Five Years of Applications of EXOCTIC radioactive ion beams at ISOLDE

new tools, new ideas, new people

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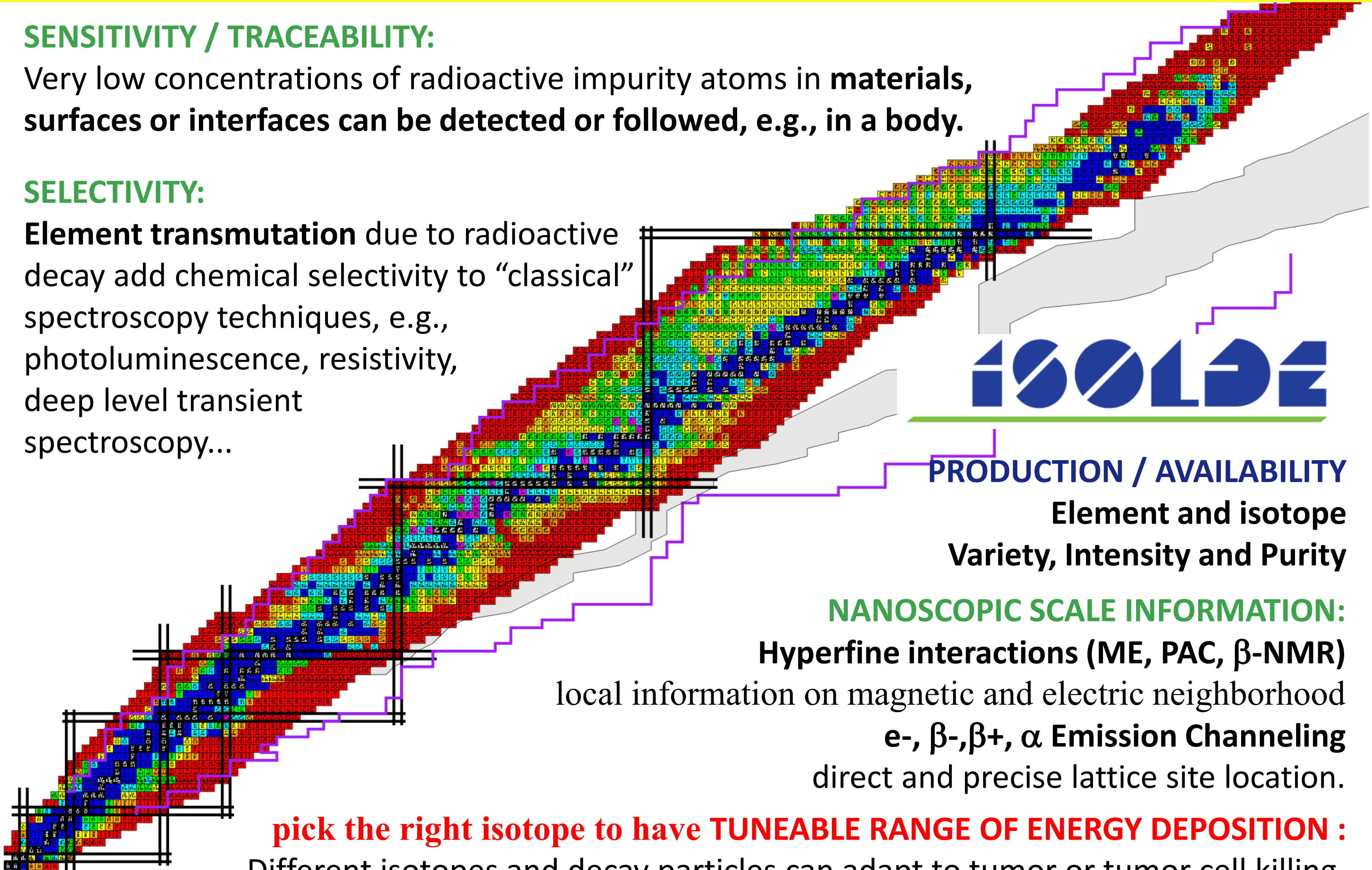
“APPLICATIONS” OF EXOTIC RADIOACTIVE BEAMS

Presenting a review of today’s offer...

- What is working and is new ...
  - What is useful and ... usable
    - Who are the users ...
      - Where ...

... aiming to work better in 10 – 15 years !

KEY Features for Sustainability of RIB Applications



SENSITIVITY / TRACEABILITY:

Very low concentrations of radioactive impurity atoms in **materials, surfaces or interfaces can be detected or followed, e.g., in a body.**

SELECTIVITY:

Element transmutation due to radioactive decay add chemical selectivity to “classical” spectroscopy techniques, e.g., photoluminescence, resistivity, deep level transient spectroscopy...

PRODUCTION / AVAILABILITY

Element and isotope Variety, Intensity and Purity

NANOSCOPIC SCALE INFORMATION:

Hyperfine interactions (ME, PAC, β-NMR)

local information on magnetic and electric neighborhood

e-, β-,β+, α Emission Channeling

direct and precise lattice site location.

pick the right isotope to have TUNEABLE RANGE OF ENERGY DEPOSITION :

Different isotopes and decay particles can adapt to tumor or tumor cell killing.

ISOLDE

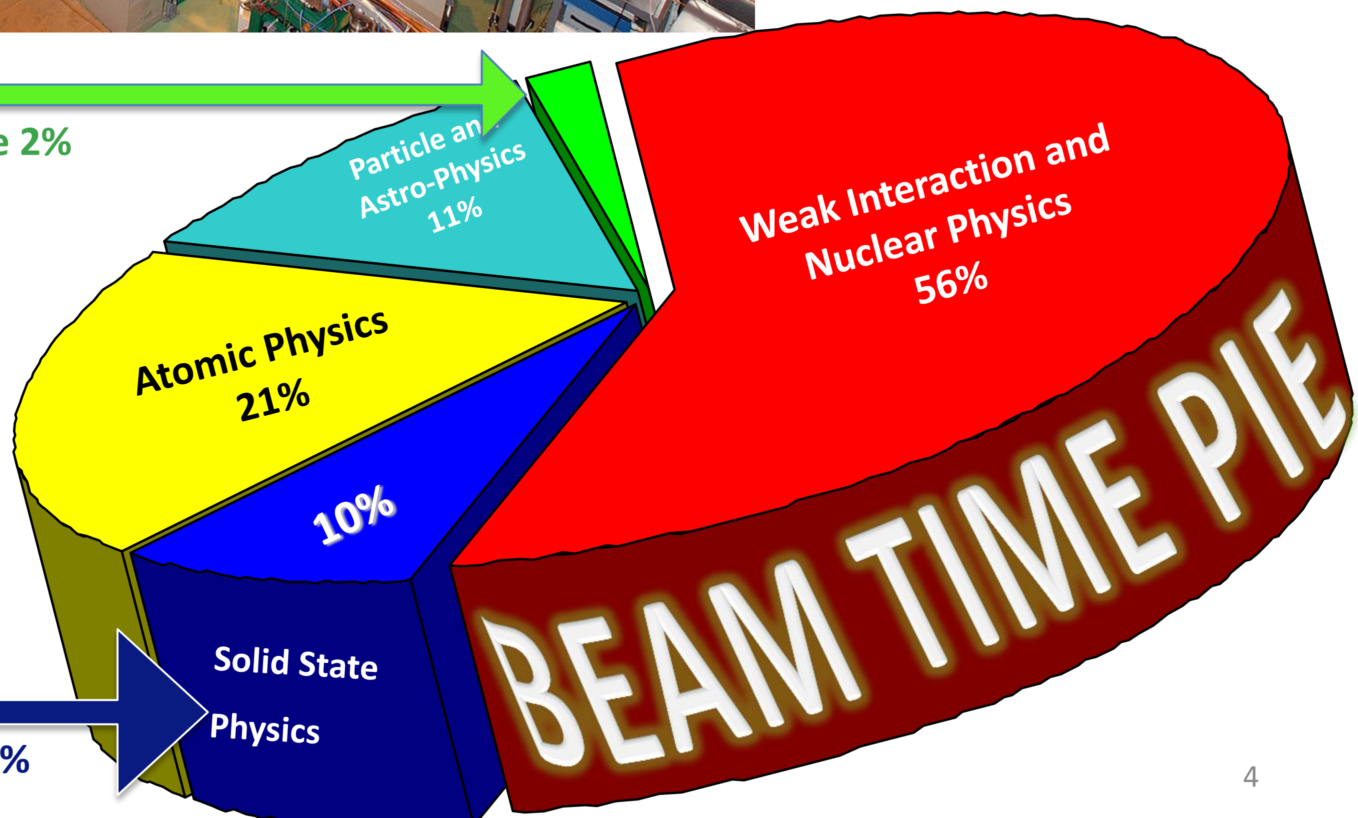
2011

37 Experiments
300 Users
96 Institutes
22 Countries
235 8h-shifts of radioactive beams

Biology/Medicine 2%

University Hospitals
Universities
Research Institutes

Material's research 10%



SSP + BIO @ ISOLDE: Diverse community

Running experiments/letters of intent	24
Participating countries	26
Scientists	160

Current and PROSPECTIVE Work using EXOTIC Radioactive isotopes

→ THINKING Materials and Molecular Properties ←

dealing with mass, electromagnetism, many body systems and scaling

Atomic-like information is the aim !

→ Semiconductor Physics (Si, Oxides, organic compounds)

→ Multi- ferroic- magnetic, Superconductors (correlated parameters}

→ Nanomaterials (geometry, downsizing and integration)

→ Surfaces and interfaces (bulk properties are modified)

→ Soft matter : liquid crystals and graphen,

→ Bio / Molecular chemistry and physics

→ THINKING Life Sciences ←

optimizing delivering and range of deposition of highly concentration of energy upon radioactive decay into the living body or cell of interest.

Enlarging the choices of radioisotopes is the aim !

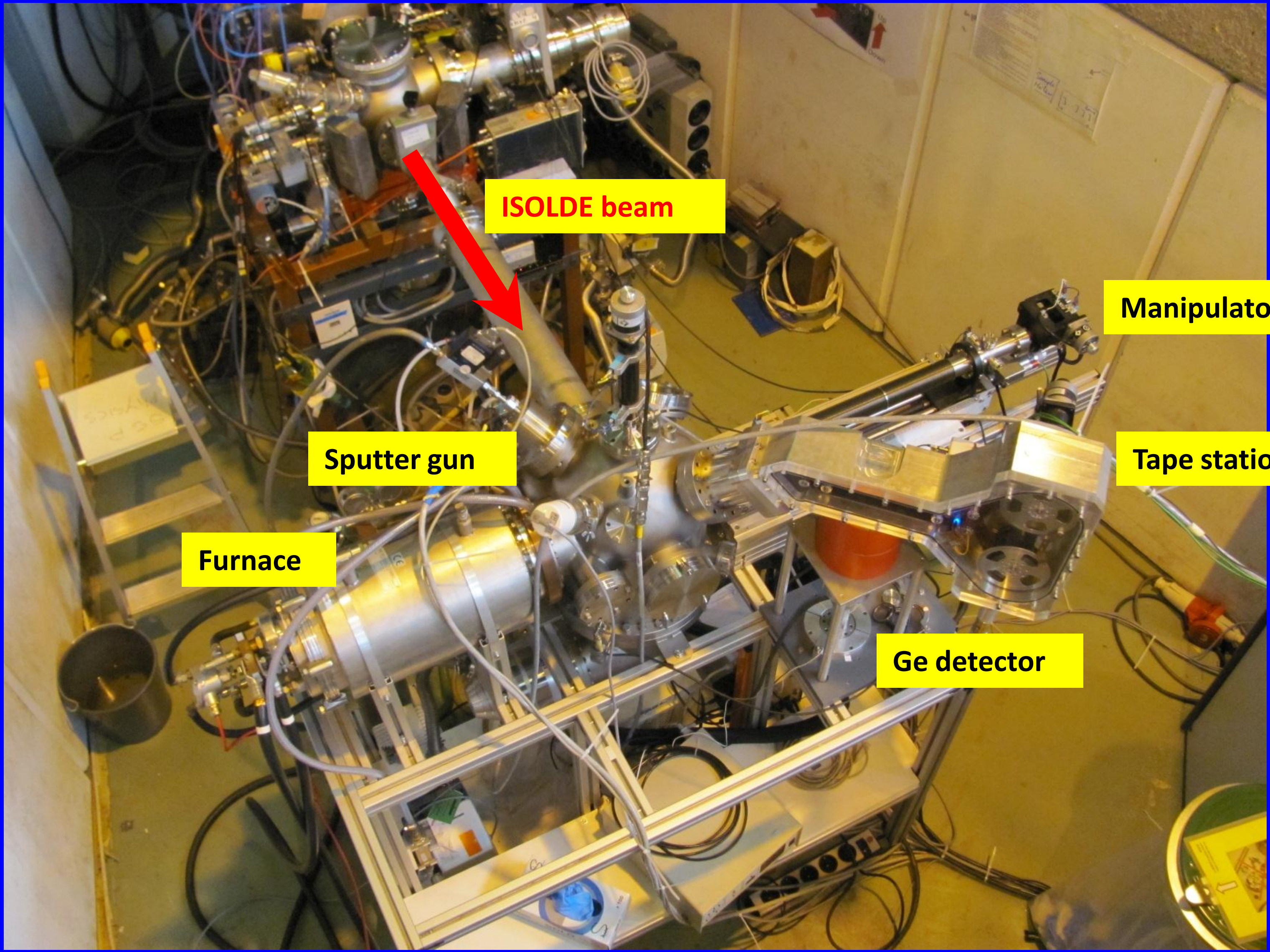
→ NEW isotopes and decay modes for diagnosis and treatments.

