Project REPARE :

Production cross-section measurement of 211 and 210 At for targeted alpha therapy

GDR: LP2i Bordeaux, 4th - 6th October, 2023

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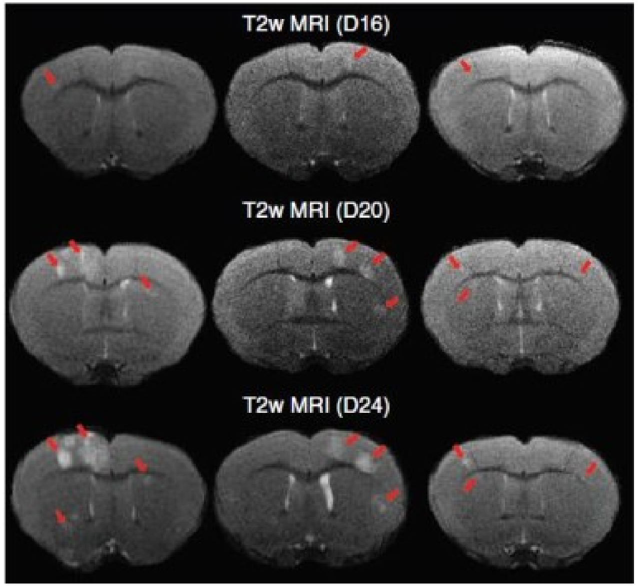
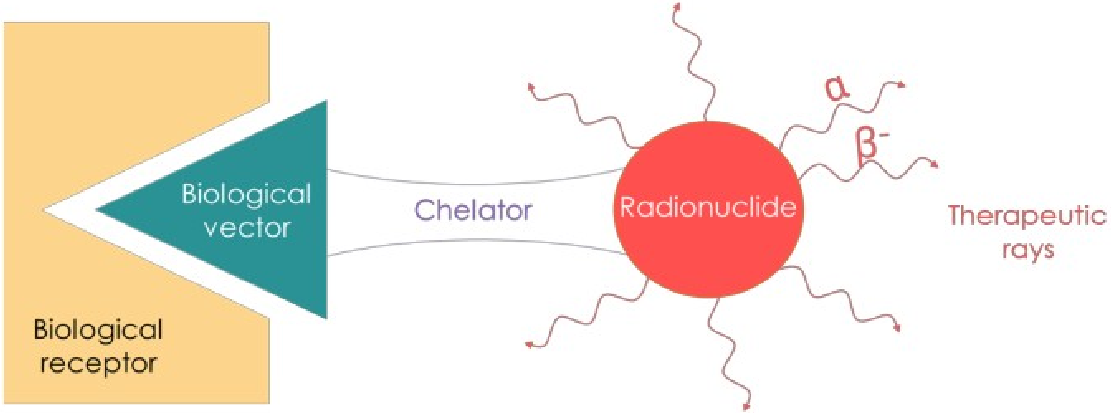
04/10/23

Targeted Radio Therapy

- Localized cancer → Surgery/ External radio therapy → Hadron therapy
- Diffused cancer → Chemotherapy / Internal Targetted Radio Therapy → using α/β emitters



Métastases cérébrales
(Corroyer 2019)



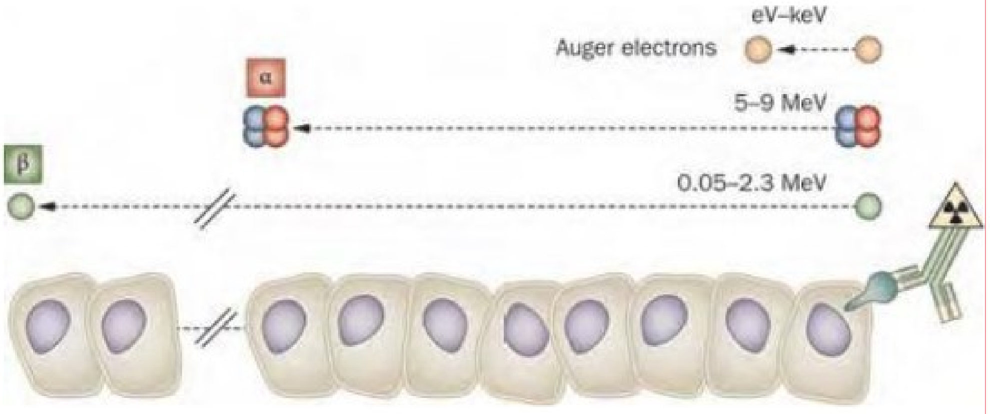
from A. Doudard seminar presentation

Targeted Alpha Therapy

- α particle are very efficient against small tumors:
  - ➔ high energy deposited: 4-9 MeV
  - ➔ high Linear Energy Transfer (LET): ~100 keV/µm

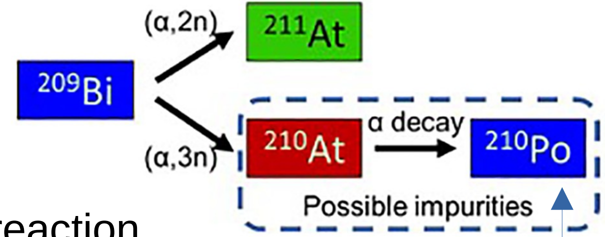
- DNA double strand breaks ++

- Oxygen Enhancement Ration (OER)
  - ➔ radioresistent cells: hypoxia



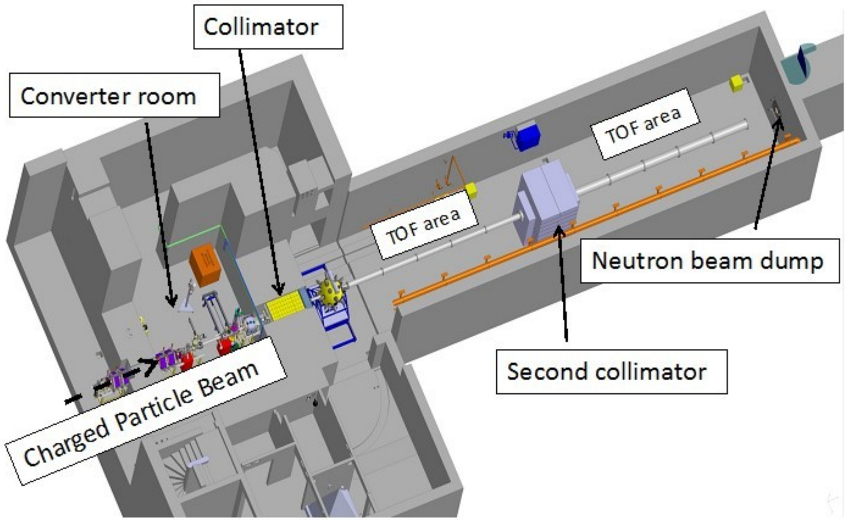
Schematic representation of Auger, *α- and β-particles range in tissue, at the cellular* scale. Source: Pouget et al. 2011.

