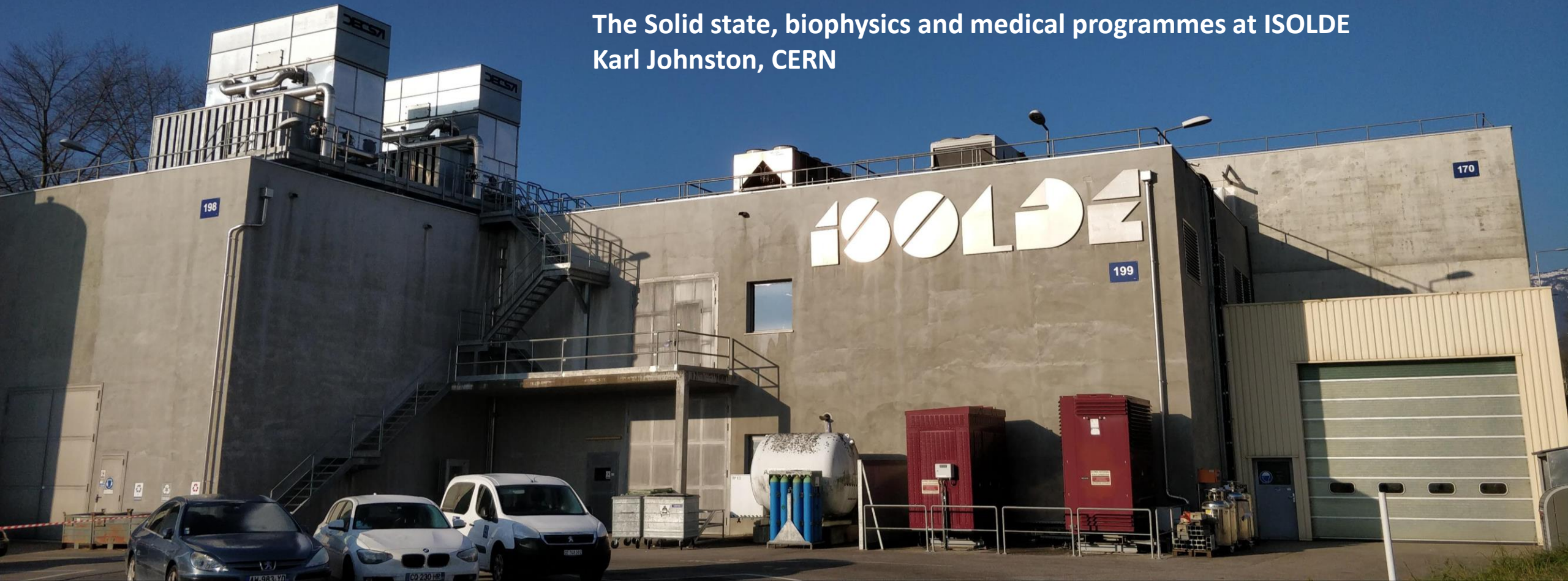


The Solid state, biophysics and medical programmes at ISOLDE

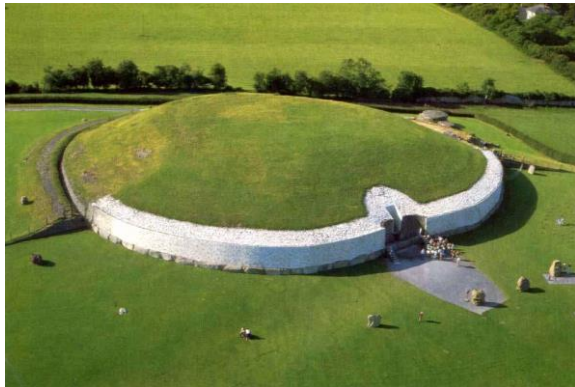
Karl Johnston, CERN



- ISOLDE facility and «applications» e.g. solid state physics, biophysics and medicine
- Why use radioactive isotopes?
- Examples of common techniques for nuclear solid state physics (and a bit of biology)
- Isotopes for medicine: where ISOLDE can play a role in developing «standard» diagnostic and treatment isotopes for the future.

Journey of a solid state physicist to a radioactive ion beam facility...