RECENT DEVELOPMENTS

A commitment for the future based on facts !

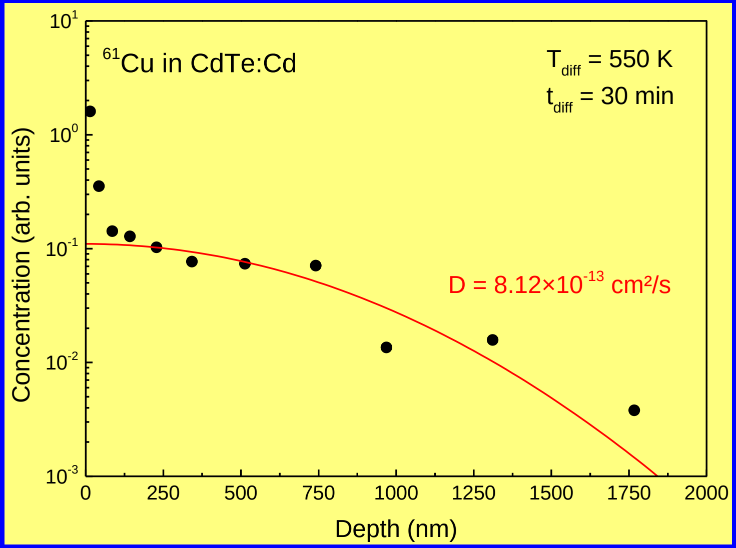
On-line diffusion chamber at ISOLDE

2011



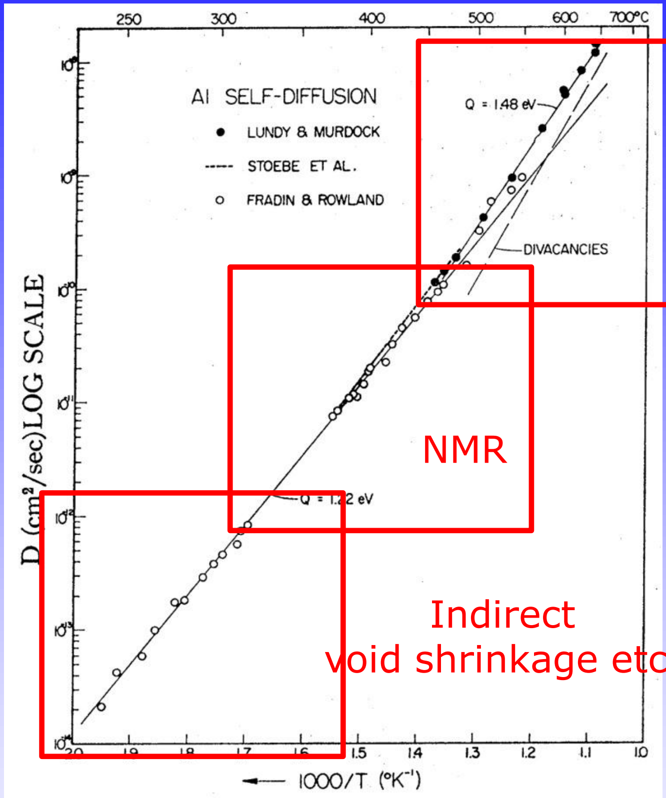
Understanding Diffusion and self diffusion ... On-line !

^{61}Cu (3.3h) diffusion in Cd saturated CdTe



Isotope	$t_{1/2}$	Detection
^{38}Cl	37.3 min	$\beta^-_{4800keV}$; $\gamma_{2168keV}$
^{11}C	20.38 min	β^+ ; γ_{511keV}
^{13}N	9.96 min	β^+ ; γ_{511keV}
^{29}Al	6.6 min	$\gamma_{1273keV}$
(^{15}O)	122 s	β^+ ; γ_{511keV}

Unknown Aluminum self diffusion



(T.G.Stoebe *et al*., Phys. Rev. 166 (1968) 621)

- Single stable Al isotope: no SIMS measurements
  Unknown activation energy of self diffusion in Al
- Unknown role of vacancies, di-vacancies at different temperatures.
- Unknown Al diffusion in Al-based compounds

From the Avogadro Project : define Kg in terms of number of Si atoms...

$$N_A = \frac{V_{mol}}{V_o}.$$

$$N_A = \frac{V_{mol}}{(a^3/n)},$$

$$N_A = \frac{M_{Si}}{m} \frac{V}{(a^3/8)},$$

Scientific American
295, 102 – 109 (2006)

PL + L-DLTS apparatus at ISOLDE

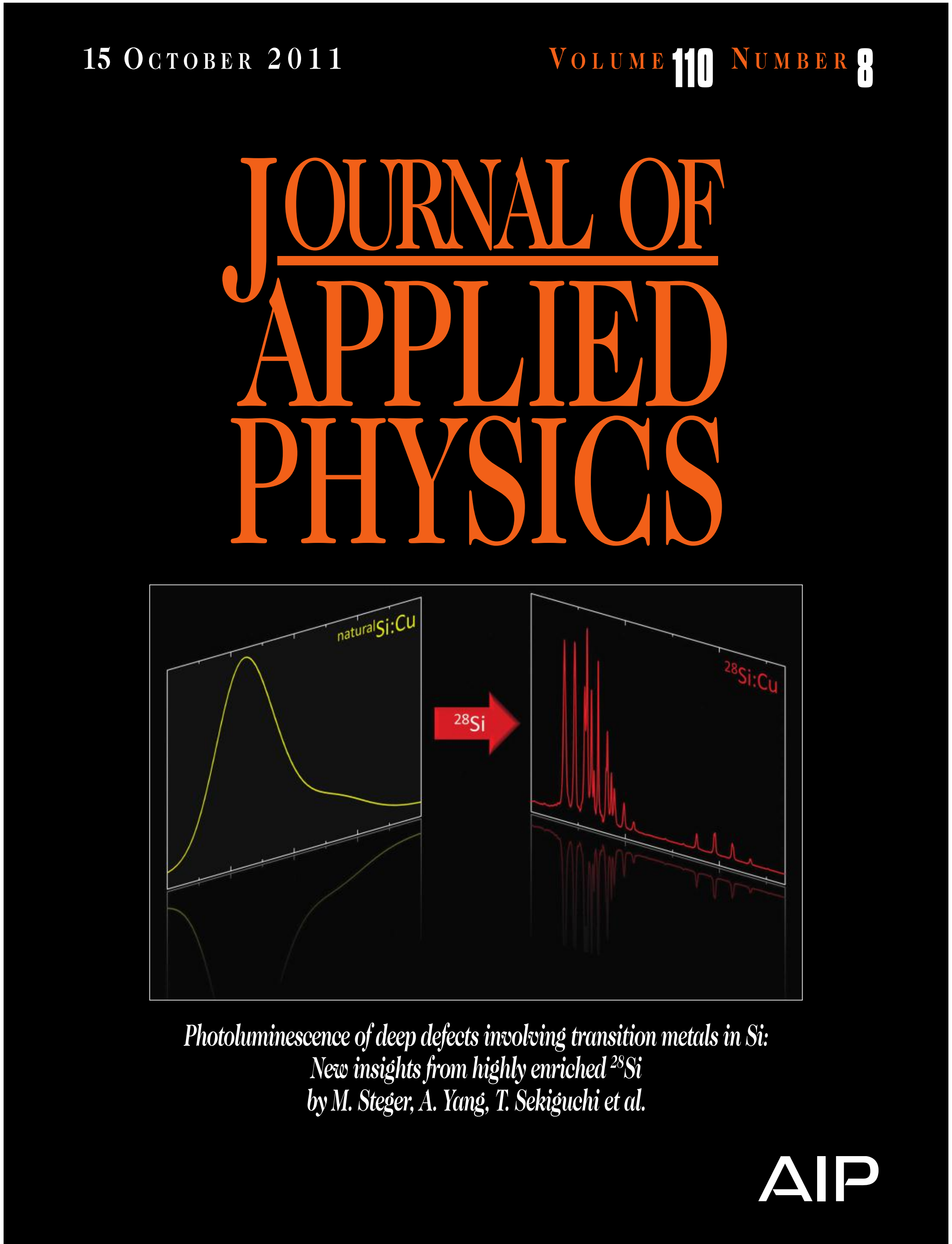
LASER
- HeCd (3,8 eV)
- Nd:YAG (2,3 nm)
- Diode (1,9 nm)

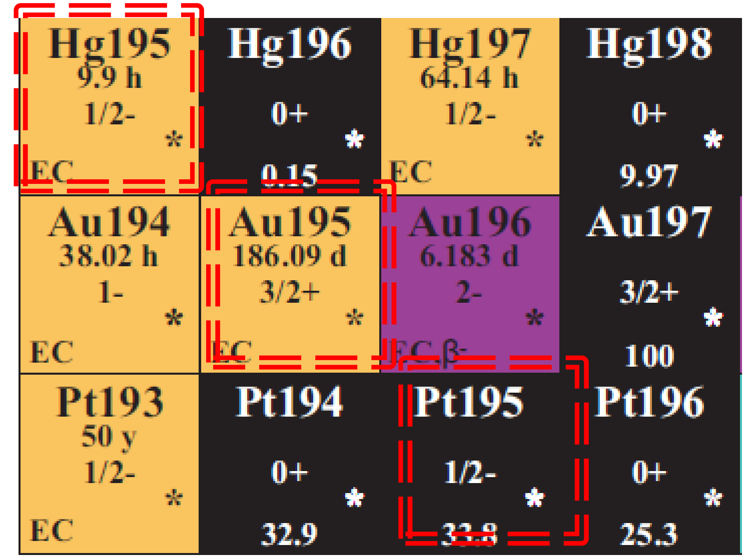
Cryostat
He-Bathcryostat (1,5 – 300 K) Closed cycle

Monochromator
- Focus: 0,75 m
- Gratings: 150 – 1800 l/mm

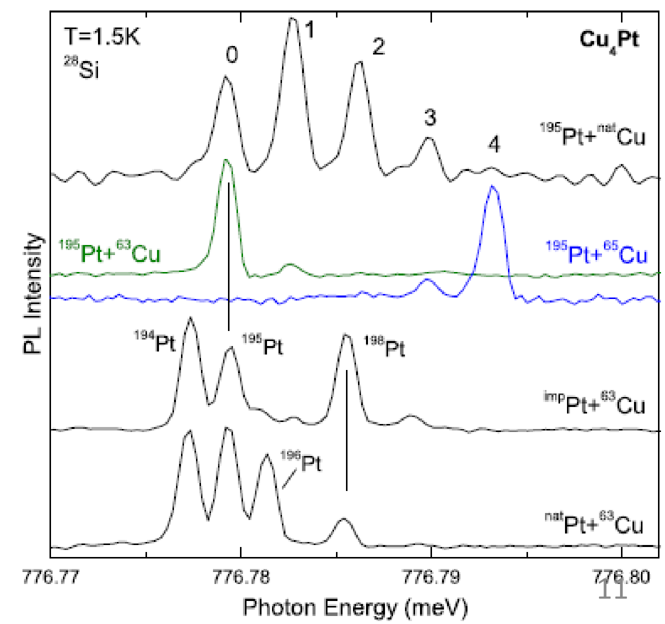
Detectors
- CCD-camera (1,1 - 6,2 eV)
- Ge-Diode (0,7 - 1,5 eV)

... to measure optical properties of mono-isotopic Si.