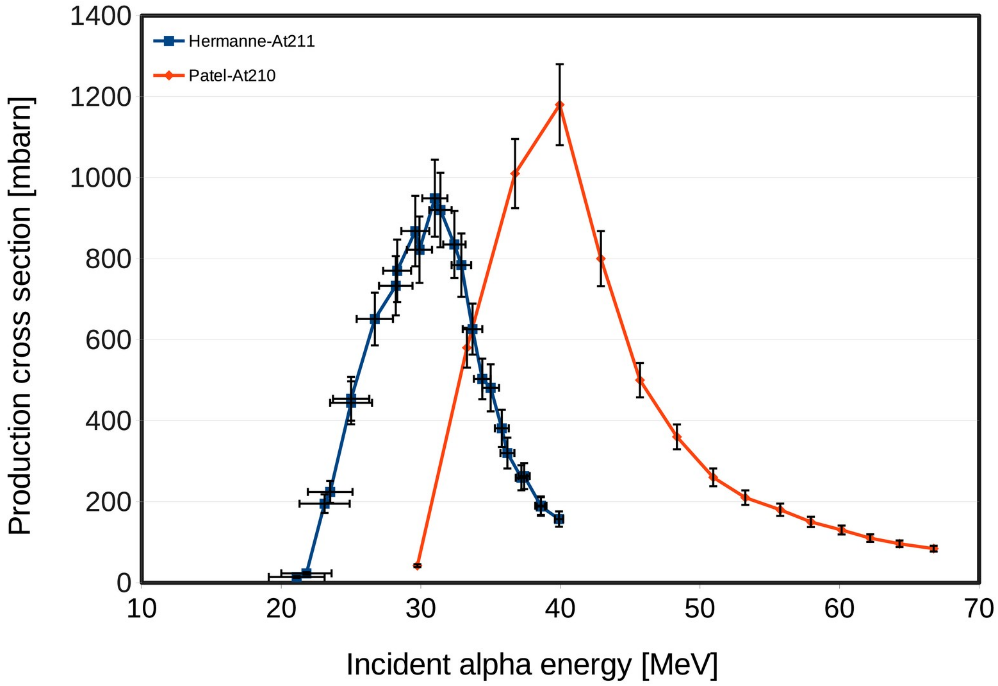
Astatine production



Polonium production

- Alpha beam at SPIRAL2, NFS for ^{211}At production → Bi(α,2n)At reaction
- Depending on the alpha energy, ^{210}At can also be produced → Bi(α,3n)At reaction





Pneumatic transfer system → developed by NPI CAS

Experimental objective

Irradiated targets

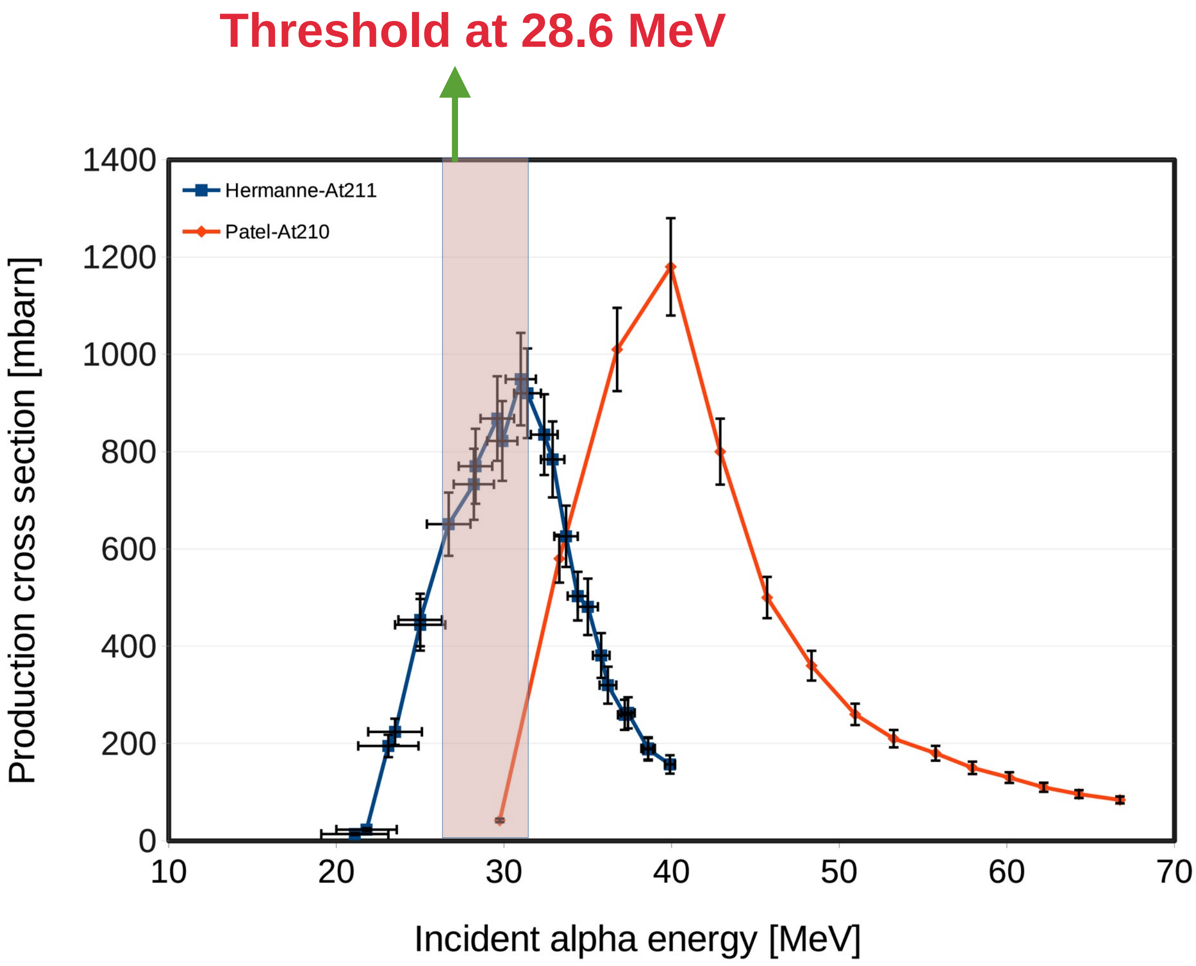
- Bi → Measure CS of At via γ-ray spectroscopy
- Cu → To cross-check flux by using known cross section from the literature

