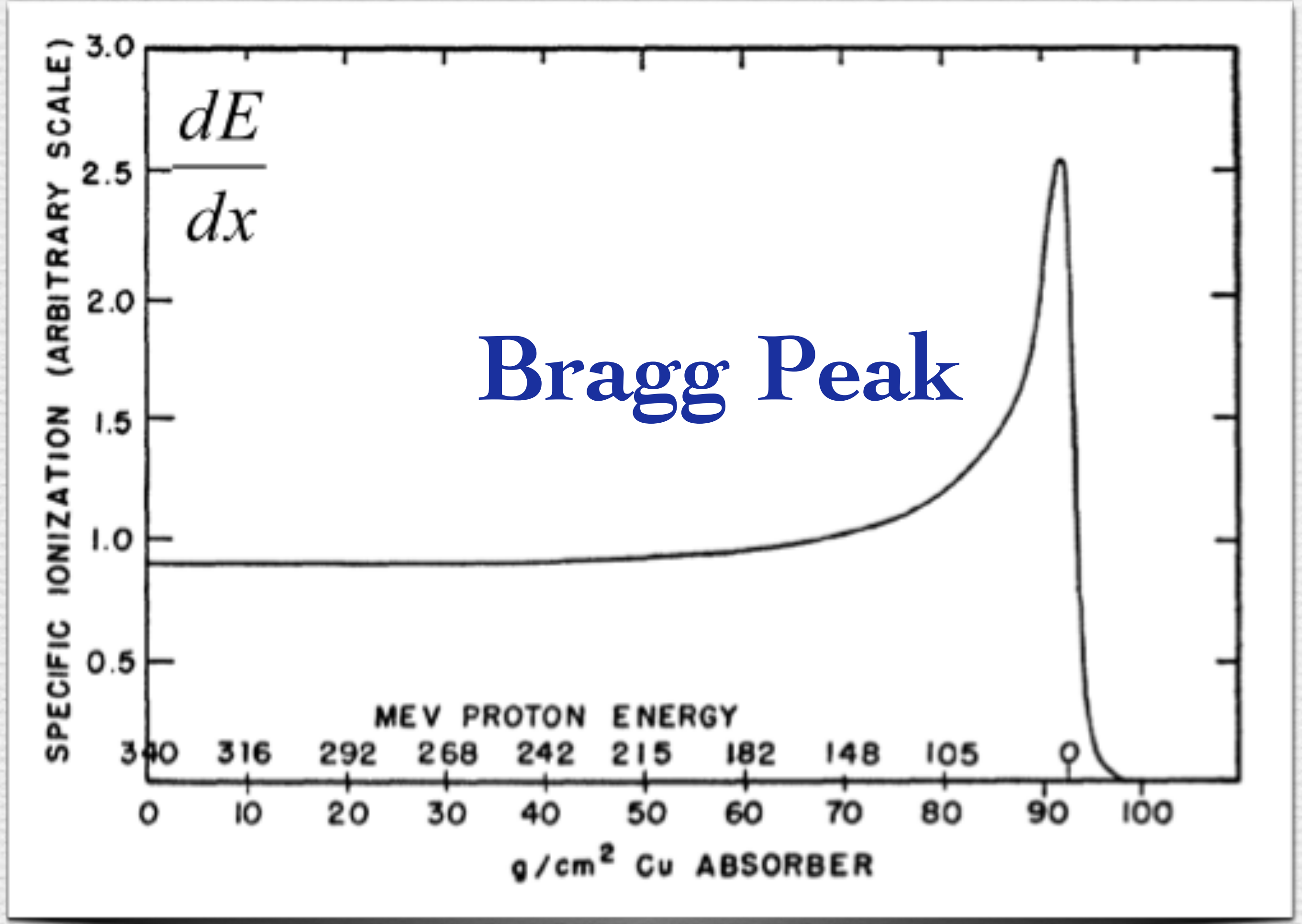
SIGLA INFN GRUPPO V

MOnitor for Neutron Dose in hadrOntherapy

Michela Marafini

Particle Therapy

Particle Therapy (PT) is an extremely effective method for destroying tumors while preserving healthy tissues that exploits the properties of energy deposit within the matter of heavy charged particles, described by the Bragg Peak distribution.



- **The most common beams are Protons and Carbon ions but new ions have been recently proposed (Helium, Oxygen);**

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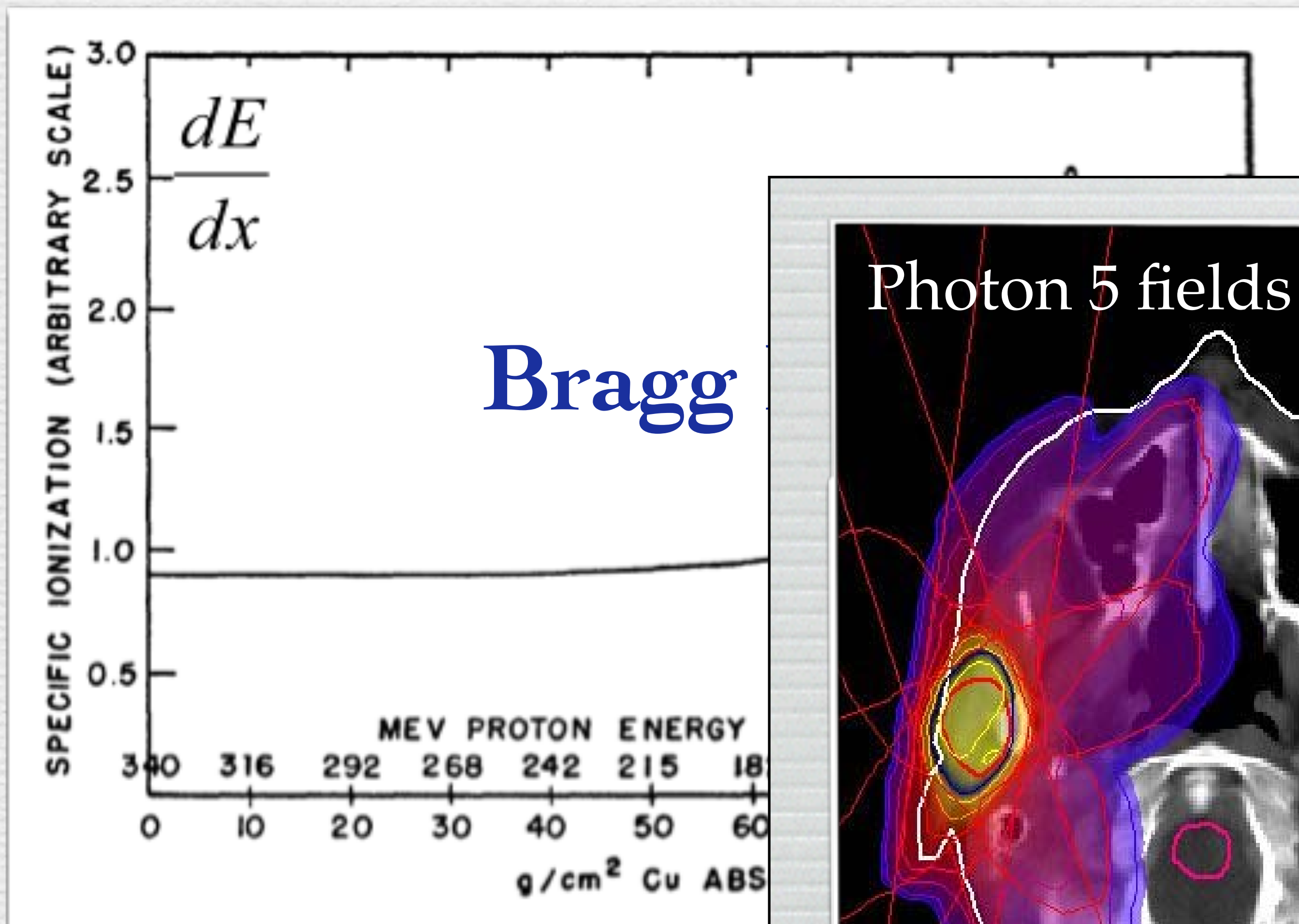

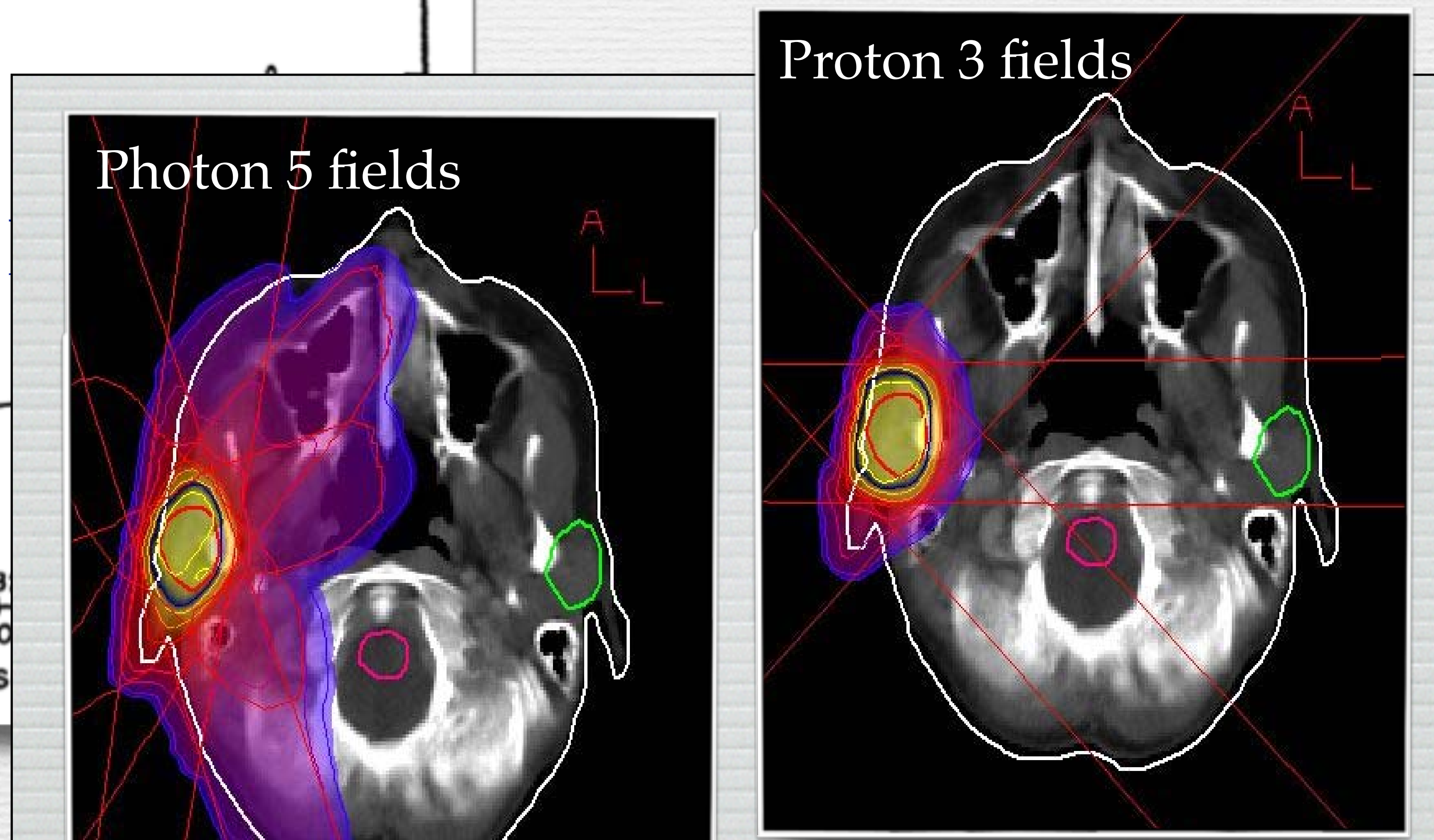

Universitätsklinik für Strahlentherapie und Strahlenbiologie, AKH, Wien

Particle Therapy

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An high precision Bragg Peak position monitoring is mandatory for PT applications. Since the primary beam is absorbed inside the patient, range monitor technologies have to exploit the abundant flux of emitted secondary particles: photons, charged nuclear fragments and neutrons.

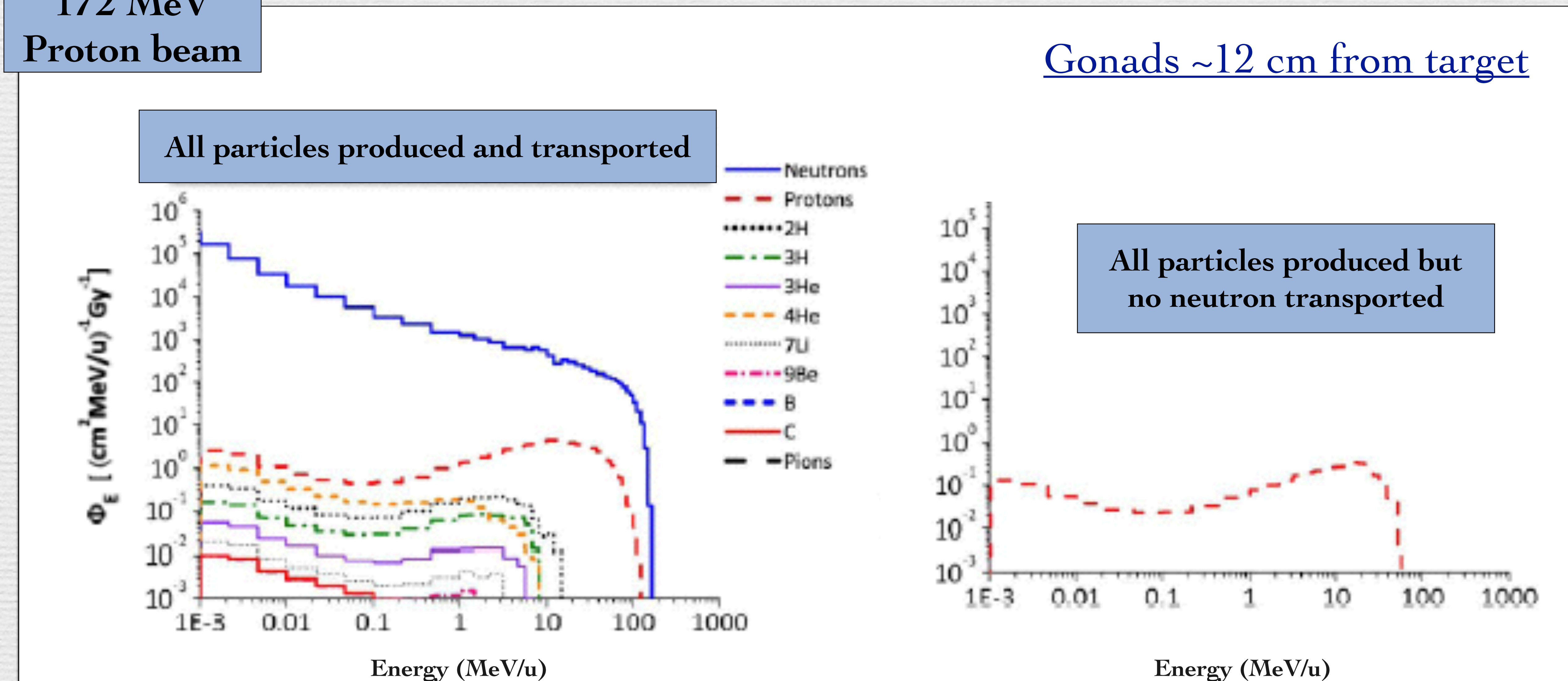
Several beam products flux measurements have been performed at different angles

Many range and dose monitor technologies based on the detection of beta+ activity, prompt photons and charged secondary particles have been proposed.

Particle Therapy

While the MC simulation are predicting a large flux of neutrons, a precise experimental knowledge of such fluxes, together with their angular distribution, is currently still missing.

172 MeV Proton beam



Hultqvist and Gudowska, PMB 55,2010

Neutrons

- Given its important biological effect it is mandatory to achieve precise knowledge of neutron flux produced during a treatment to minimize the patient secondary complications risk (E.g Secondary Malignant Neoplasm)

The SMNs can be developed in tissues that are located *in-field* (in the path of the therapeutic beam) and *out-of-field* (outside the path of the therapeutic beam).

The risk of developing a radiogenic second malignant neoplasm (SMN), years or decades after undergoing a PT treatment is one of the main concerns in PT administration and planning, in particular in pediatric treatments

The children prospect of long-term survival has increased impressively as an effect of the major advances in cancer therapies. Approximately 80% of children and adolescents that are now treated for cancer survive more than 5 years, but unfortunately nearly 73% of them develop anyway treatment-related complications.

W.D.Newhauseret al., PMB 54 (2009) 2277–2291

M. Durante, Nature 11 2011

Neutrons

- Given its important biological effect it is mandatory to achieve precise knowledge of neutron flux produced during a treatment to minimize the patient secondary complications risk (E.g Secondary Malignant Neoplasm)
- for radio-protection calculations, like shielding=> e.g. shielding, staff safety,
- for induced radioactivity evaluations;

Neutron measurements are elaborate due to the low neutron interaction probability in matter

⇒ The development of a detector capable of measuring the secondary neutrons direction and energy in thus fundamental

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MOnitor for Neutron Dose in hadrOntherapy

NEUTRON TRACKER DETECTOR

By exploiting elastic scattering of emitted neutrons in the 20-200 MeV energy range we propose to measure their energy and emission point.

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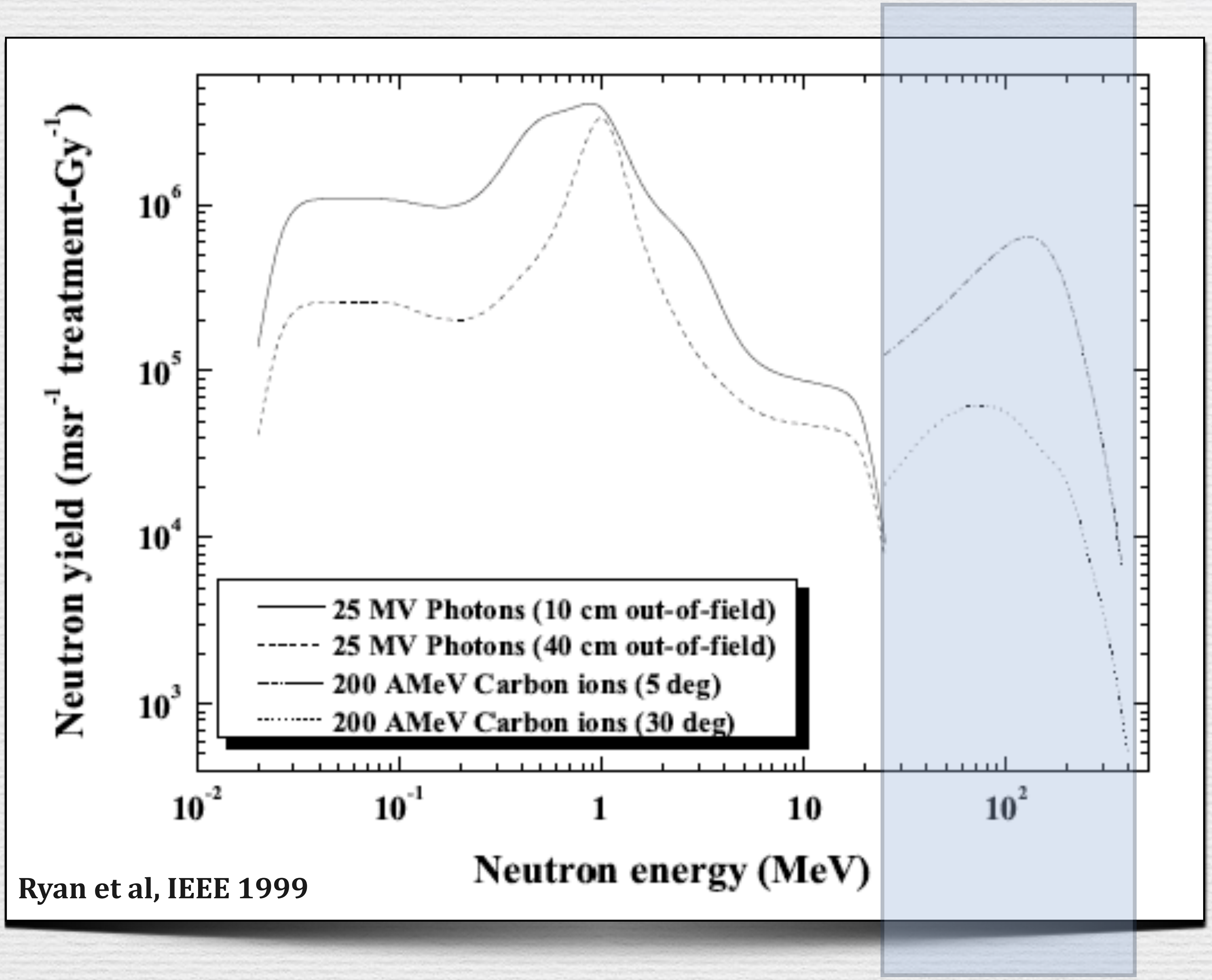
TRACKER DETECTOR for [20-200] MeV NEUTRON



Ryan et al, IEEE 1999

The expected neutron flux is dominating, by orders of magnitude, the total secondary flux nearly at all energies. While secondary neutrons produced during PT treatments by the beam interaction with the patient are mainly fast neutrons, their energy is degraded after several scattering interactions with the target nuclei so that a large flux of slow neutrons is expected

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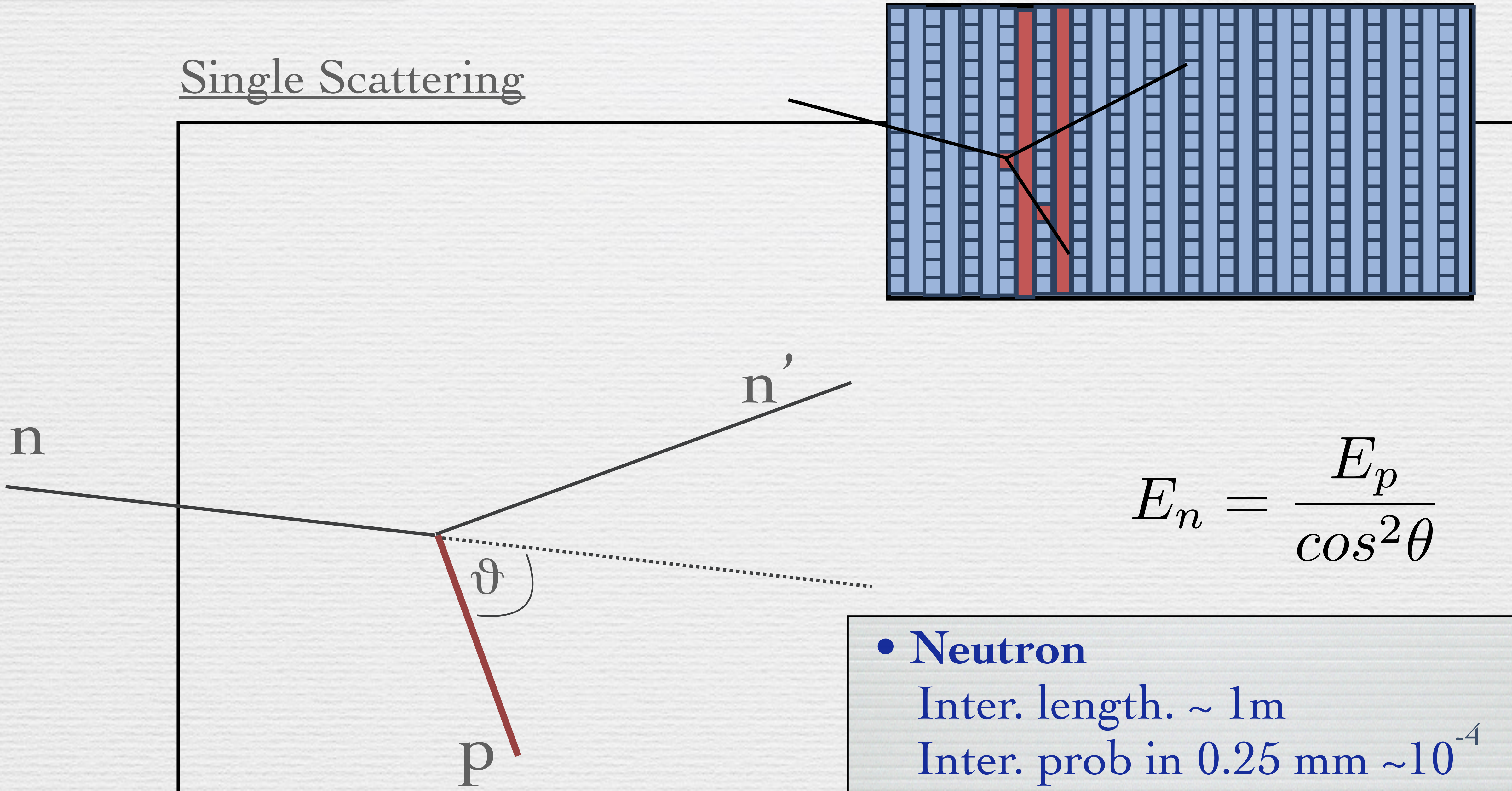
Single Scattering