Born in Ireland



BSc in Dublin
(Dublin City
University)
(1996)



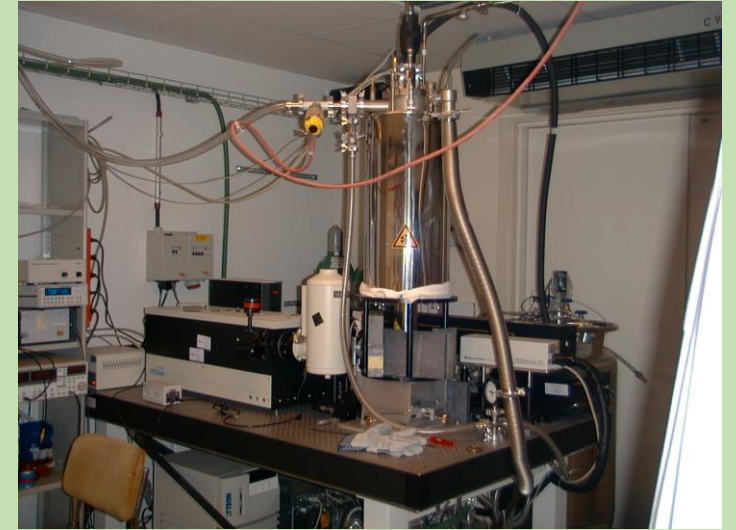
PhD (2000) + postdoc (2002) in London (King's College
London)

Thesis on properties of metal-N complexes in
diamond

Finally....some radioactive isotopes!



(2003) First experiments at ISOLDE
Built radiotracer PL laboratory at ISOLDE and studied semiconductors such as ZnO implanted with radioactive isotopes.



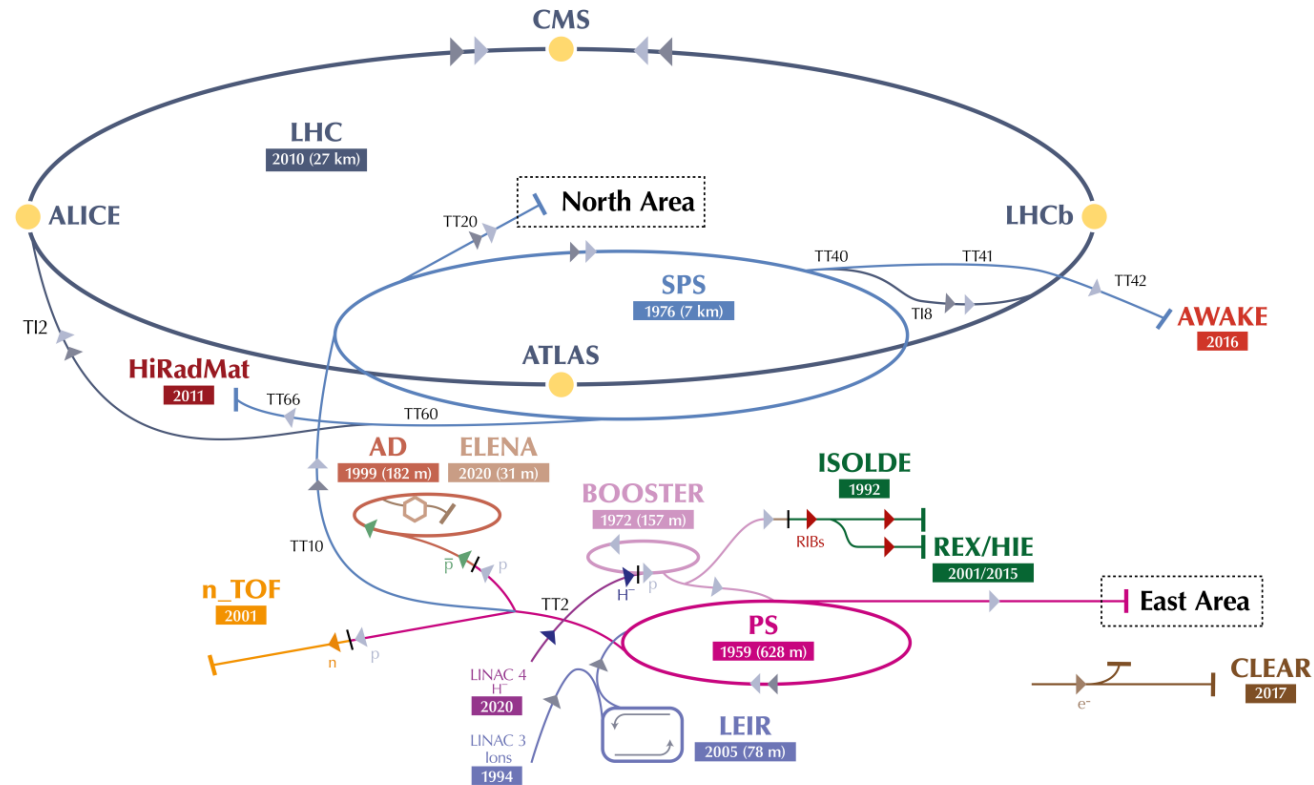
(2005) Brief interlude in Prague to work on nanodiamonds