α beam

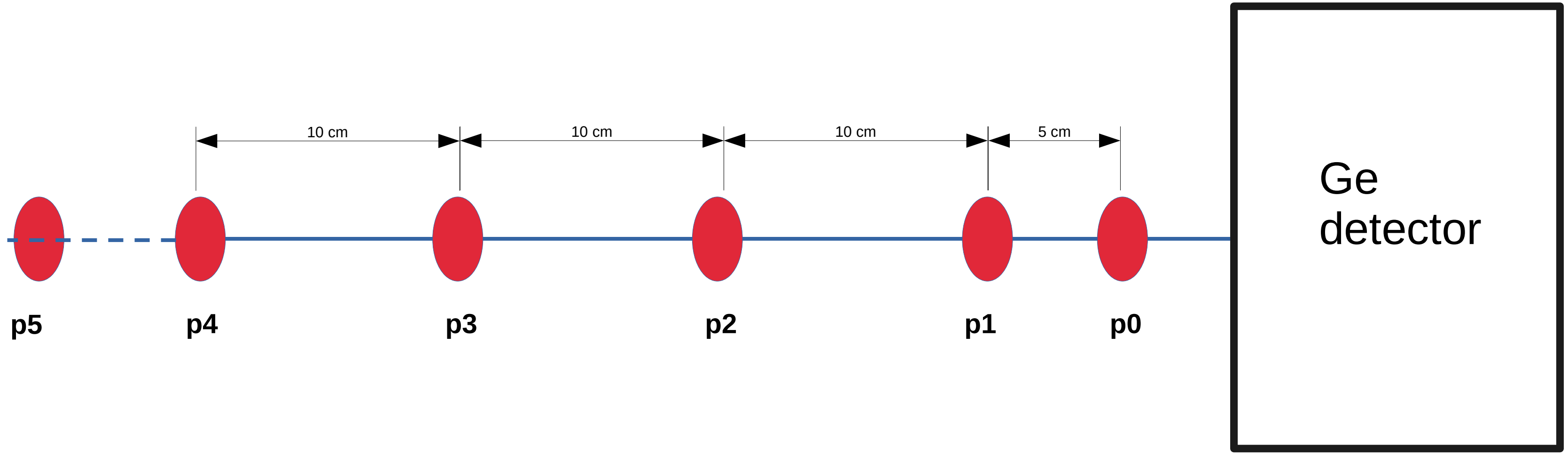
- 28 MeV < E < 31 MeV

Setup : 2 spectral measurement

- Using a Ge detector in ToF hall
- Using 2 Exogam detectors remotely

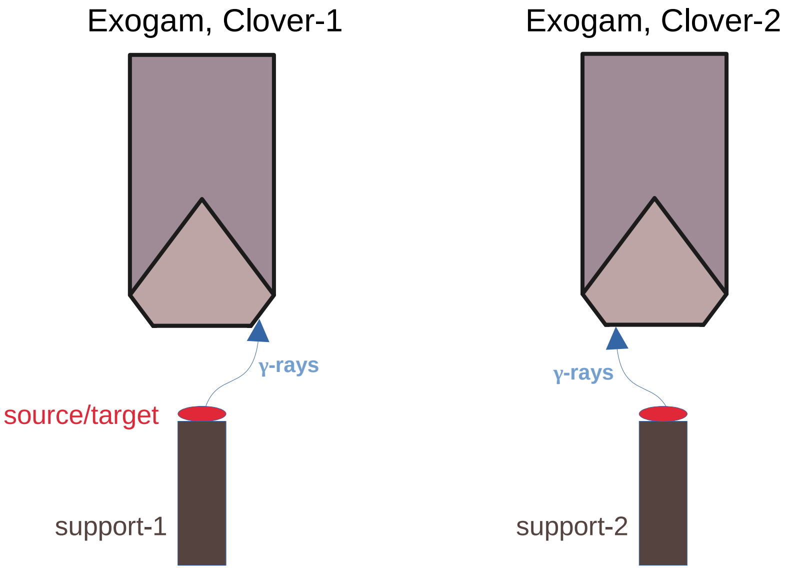


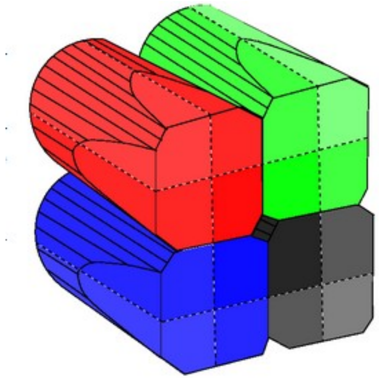
Experimental setup-1



- Bi and Cu were irradiated with alpha energy 28-31 MeV
- Measurements taken at 6 different position
- 1 Ge detector used
- Time between Irradiation and measurement: ~ 1 min to 22 mins, for different Bi targets.

Experimental setup-2



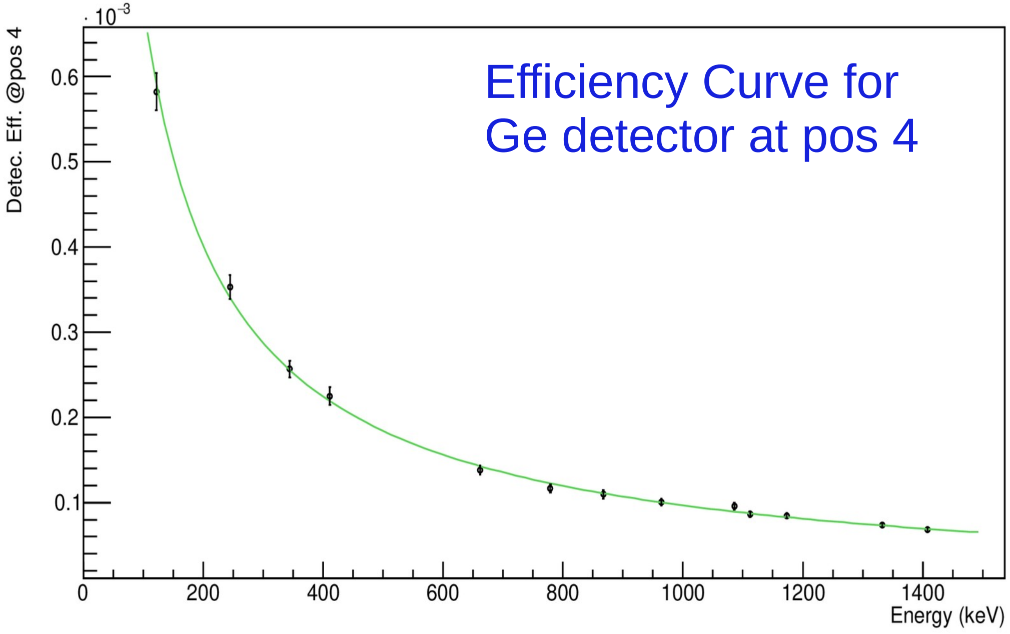

Exogam clover: 4 crystals

- Bi and Cu were irradiated with alpha energy 28-31 MeV
- Measurements taken with 2 Exogam clovers
- Different targets were placed under each clover
- Time between Irradiation and measurement: ~ several hours