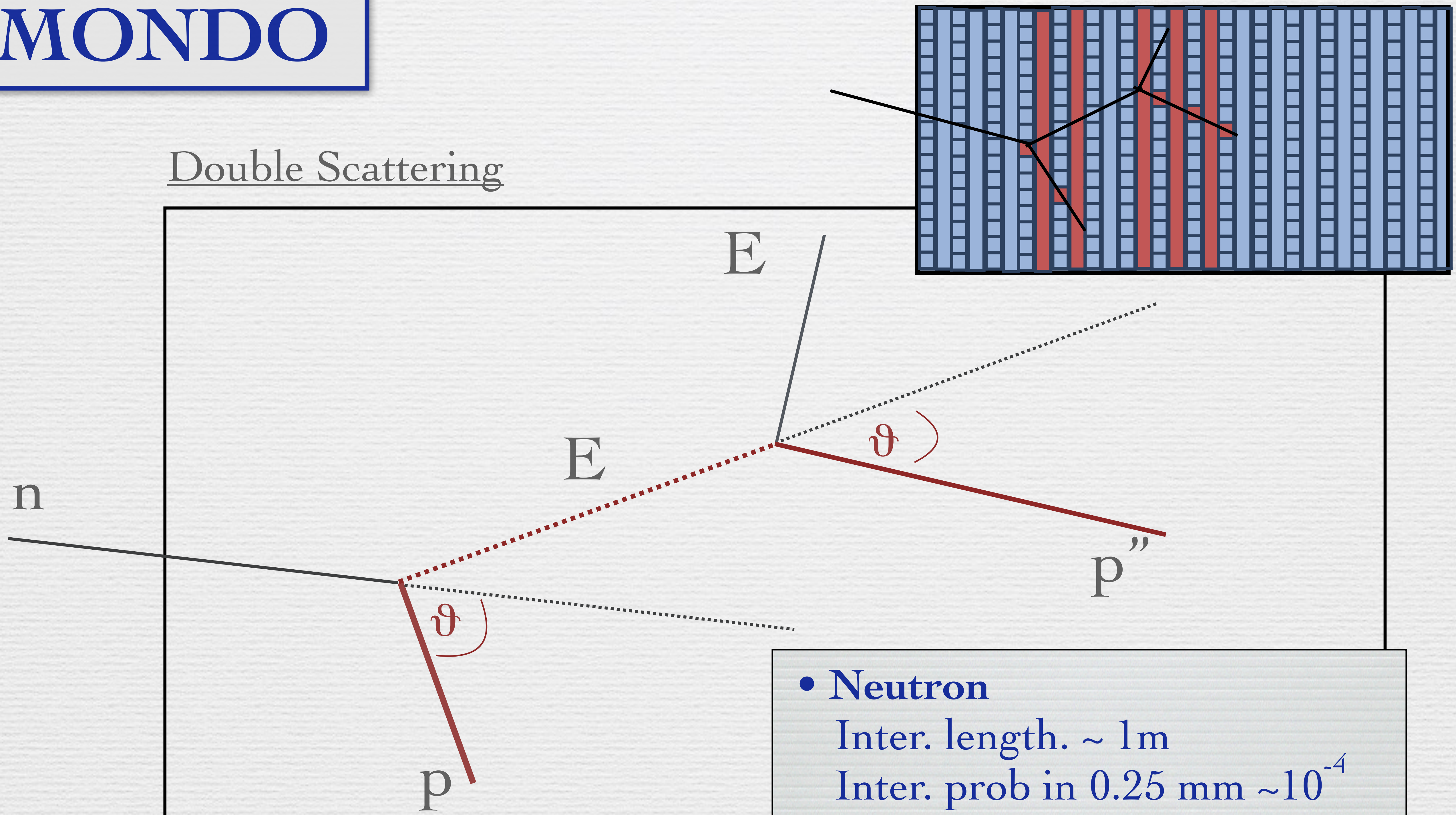


$$E_n = \frac{E_p}{cos^2\theta}$$

- **Neutron**
  Inter. length. ~ 1m
  Inter. prob in 0.25 mm ~10^{-4}
  P(single scatt.) ~ 7%
- **Proton mean path**
  T = 100 MeV=> 8 cm
  T = 50 MeV=> 2 cm
  T = 30 MeV=> 1 cm
  T = 10 MeV=> 0.1 cm

MONDO

Double Scattering



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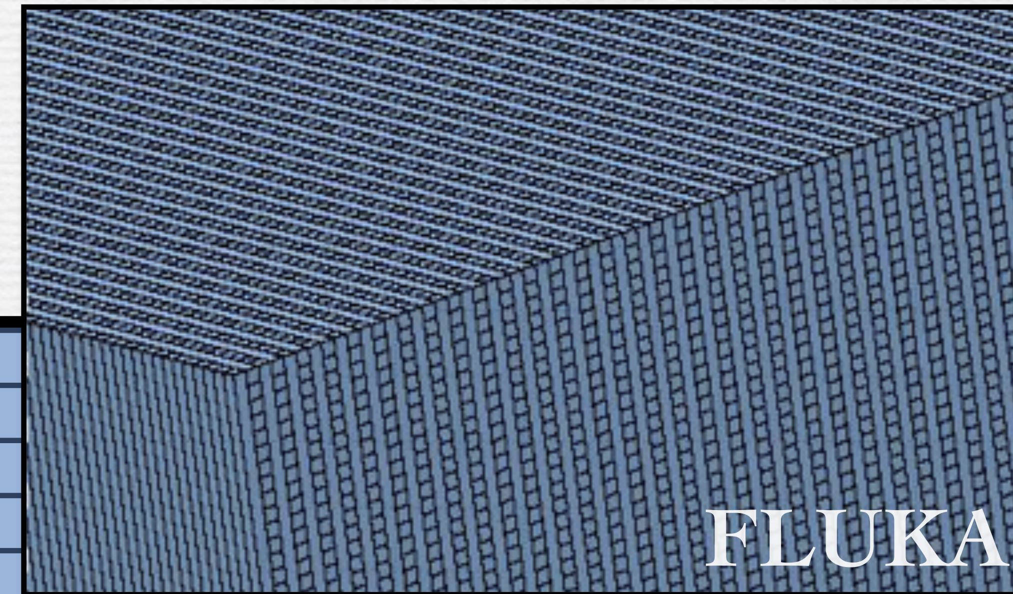
MONDO Design



Plastic Scintillator

- 4 x 4 x 8 cm^3;
- scintillating fibres 250 μm;
- 160 squared fibres per layer;
- 320 layers;