Since 2005 first solid state, now physics coordinator at ISOLDE, CERN

The CERN accelerator complex

Complexe des accélérateurs du CERN



▶ H^- (hydrogen anions) ▶ p (protons) ▶ ions ▶ RIBs (Radioactive Ion Beams) ▶ n (neutrons) ▶ \bar{p} (antiprotons) ▶ e^- (electrons)

LHC - Large Hadron Collider // SPS - Super Proton Synchrotron // PS - Proton Synchrotron // AD - Antiproton Decelerator // CLEAR - CERN Linear Electron Accelerator for Research // AWAKE - Advanced WAKEfield Experiment // ISOLDE - Isotope Separator OnLine // REX/HIE - Radioactive Experiment/High Intensity and Energy ISOLDE // LEIR - Low Energy Ion Ring // LINAC - LINear ACcelerator // n_TOF - Neutrons Time Of Flight // HiRadMat - High-Radiation to Materials

AD: Antiproton Decelerator for antimatter studies

AWAKE: proton-induced plasma wakefield acceleration

CAST, OSQAR: axions

CLOUD: impact of cosmic rays on aerosols and clouds → implications on climate

COMPASS: hadron structure and spectroscopy

ISOLDE: radioactive nuclei facility

NA61/Shine: heavy ions and neutrino targets