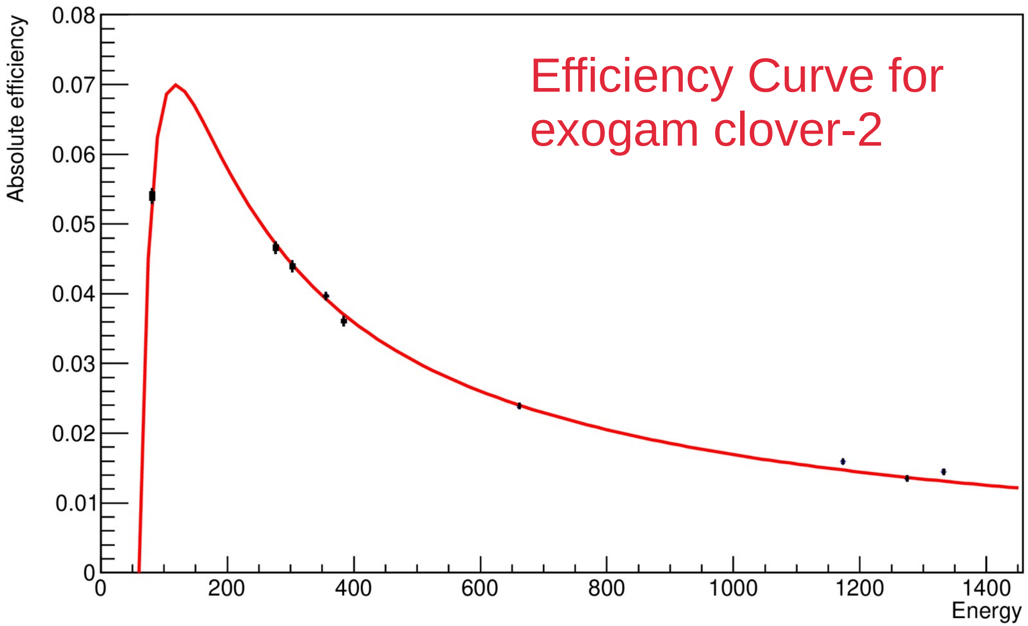
Energy and Efficiency Calibration

Sources used:

^{60}Co, ^{137}Cs, ^{88}Y and ^{152}Eu for Ge detector (TOF room)
^{60}Co, ^{137}Cs, ^{22}Na, ^{133}Ba for Exogam clovers



Efficiency is 0.15% @ pos 0 for 687 keV from ^{211}At



Efficiency is 2.3% for 687 keV from ^{211}At

Analysis

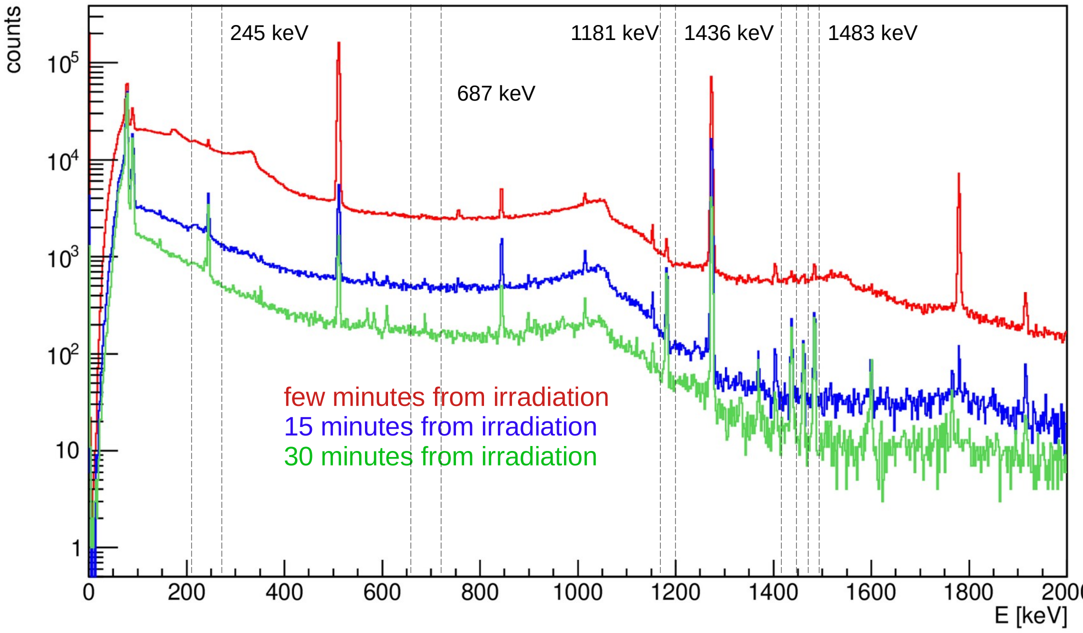
Nuclei	Energy [keV]	BR
^{210}At	245	0.69
^{210}At	1181	0.99
^{210}At	1436	0.29
^{210}At	1483	0.465
^{211}At	687	0.00245

γ-spectrum from 2 different setups

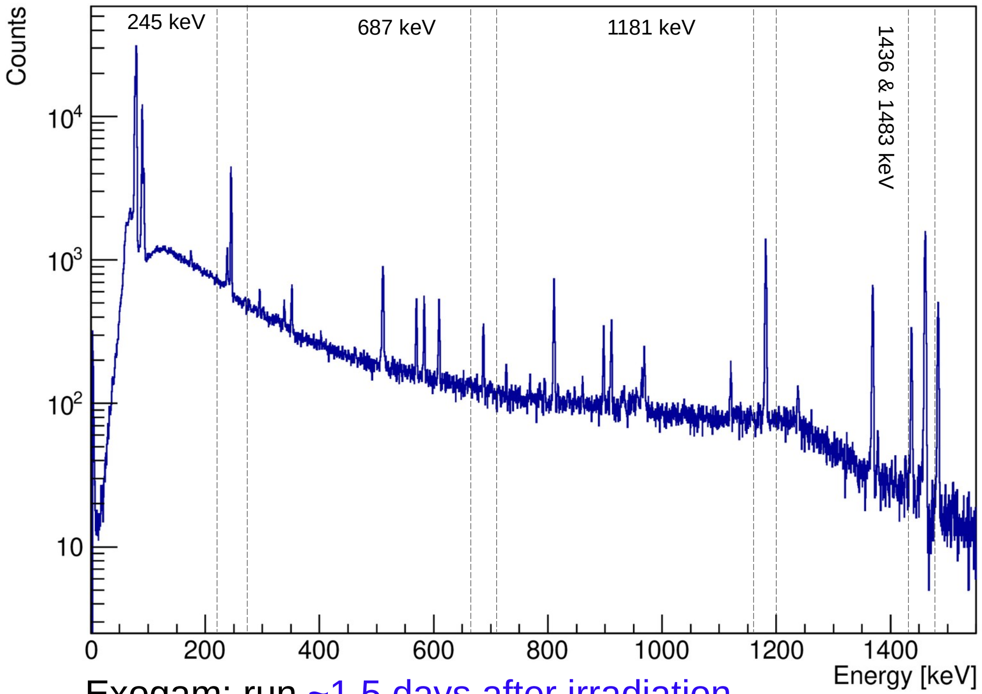
^{210}At $T_{1/2}$ = 8.1 h
^{211}At $T_{1/2}$ = 7.2 h

^{209}Bi spectrum

Same Bi target with different times between irradiation and measurements



Ge (ToF room)