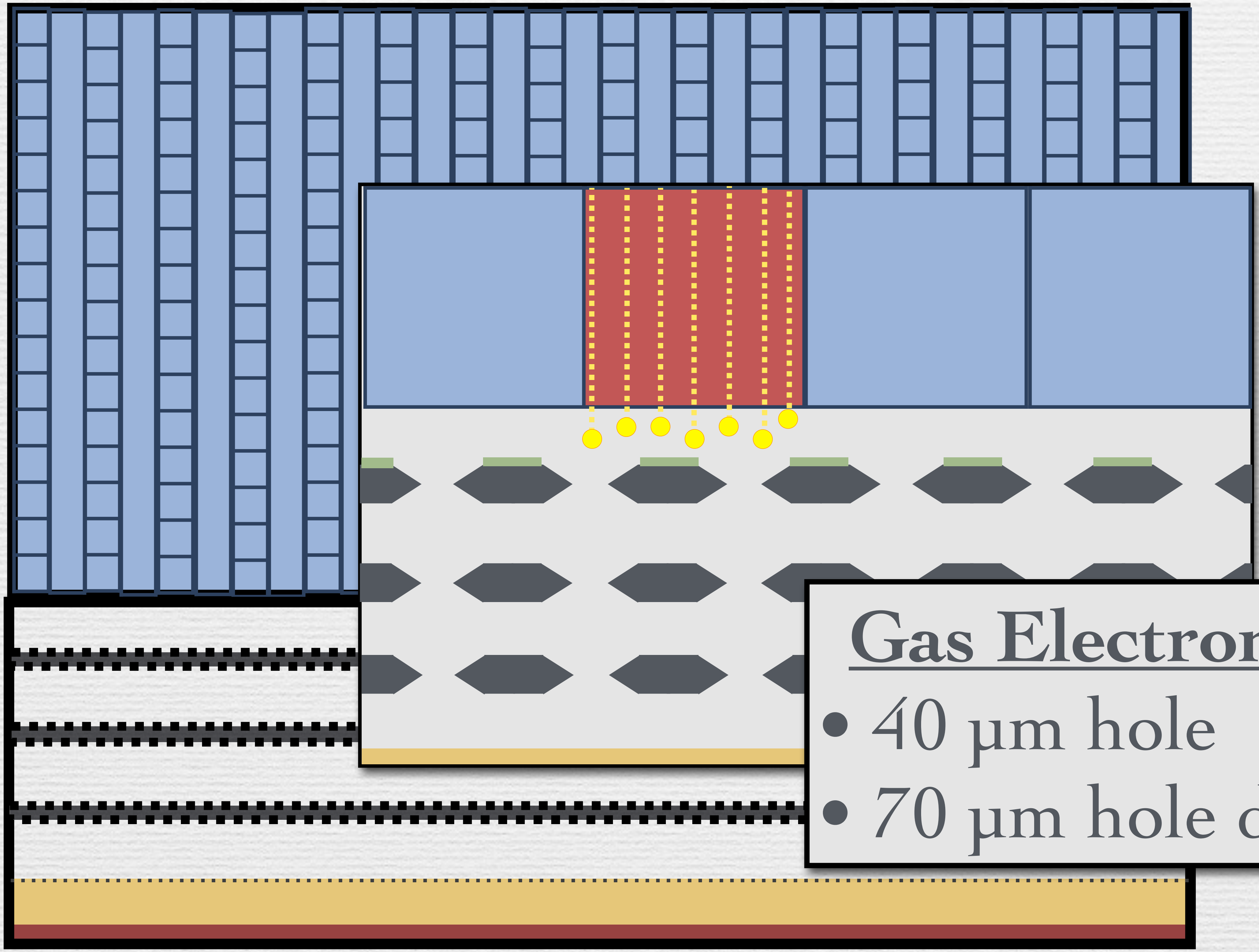
Image Intensifier

- Triple GEM

Read Out

- CMOS

MONDO Design

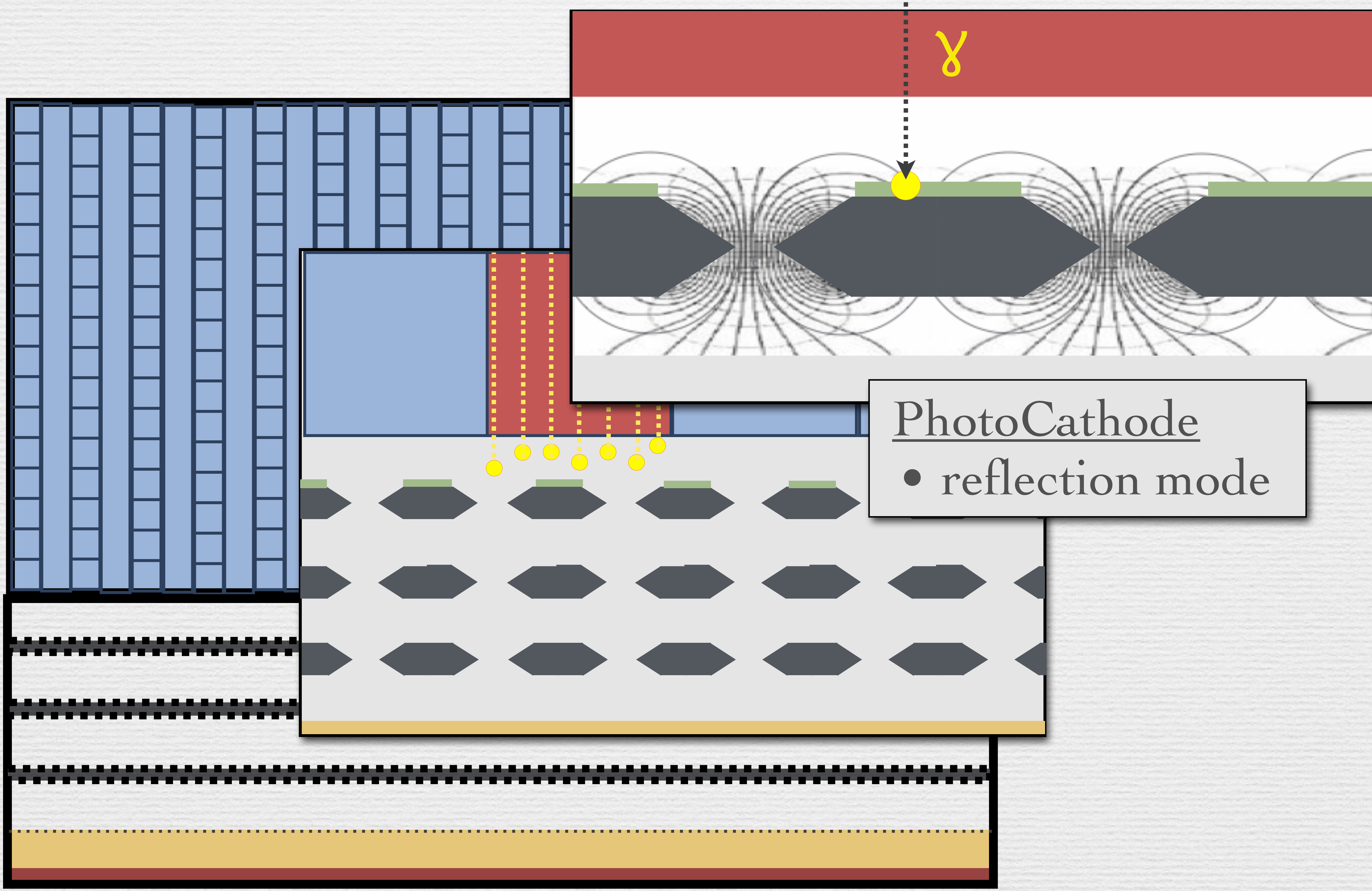


Gas Electron Multiplier

- 40 μm hole
- 70 μm hole distance

MONDO Design

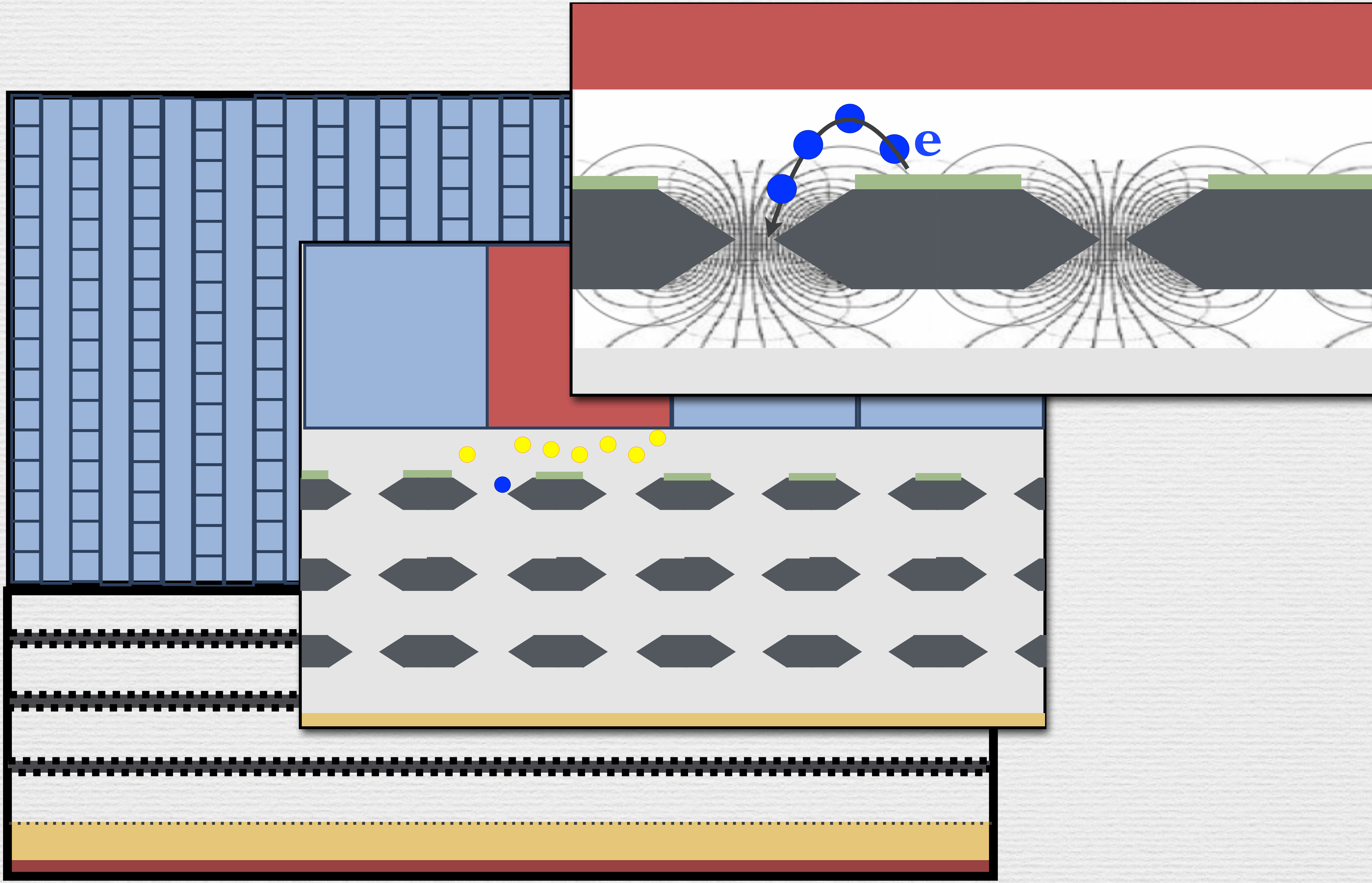
GEM



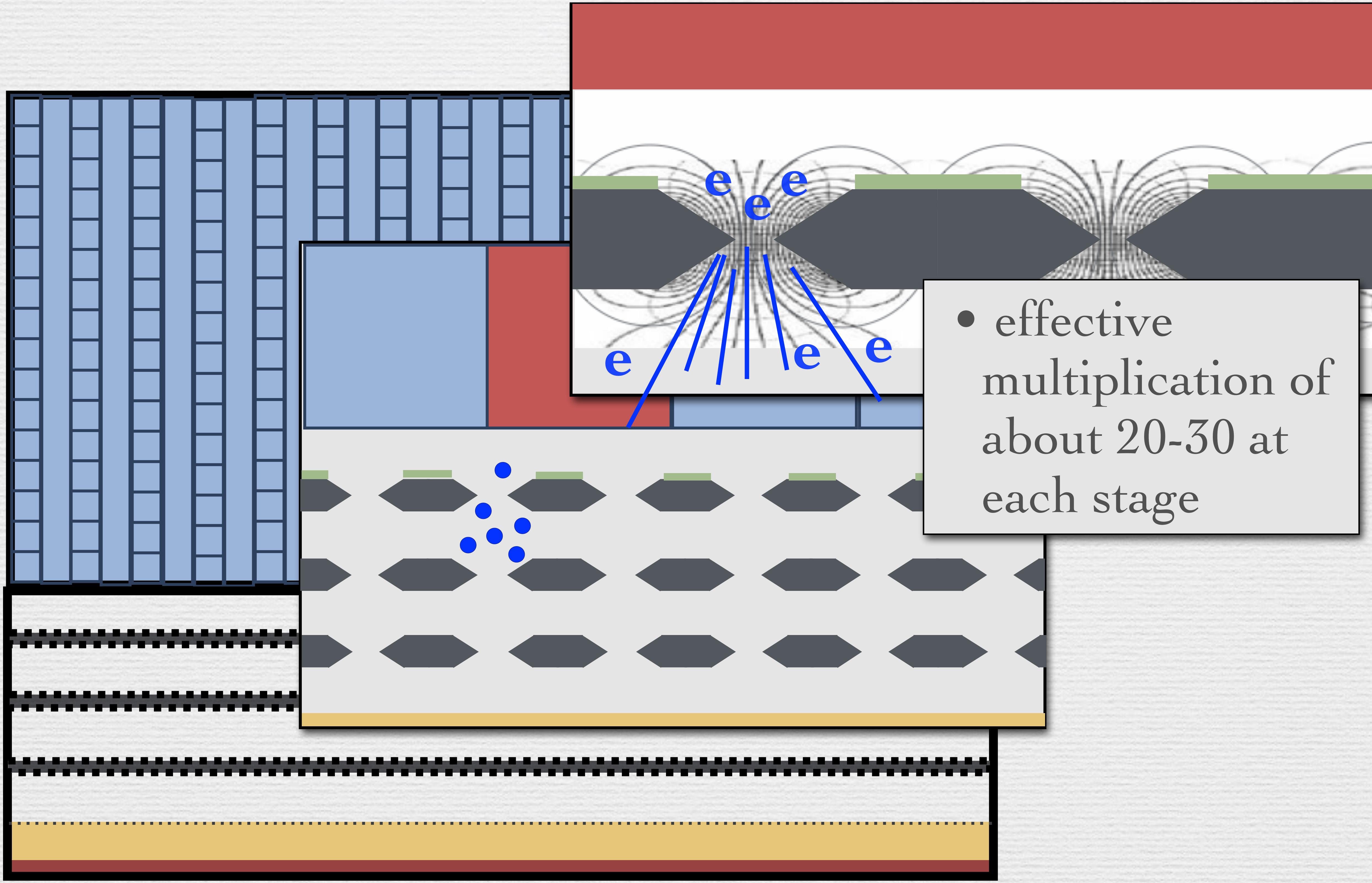
PhotoCathode
- reflection mode

MONDO Design

GEM



MONDO Design



- effective multiplication of about 20-30 at each stage

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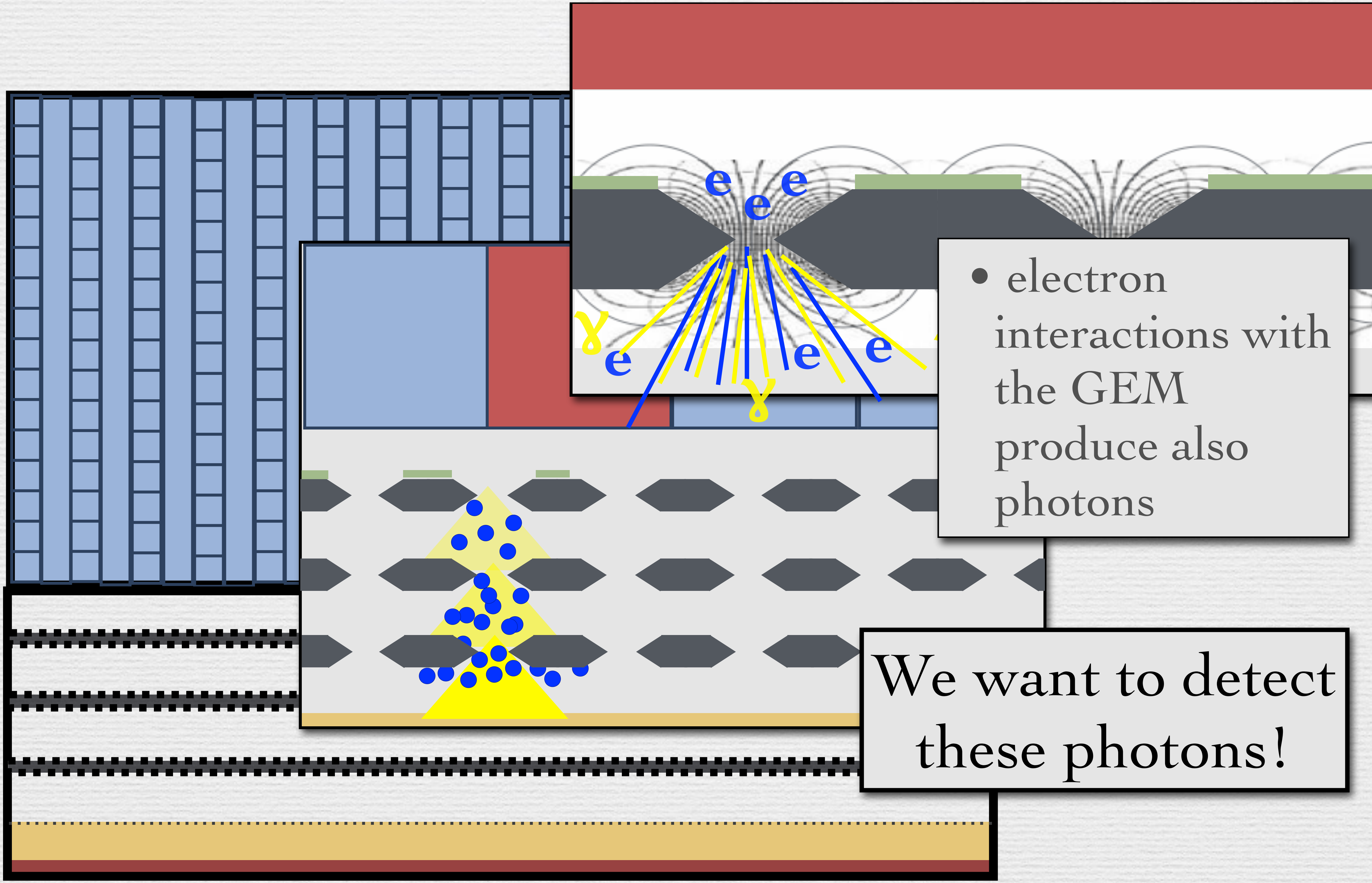
GEM

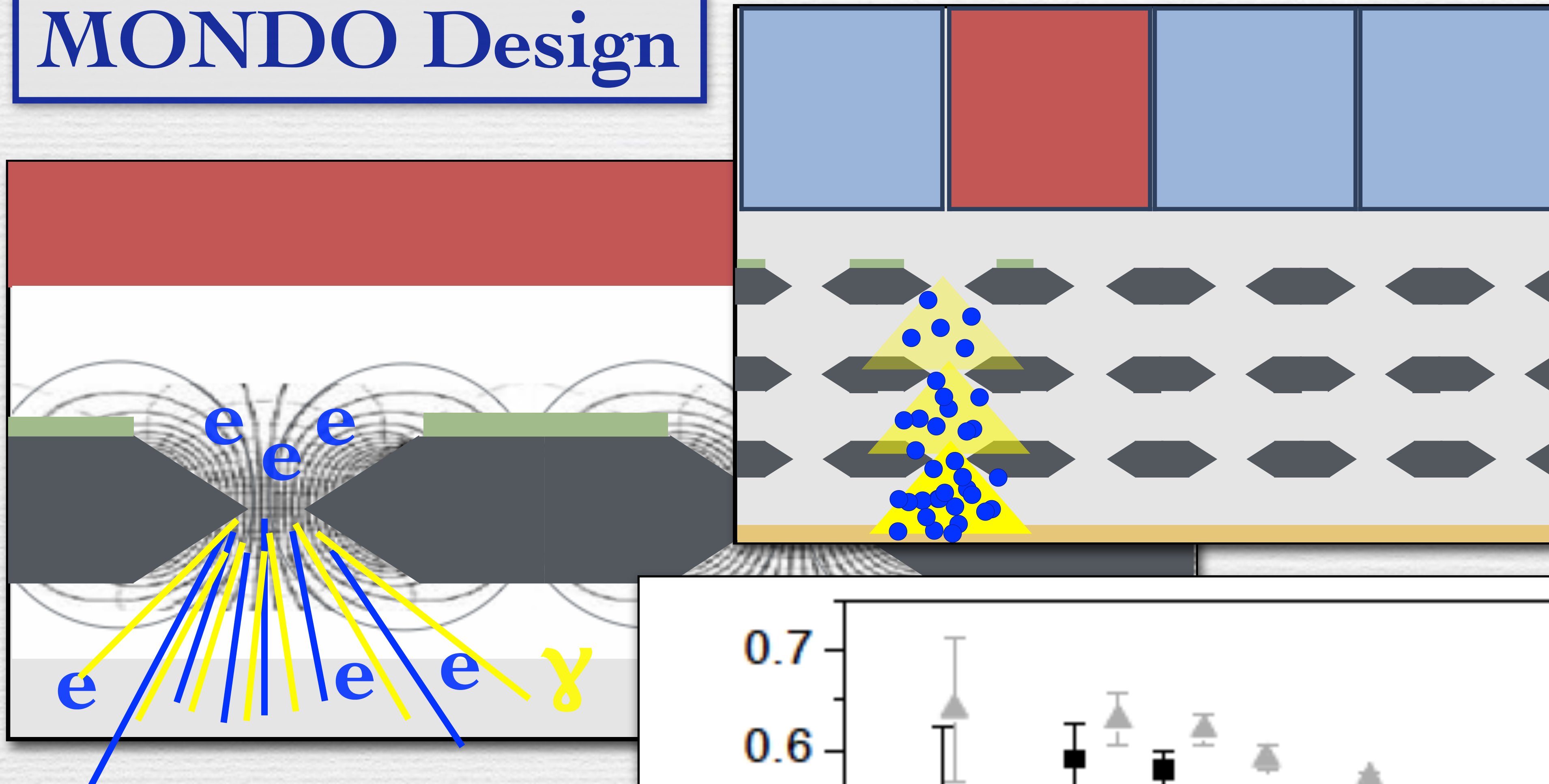


- electron interactions with the GEM produce also photons

We want to detect these photons!

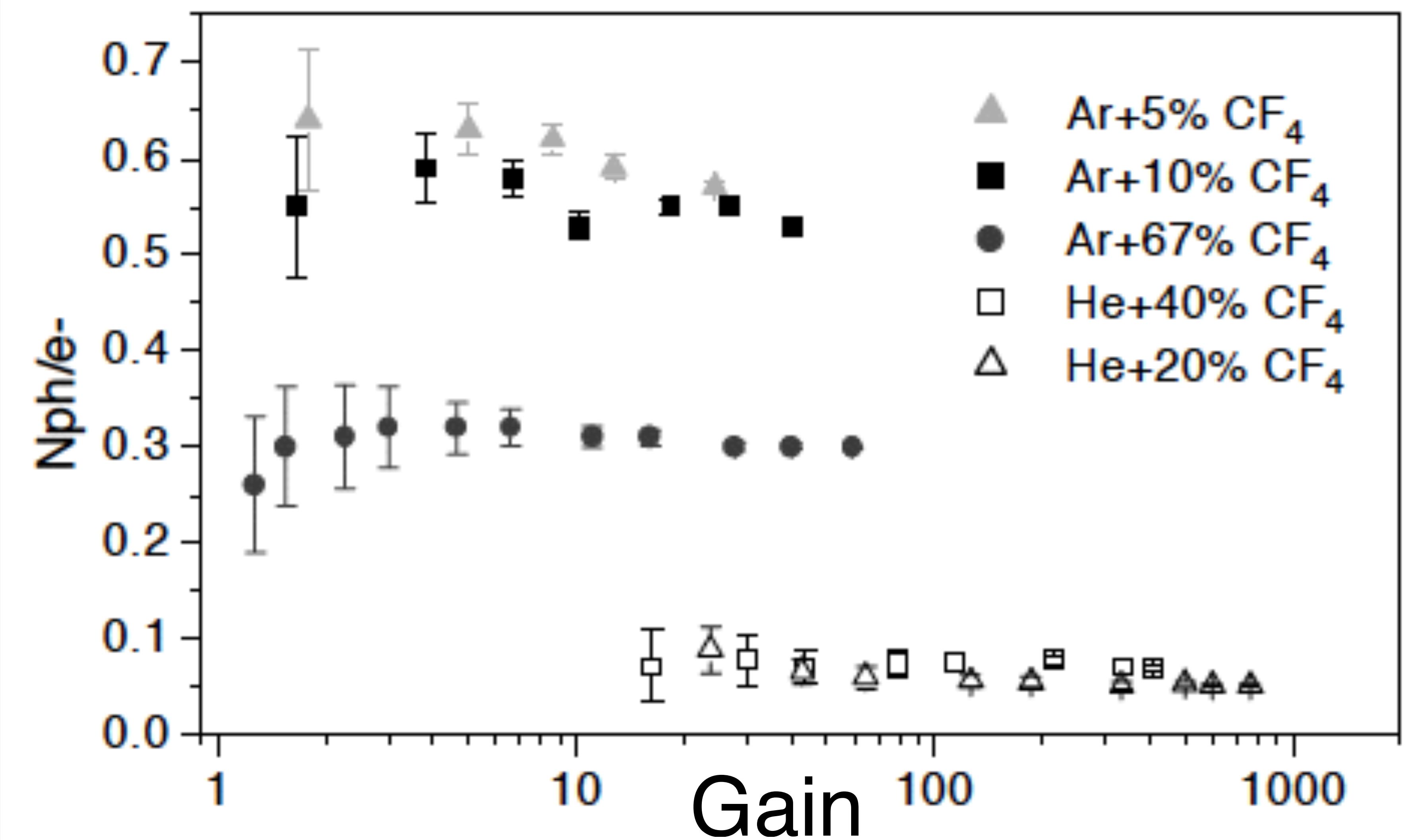
MONDO Design

GEM



N_γ / N_e
depends on the gas mixture and on the hole size (best for 45 μm)