NA62: rare kaon decays

NA63: radiation processes in strong EM fields

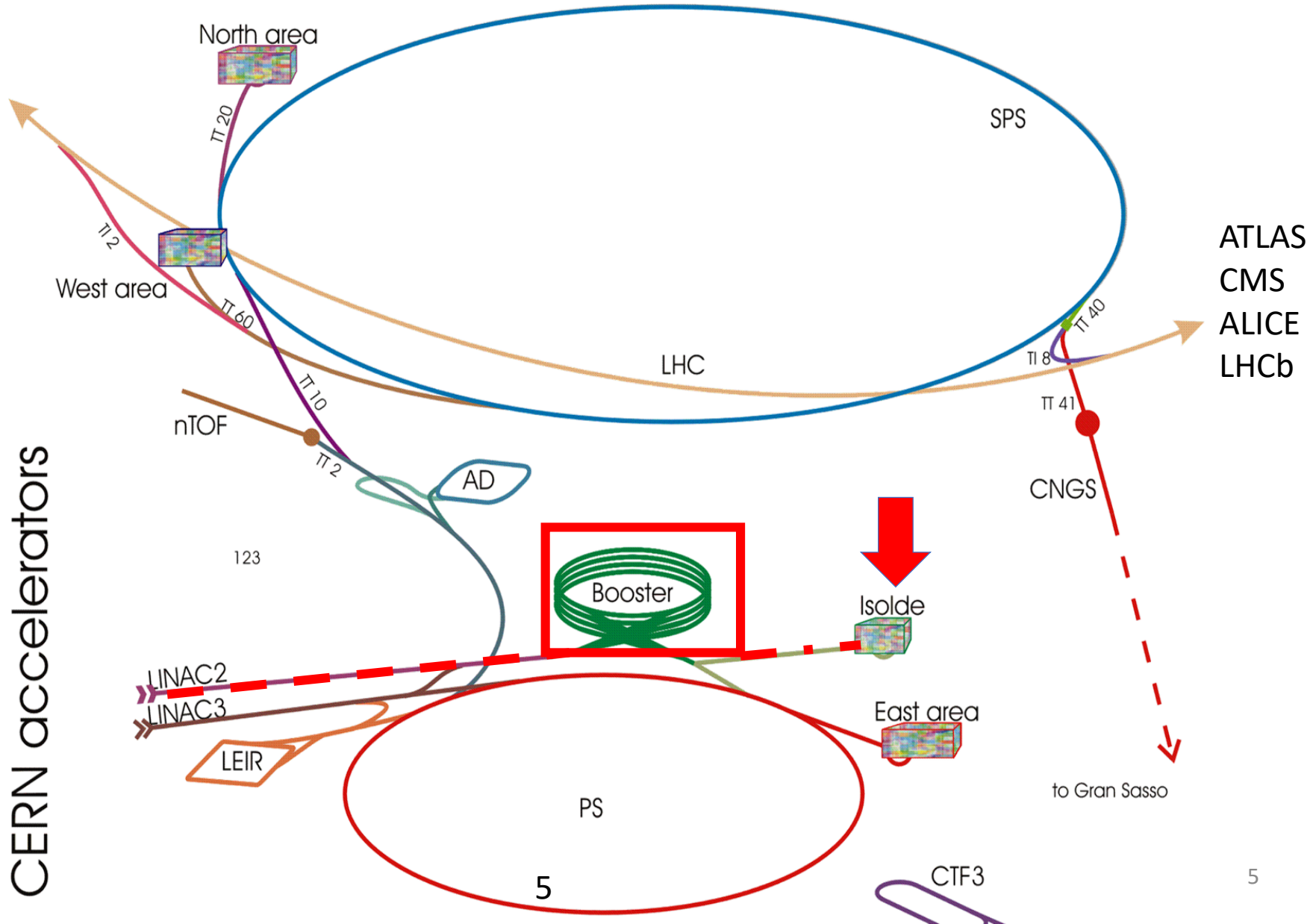
NA64: search for dark photons

Neutrino Platform: ν detectors R&D for experiments in US, Japan

n-TOF: n-induced cross-sections

UA9: crystal collimation

ISOLDE = Isotope Separator On Line



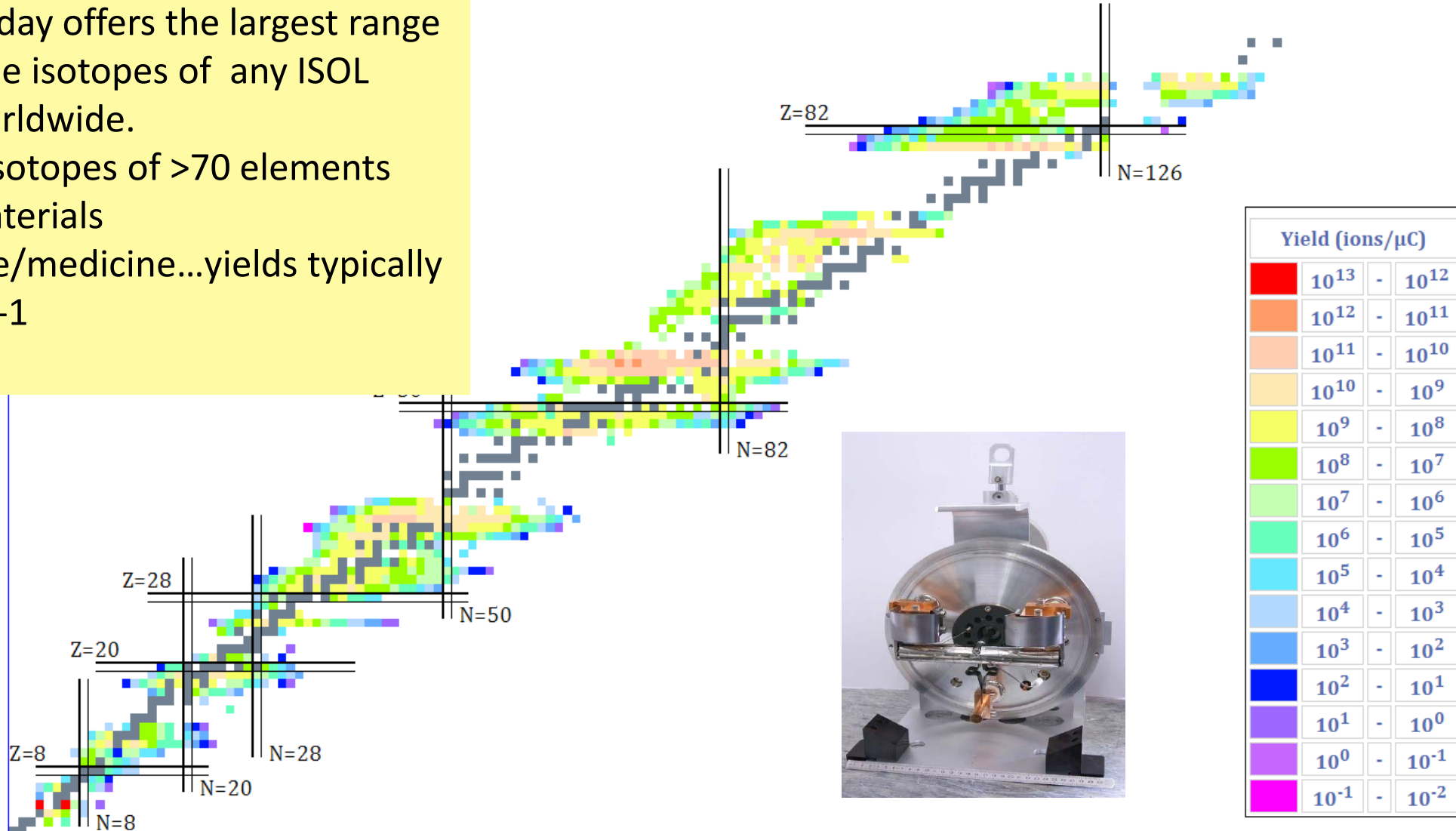
CERN accelerators

ISOLDE uses about 65% of CERN's protons....

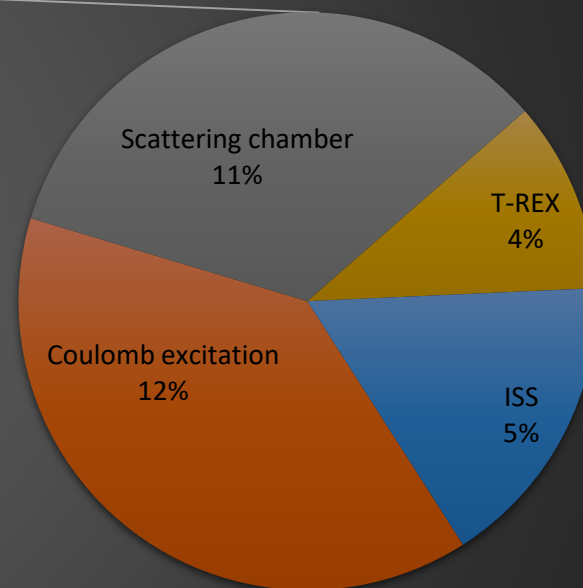
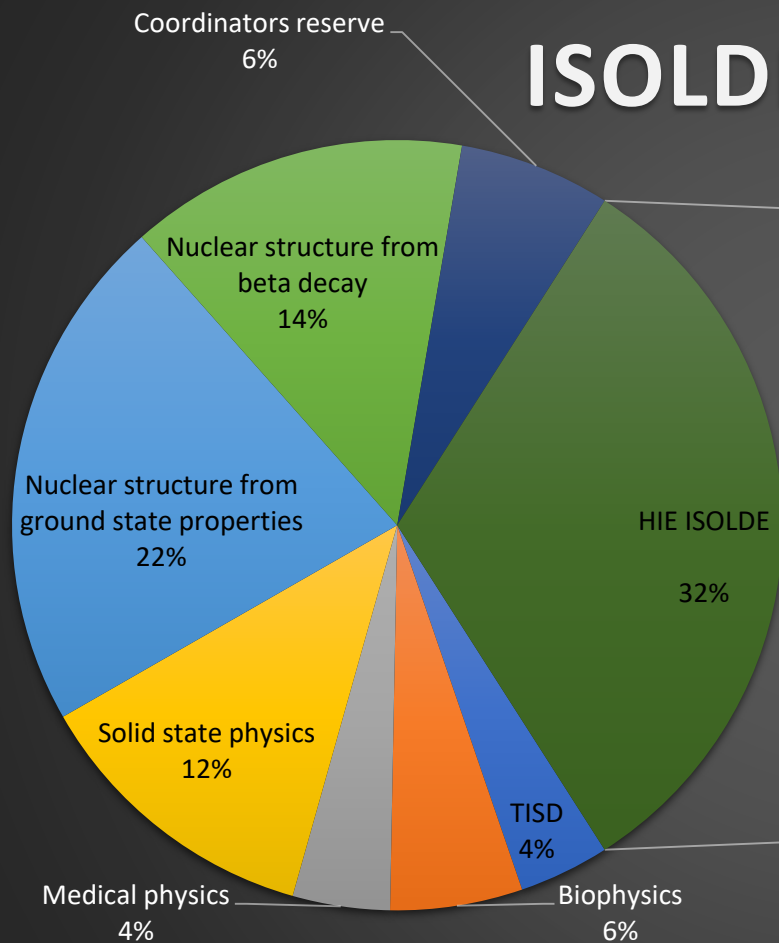
Nuclear chart for ISOLDE