Exogam: run ~1.5 days after irradiation

Cross section measurement

$$A_{ct} = \frac{\lambda}{\left(e^{-\lambda t_1} - e^{-\lambda t_2}\right)} \times \frac{M}{r \times \epsilon}$$

$$\sigma = \frac{A_{ct}}{\phi \cdot \chi \cdot \left(1 - e^{-\lambda \cdot t_{irr}}\right)} \cdot \frac{A}{N_A \cdot M_S}$$

First approximation: $\phi = \frac{I_{CF}}{C \cdot 2 \cdot e}$

I_{CF}: current measured by the faraday cup	$[1.10^{10}\ C.s^{-1}]$
C: calibration factor , C =1.10^{10}	$[s^{-1}]$
e: the elementary charge	[C]

A_{ct}: Activity at the end of the irradiation

λ: radioactive decay constant of the isotope $[s^{-1}]$

t1,t2: time between irradiation end and Acqu. Start & stop

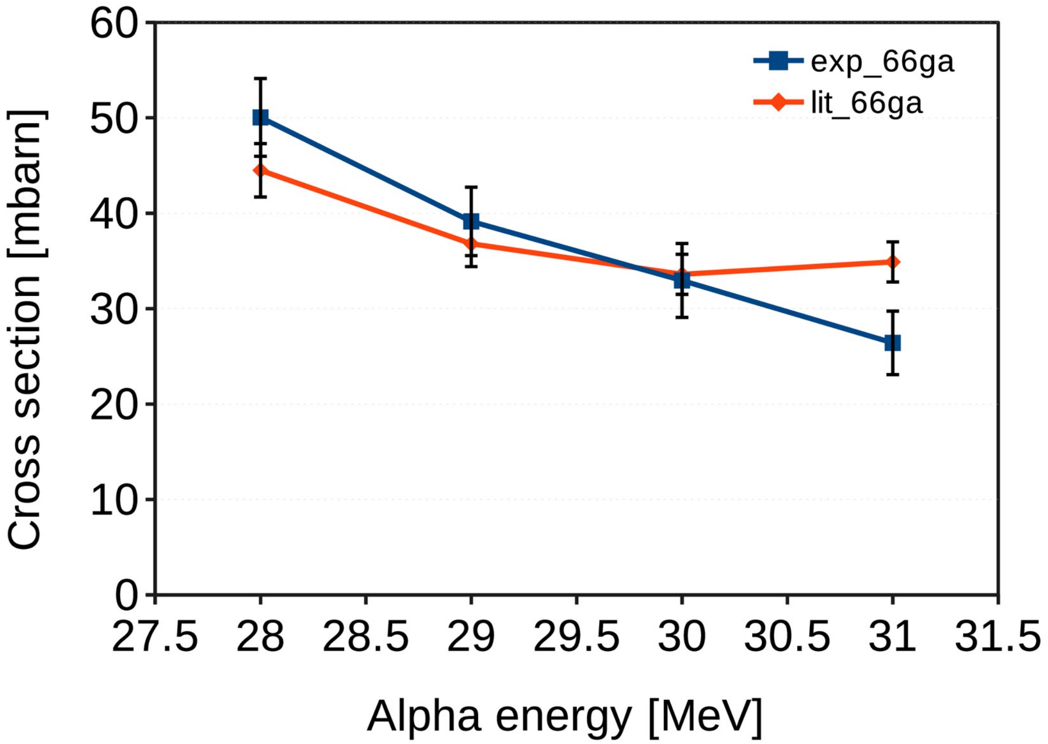
M: Number of detected γ-rays

r: branching ratio of the measured γ-ray

ϵ: detection efficiency at the corresponding energy

σ: cross section	[b]
ϕ: incident particle fluence	$[s^{-1}]$
χ: chemical purity of the target	
t_{irr}: Irradiation duration	[s]
A: Target atomic mass	$[g.mol^{-1}]$
N_A: Avogadro constant	$[mol^{-1}]$
Ms: Target surface mass	$[g.cm^{-2}]$