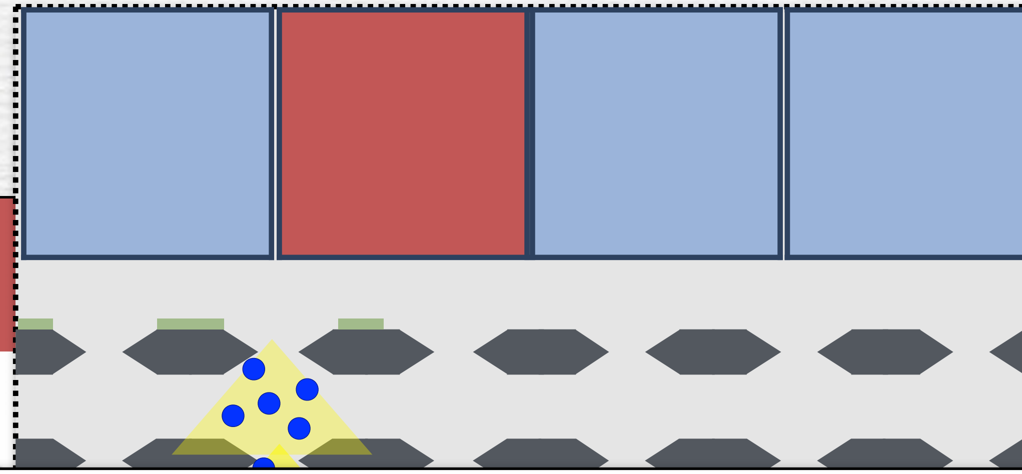
Fraga et al, NIM A 478 (2002) 357-361

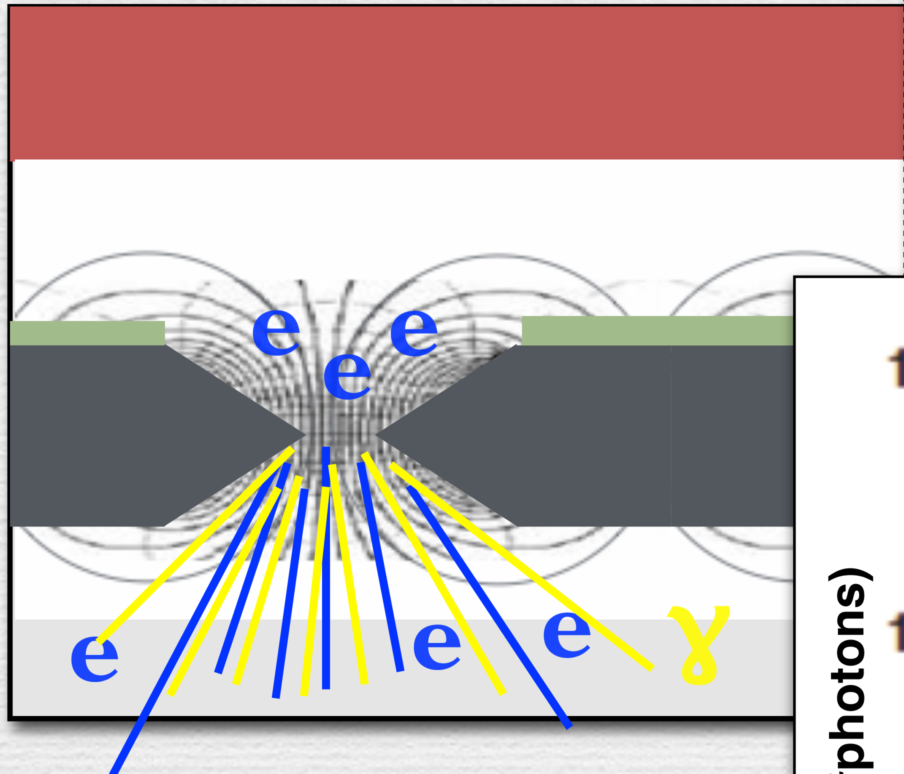


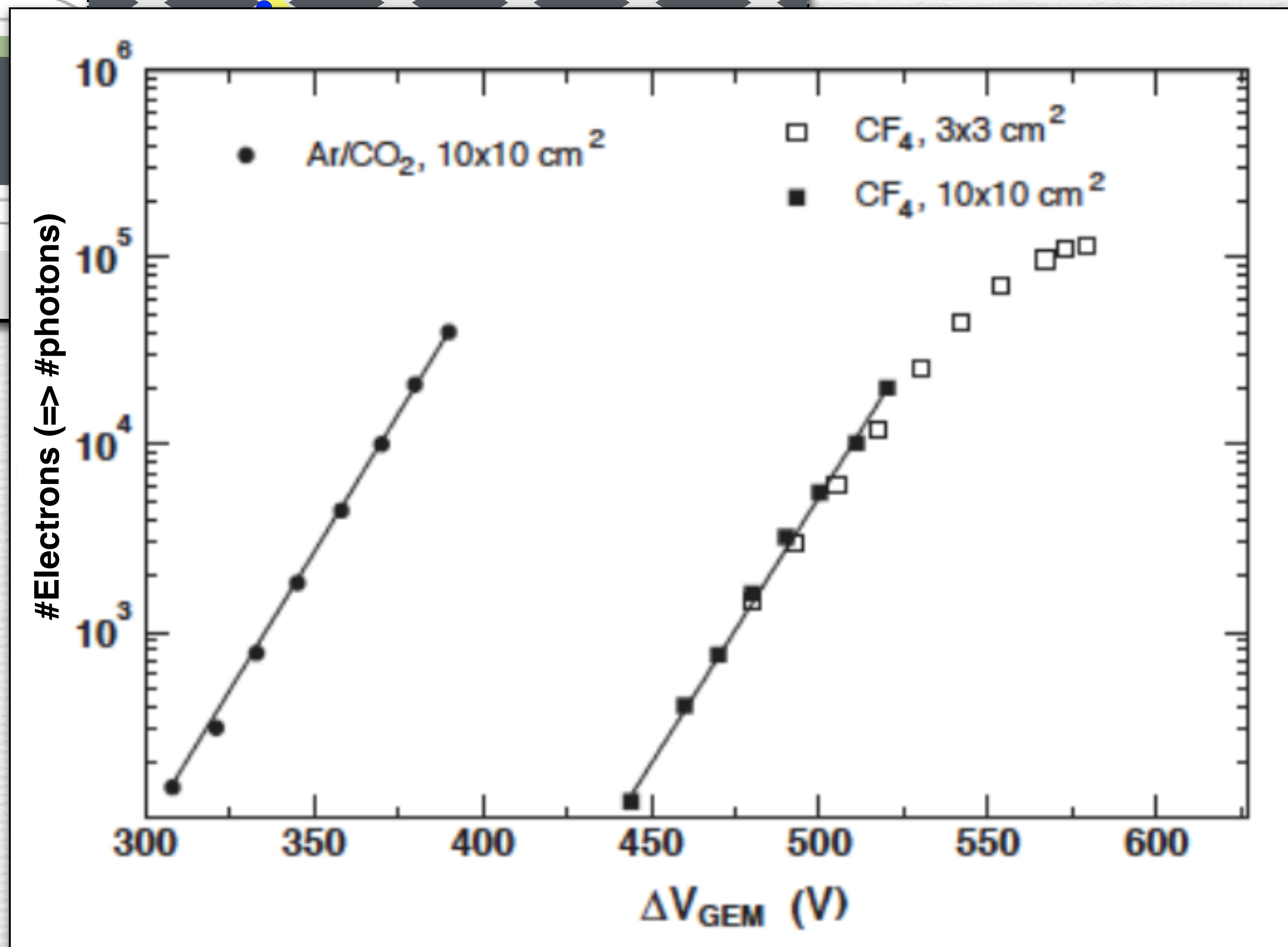
Fraga et al, NIM A 504 (2003) 88-92

MONDO Design

GEM





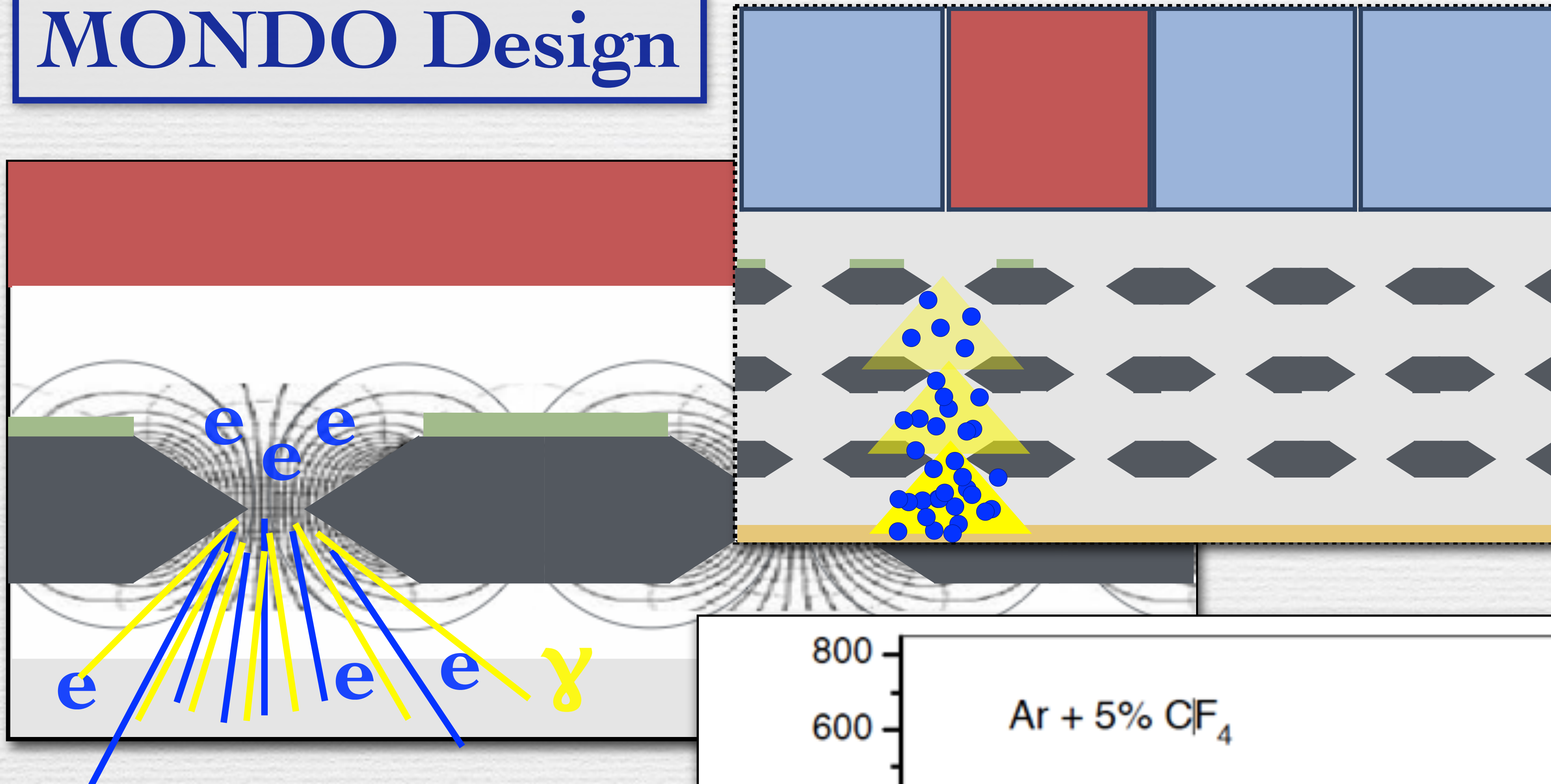


With a triple GEM system a gain of 10^4 is achievable

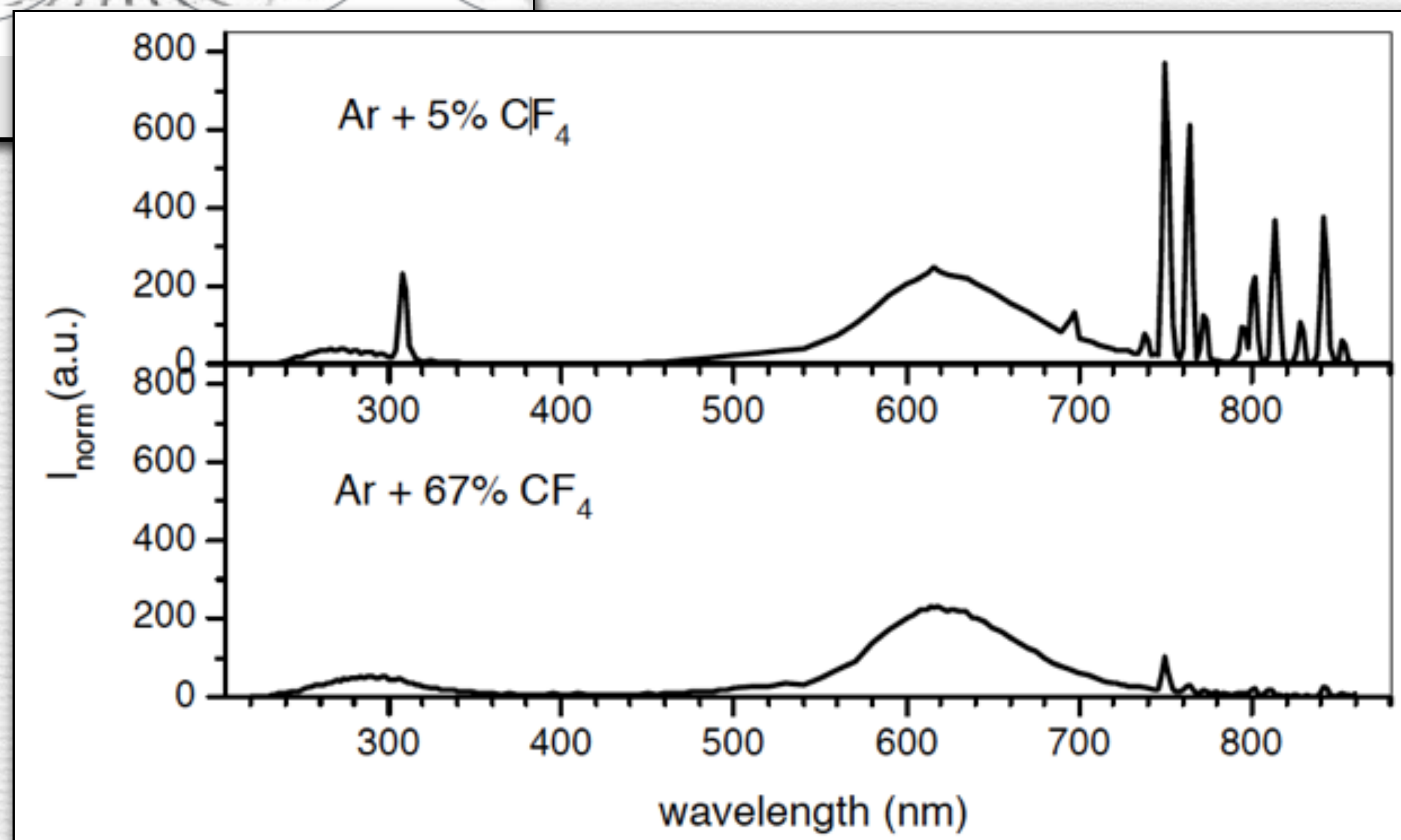
Fraga et al, NIM A 504 (2003) 88-92

MONDO Design

GEM



The emitted photons energy spectra depends on the gas mixture

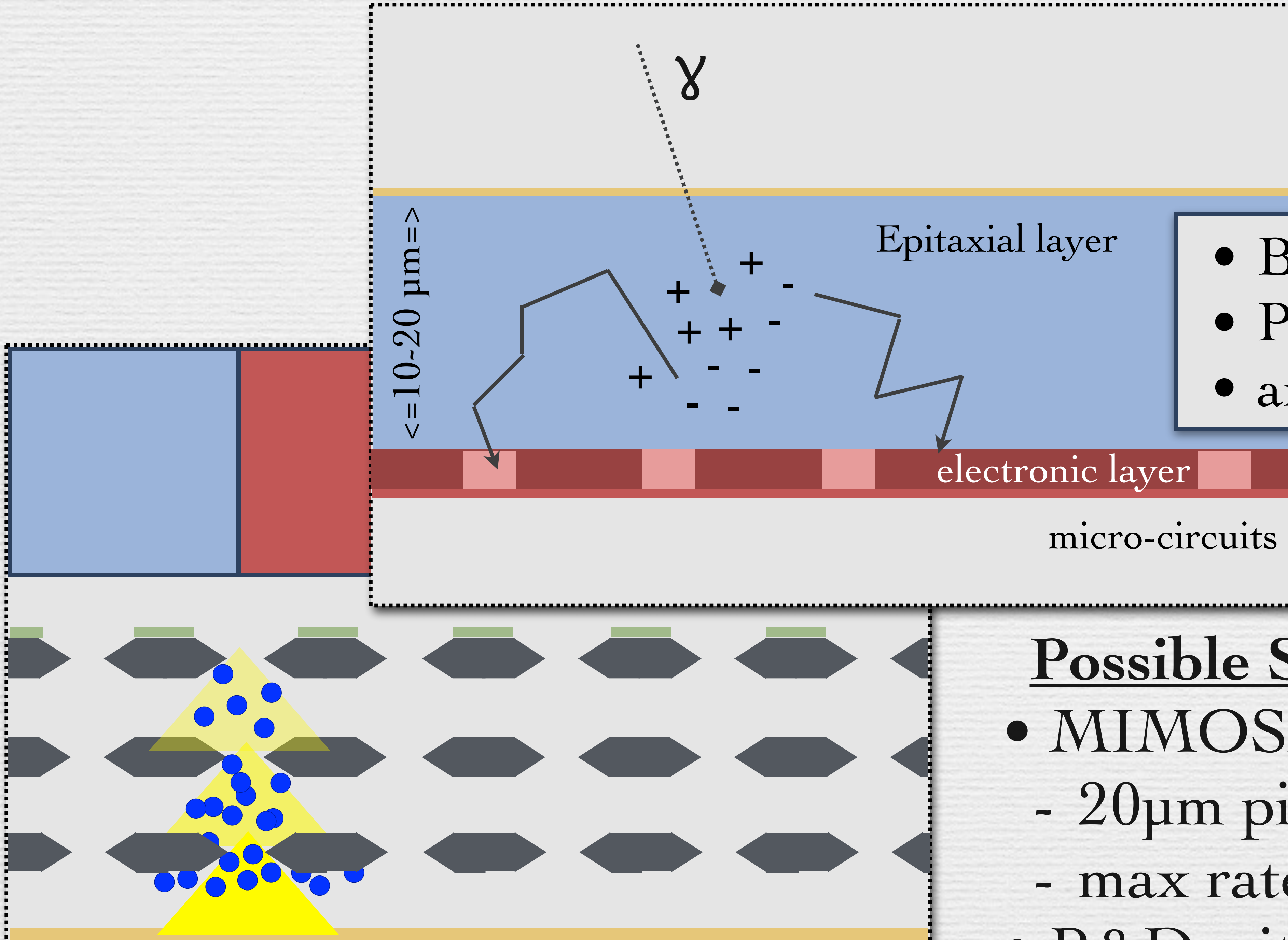


Fraga et al, NIM A 504 (2003) 88-92

M.Marafini

MONDO Design

CMOS

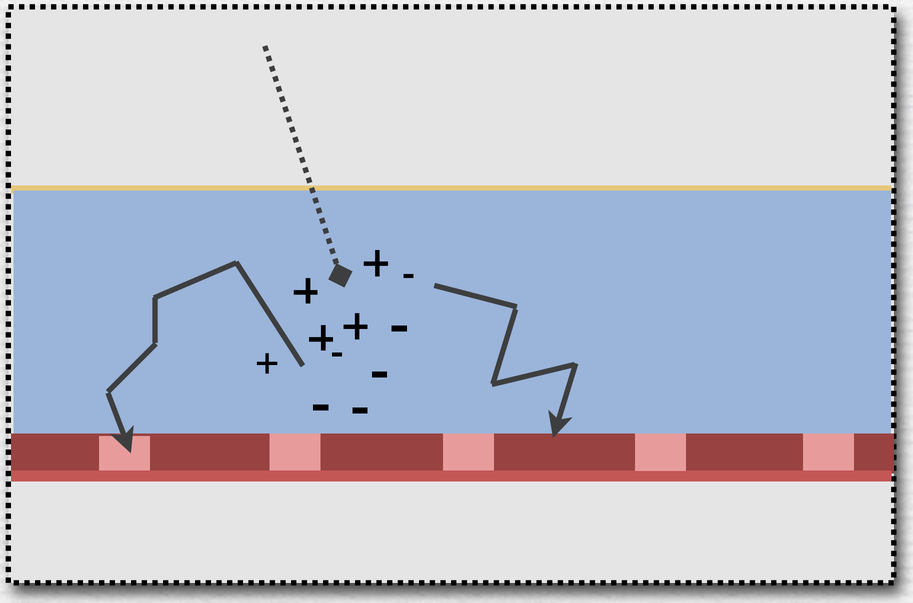


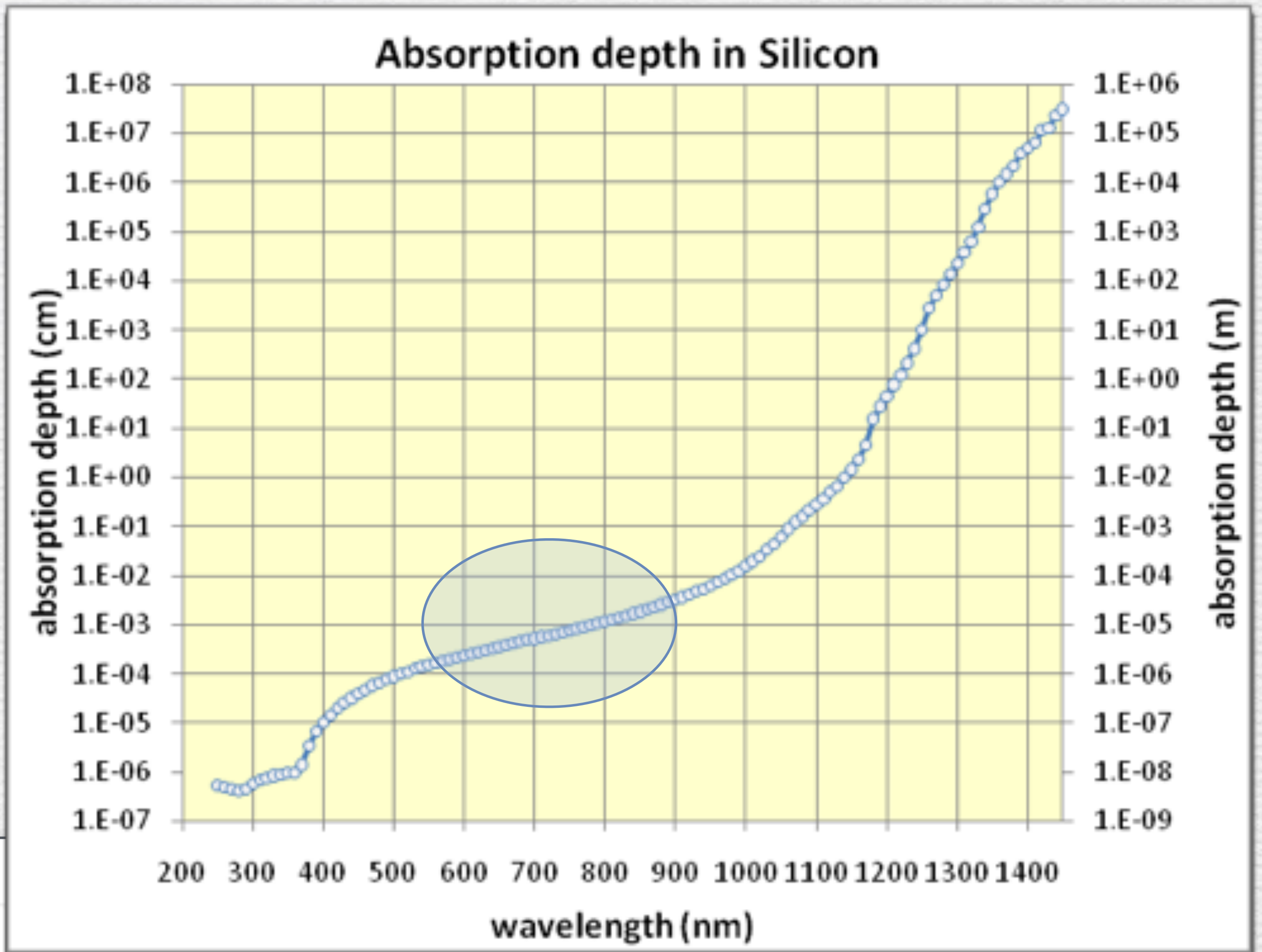
- Back-illuminated
- Passivated face ~1µm
- antireflective coating

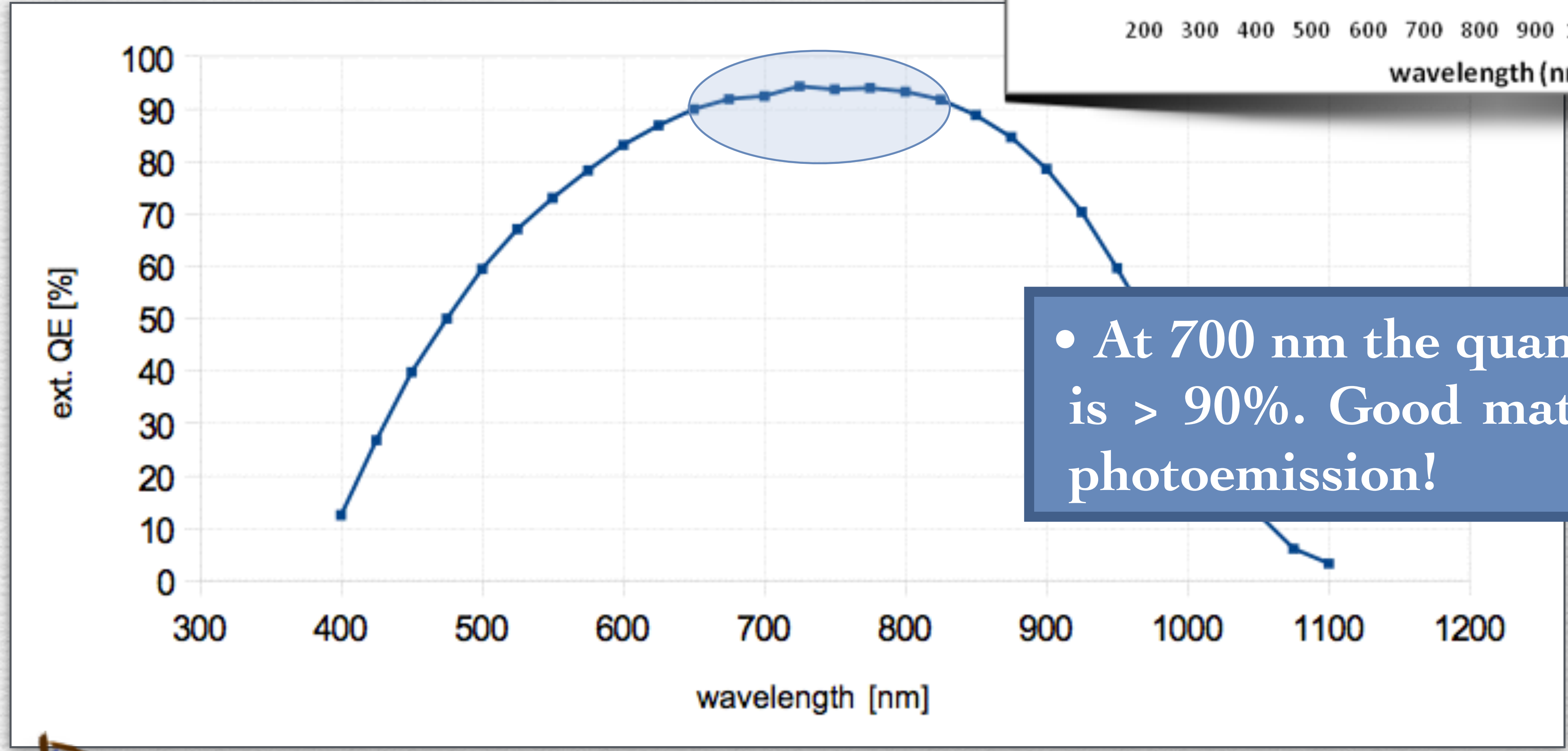
Possible Sensors:

- MIMOSA28
  - 20µm pixel
  - max rate 10kHz
- R&D with Strasbourg
  - 50µm pixel
  - rate 100kHz
- ...

MONDO Design







- At 700 nm the quantum efficiency is > 90%. Good match with GEM photoemission!

Resolution

The expected performances on neutron energy and direction angle are based on what obtained by [SONTRACK]

$\sigma_E/E \sim 5\%$

$\sigma_\theta \sim 4.6\ degrees$

at 35 MeV, improving with energy

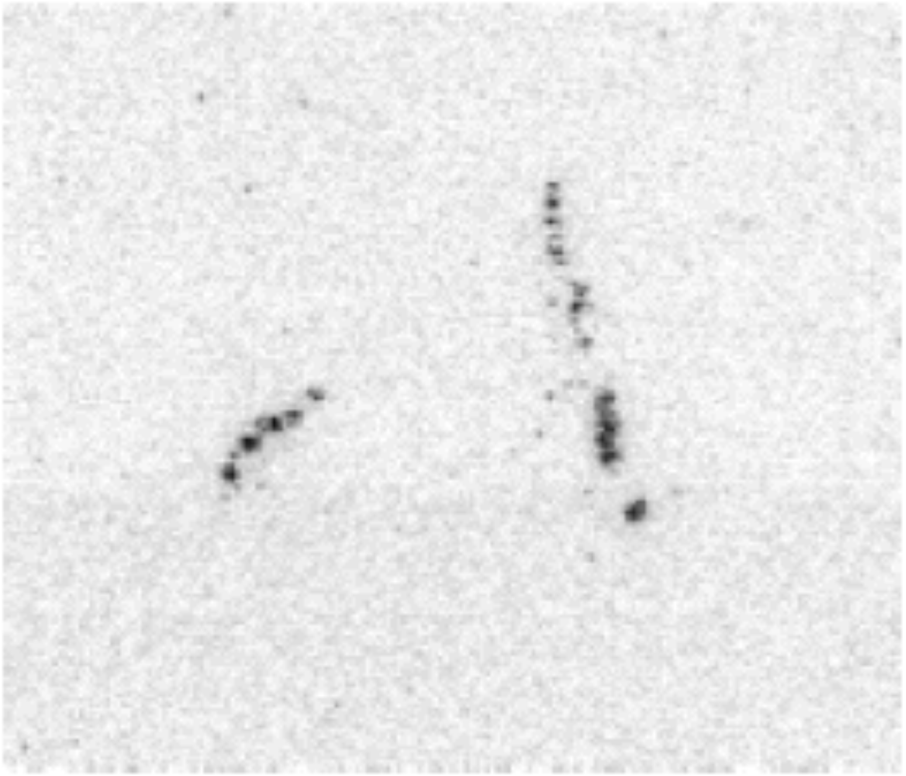


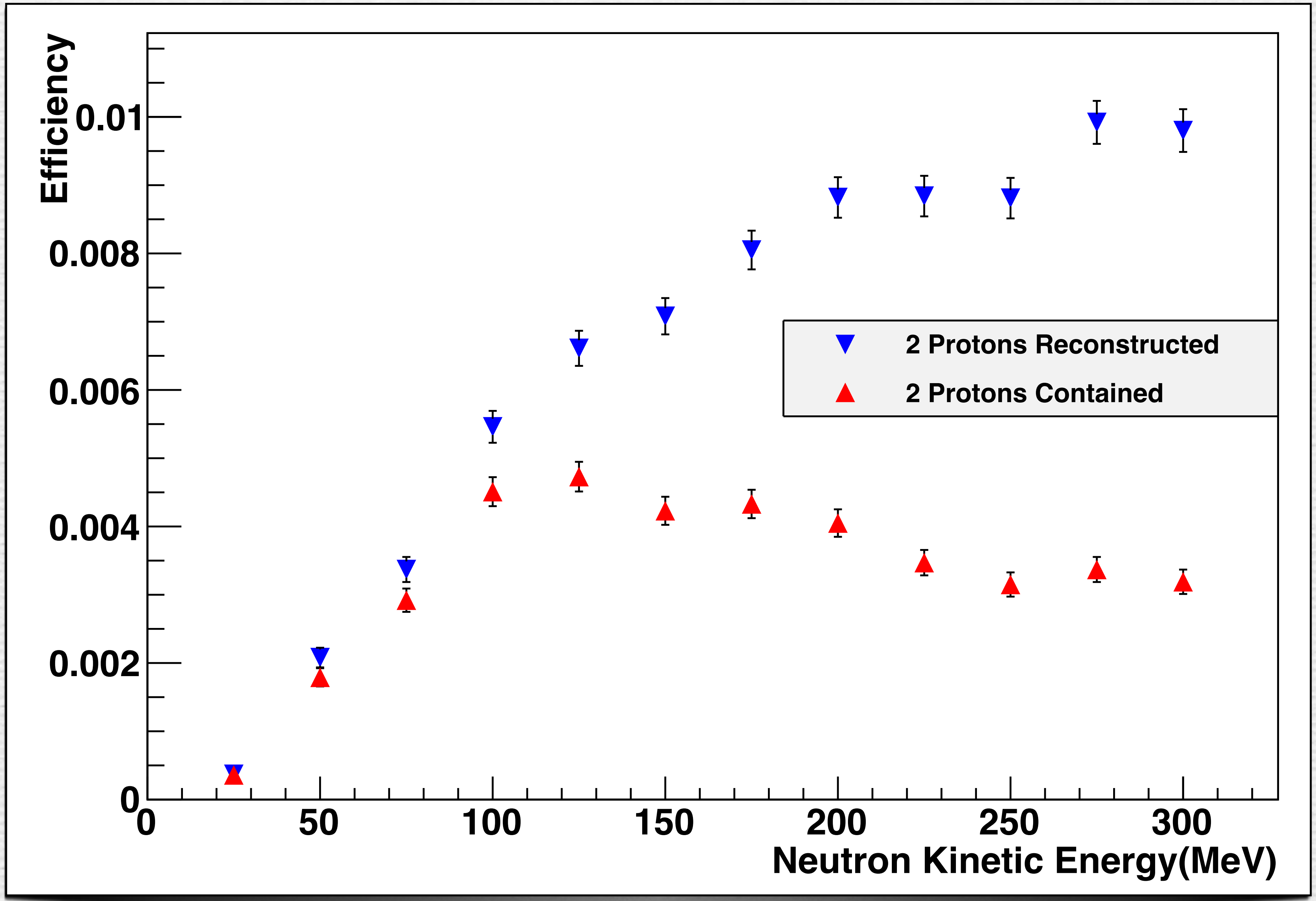
Figure 3. Raw CCD image of a double scatter from a ~65 MeV neutron incident from the top.