ISOLDE today offers the largest range of available isotopes of any ISOL facility worldwide.

- 1000 isotopes of >70 elements
- For materials science/medicine...yields typically $>1e7 \text{ s}^{-1}$

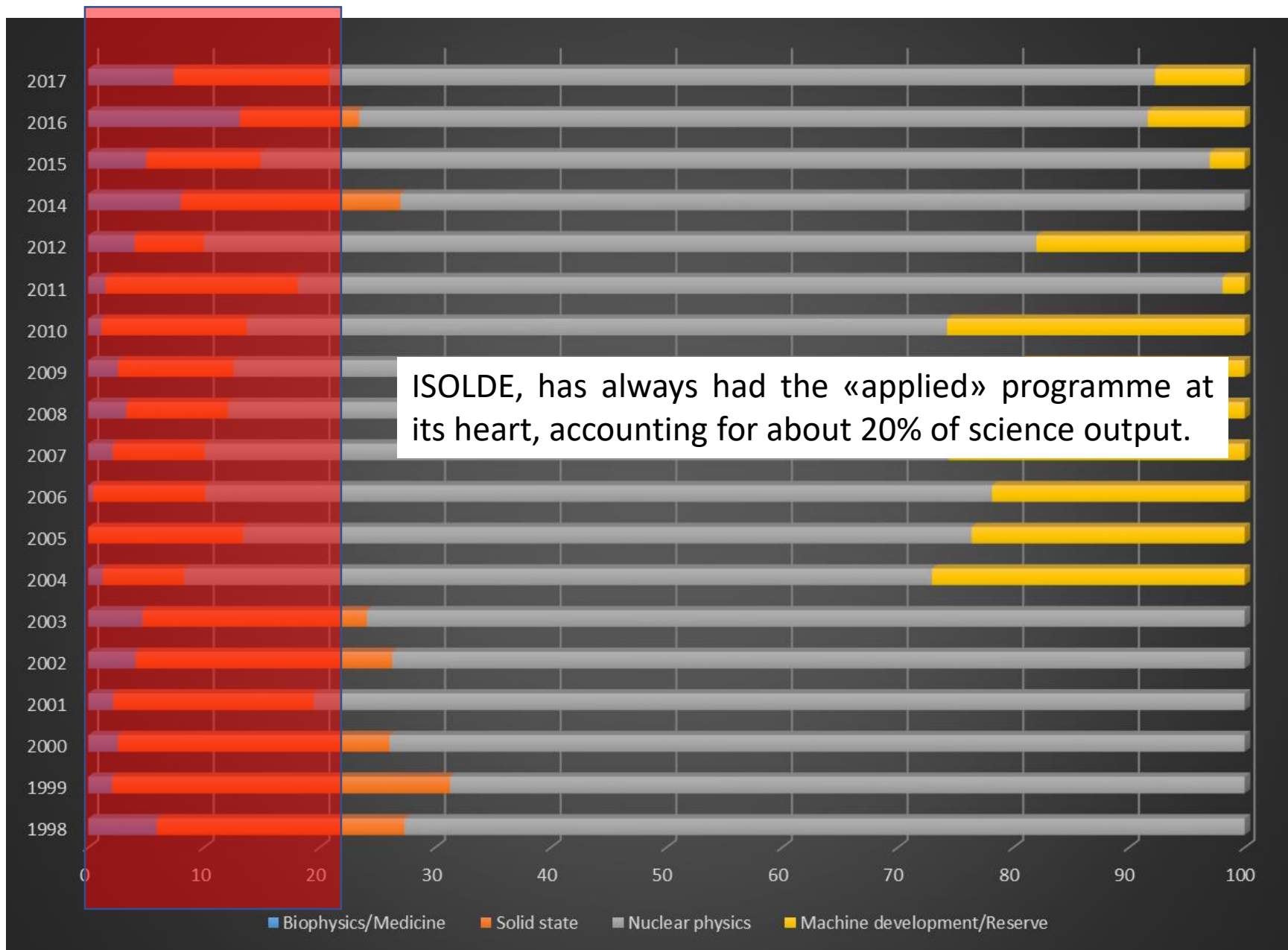


ISOLDE PIE 2018



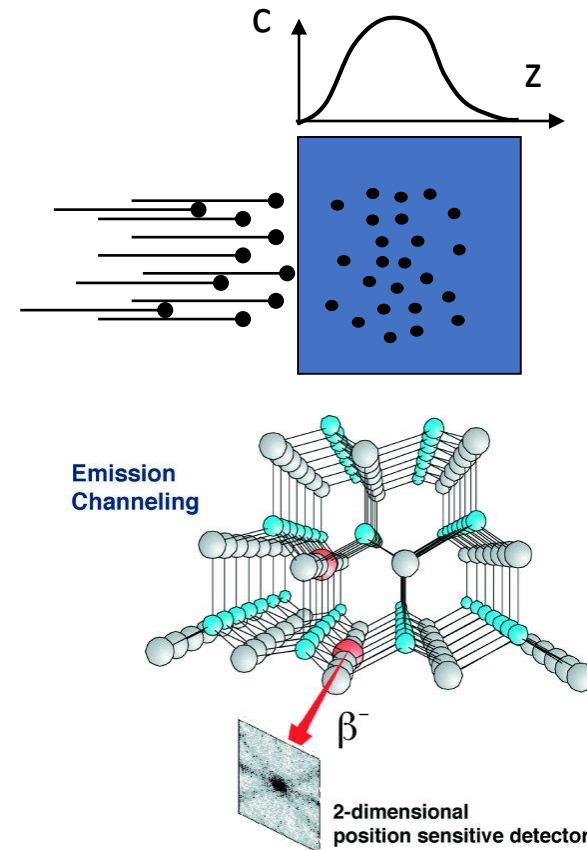
Étiquettes de lignes	Nombre de Delivered 2018
Biophysics	4
COLLAPS	3
CRIS	4
Gandalph	1
HIE	12
IDS	5
ISOLTRAP	2
la1	1
MEDICAL	2
REX	1
Special	1
SSP	13
Windmill; ISOLTRAP	1
WITCH	1
Total général	51

Applications: Solid state and biophysics/medicine long at the core of the ISOLDE programme