Flux 2nd approximation using lit. Copper CS

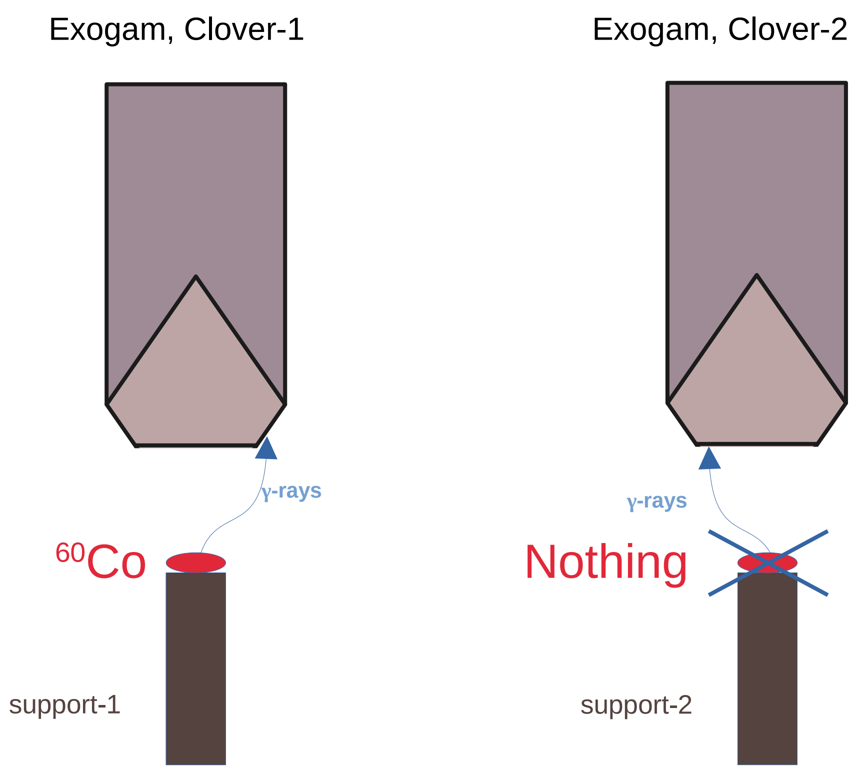


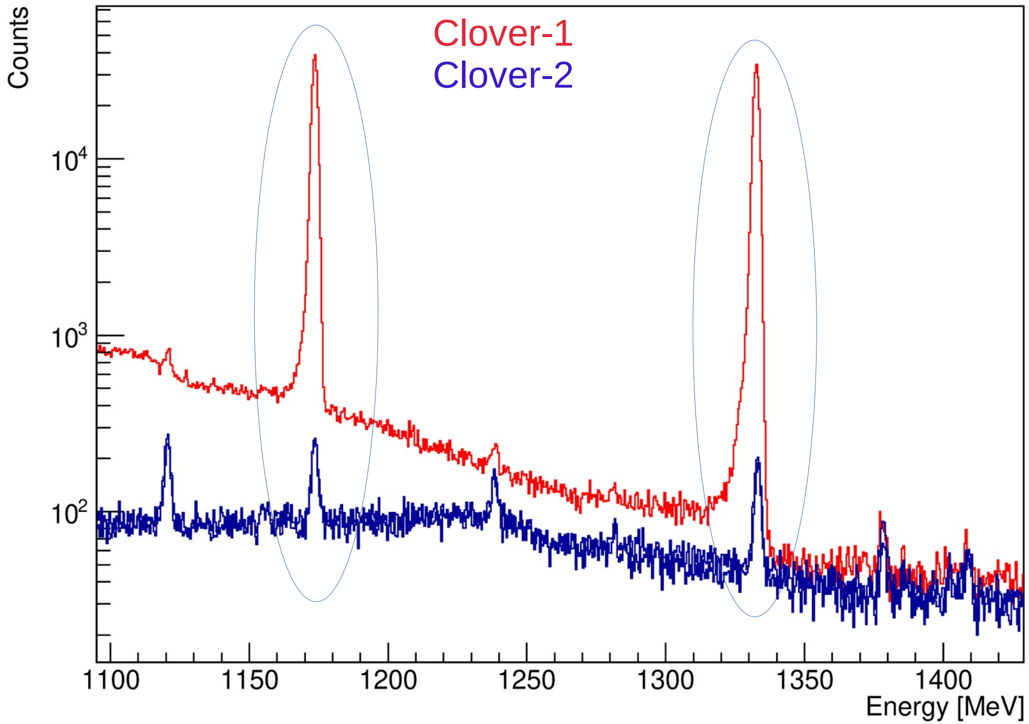
- Ratio between the Lit. and Exp. flux values:

  @ 28 MeV: 0.89
  @ 29 MeV: 0.94
  @ 30 MeV: 1.01
  @ 31 MeV: 1.32

- Flux calculated by using 1st approximation (current measured by faraday cup) is rather close to the one calculated from the literature CS of Cu.

