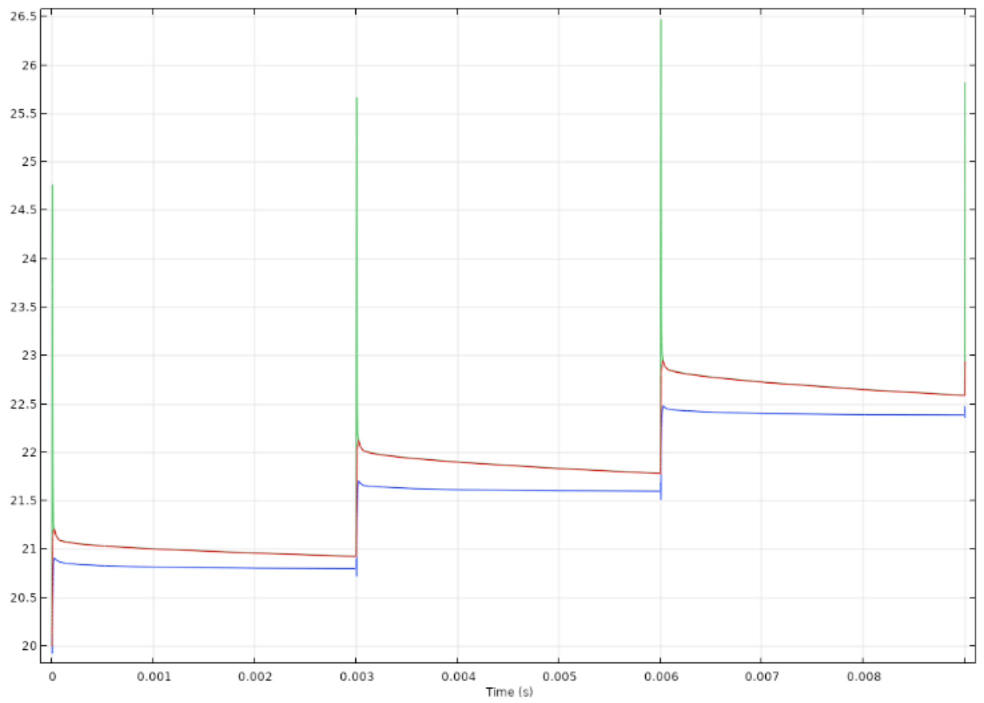
Cahier des charges :

- Irradiation en mode flash : 0,3 secondes (environ 100 impulsions de Linac à 330 Hz)
- Puissance du faisceau jusqu’à 100 kW
- Système de contrôle du faisceau en **temps réel** (acquisition des charges, numérisation du signal disponible en moins de 800 µs après chaque impulsion)
- Précision globale de la mesure meilleure que le %

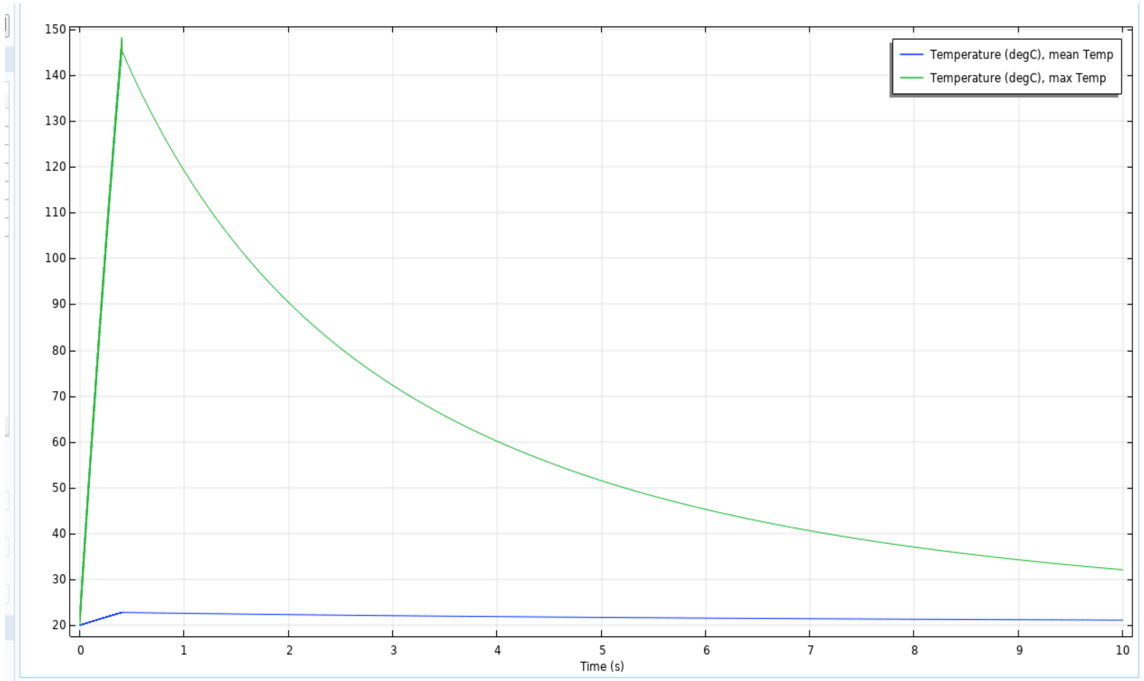
Brevet en cours de rédaction par le cabinet mandaté par CNRS Innovation