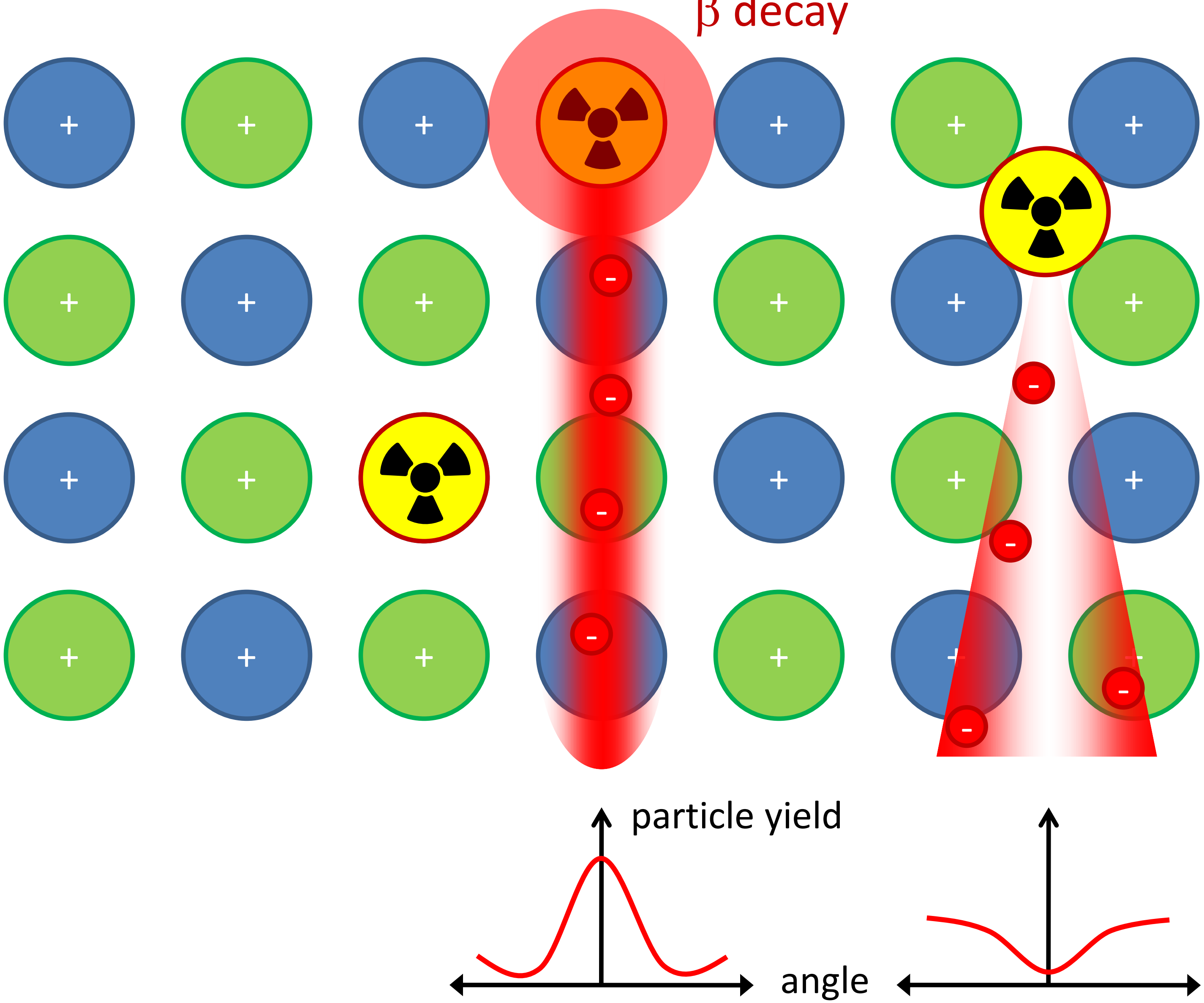




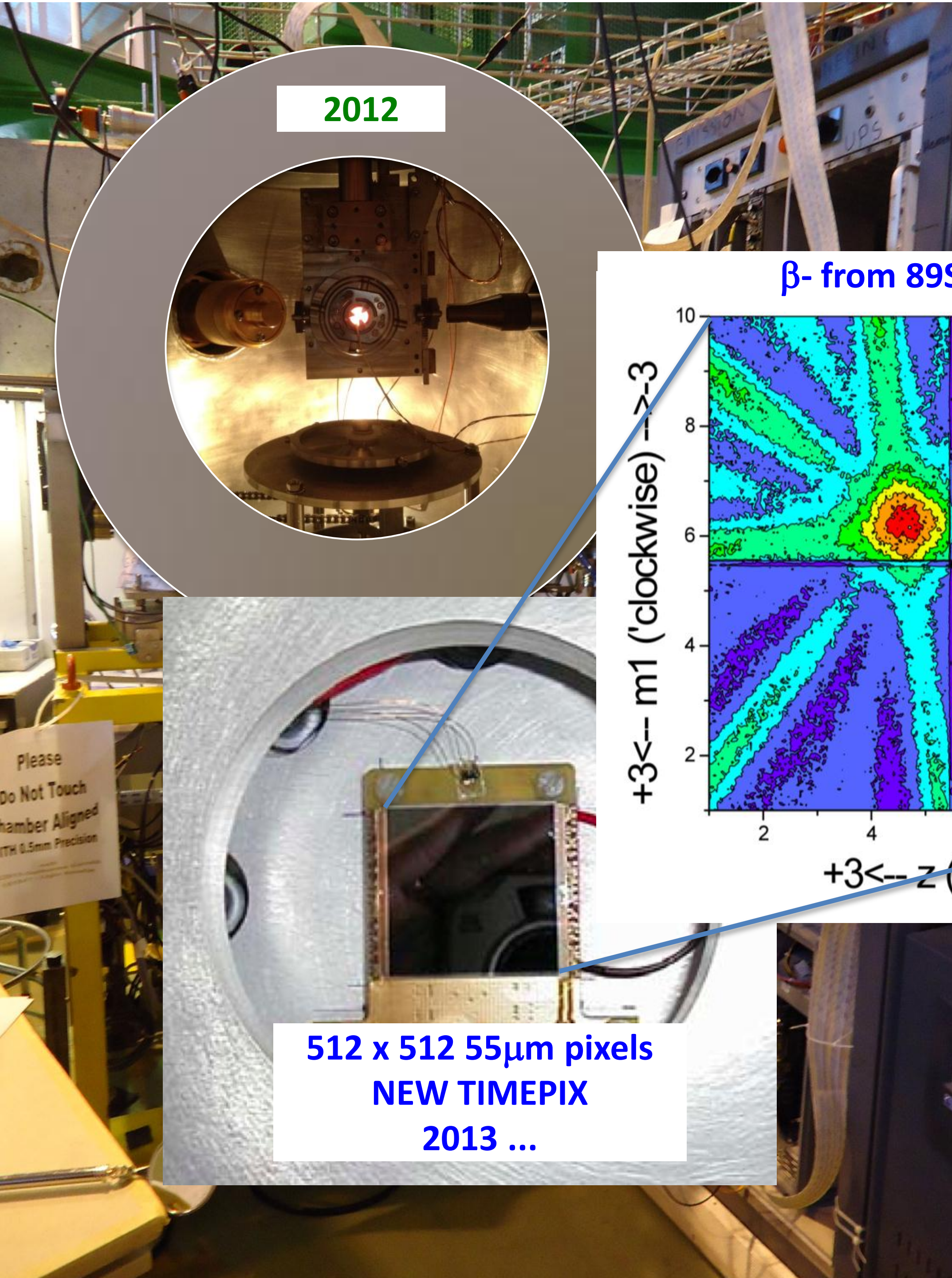
777meV feature, now shown to include Pt and 4 Cu atoms!



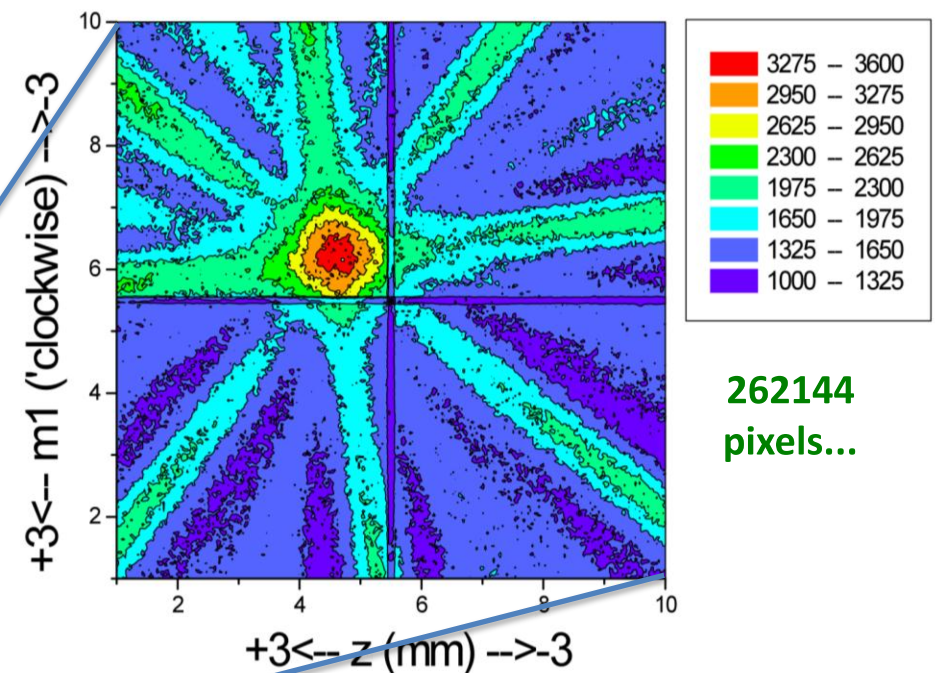
Emission Channeling of decay particles, on single crystals (β^-, β^+, c.e., α)



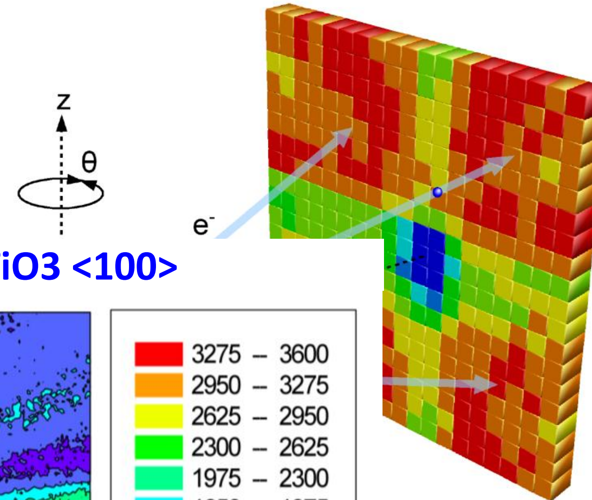
β- from 89Sr(50d) SrTiO3 <100>

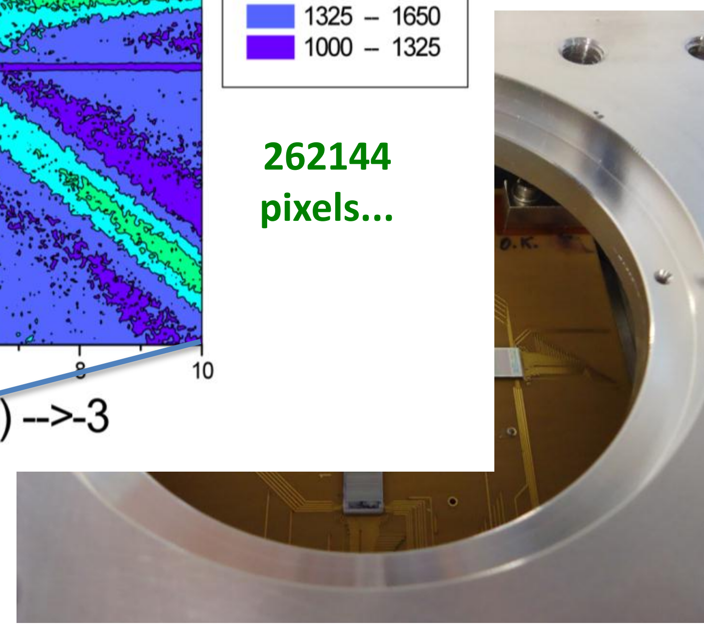


512 x 512 55µm pixels
NEW TIMEPIX
2013 ...