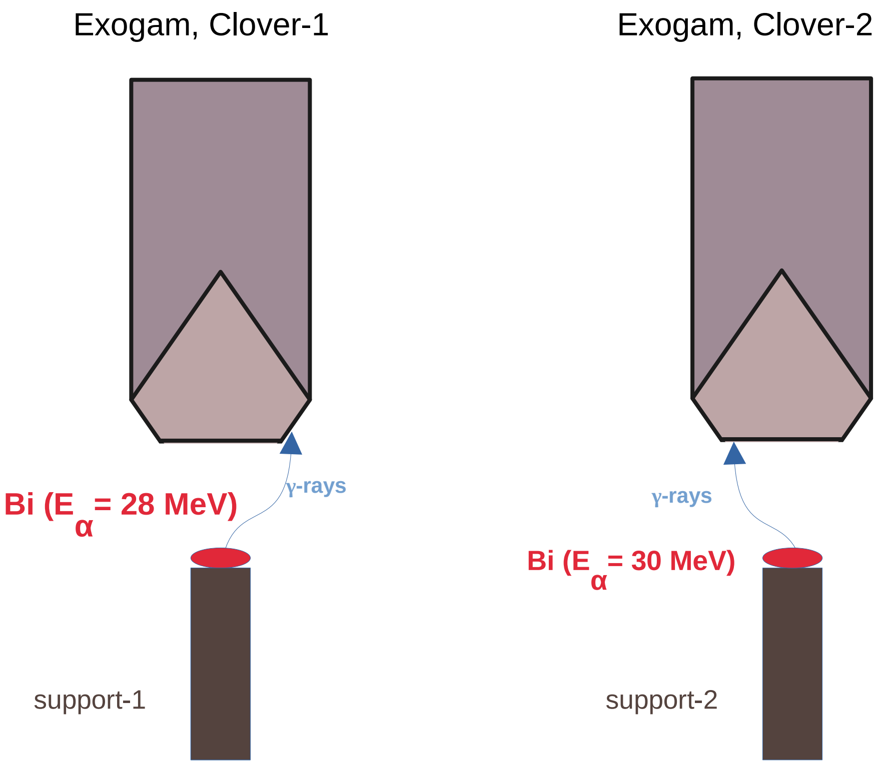
“Cross talk” between 2 clovers

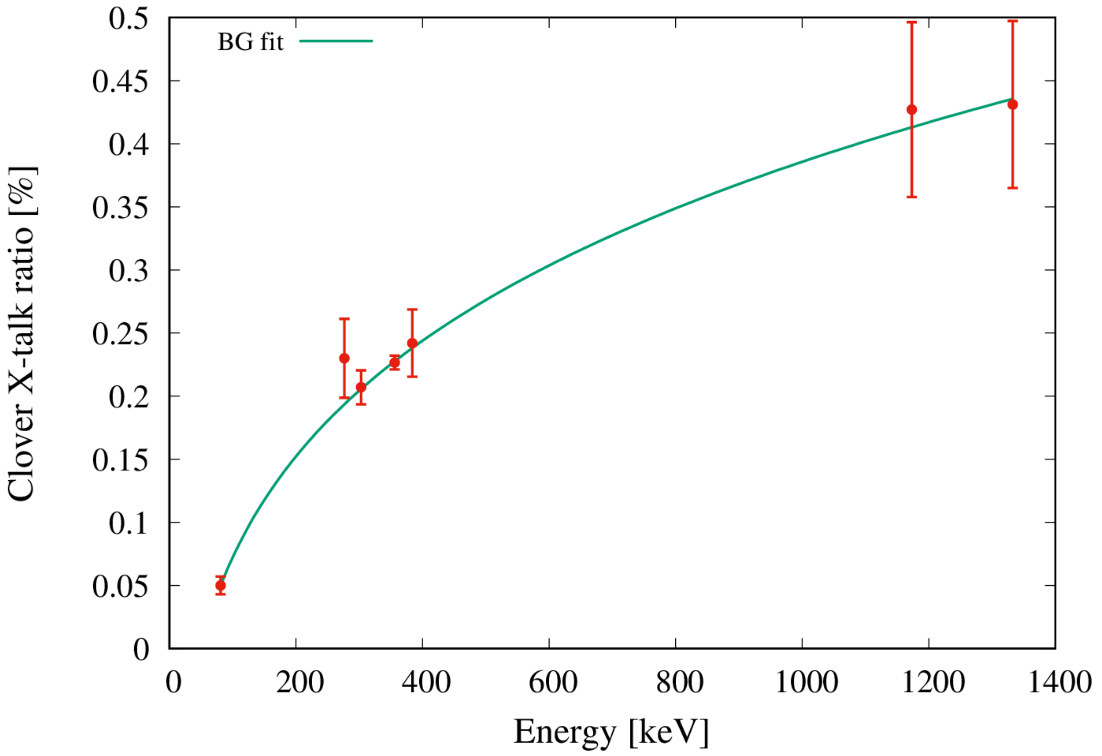




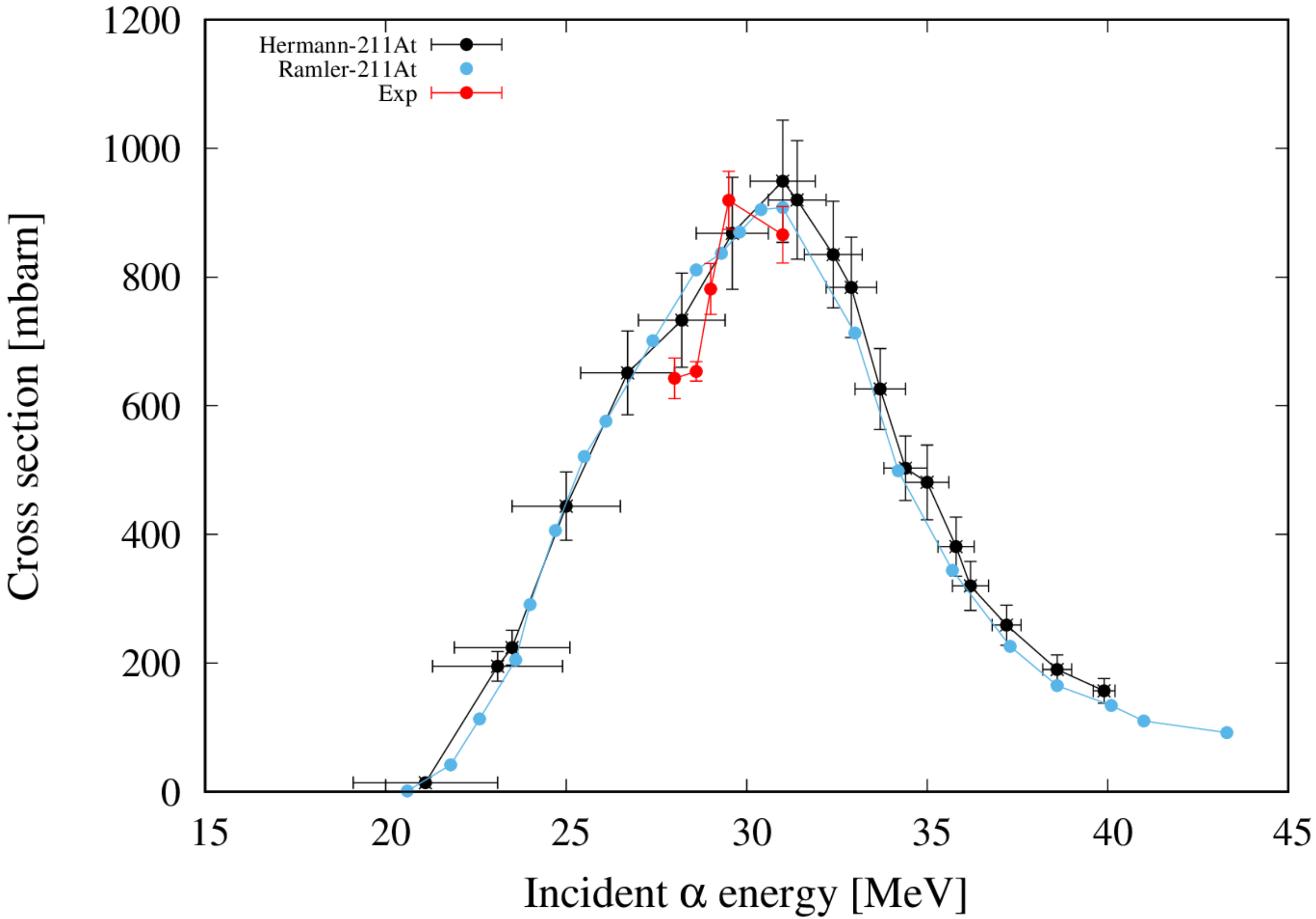
0.3% of counts from Co peaks of clover 1 in clover 2

“Cross talk” between 2 clovers





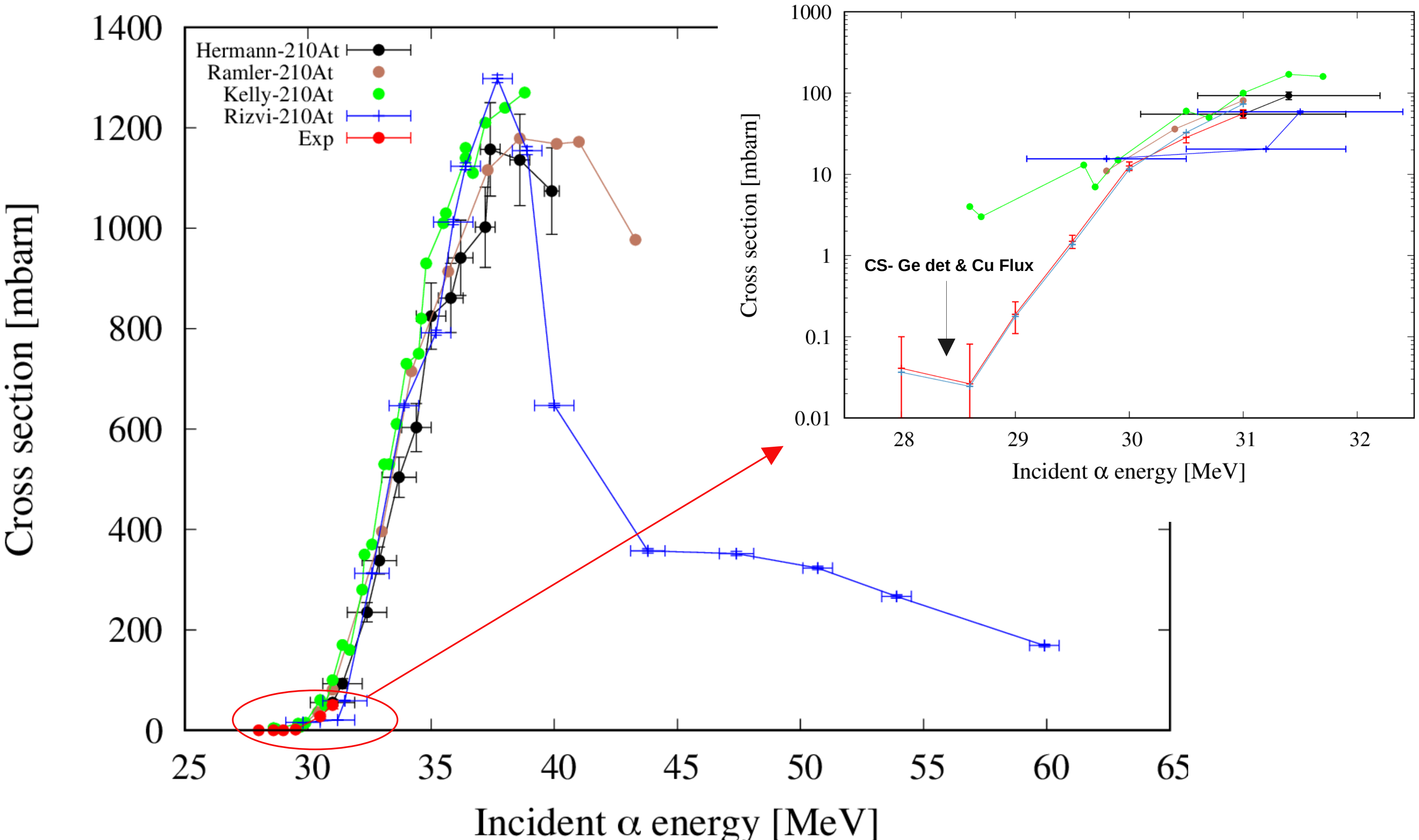
^{211}At production cross-sections using Exogam