R.S. Miller et al, NIM A 505 (3003) 36-40

Efficiency

- Events are reconstructed only if 2 protons have a signal over threshold in more than 6 fibers;
- To release a signal over threshold in a given fiber, the proton must deposit more than 100 KeV

The neutron energy can be computed by measuring the proton range ONLY if both protons are contained.



TEST planning

Several test will be performed in different laboratories with different beams

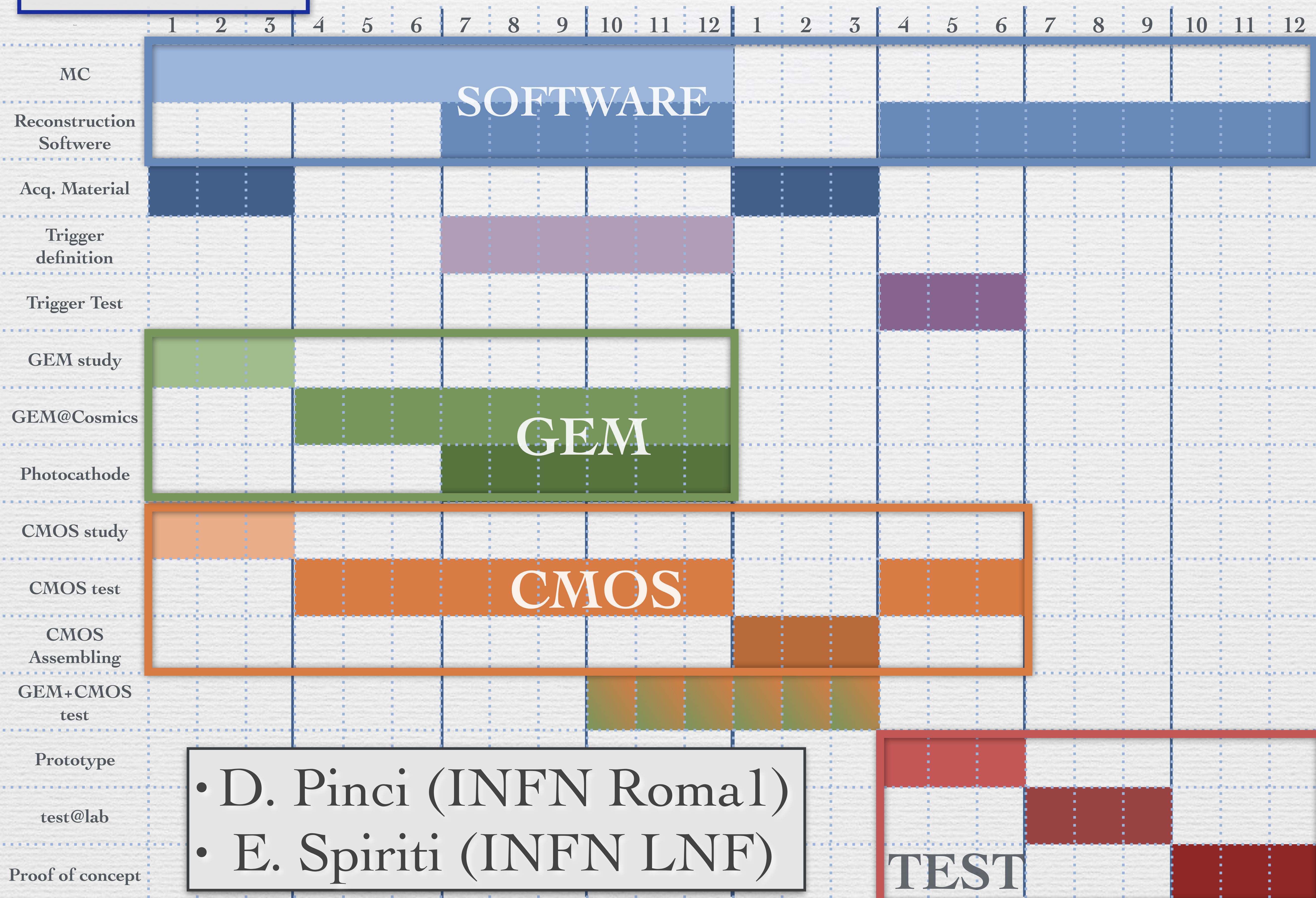
- charged particles
  - cosmic (at SBAI lab)
  - protons (at CNAO)

→ To test the tracking capabilities of the detector

- neutrons
  - neutron facility
  - neutrons emitted from a therapeutical beam on phantom (at CNAO)

→ To measure the detector performances

Timetable



- D. Pinci (INFN Roma1)
- E. Spiriti (INFN LNF)

CONCLUSIONS

- Neutrons are emitted during the patient irradiation and are responsible for the uncorrelated dose released "far" from the affected volume.

- **The MONDO project is dedicated to the development of a neutron tracking device tailored for flux and energy spectra measurements.**

- MONDO is the answer to the compelling need of more detailed information on neutron production in PT. MonteCarlo simulations, therapy centers and physicist community in general would profit of such measurements.

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- The MONDO proof of principle will seed the neutron tracking based range monitoring technique.

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- The MONDO detector can measure **charged secondary particles**, tracking easily the p,d,t profiting form the knowledge acquired with the INSIDE project.
- The detector can also work as Compton Camera for tracking **prompt photons**.

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The **GEM-CMOS system** is the first attempt combining there two technologies in a single device The system will be largely exploitable in many fields of applied and fundamental physics.

THANKS

- GSI Center (M. Durante)
- Karolinska University (I. Gudowska)
- CNAO foundation (S.Rossi)

expressed their interest in the MONDO project.

INFN GRUPPO V

Grant per Giovani Ricercatori

GSI

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TECHNISCHE UNIVERSITÄT DARMSTADT

fondazione CNAO
Centro Nazionale di Adroterapia Oncologica

Il Segretario Generale

Pavia, 01.08.2014
SR/sm
Prot. 562

Gent.ma
Michela
CENTR
Compen
P.zza de
00184 -

Comunicazione inviata via email

Oggetto: INFN CSN5 Call for young researchers 2014.

Gentile dott.ssa Marafini,

il Centro Nazionale di Adroterapia Oncologica è molto in
for young researchers 2014, da Lei proposto nell'ambito di un band

Confidiamo nell'autorizzazione e nel finanziamento della Sua pro
rimarchevole e significativo obiettivo di effettuare al CNAO le
prodotti durante i trattamenti adroterapici dei pazienti, e di valutar
neoplasie maligne secondarie.

Restiamo in attesa di un riscontro, e porgiamo distinti saluti.

Sandro

Sede legale: via Caminadella, 16 – 20123 Milano - Sede operativa: strada Campeggi, 53 – 27100 P
info@cnao.it - www.cnao.it

Karolinska Institutet

MEDICAL RADIATION PHYSICS
KAROLINSKA INSTITUTET
STOCKHOLM UNIVERSITY

Stockholm University

Stockholm, March 10 2014

To whom it may concern

The group of researcher at the Medical Radiation Physics, Inst. of Oncology and Pathology, Karolinska Institute and Dept. of Physics, Stockholm University since a long time has been involved in the research projects related to hadron therapy. We have extended experience in the areas of treatment planning, radiobiological modelling and studies of secondary doses to patients undergoing radiation therapy. Special attention was given to evaluation of secondary radiation in the patient under proton and heavy charged ion therapy generated by nuclear fragmentation processes. This secondary radiation contributes to the dose delivered both to tumour and to healthy tissues outside the treated volume and consequently may generate damage to the healthy cells, which could lead on the long term to the occurrence of secondary cancers.
Our studies were performed using Monte Carlo (MC) simulations with the SHIELD-HIT code, which still requires benchmarking for nuclear interactions of different ion beams and the particle spectra of the produced secondary radiation including high energy neutrons.

There is a lack of experimental data of neutrons in energy range 10 - 600 MeV produced in tissue equivalent materials by therapeutic ion beams of ^{1}H, ^{4}He, ^{12}C and ^{16}O.

The project MONDO proposed by Italian colleagues is of high importance for benchmarking of the nuclear models applied in the MC codes, design of the measurement techniques for high energy neutrons as well as for further development of the risk models for inductions of secondary cancers in patient undergoing hadron therapy.
Several international projects would benefit from the measurements of secondary neutron radiation in clinical ion beams for cancer therapy.
A scientific level of the MONDO project is highly motivated for the research on the development of light ion therapy and we fully support this program.

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Backup

Personal career

Michela Marafini
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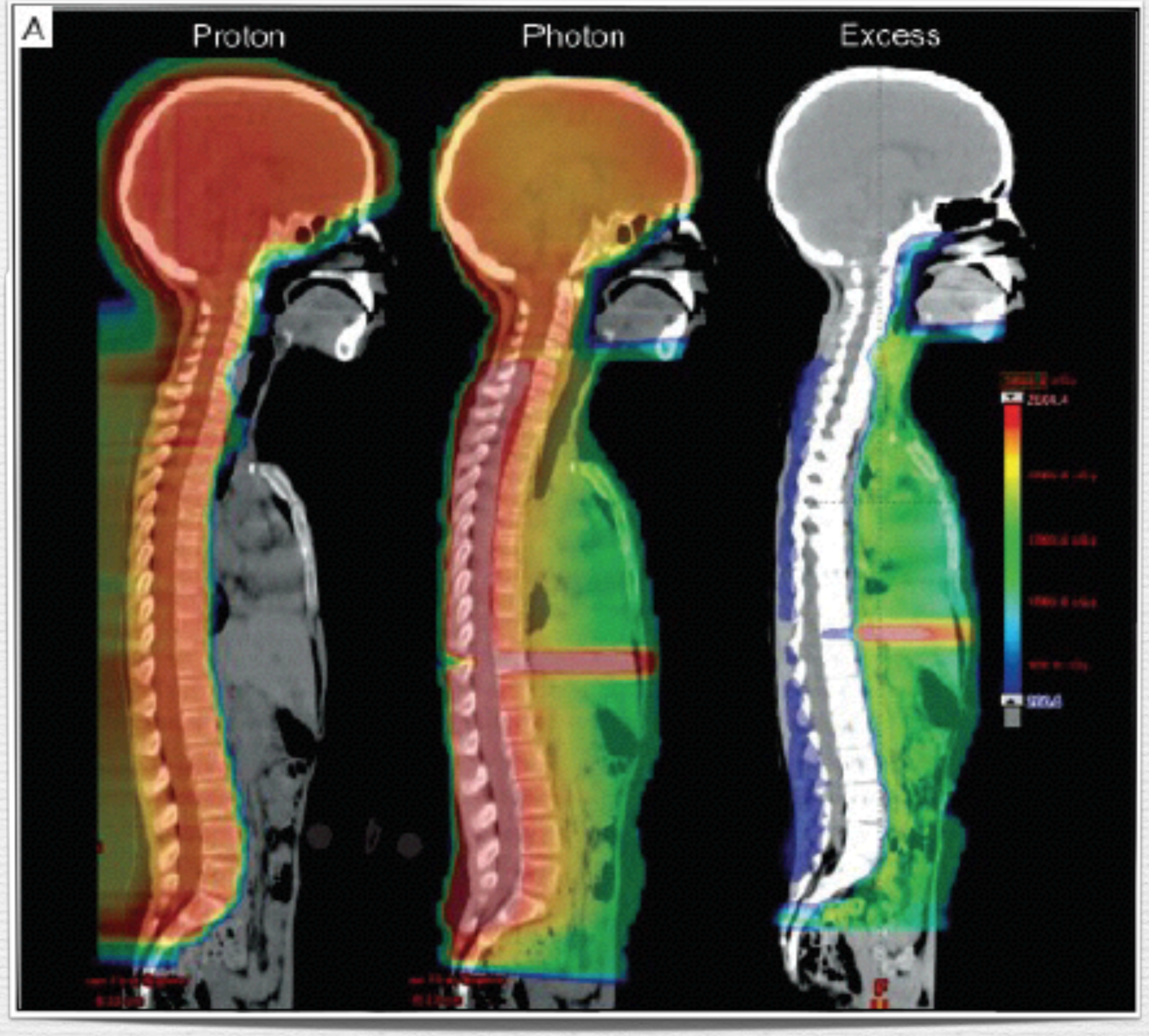
- **Ph.D.** at Paris7 APC Laboratory
  - => MEMPHYS project in LAGUNA
  - Responsible of MEMPHYno prototype
- **PostDoc** CentroFermi at SBAI lab
  - => INSIDE project with CNAO

Neutrino physics next generation experiments

Medical Application: Particle Therapy

- R&D detectors
- photodetection
- Design and implementation of DAQ systems
- Particle Therapy center measurements: GSI, HIT

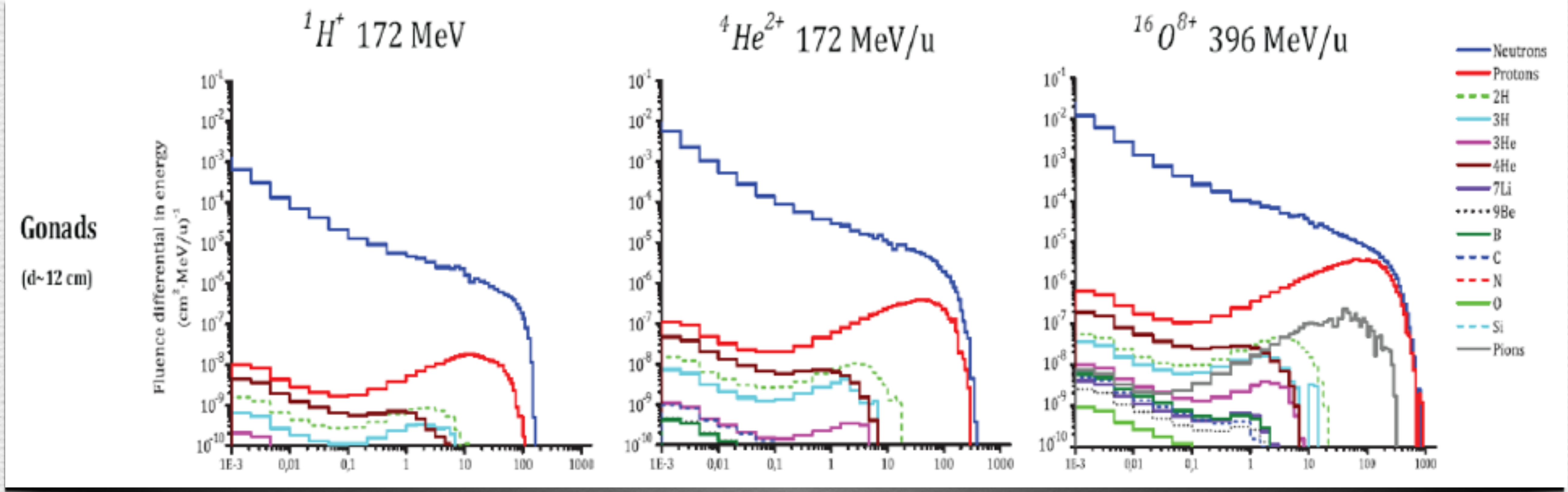
PT



Courtesy of M.Durante

SIMULATION

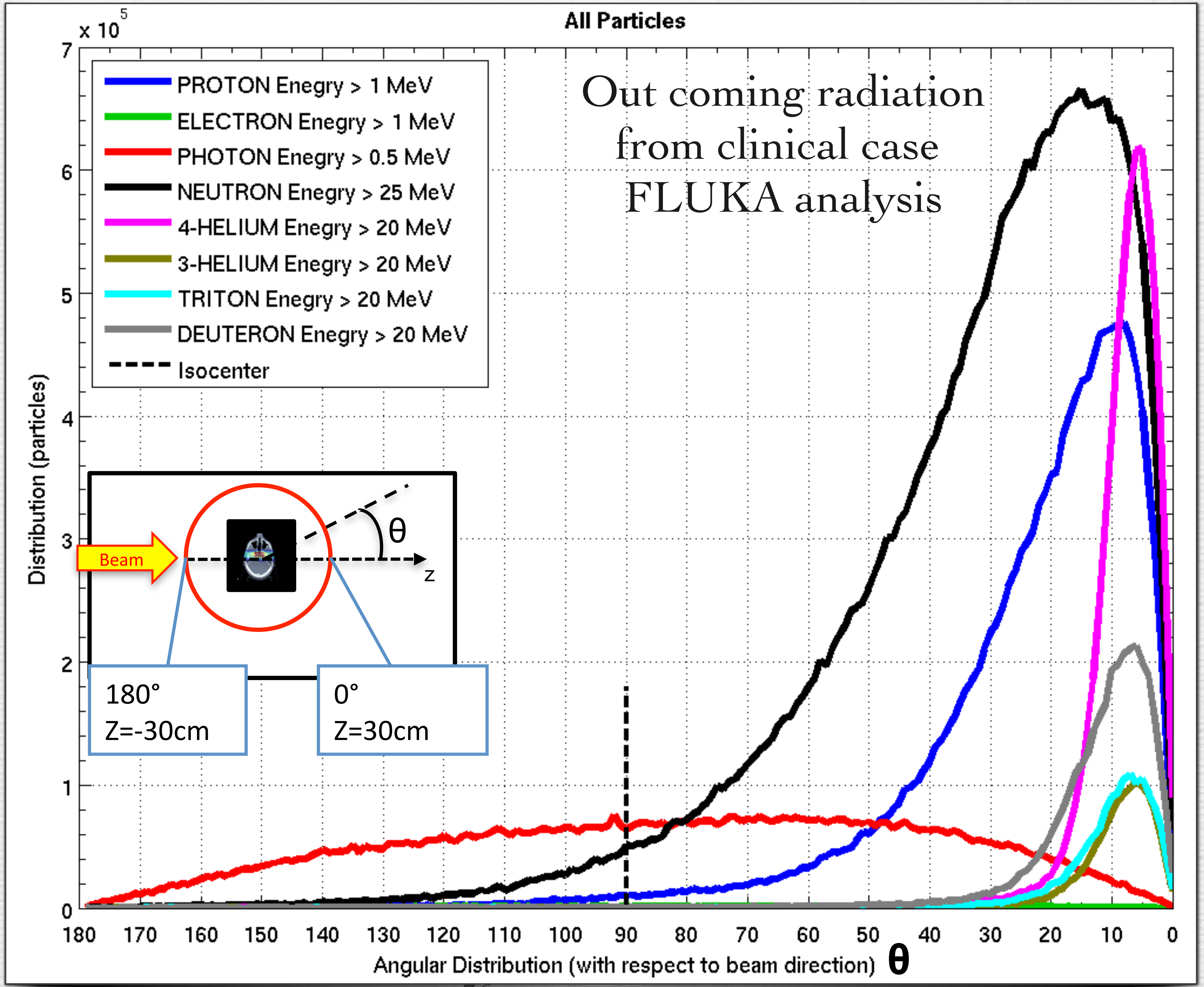
ADAM-HIT: prostate irradiation - secondary particle spectra



SIMULATION

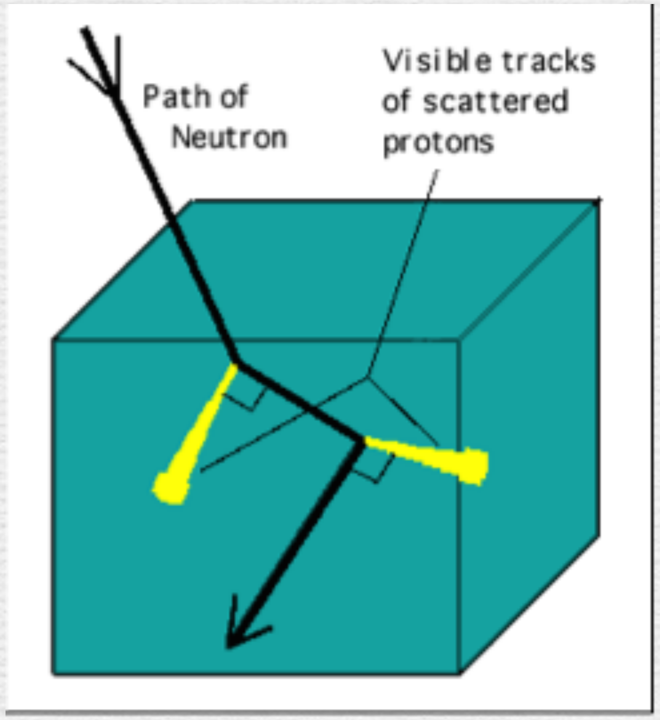
Courtesy of F.Cappucci

One slice
12C beam
228 MeV/u



M.Marafini

Neutron detectors



SONTRACK Astronomical neutrons [20-200]MeV

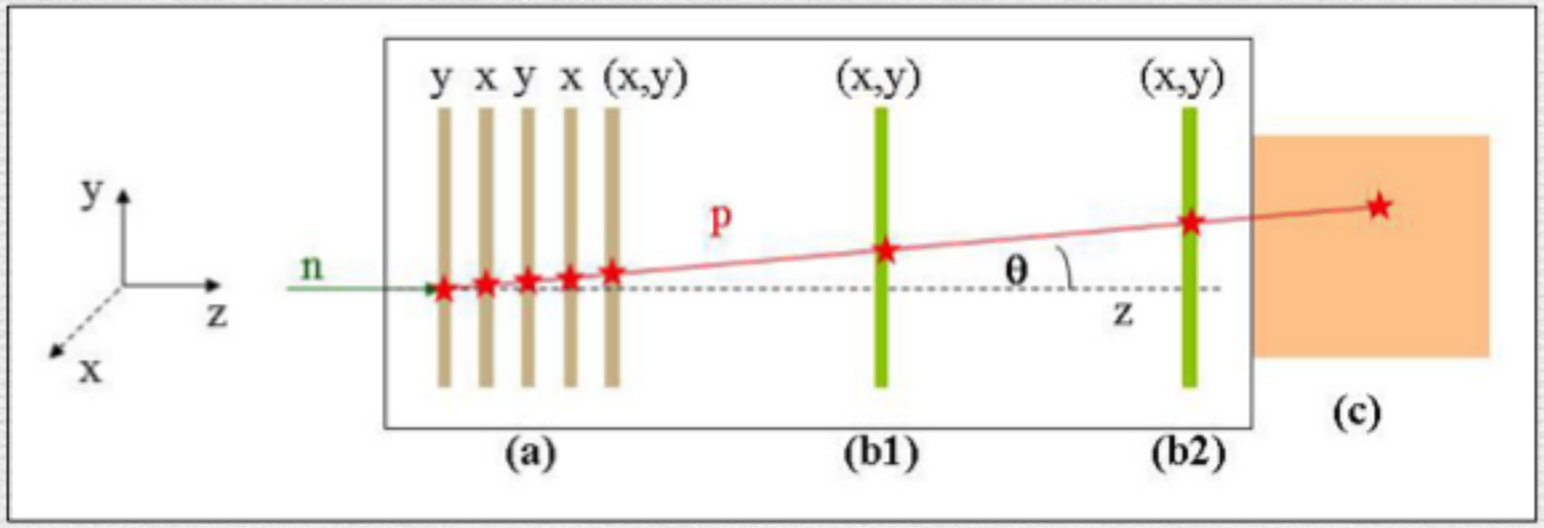
R.S. Miller et al, NIM A 505 (3003) 36-40

Prototype: Scintillating fibers (0.250 mm) are used as target material (allowing for fast neutrons elastic scattering) as well as active volume, detecting the light produced by the recoiling protons. The read- out is based on optically focused CCD commercial devices.