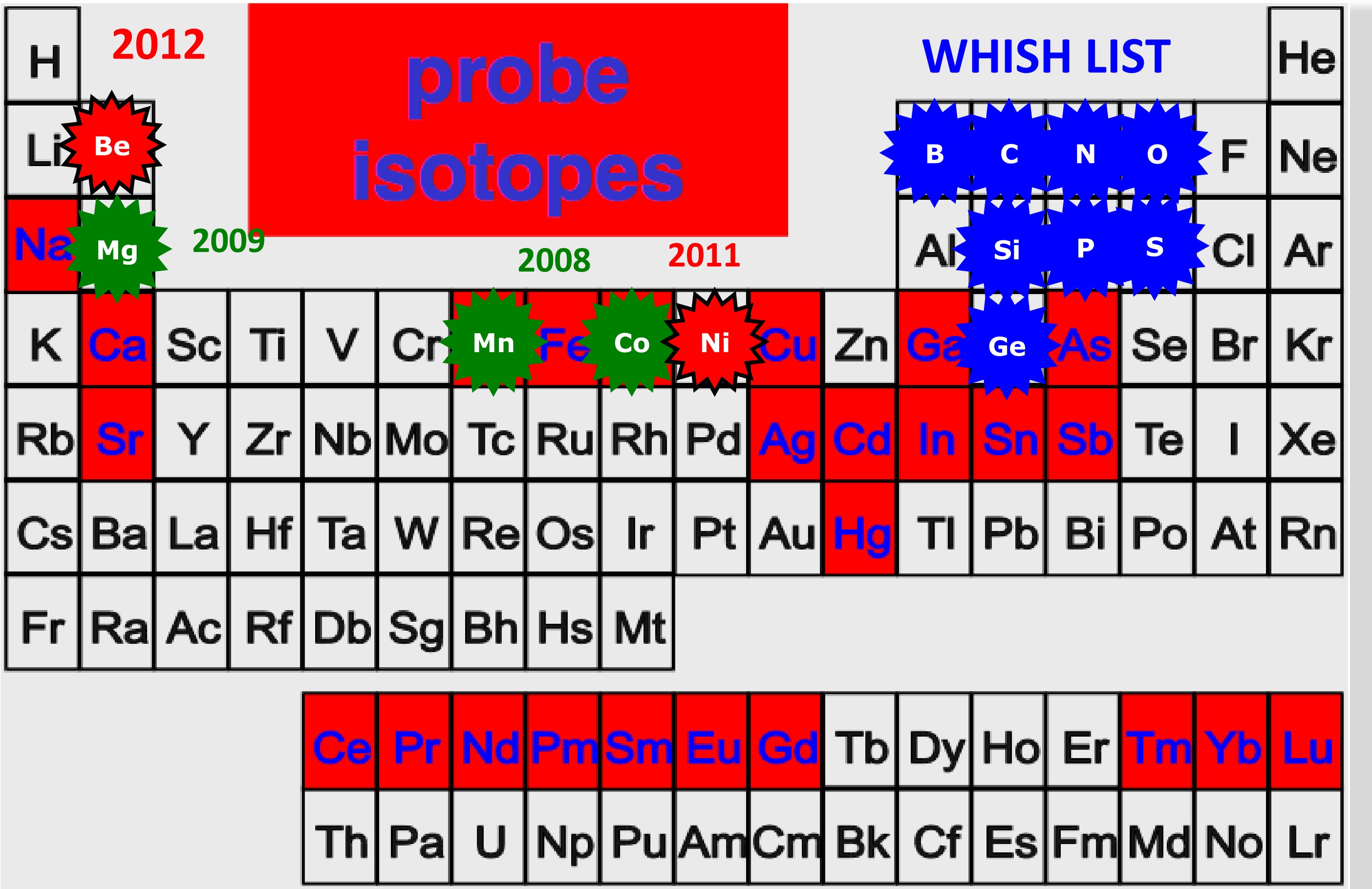


262144 pixels...

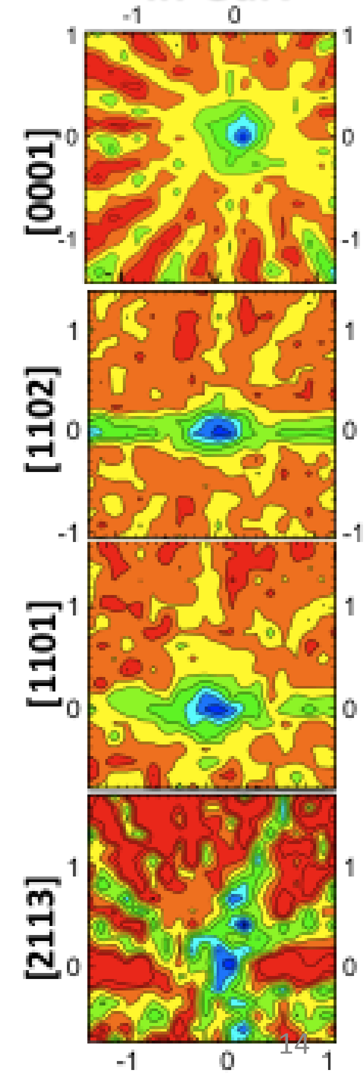


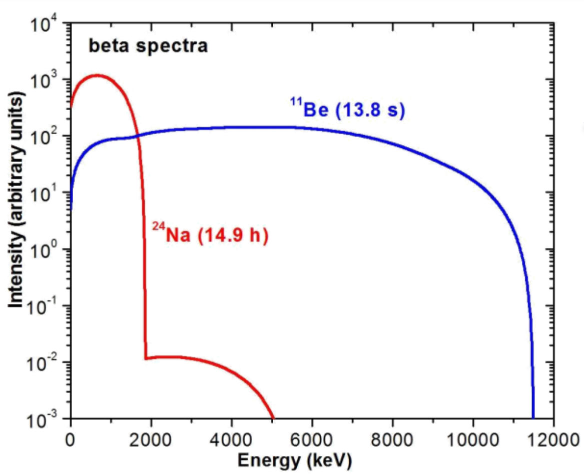


2012 NEW FAST VATAGP7
PAD detector
(22x22 = 484 pads 1.4 x 1.4 mm^2
> 5.5 kHz

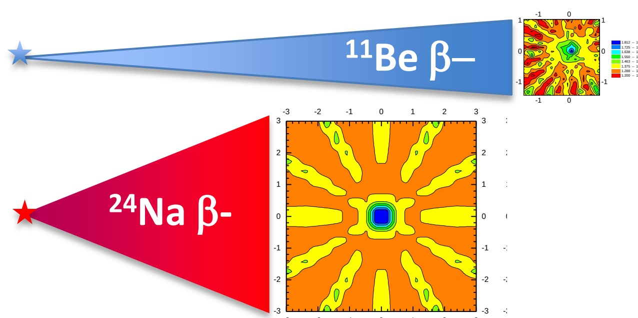


2012
first ever done β⁻ EC patterns using ^{11}Be(14 s) in GaN





Source <-> detector : 60 cm

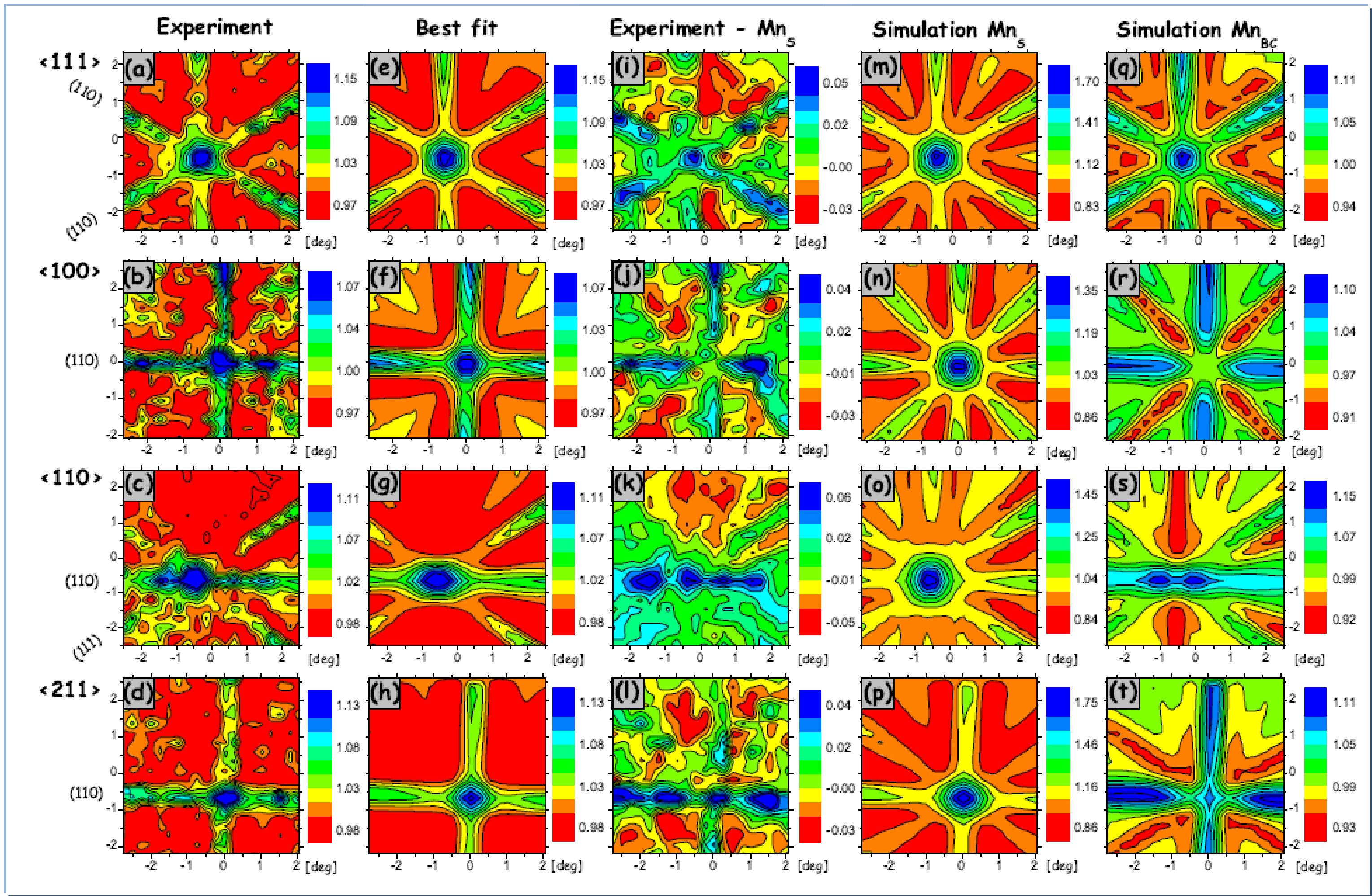


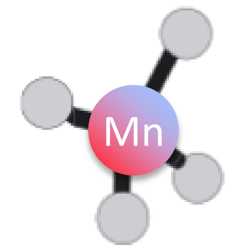
Source <-> detector : 30 cm

Lattice location study of implanted ^{56}Mn (2.6h) : Ge Implantation at 300°C

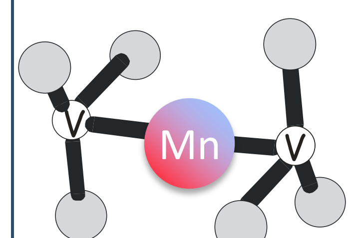
S. Decoster, U. Wahl et al., Applied Physics Letters 97, 151914 (2010)

Mn-doped Ge ←(?)→ spintronic devices, Mn_xGe_{1-x} ferromagnetic 25K… 116 K, TC increases linearly 0.6% <[Mn] < 3.5%.

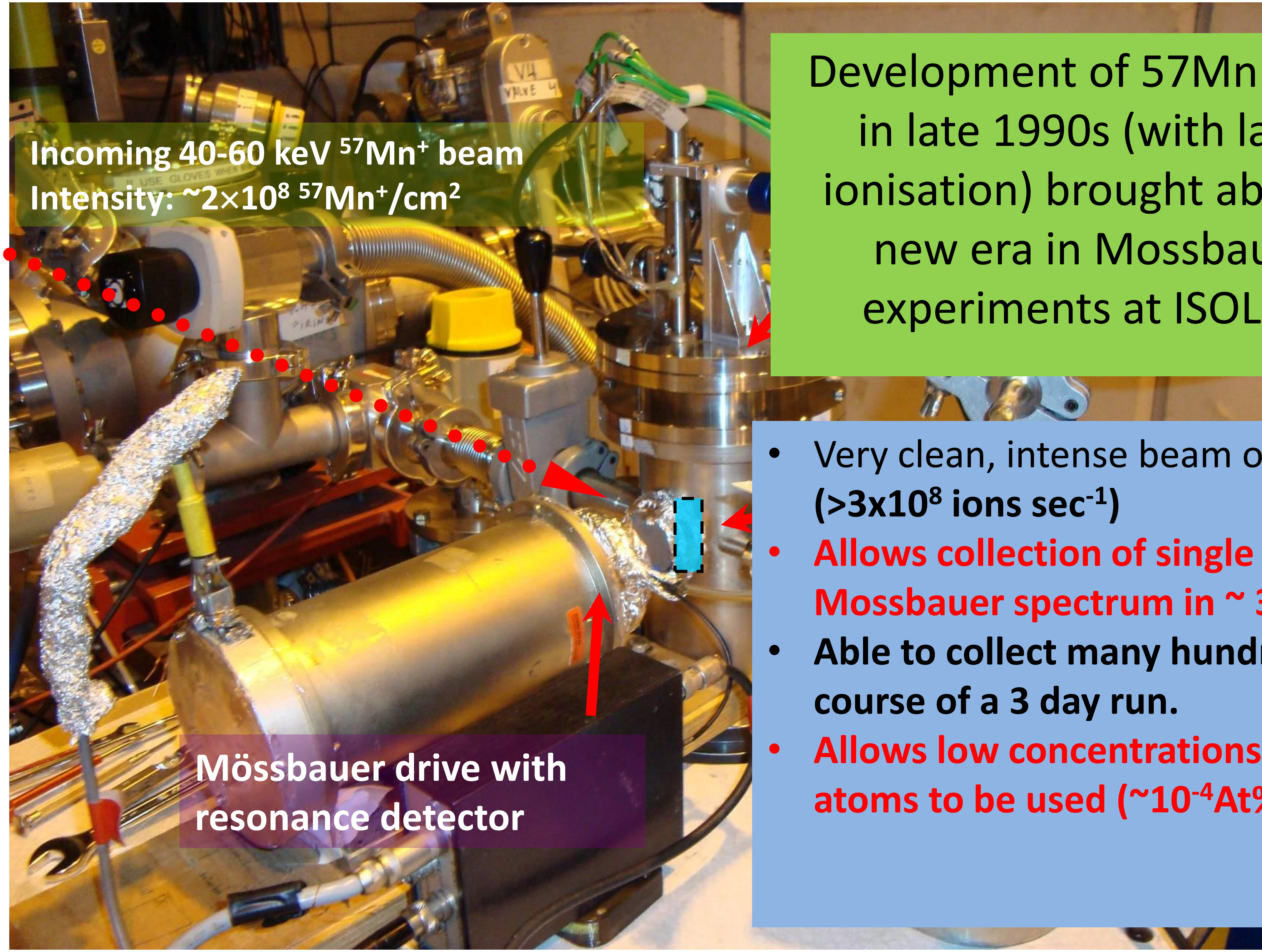




38(7)%
Mn(S)
+
59(8)%
Mn(BC)



Hyperfine Interactions with Mossbauer spectroscopy



Development of 57Mn beam in late 1990s (with laser ionisation) brought about a new era in Mossbauer experiments at ISOLDE.