Etude thermique du capteur sous e-beam de $10\ MeV$, $P_{peak} = 1\ MW$

Choix des matériaux : dissipation, optimisation du dépôt d’énergie / transparence

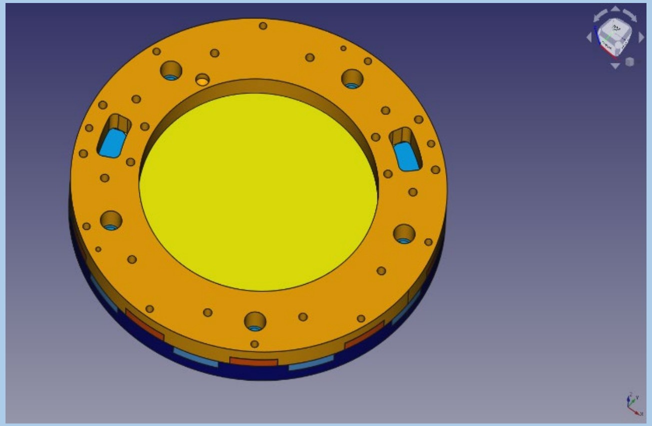


Pic de température à chaque impulsion



Elévation de température de 130°
Relaxation rapide

Capteur



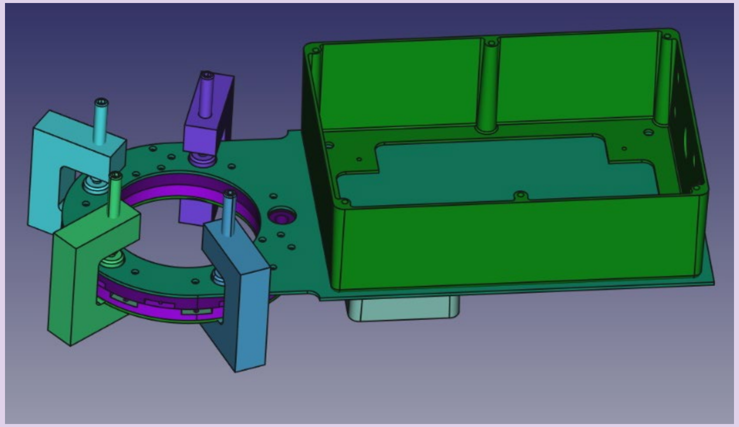
En cours de fabrication
(collab. avec institut Néel)

Electronique

Module éprouvé avec ASIC *QDC DAMe* (sensibilité ~10 pC)

Module avec en composants discrets à faible bruit
Gamme dynamique $1 : 10^6$

Intégration



Tests à l’automne

Preuve de principe

Fabrication de 2 modules à anodes segmentées

Et après

Applications académiques et médicales

Chambre d’ionisation
Profileur de faisceau X, e-, ions