Preliminary

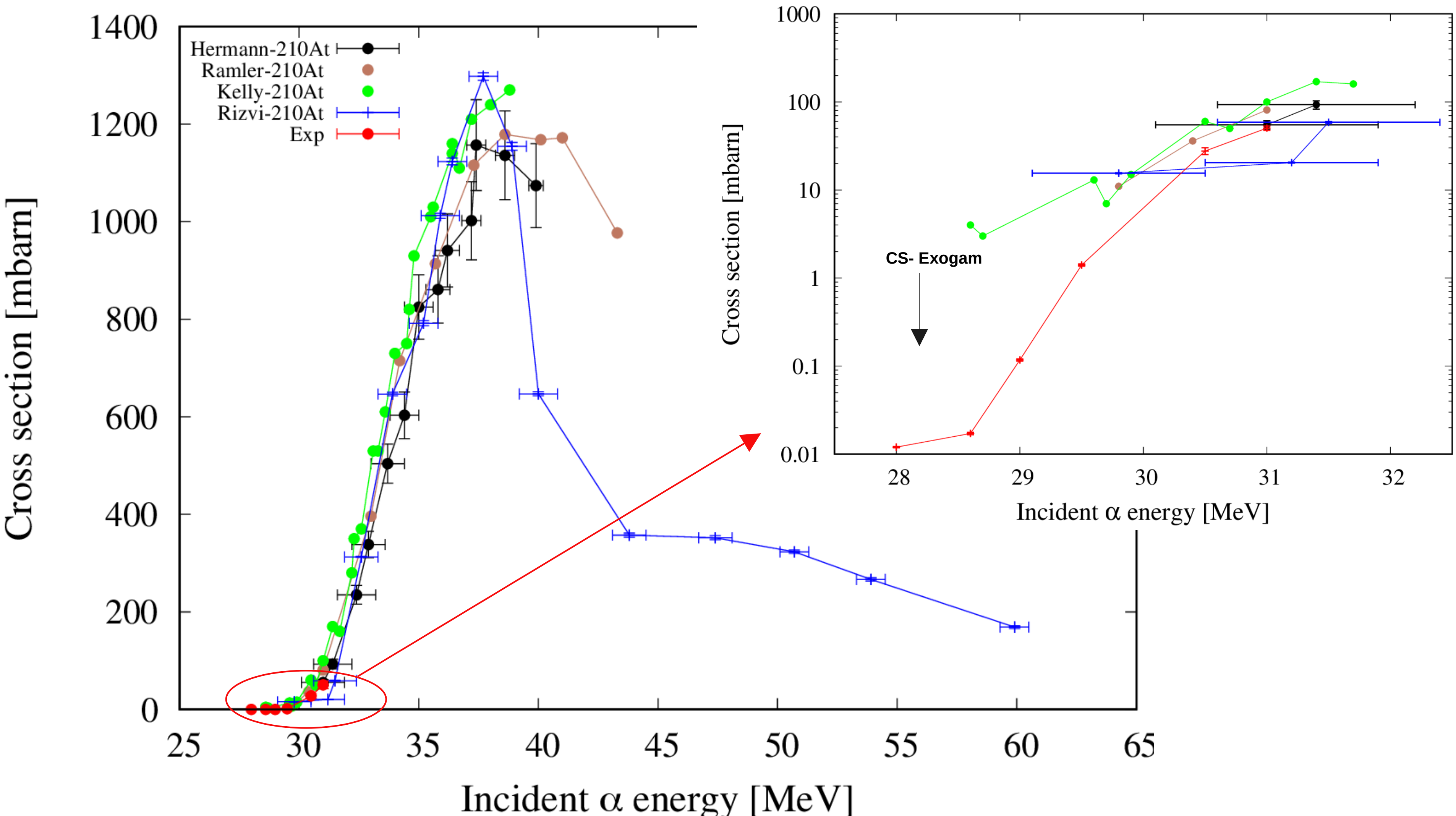
^{210}At production cross-sections from Ge detector (ToF room) & using Cu flux

Preliminary



^{210}At production cross-sections using Exogam

Preliminary



Conclusion

- Successfully measured the cross-section of both ^{211}At and its contaminant, ^{210}At at critical incident alpha energies.

- These accurate CS measurements will allow us to determine optimal energy to produce ^{211}At with least amount of contribution from ^{210}At.

- First production studies of Astatine at NFS open doors for a broad and continued interdisciplinary collaboration with french laboratories, Cyceron, Arronax and Subatech in TAT.

- These first results are promising first steps for the integration of ^{211}At at a preclinical level.

Thank you!

Error Propagation

$$\delta\sigma^2 = f\left(\delta\lambda, \delta M, \delta r, \delta\epsilon, \delta\phi\right)$$

$$\delta\sigma^2 = \overbrace{\left(\frac{\partial\sigma}{\partial\lambda}\right)^2 \delta\lambda^2}^{1^{st}\,term} + \overbrace{\left(\frac{\partial\sigma}{\partial M}\right)^2 \delta M^2}^{2^{nd}\,term} + \overbrace{\left(\frac{\partial\sigma}{\partial r}\right)^2 \delta r^2}^{3^{rd}\,term} + \overbrace{\left(\frac{\partial\sigma}{\partial\epsilon}\right)^2 \delta\epsilon^2}^{4^{th}\,term} + \overbrace{\left(\frac{\partial\sigma}{\partial\phi}\right)^2 \delta\phi^2}^{5^{th}\,term}$$

$$\delta\sigma^2 = \frac{\sigma}{\lambda}\left[1 - \lambda\frac{\left(-t_1 e^{-\lambda t_1} + t_1 e^{-\lambda t_2}\right)}{\left(e^{-\lambda t_1} - e^{-\lambda t_2}\right)} + \frac{t_{irr} e^{-\lambda t_{irr}}}{1 - e^{-\lambda t_{irr}}}\right]^2 \cdot \delta\lambda^2 + \left(\frac{\sigma}{M}\right)^2 \cdot \delta M^2 + \left(\frac{\sigma}{r}\right)^2 \cdot \delta r^2 + \left(\frac{\sigma}{\epsilon}\right)^2 \cdot \delta\epsilon^2 + \left(\frac{\sigma}{\phi}\right)^2 \cdot \delta\phi^2$$

Backup slide