- Very clean, intense beam of ^{57}Mn **(>3x10^{8} ions sec^{-1})**
- **Allows collection of single Mossbauer spectrum in ~ 3 mins.**
- **Able to collect many hundreds over course of a 3 day run.**
- **Allows low concentrations of probe atoms to be used (~10^{-4}At%)**

Fe: ZnO a ferromagnetic semiconductor? (nope!)

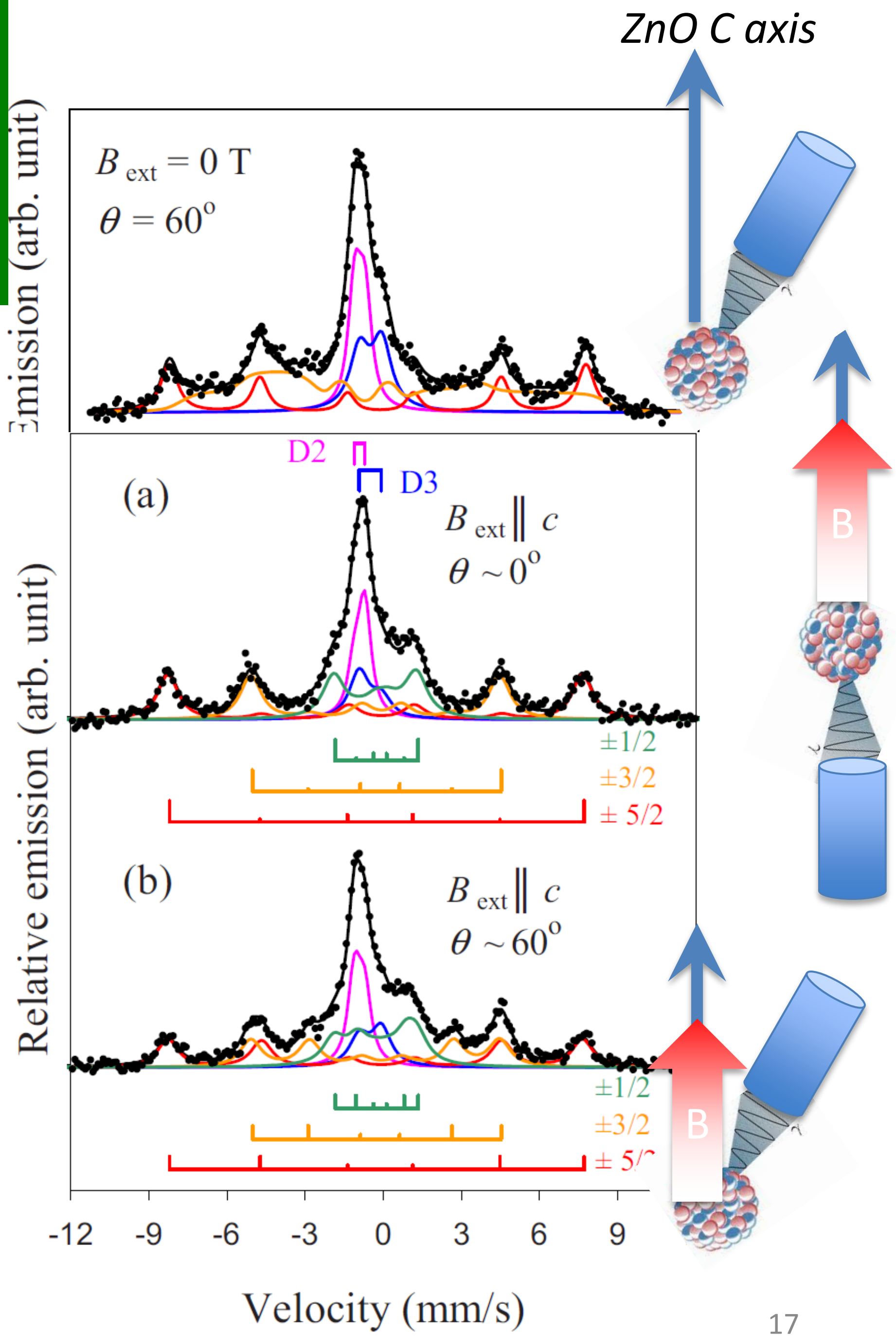
6 fold spectrum: characteristic of magnetic structure (at room temperature!!!).

Results in an external magnetic field show that the spectrum shown to be a **slowly relaxing paramagnetic system** .

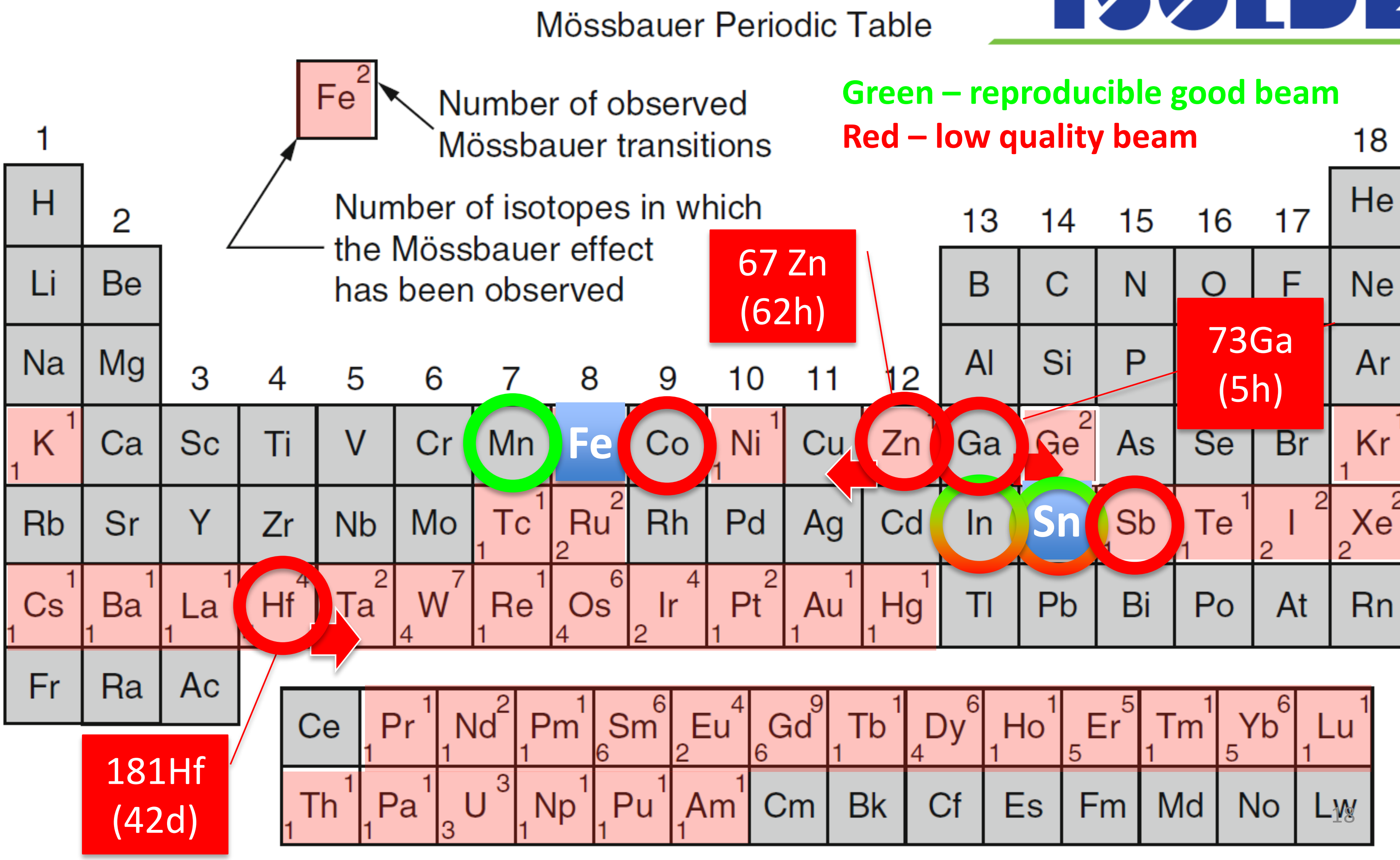
Gunnlaugsson *et al* (APL **97** 142501 2010)

After high-dose implantations, precipitates of Fe-III are formed. These form clusters yielding misleading information about the nature of magnetism in ZnO (as reported by many groups over the last number of years).

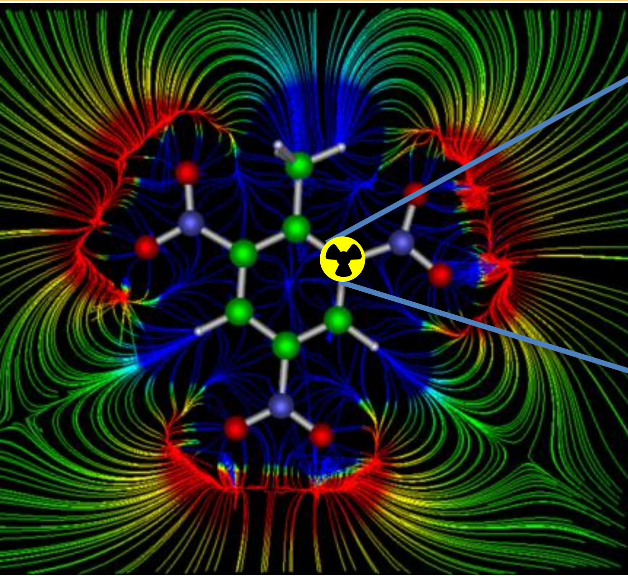
Gunnlaugsson *et al* APL **100 042109** 2012

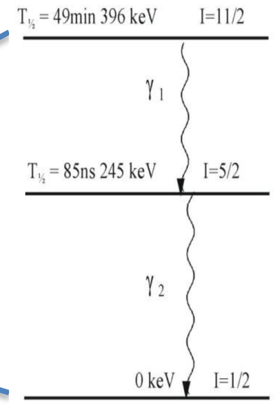


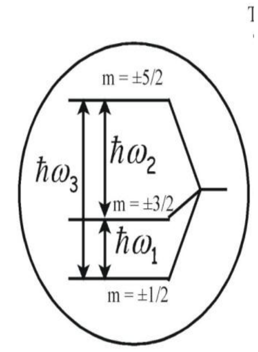
Mössbauer periodic table



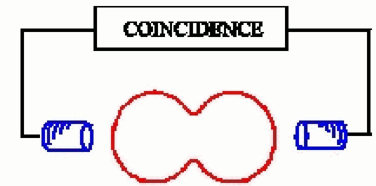
Perturbed angular correlation (PAC) Spectroscopy applied to BIOPHYSICS