Science model proton track reconstruction

Proton energy (MeV)	σ_E/E	Angular resolution (degree, 1σ)
35	4.8	4.6
46.5	3.4	4.0
55	2.8	3.2
67.5	2.1	2.3

Proposal: carbon ion beam characterization (total fluency of the beam measured with respect to known standard cross-sections and energy spectrum and angular distribution of the emitted neutrons.)

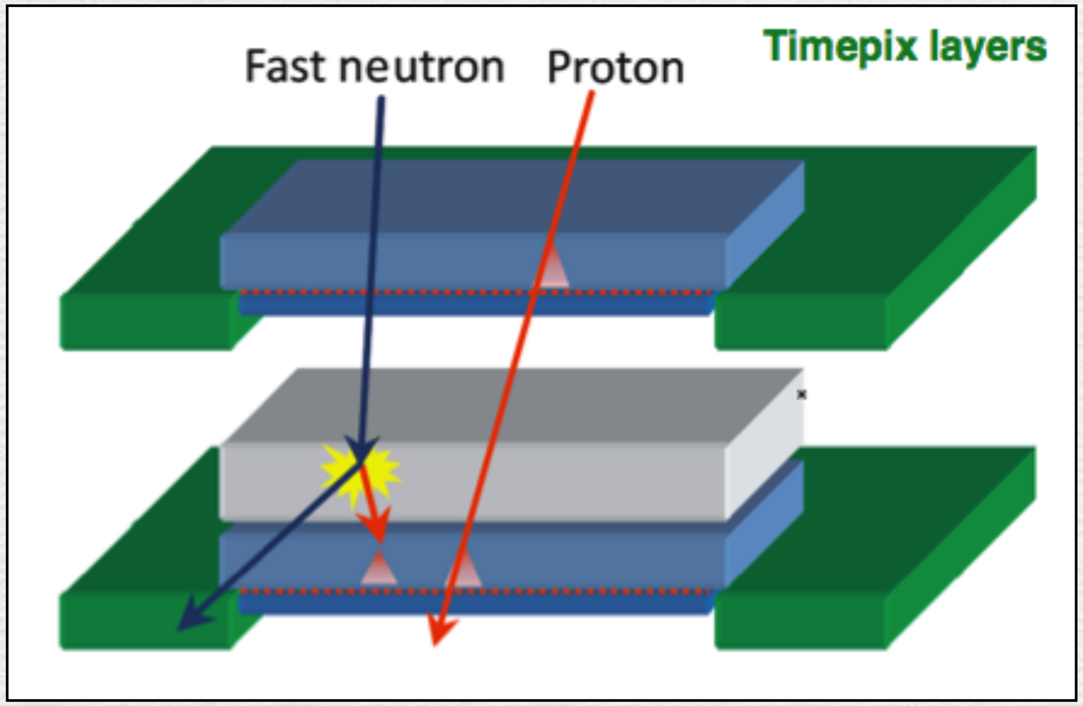


Energy resolution that ranges from about 20% at the lowest neutron energy to about 2% at 160 MeV.

A. Donzella et al, NIM A 613, I 1, (2010) 58–64

- 4 plastic scintillator strips 12 mm wide, 50 mm long and 0.4 mm thick;
- a cylindrical plexiglass light guide connects each strip to a photomultiplier tube. The plastic strips (active target) are followed by silicon detectors (300 µm of thickness) for a total active area of 5 cm x 5 cm divided into 16 strips in both sides but orthogonally oriented.
- For the residual proton energy measure, a cylindrical 3” x 3” CsI(Tl) scintillator coupled by a photomultiplier tube is used.

Neutron detectors

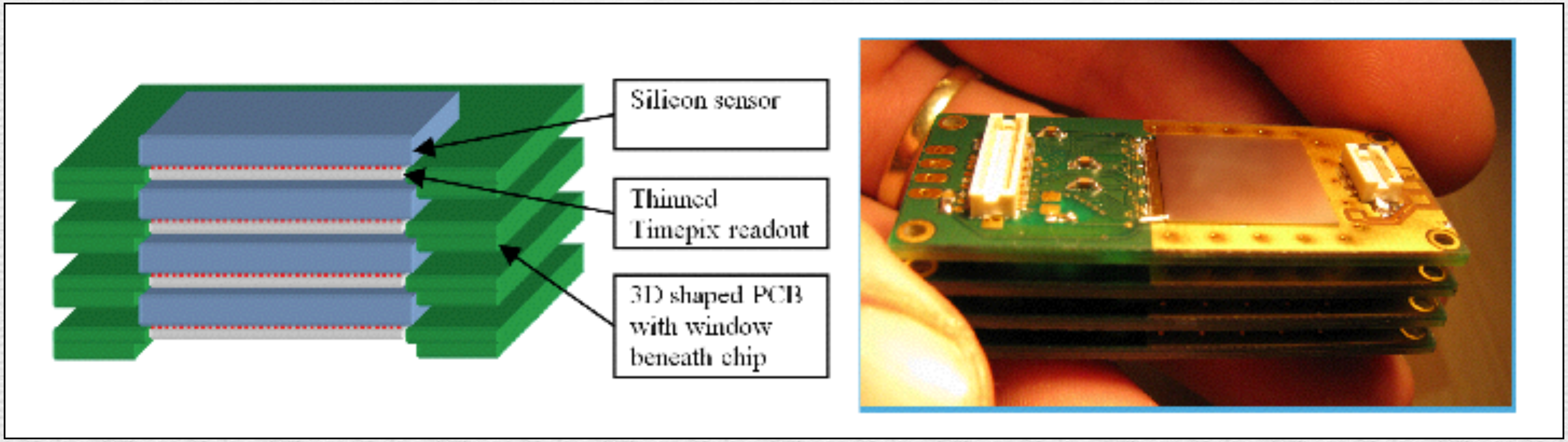


TIMEPIX

J. Jakubek et al.

The technique uses a 3D sensitive voxel detector composed of several layers of Timepix pixel detectors. These layers are interlaced with an hydrogen rich material (plastic) that maximize the elastic scattering cross section and the relative production of recoiling protons.
corresponding to different particles: photons, light charged particles, heavy charged particles and neutrons (slow and fast).

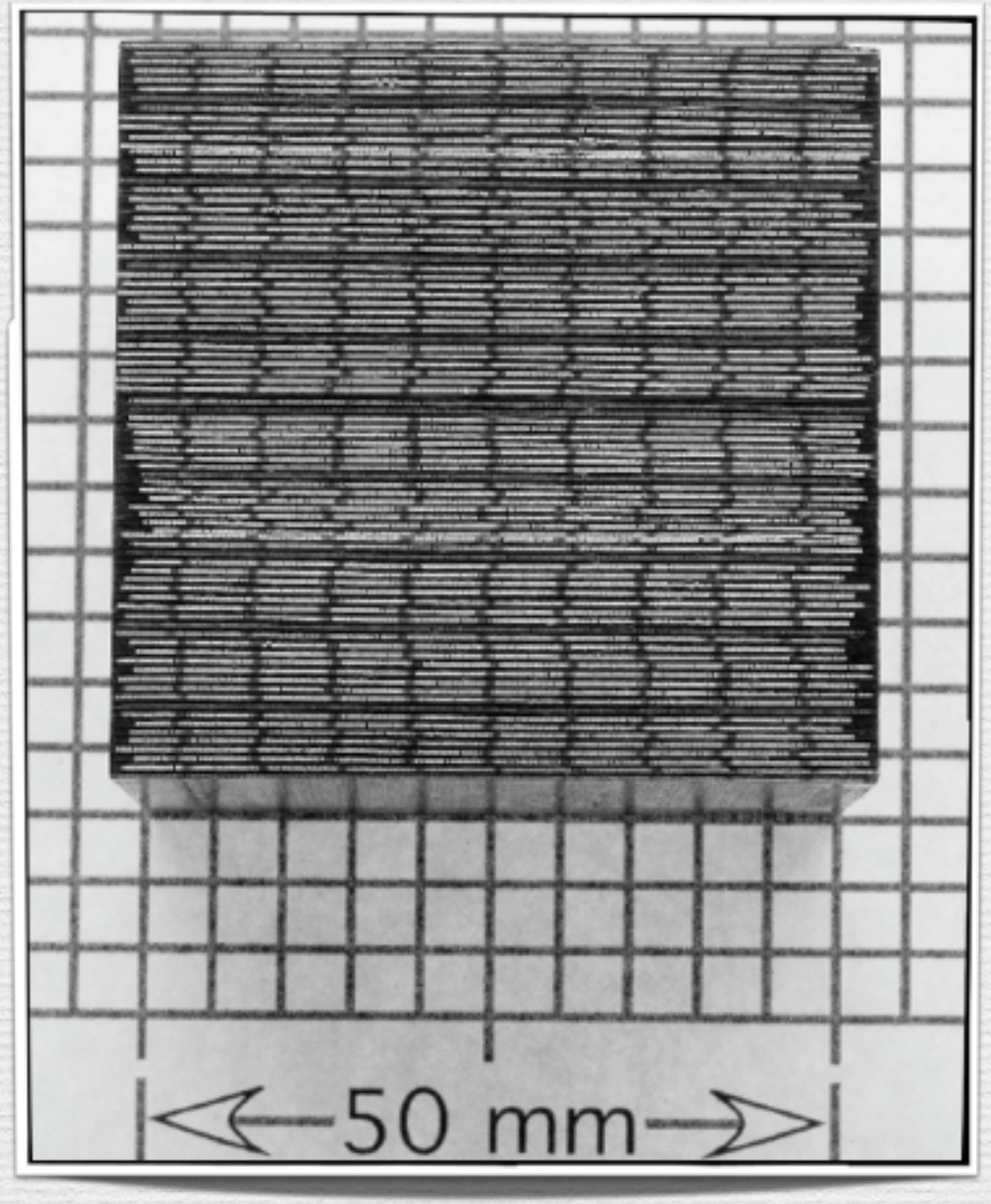
For certain particle types (ions) it is even possible to generate their 2D distribution on the surface of the irradiated volume.
the device to neutrons needs to be determined and calibrated.

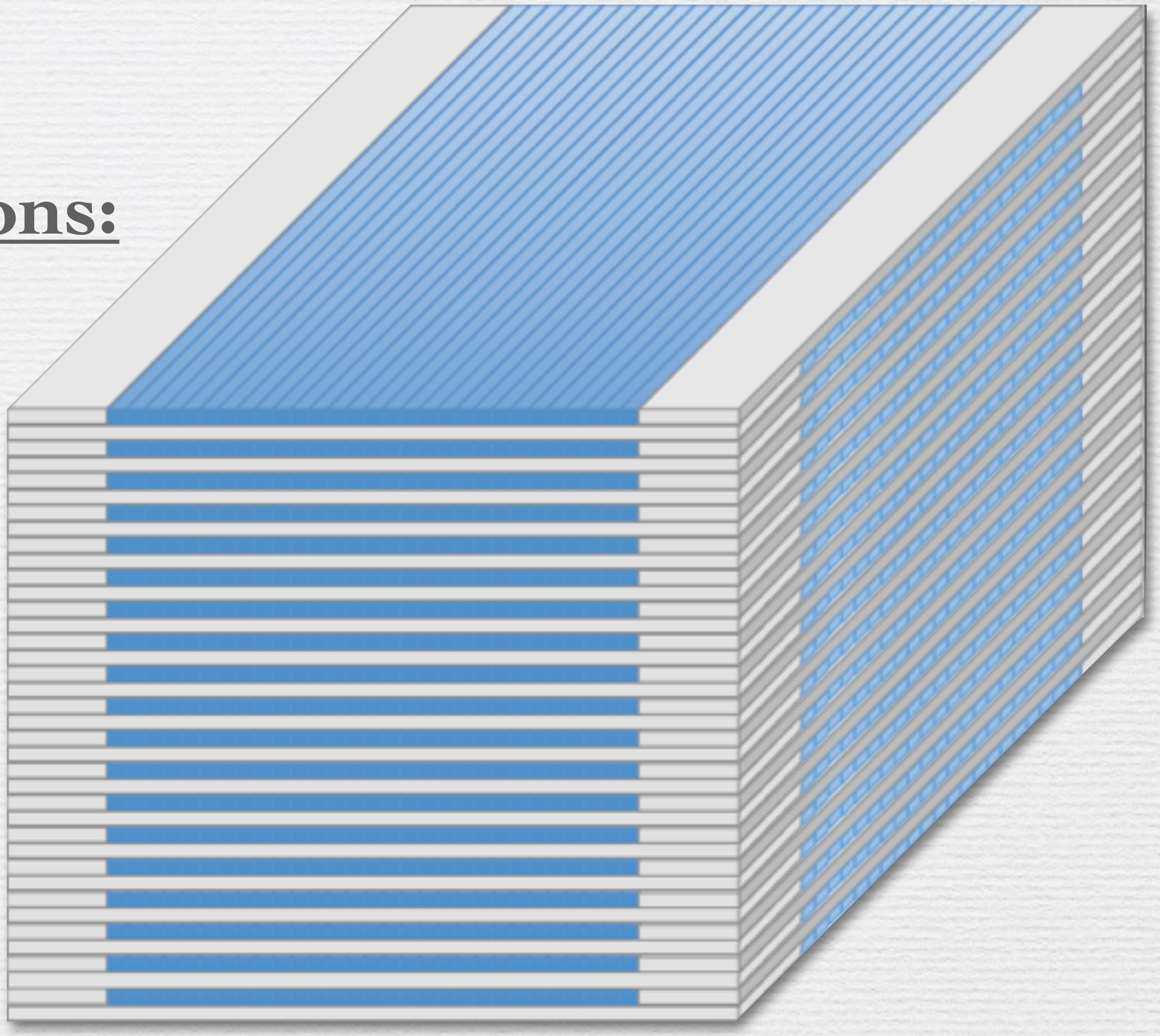


MONDO Design

Possible mechanical solutions:

- San Gobain fibers package
- Homemade assembling





SONTRAC

- 5 x 5 x 5 cm^3 detector (0.250 mm fibres)

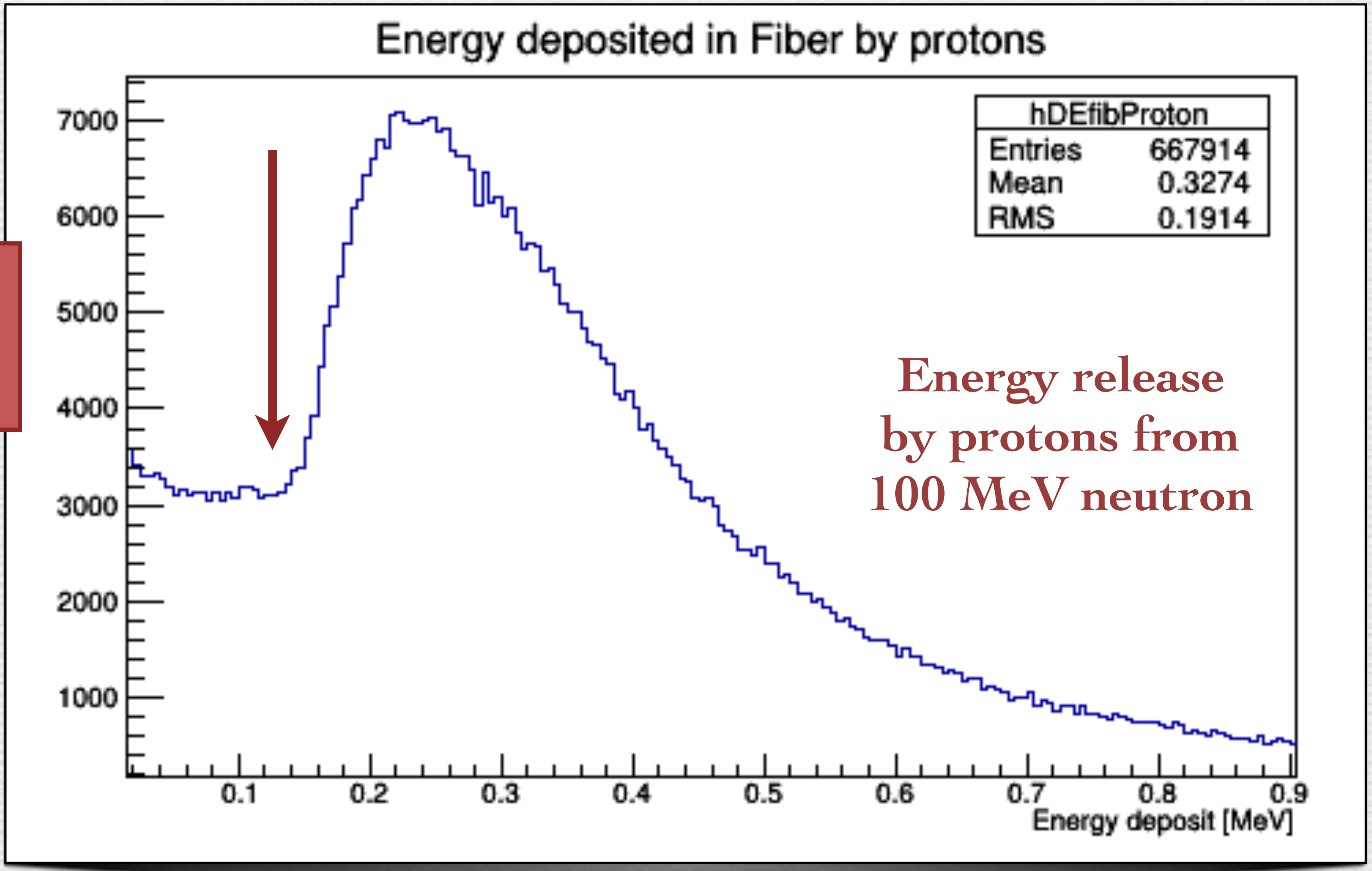
R.S. Miller et al, NIM A 505 (3003) 36-40

Ph.Electrons

The ph.e. produced by the GEM cathode, due to a proton signal in a can be estimated using realistic parameters:

- Minimum Energy: >150 KeV (50 KeV m.i.p.)
- Fiber light yield: $9x10^3$photons/MeV
- Fiber collection eff: 4%
- Photo Cathode eff: 20%

p produces ~ 10 ph.e.
m.i.p produces 5 ph.e.

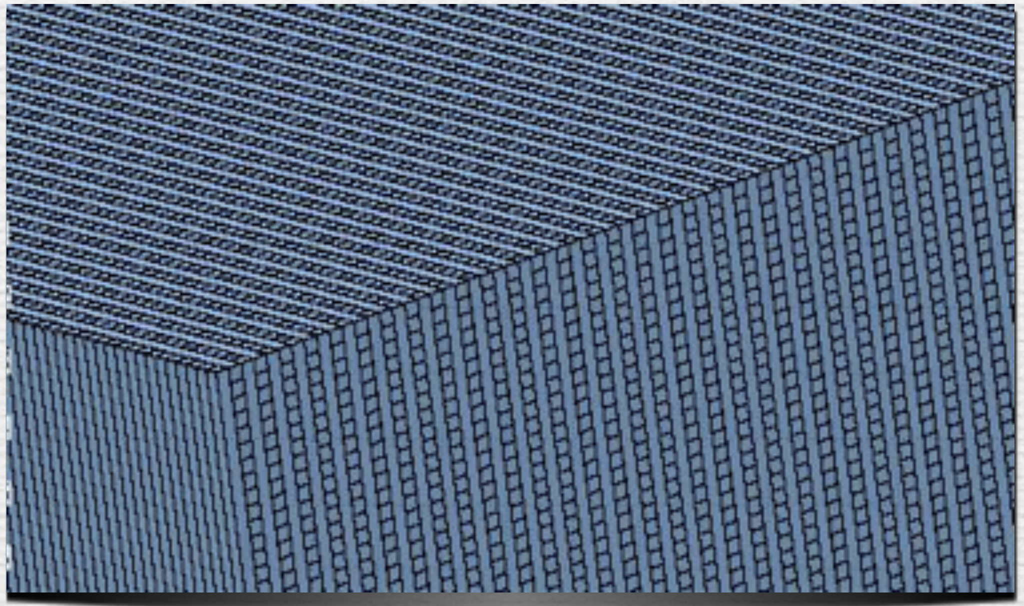


Ph.Electrons

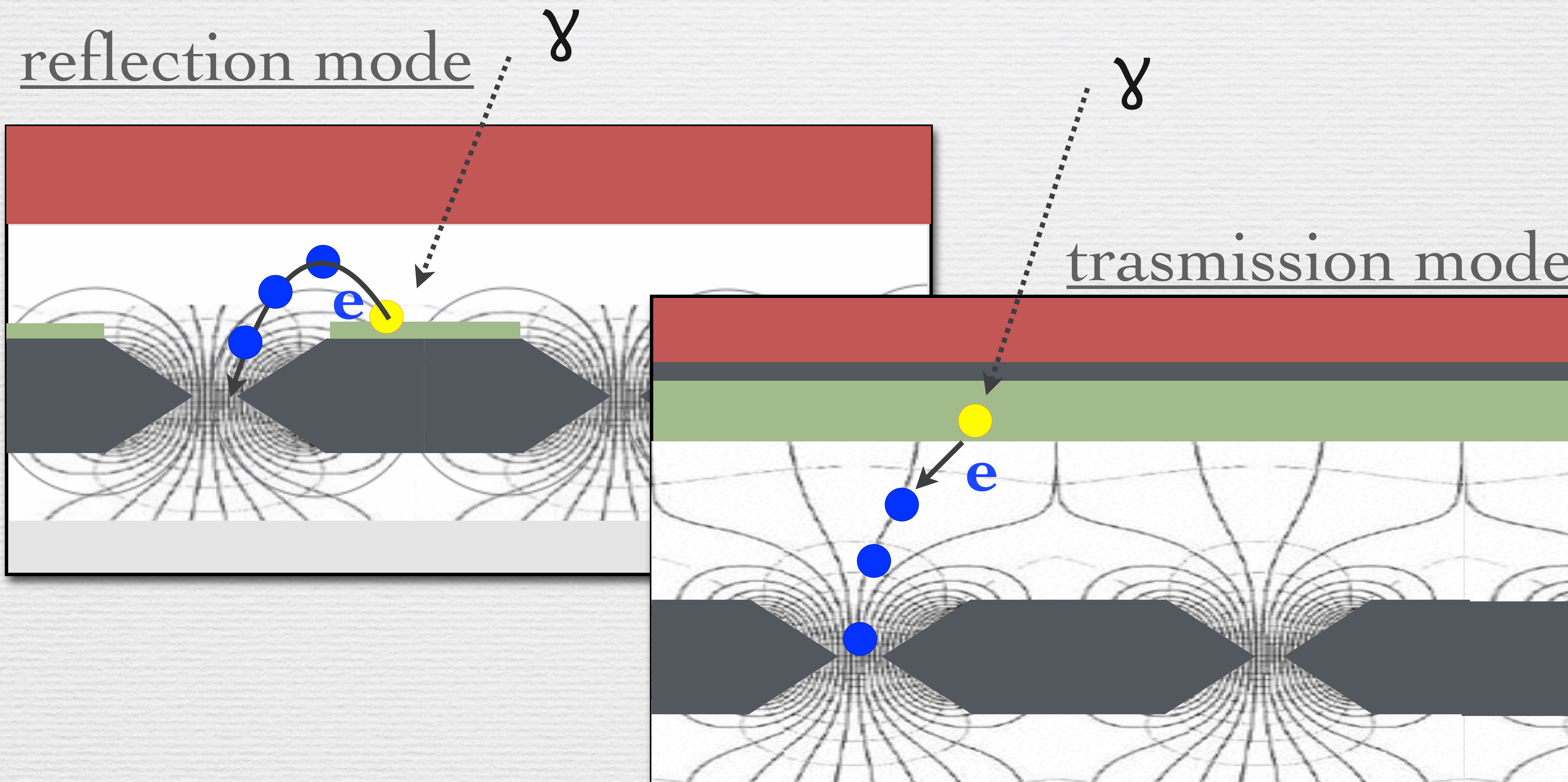
The photons reaching a single CMOS pixel
realistic parameters:

- 50 ph.e per fiber
- 50 ph.e x 20% photocathode effQ => 10 ph.e
- 10 ph.e x 30% photocathode effGeo => 3 ph.e
- 3 x 10^4 photons after the last stage
- x 50% GEM effGeo [half of the electrons (and photons) goes in the wrong direction]
- 15000 from 250 µm => 600 ph per pixel (50µm)
  => 100 ph per pixel (20µm)

in CMOS sensor: 15 pair of bkg
=> 100 ph -> 100 pairs
=> 50 ph -> 50 pairs

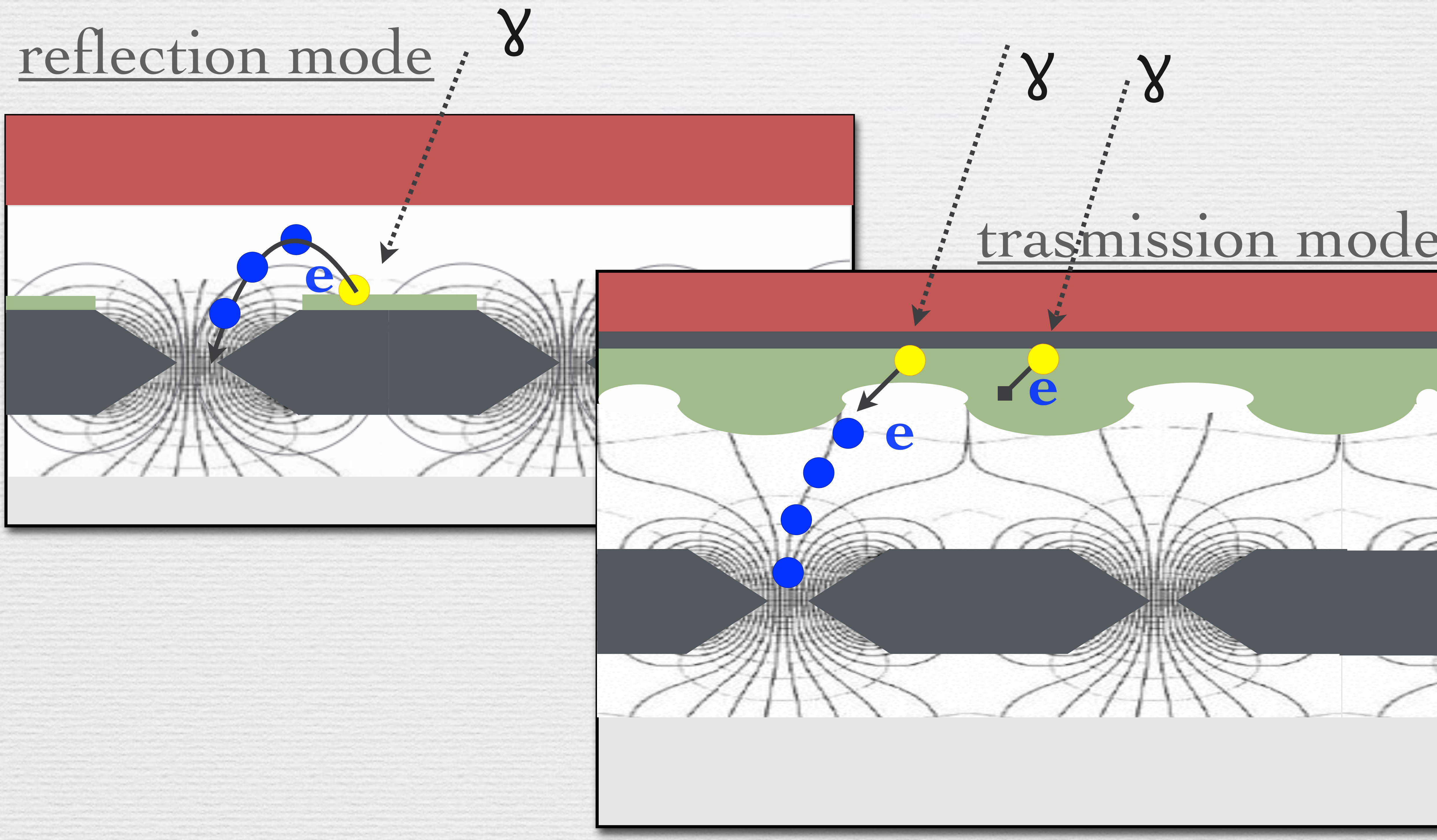


PHOTOCATHODE



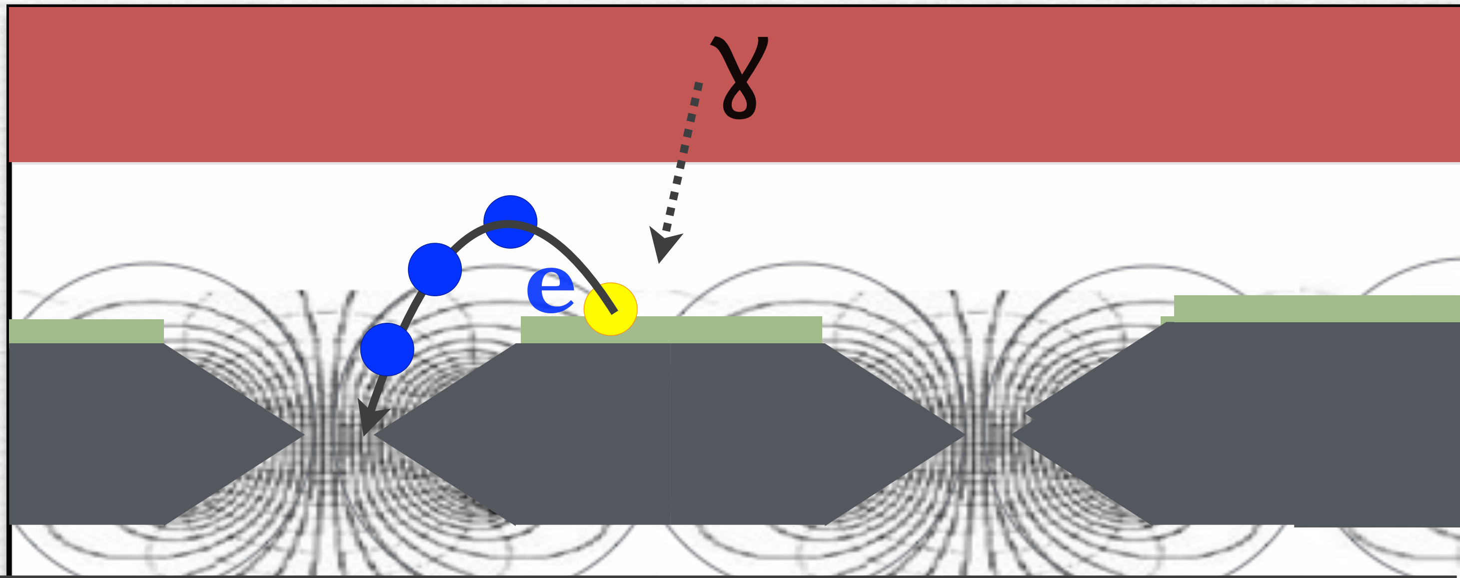
- Ec ~ 50%

PHOTOCATHODE

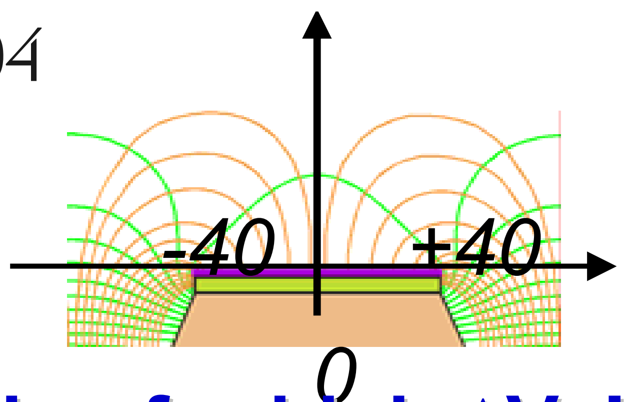


PHOTOCATHODE

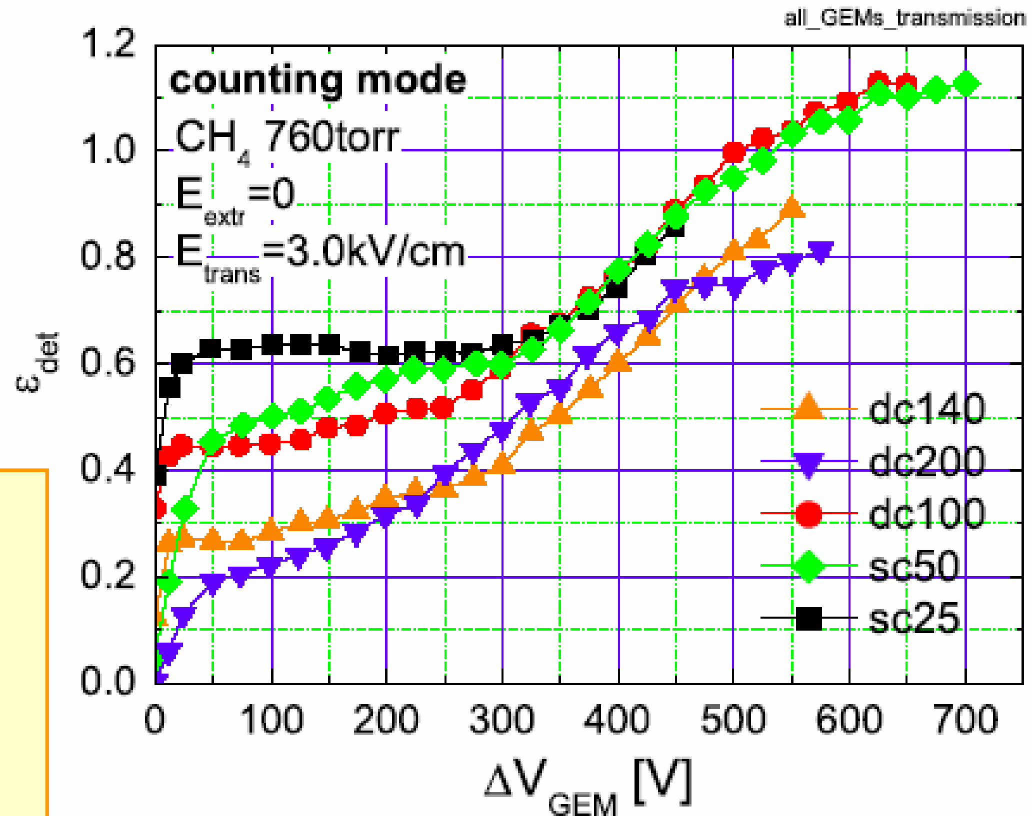
reflection mode



S.della Torre, RICH 2004

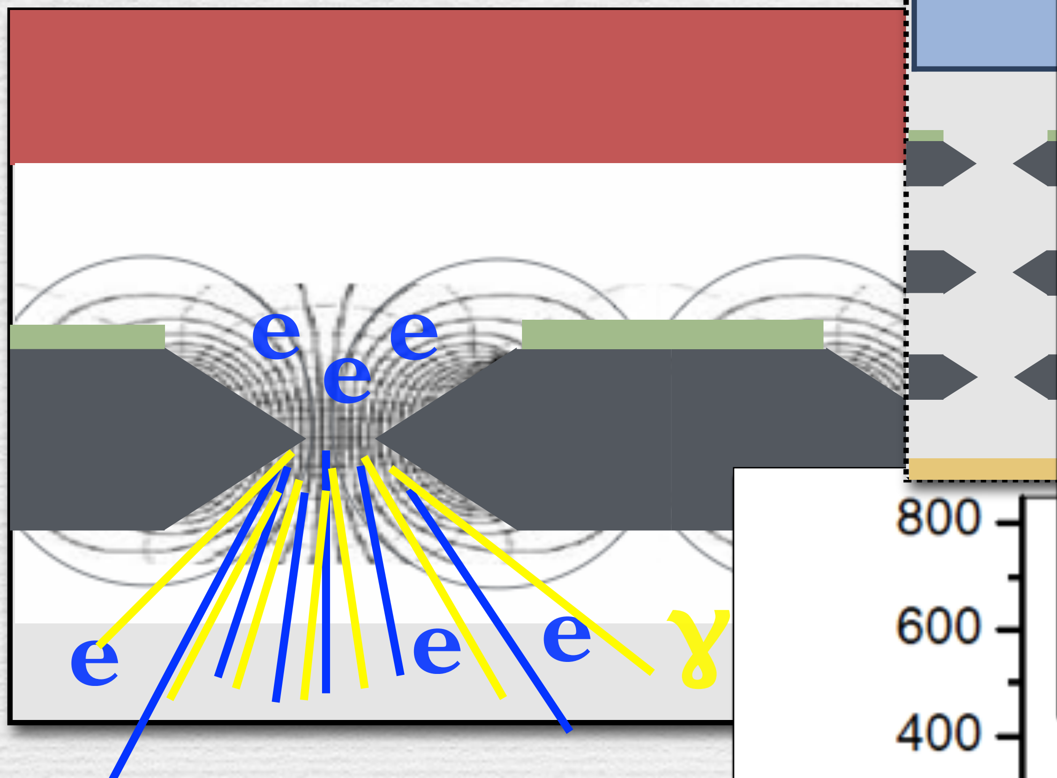


pushing for high ΔV !!

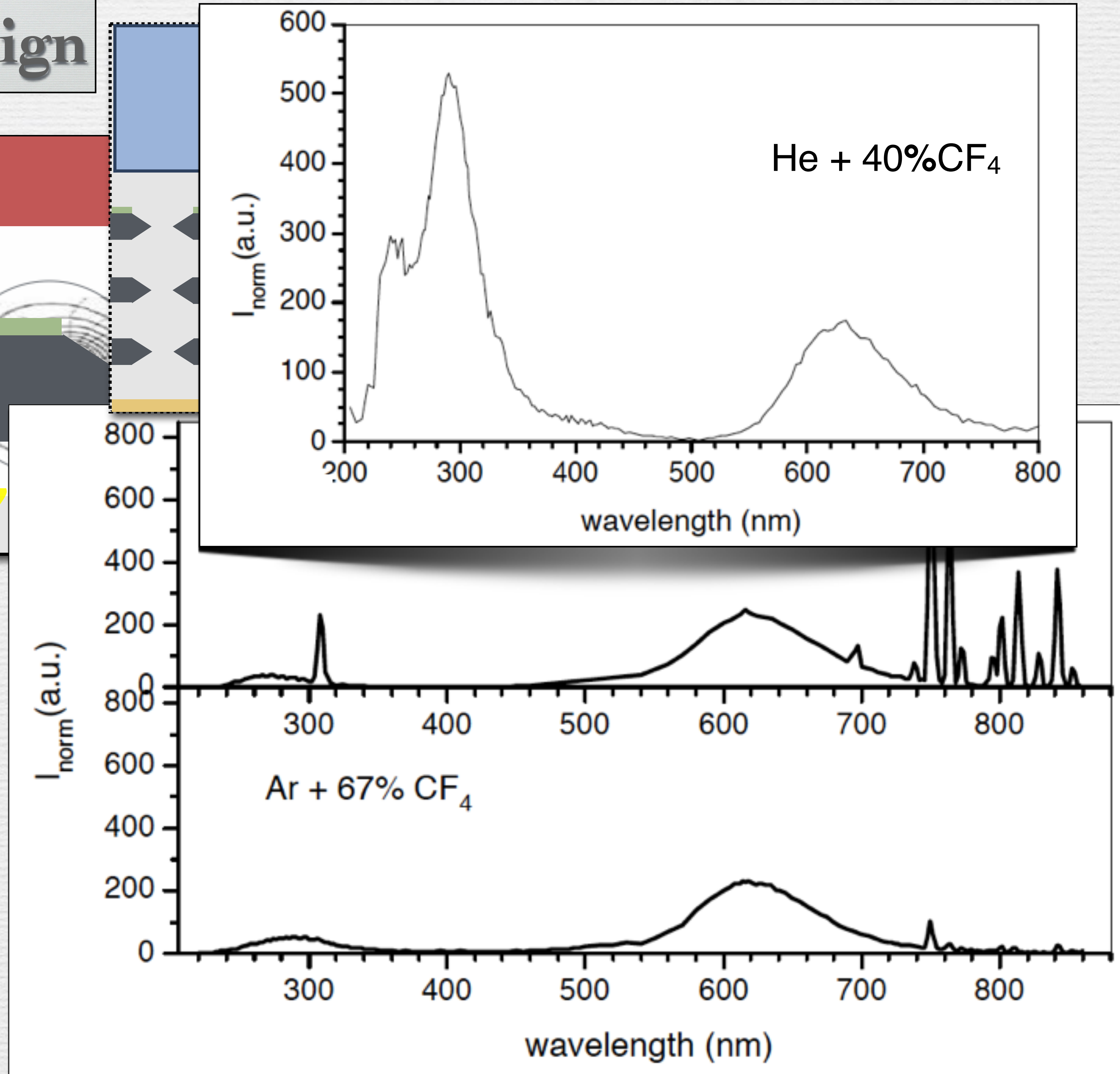


- Reflective PC (compared to ST), higher QE, low sensitivity to ionizing BG radiation
- Reduced secondary effects → high gains 10^6 - 10^7
- Fast: with CF_4 σ = **1.6ns** w\single electrons
  σ = **0.33ns** w\150 electrons

MONDO Design



The emitted photons energy spectra depends on the gas mixture



Fraga et al, NIM A 504 (2003) 88-92

M.Marafini

GEM

The GEMs with 45 um holes have higher light emission than the other GEMs

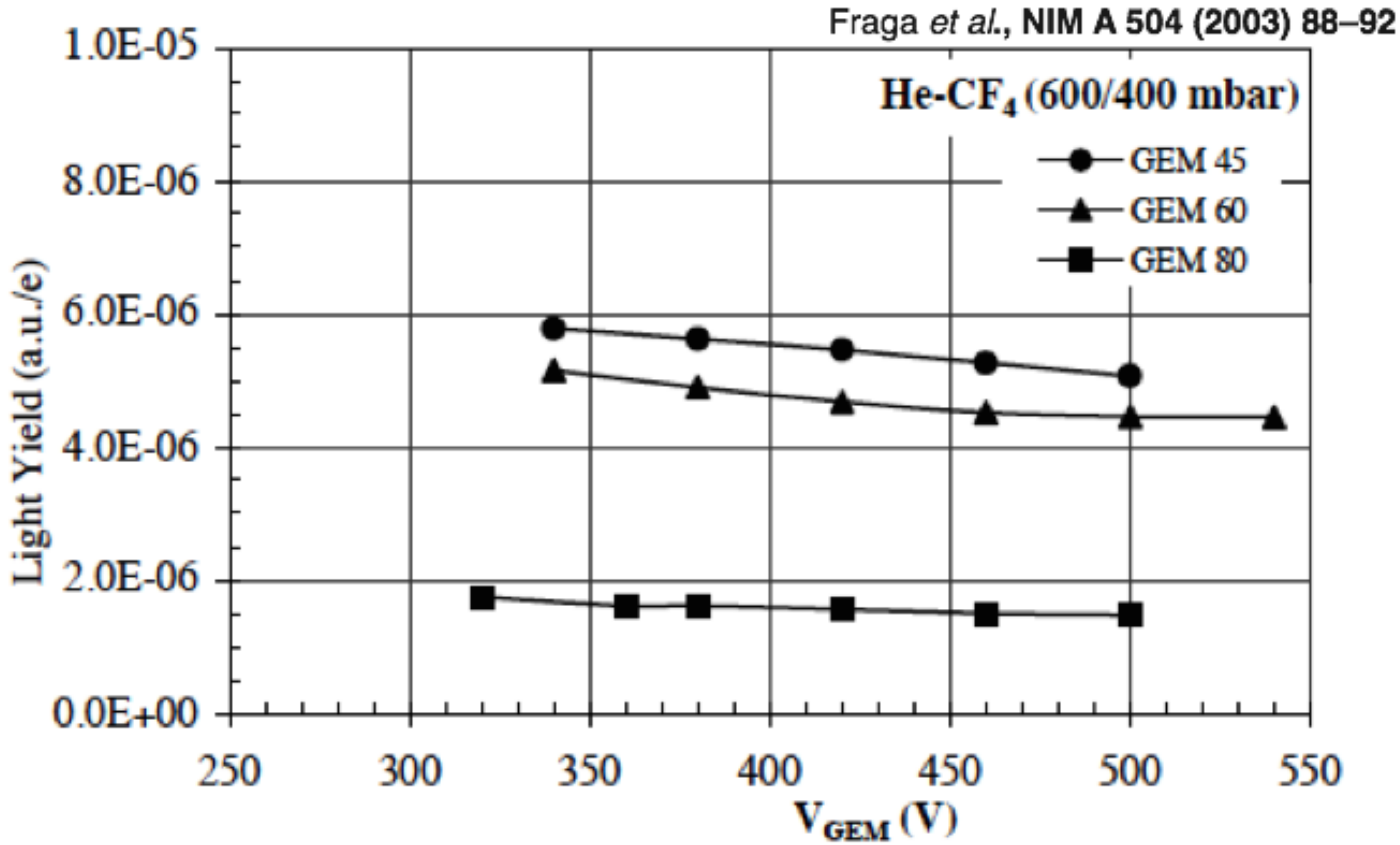
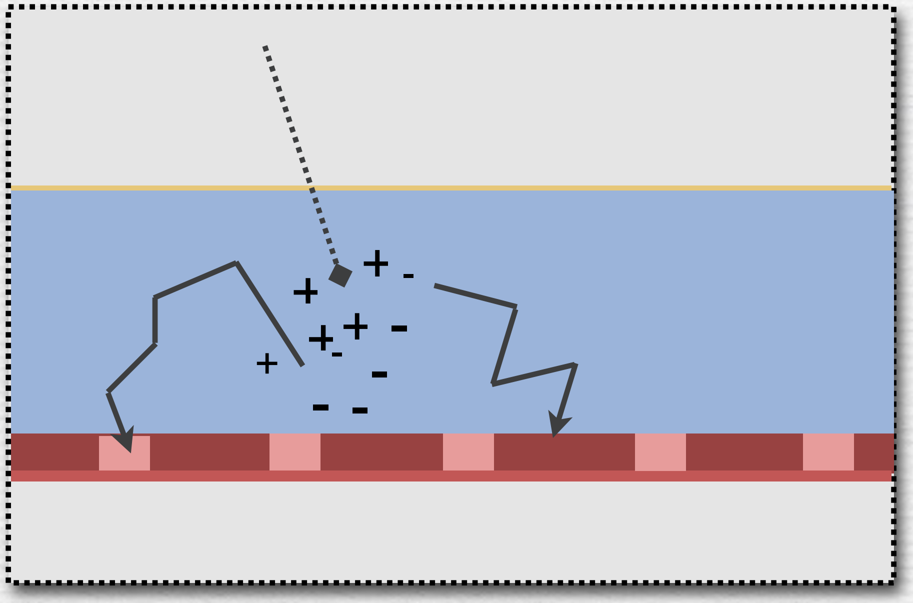
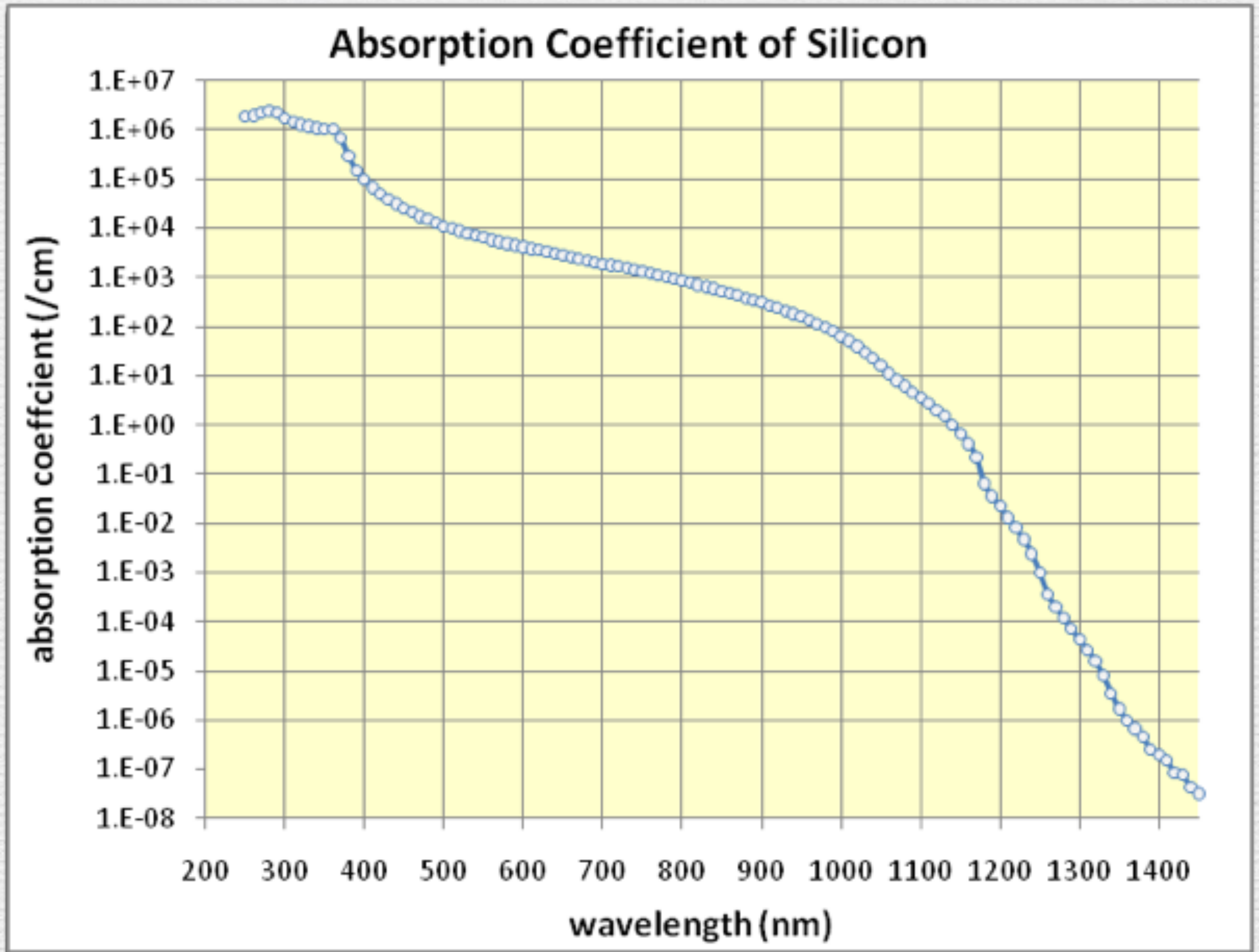