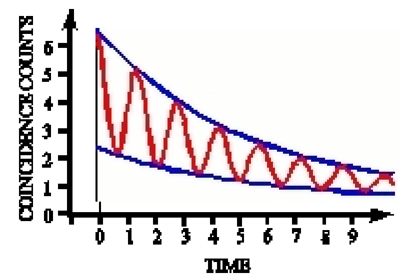




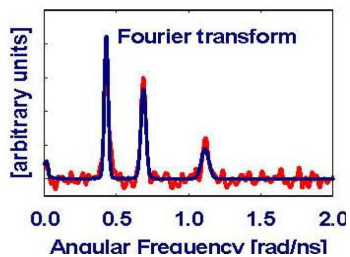


$\eta = 0$

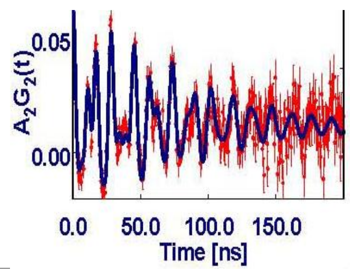




Fourier transform



Least χ^2 analysis



$$A_{22}G_{22}(t) = 2\frac{W(180°,t)-W(90°,t)}{W(180°,t)+2W(90°,t)}$$

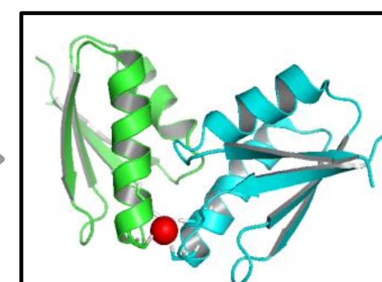
6·180º spectra and 24·90º spectra

ω_Q and η

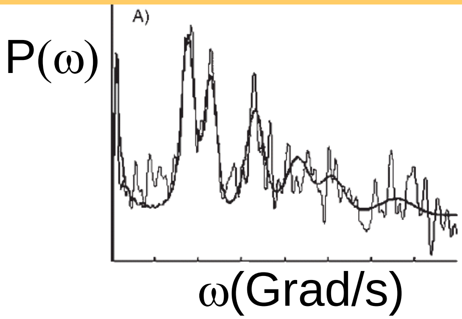
+

BASIL model

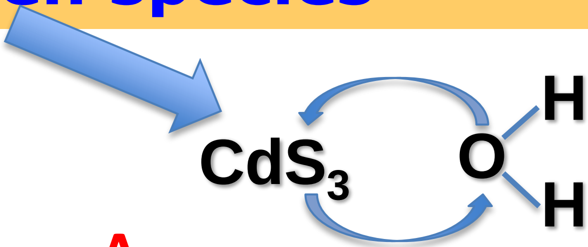
QM calculations



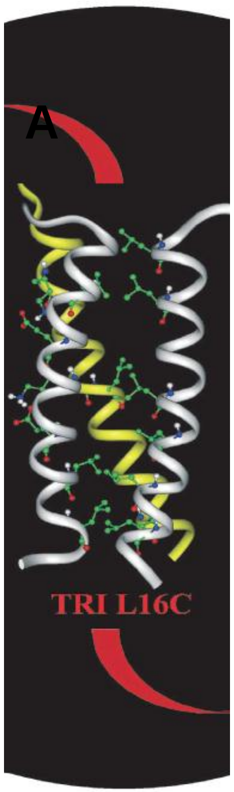
^{111m}Cd(48m) PAC - Metal Ion Binding Site Structure: Fast inter-conversion between species

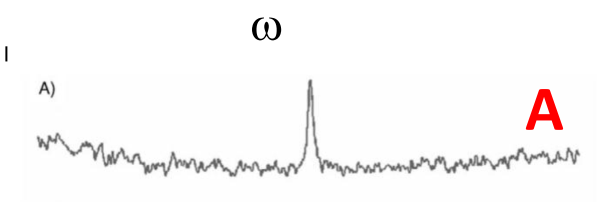


A ^{111m}Cd-PAC



A

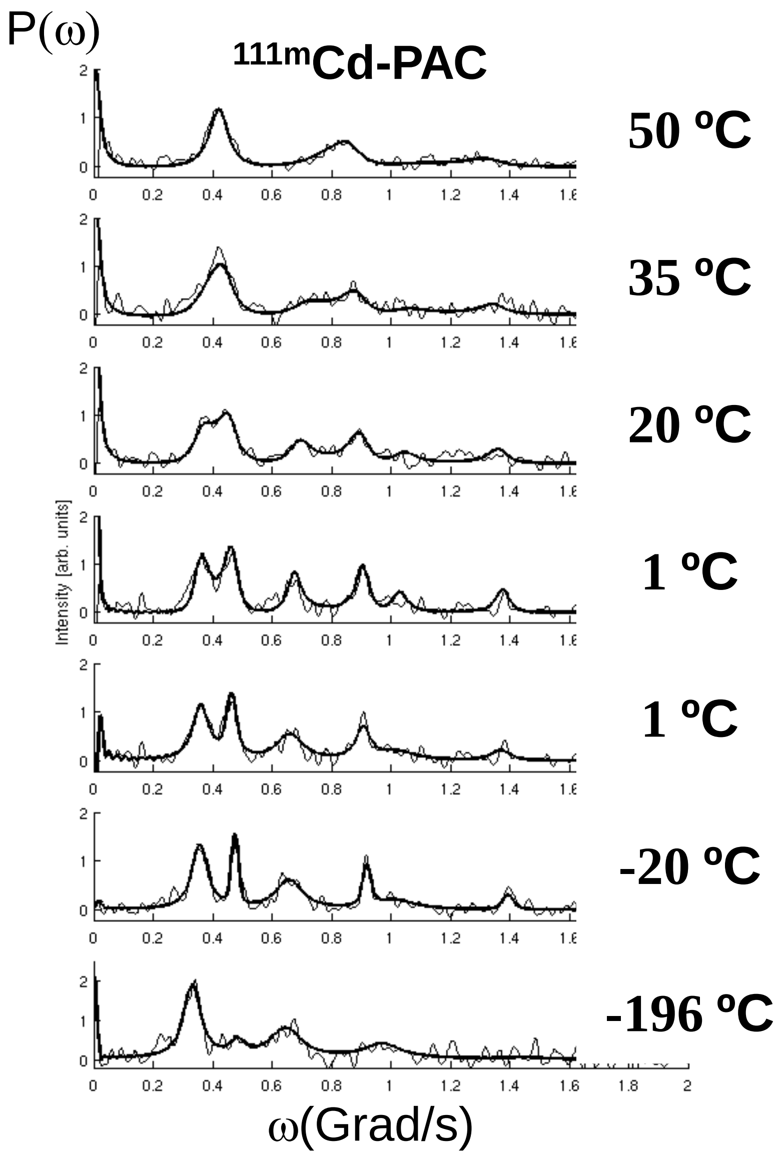


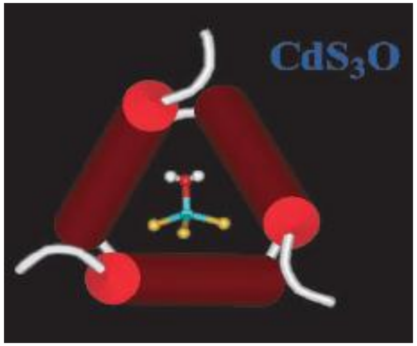


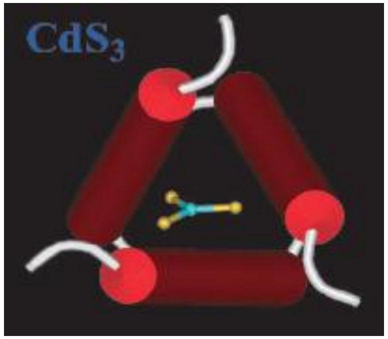
A ^{113}Cd-NMR

Matzapetakis *et al*. J. Am. Chem. Soc. **2002**, 124: 8042; Lee *et al*. Angew. Chem., **2006**, 45: 2864; Peacock *et al.* Proc. Nat. Acad. Sci. **2008**, 105: 16566

^{111m}Cd PAC (48M) - De novo designed heavy metal Ion binding proteins: ns dynamics





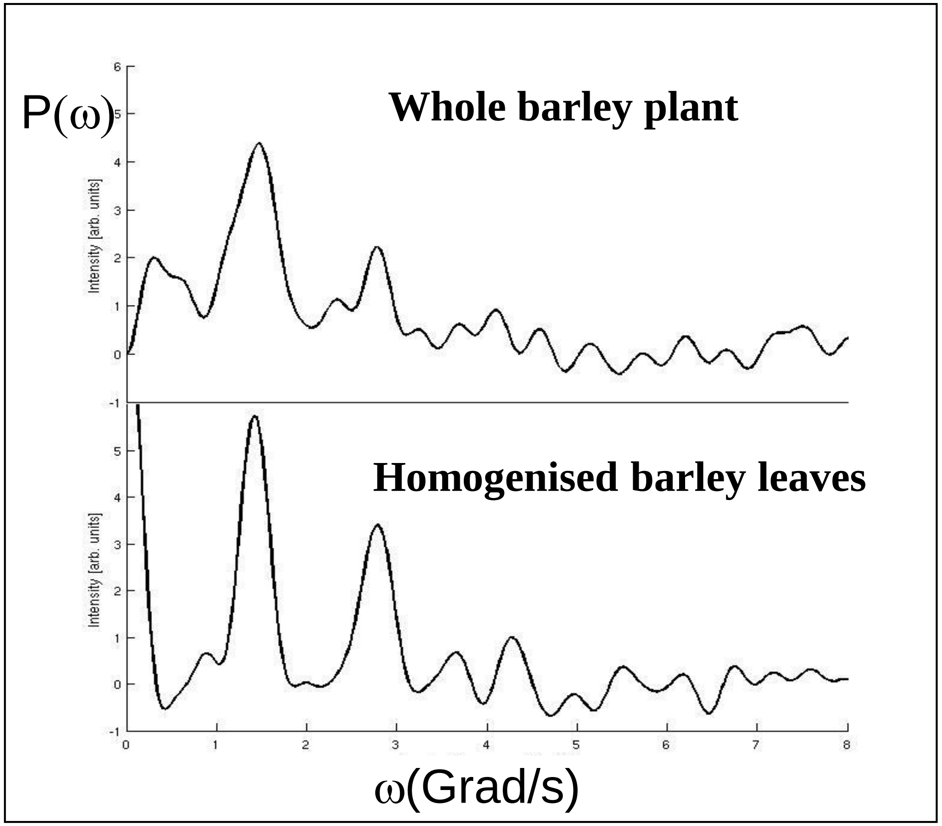


Temp [°C]	τ_1 [ns]	τ_{-1} [ns]
1	52	48
20	42	36
35	28	20
50	19	12

Stachura et al. Manuscript Science in preparation

In vivo experiments Hg(II) binding to barley
^{199m}Hg PAC (42M)

Adolph et al. *Chem. Eur. J.*, **2009**, 15, 7350 – 7358

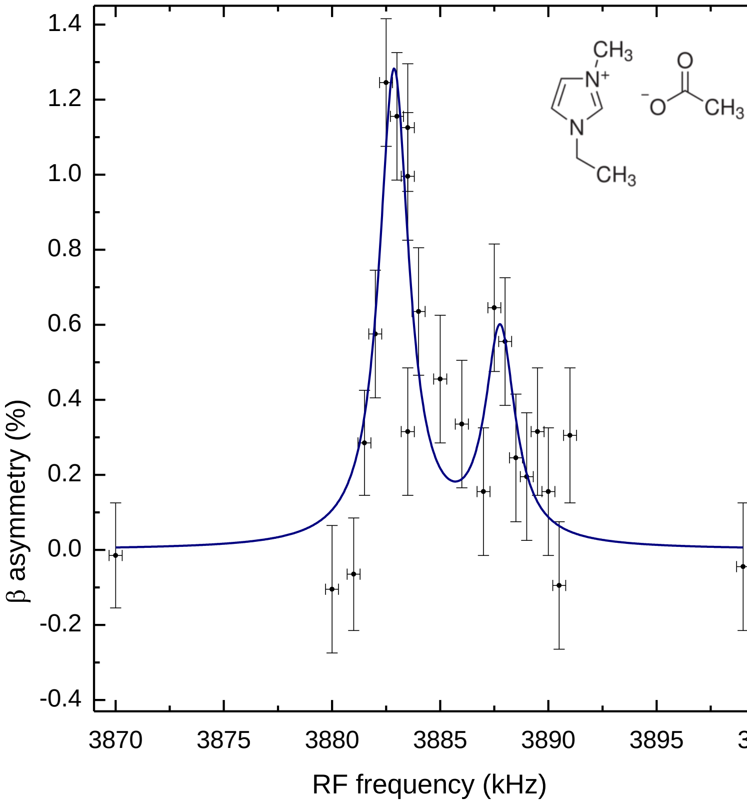


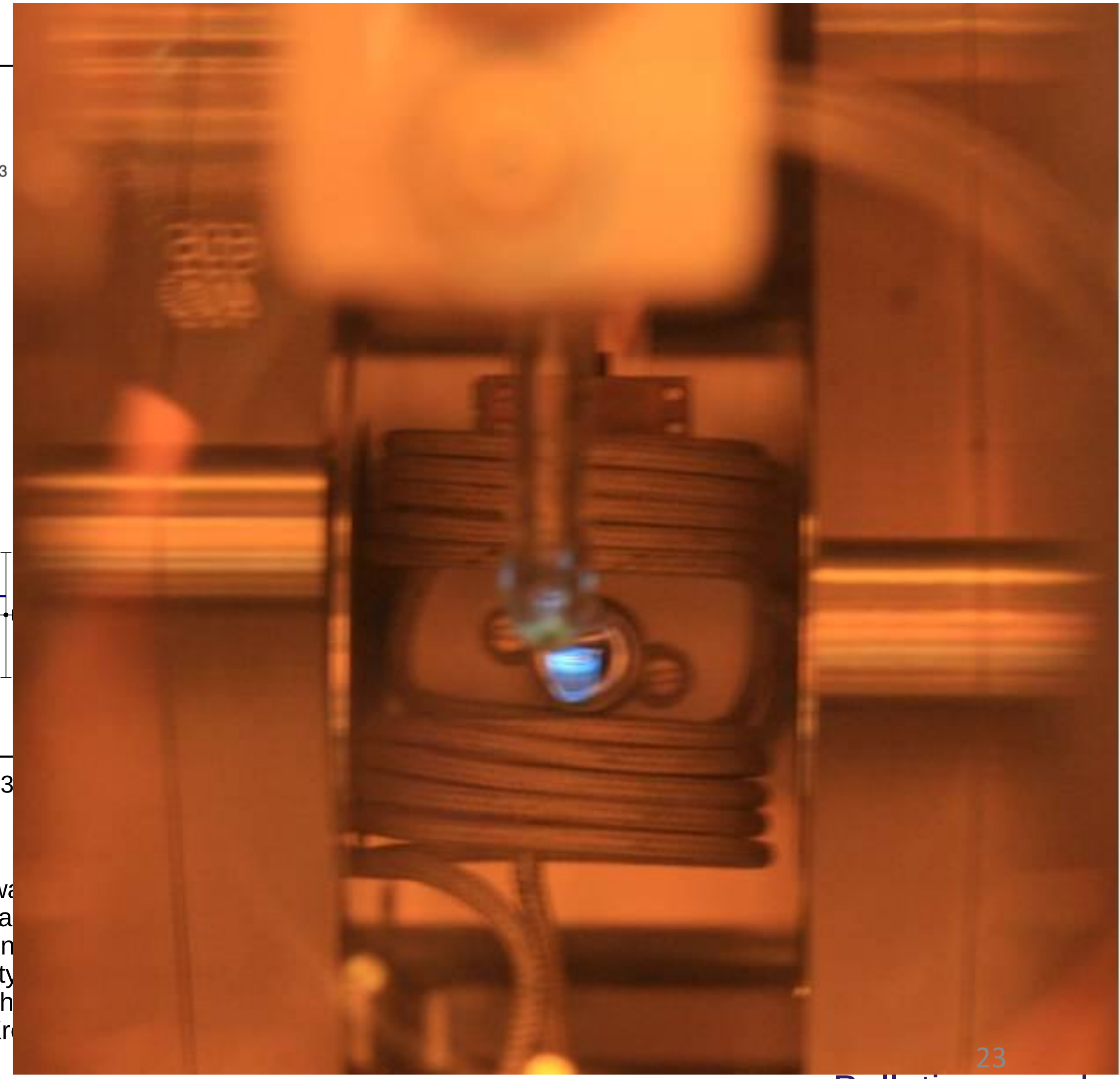
- 5-7 days-old plants
- Plant inserted into test tube.
- Fast uptake of Hg(II) (<1h)
- Bound to large molecules, similarities to HgS_2 compounds

2012 – first (and successful) $^{31}Mg^{+}$ β-NMR experiment applied to soft condensed matter

$^{31}Mg^{+}$ implanted into an ionic liquid (EMIM-Ac):

Differential pumping and drop
Mounted @ COLLAPS experiment





Monika Stachura, University of Copenhagen; Magdalena Kowa
CERN, Geneva; Alexander Gottberg, CSIC, Madrid; Klaus Bla
Planck Institute for Nuclear Physics, Heidelberg; Gerda Neyen
Leuven University, (Leuven); Rainer Neugart, Mainz University
(Mainz); Deyan Yordanov, Max Planck Institute for Nuclear Ph
Heidelberg; Mark Bissell, Leuven University, (Leuven); Kim Kr
Planck Institute for Nuclear Physics, Heidelberg

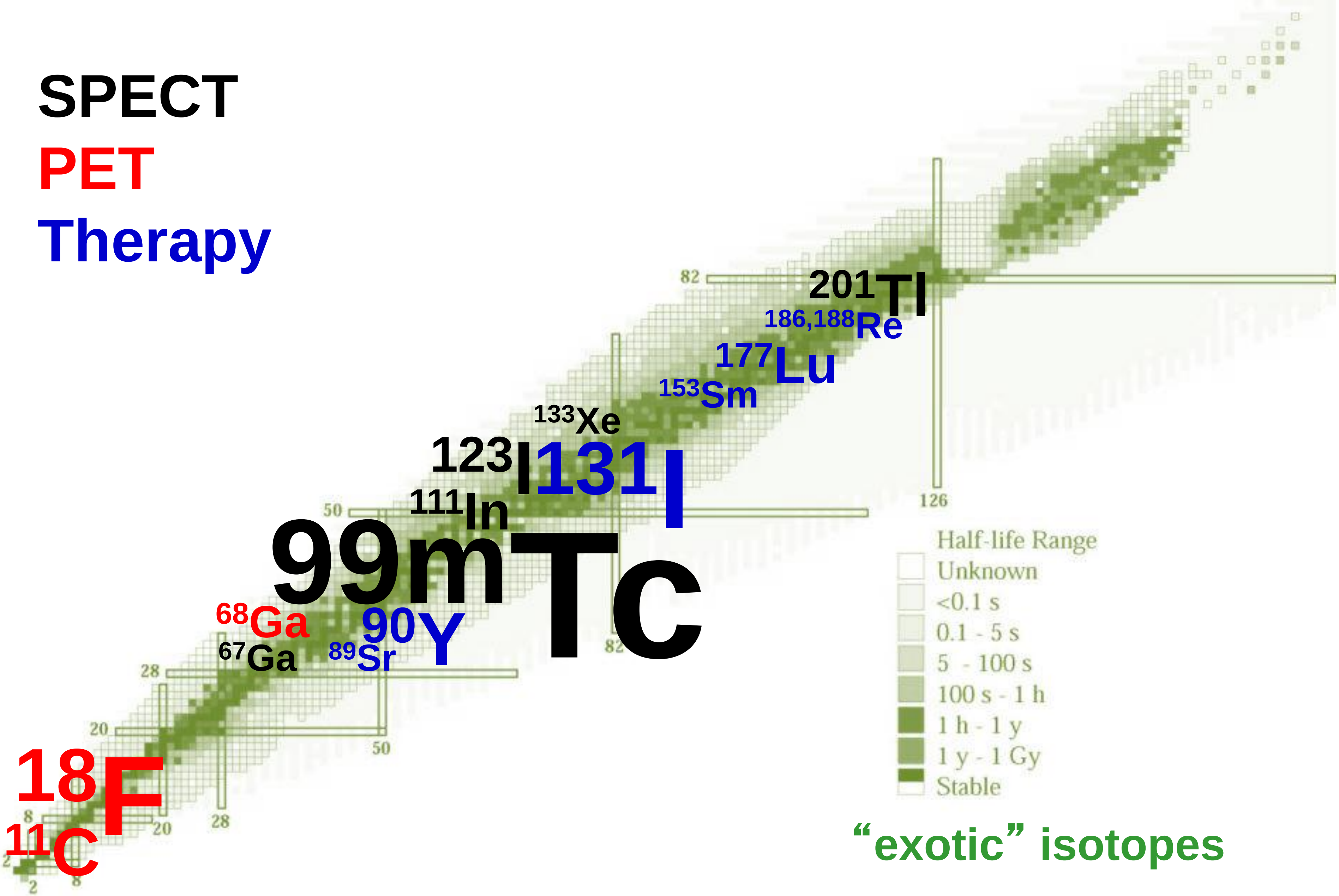
Bulletin.cern.ch

Radionuclides for diagnosis and therapy

SPECT

PET

Therapy



"exotic" isotopes

Radionuclides for therapy

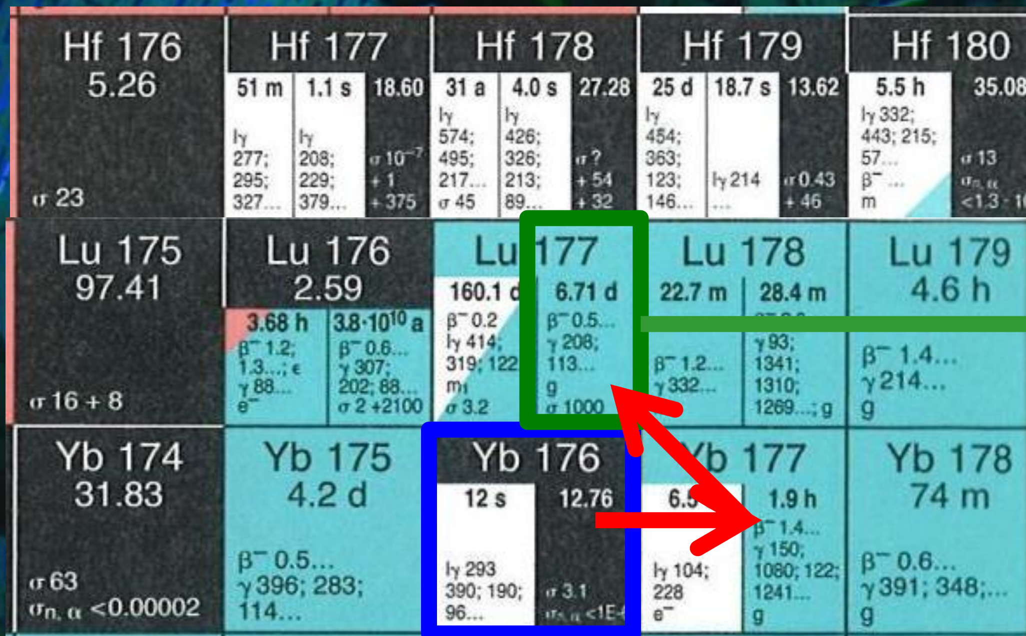
Radio-nuclide	Half-life	E mean (keV)	Eγ (B.R.) (keV)	Range
Y-90	64 h	934 β	-	12 mm
I-131	8 days	182 β	364 (82%)	3 mm
Lu-177	7 days	134 β	208 (10%) 113 (6%)	2 mm

Estab-lished isotopes

Emerging isotopes

localized radiation

Production of non-carrier-added ^{177}Lu



Irradiation in high flux reactor (e.g. ILL Grenoble), then chemical separation of ^{177}Lu from stable Yb.

Radionuclides for therapy

Radio-nuclide	Half-life	E mean (keV)	Eγ (B.R.) (keV)	Range
Y-90	64 h	934 β	-	**12 mm**
I-131	8 days	182 β	364 (82%)	**3 mm**
Lu-177	7 days	134 β	208 (10%) 113 (6%)	**2 mm**
Tb-161	7 days	154 β 5, 17, 40 e^-	75 (10%)	**2 mm** **1-30 µm**
Tb-149	4.1 h	3967 α	165,..	**25 µm**
Ge-71	11 days	8 e^-	-	**1.7 µm**
Er-165	10.3 h	5.3 e^-	-	**0.6 µm**

cross-fire

Estab-lished isotopes

Emerging isotopes

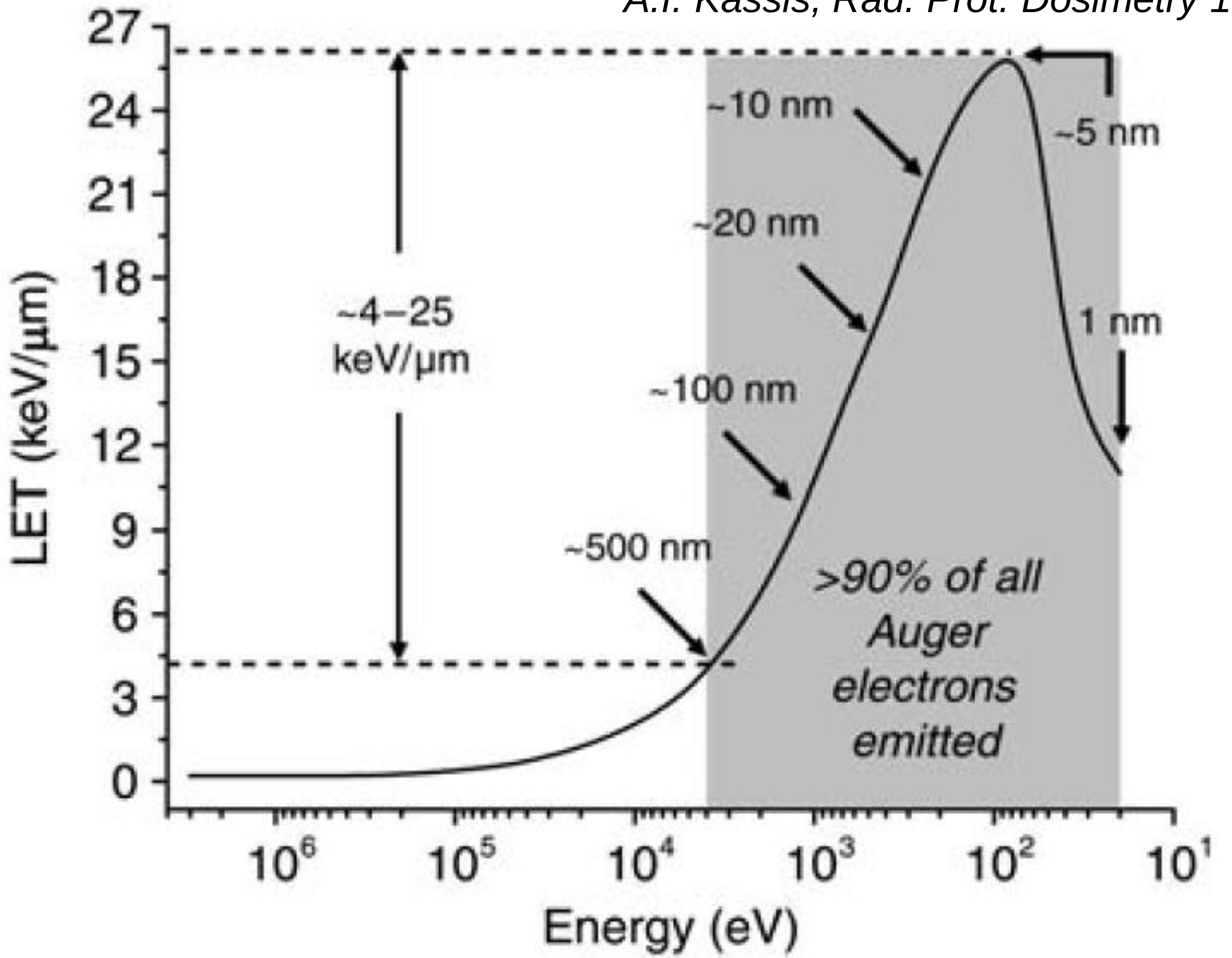
R&D isotopes: supply-limited!

localized

Modern, better targeted vectors require shorter-range radiation ⇒ need for adequate (R&D) radioisotope supply.