Fig. 2. Ratio of emitted light over secondary electron current versus V_{GEM} measured in He (600 mbar) + CF_4 (400 mbar) for GEMs with 45, 60 and 80 μm hole diameter.

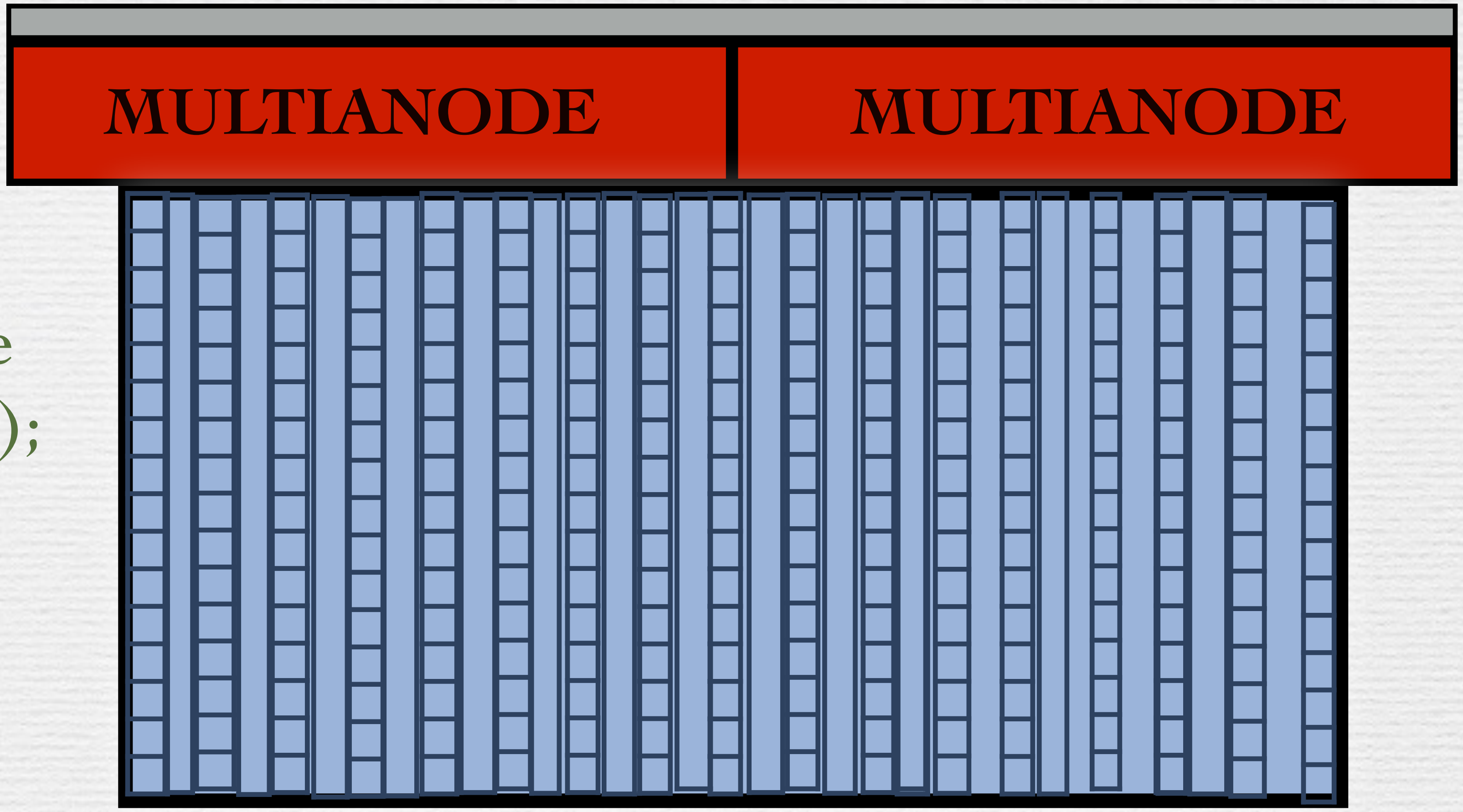
M.Marafini

MONDO Design





TRIGGER



- The trigger will be performed with Multi-anode PMTs (64 ch. 5.8 x 5.8 mm^2);

- PMTs readout chip [AGE Scientific s.r.l.]

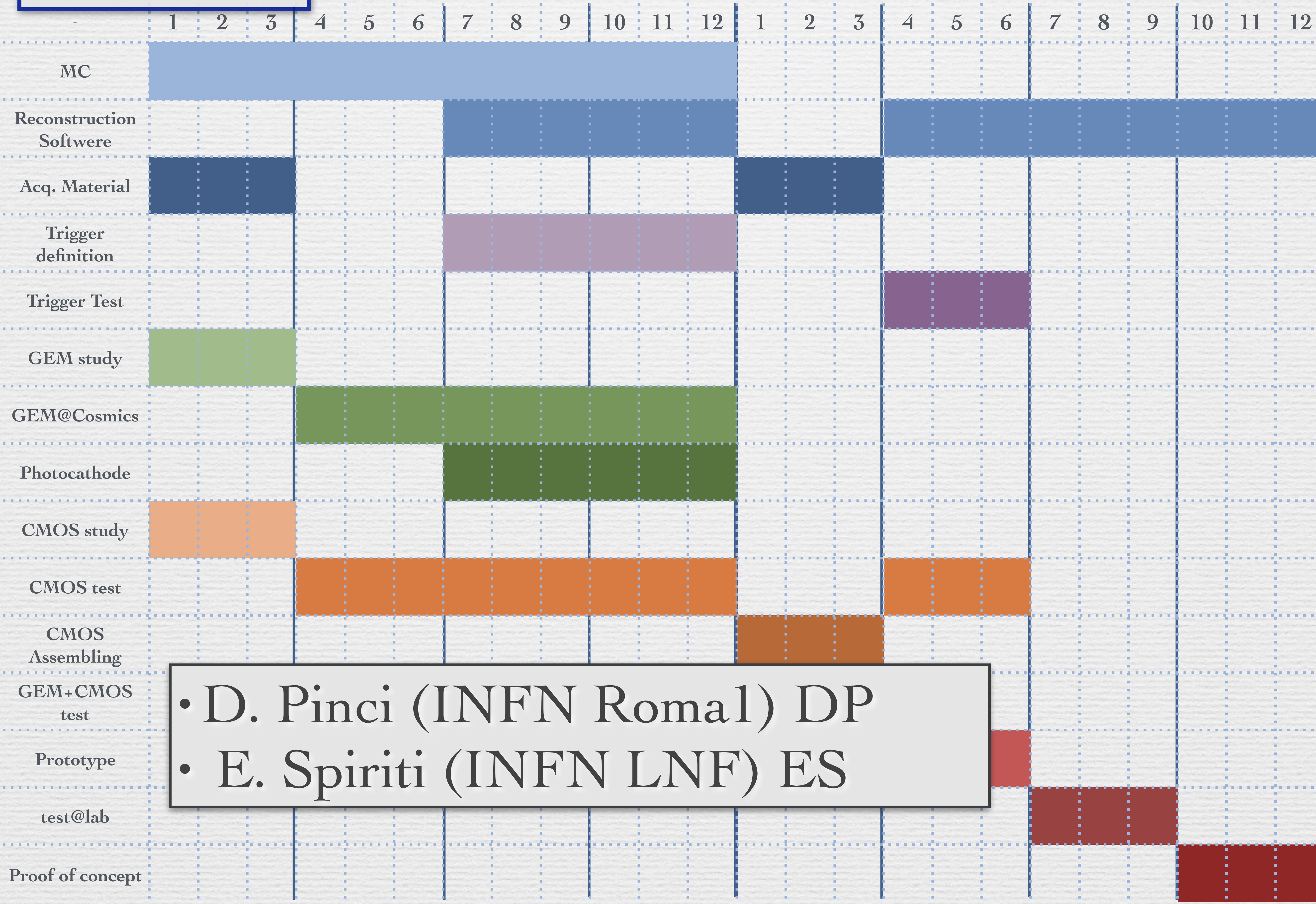
- TRIGGER STRATEGY:

=> Fast (using the first two dynodes of each PMTs)

=> Slow (logic programmable with the total information of the devices)

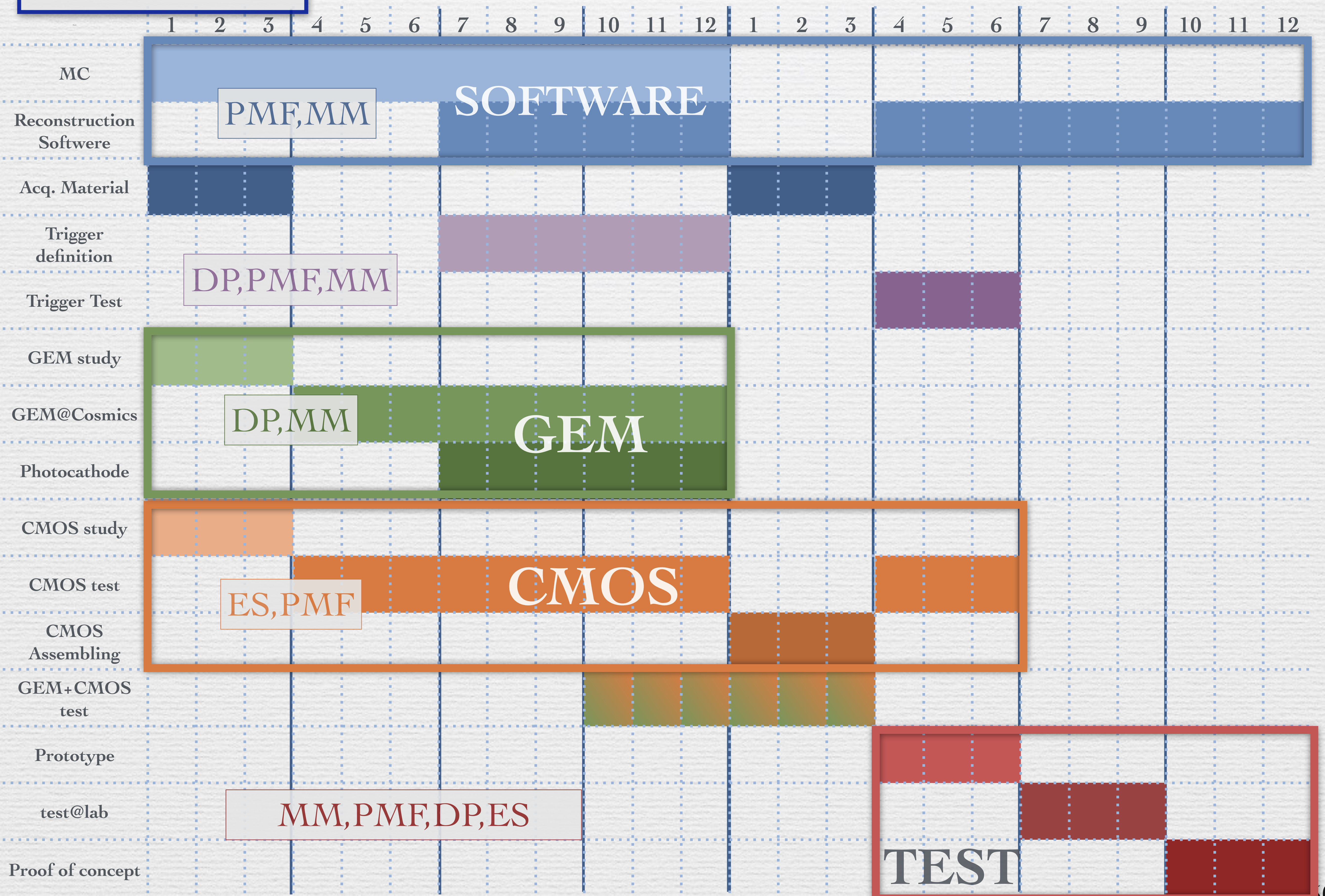
=> For the first measurements (total flux, device background study, implementation of the patter recognition, etc.) an easier one-level trigger is more coherent with the effectively man power of the project.

Timetable



- D. Pinci (INFN Roma1) DP
- E. Spiriti (INFN LNF) ES

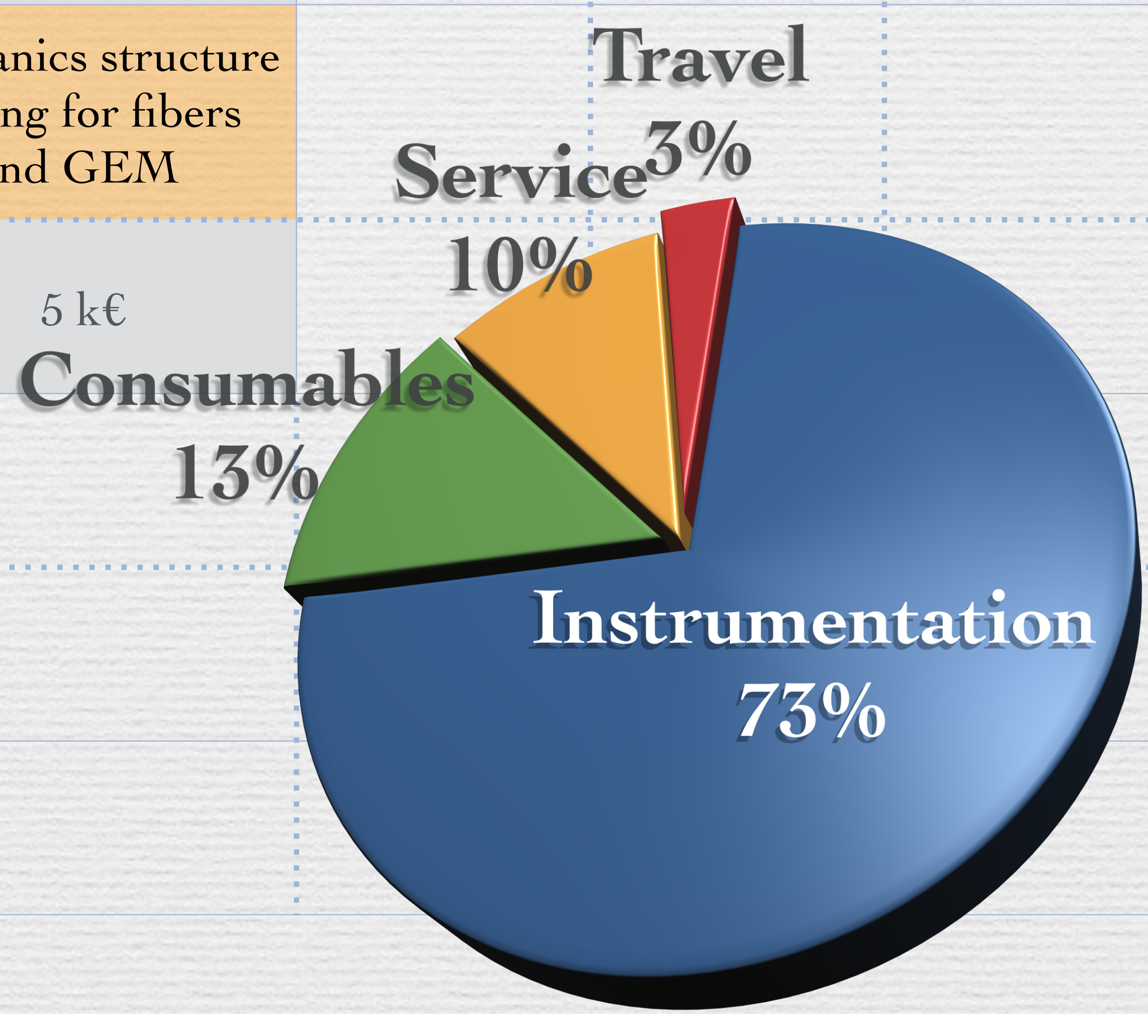
Timetable



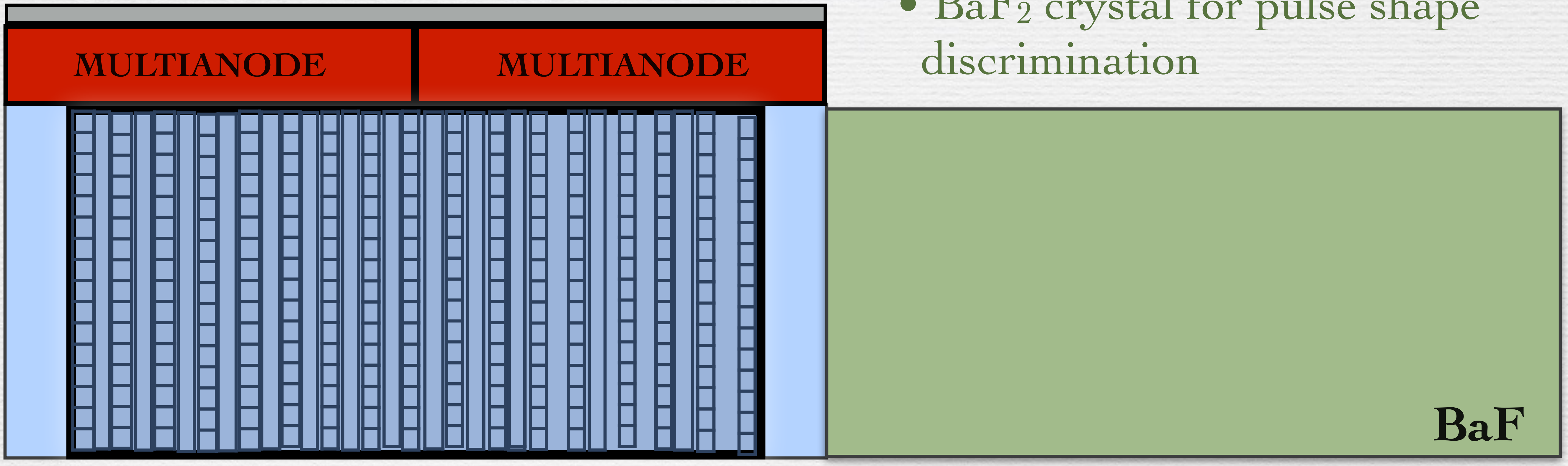
1 2 3 4 5 6 7 8 9 10 11 12 1 2 3 4 5 6 7 8 9 10 11 12
MC
Reconstruction Softwere
Acq. Material
Trigger definition
Trigger Test
GEM study
GEM@Cosmics
Photocathode
CMOS study
CMOS test
CMOS Assembling
GEM+CMOS test
Prototype
test@lab
Proof of concept
SOFTWARE
PMF,MM
DP,PMF,MM
GEM
DP,MM
CMOS
ES,PMF
TEST
MM,PMF,DP,ES

Cost Table

						Total
Instrumentation	CMOS	CMOS Readout	BaF	Multianods PMT	Commercial Electronics (CAEN)	
	60 k€	10 k€	10 k€	10 k€	20 k€	**110 k€**
Consumables	GEM + Phtocathode	Fibres				
	15 k€	5 k€				**20 k€**
Services	HV, LV, cables, gas	Mechanics structure tooling for fibers and GEM				
	10 k€	5 k€				**15 k€**
Travel	Mission and Test Beam					
	5 k€					**5 k€**
MONDO BUDGET						**150 k€**



TEST SYSTEM



- BaF_2 crystal for pulse shape discrimination

Simulation