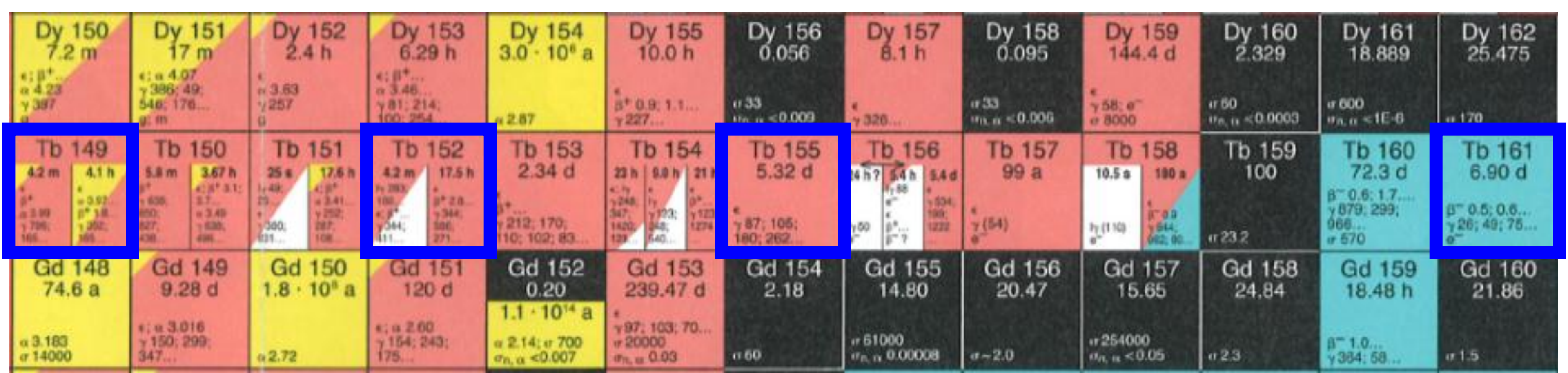
Linear Energy Transfer of Auger electrons

A.I. Kassis, Rad. Prot. Dosimetry 143 (2011) 241.

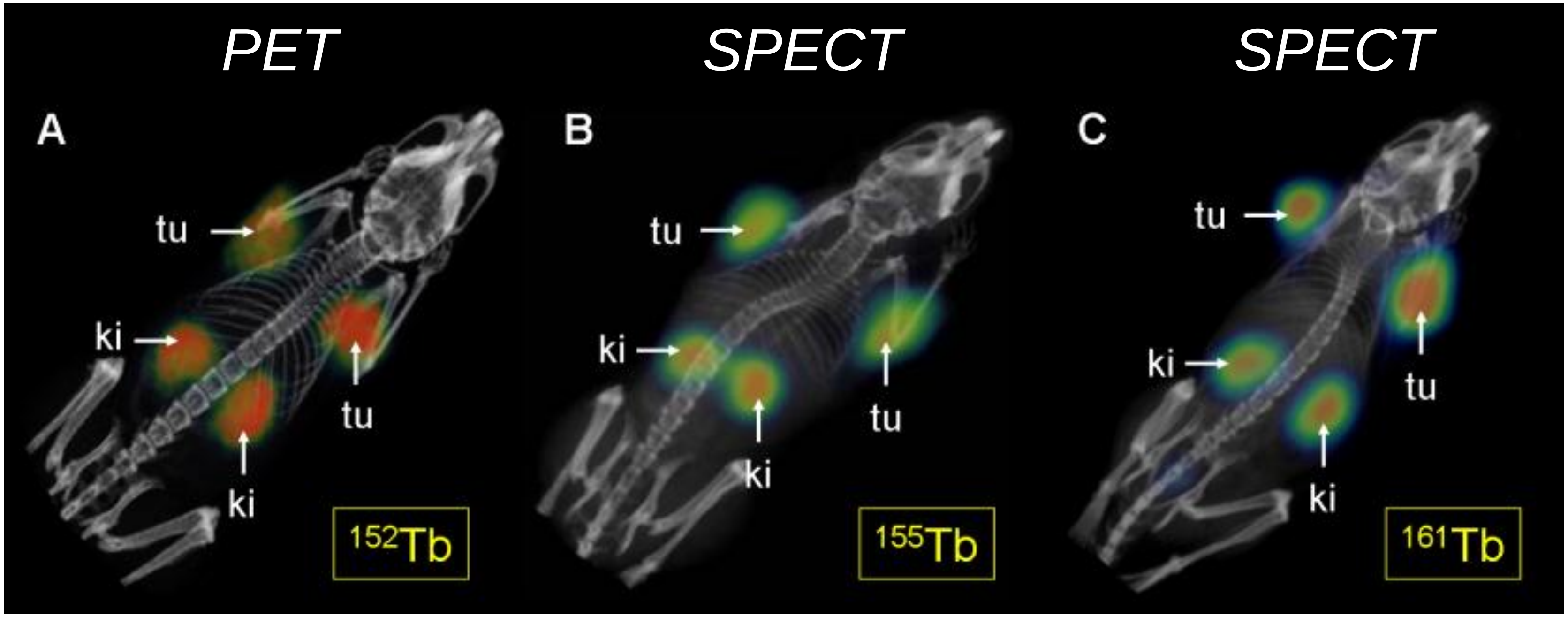


Very targeted therapy (high efficacy/low side effects) possible if "internalizing" vectors (peptides, antibodies,…) are found that penetrate the cancer cell's nucleus.

Terbium: a unique element for nuclear medicine



Imaging Studies Using PET and SPECT

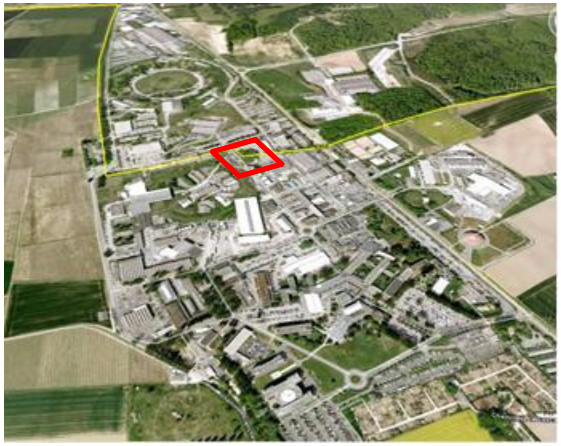


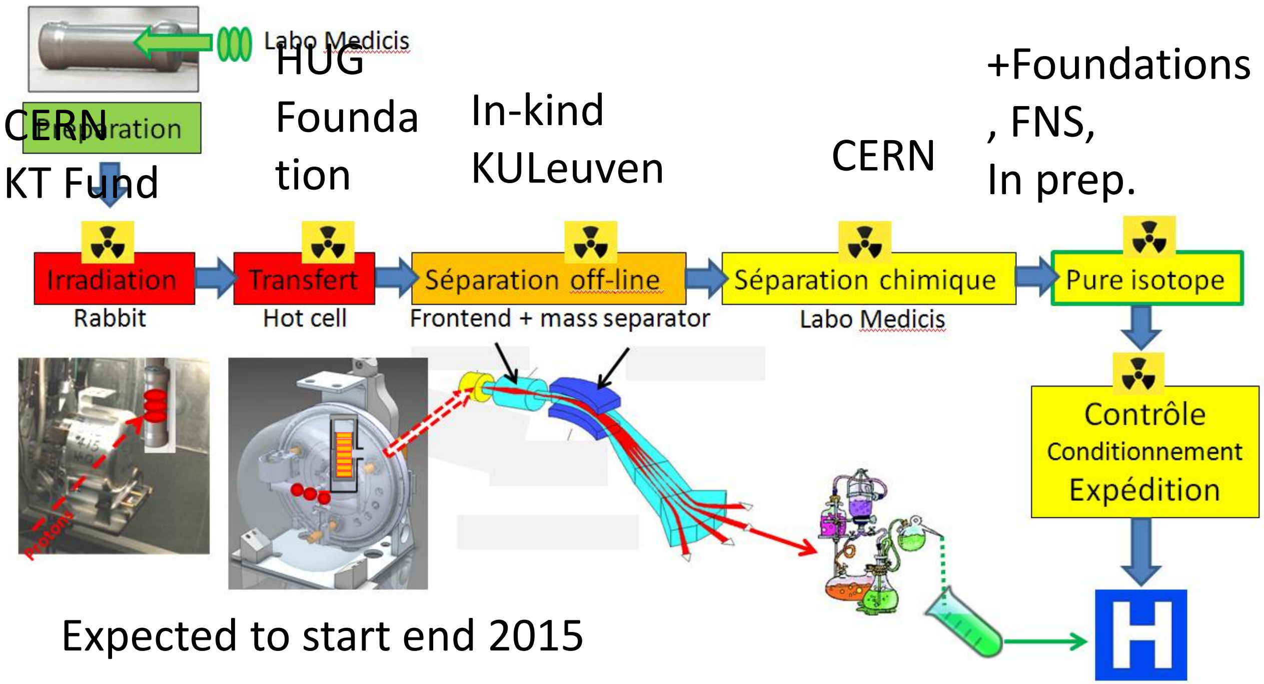
C. Müller et al., J. Nucl. Med. (2012), in press.
IS528 collaboration: supported by ENSAR, Swiss National Science Foundation and Swiss South African Joint Research Program.

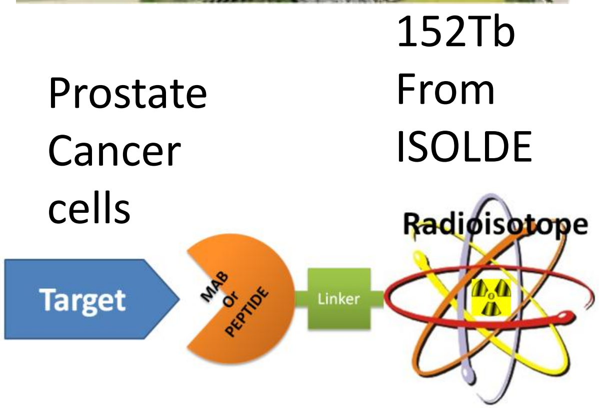
CERN-MEDICIS:
Medical isotopes collected from ISOLDE

R. Catherall, M. Dias, T. Giles, Z. Lawson, S. Marzari, **T. Stora** (**CERN**)

Dr. Forni (**Clin. Carouge**),L. Vouga, Prof. P. Morel, Prof. L. Buehler, Prof. Y. Seimbille, Prof. O. Ratib (**HUG**, Geneva), Prof. D. Hanahan (**ISREC-EPFL**, Lausanne), Prof. J. Prior, Dr. F. Buchegger (**CHUV**, Lausanne), Prof M. Huyse, Prof. P. van Duppen (**Univ. Leuven**), Prof. S. Lahiri (**SINP**, Kolkata)







The (potential) role of ISOL in nuclear medicine

1. Samples of R&D isotopes which are not commercially available or easily producible by other means.
2. Isotopes with ultimate specific activity for R&D, e.g. studies of efficacy versus specific activity.
3. Isotopes that are best produced by spallation (^{149}Tb,…).

Existing ISOL beams are sufficiently intense for preclinical studies, in certain cases even for clinical studies.

How to organize R&D with RIBs in nuclear medicine?
Physicists are used to "travel to the isotopes",
but isotopes must "travel to physicians and patients".

CONCLUSIONS

"Applications" of EXOCTIC radioactive isotopes

- Specific areas are identified:

  Life Sciences Materials Soft Matter Chemistry...

- The methods follow the needs with progressing quality...

- Viability and Visibility of "Applications"

  depend at the long term from diversifying and optimizing RIB infrastructures with:

  Dedicated BEAM TIME and BEAM LINES

  Dedicated LABORATORY SPACE

  ...the future of "Applications" depend very much on the concept of the next generation of RIB facilities ....

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