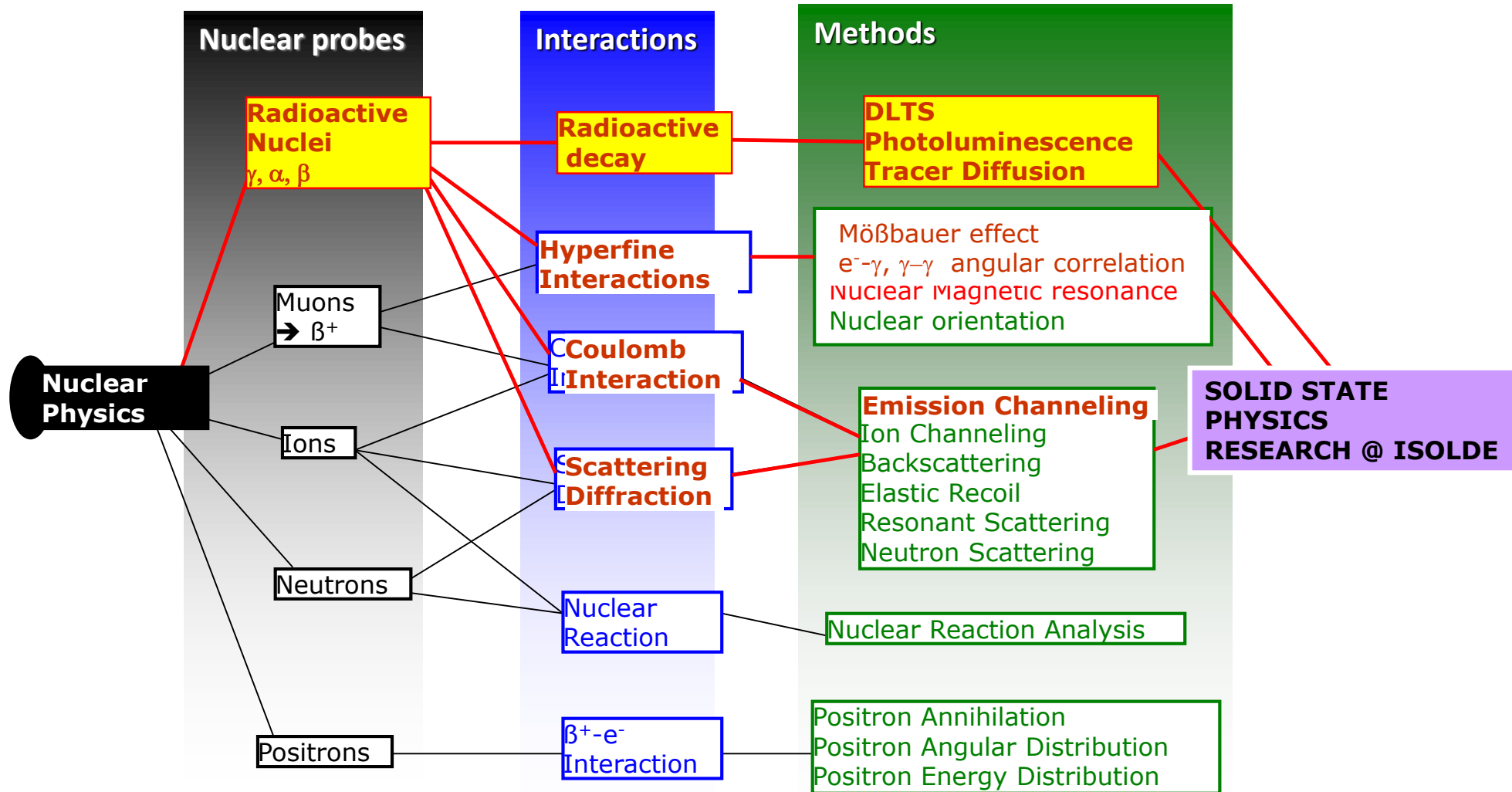
Unique features of radioactive probe atoms for SSP/biology applications

- **Chemically selective and isotope specific**
- **Extremely good detection limit**
 - among the most sensitive methods, no reaction cross section limitation
 - $10^{15} - 10^{18}$ probes/cm³
 - $10^{11} - 10^{12}$ probe atoms
- **Depth distribution and concentration control**
 - Ion energy and ion fluence control
 - Circumventing solubility and diffusion limits
- **Highly local Information**
 - Nucleus-size sensors for **local** magnetic and electric fields
 - Electric Field Gradient $\sim r^{-3}$
 - Emission channeling: ~ 0.02 nm position resolution



Why radioactive probes ? Sensitive – Selective - Controllable – Local
Often relatively easy isotopes for RIB facilities to produce (not always a good thing...)

Applying radioactivity to solid state physics



ISOLDE table of elements


The table shows ionization methods for various elements:

- surface ionization (+/-):** H, Li, Na, K, Rb, Cs, Fr, Ra, Ac, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, Ge, As, Se, Br, Kr, Xe, Rn.
- laser selective ionization:** Be, Mg, Ca, Sr, Ba, La, Hf, Ta, W, Re, Os, Ir, Pt, Au, Hg, Tl, Pb, Bi, Po, At, Rn.
- hot plasma discharge (hot/cold):** B, C, N, O, F, Ne, Al, Si, P, S, Cl, Ar, Zn, Ga, Ge, As, Se, Br, Kr, Xe, Rn.

Yellow circles indicate isotopes used for solid state physics or life science. These include: H, Li, Na, K, Rb, Cs, Fr, Ra, Ac, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, Ge, As, Se, Br, Kr, Xe, Rn, Ce, Pr, Nd, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu, Th, Pa, U, Np, Pu, Am, Cm, Bk, Cf, Es, Fm, Md, No, Lr.




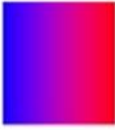

Workhorse probes:
 ^{111}Cd , ^{199}Hg , ^{117}Cd , ^{57}Mn , ^{73}As

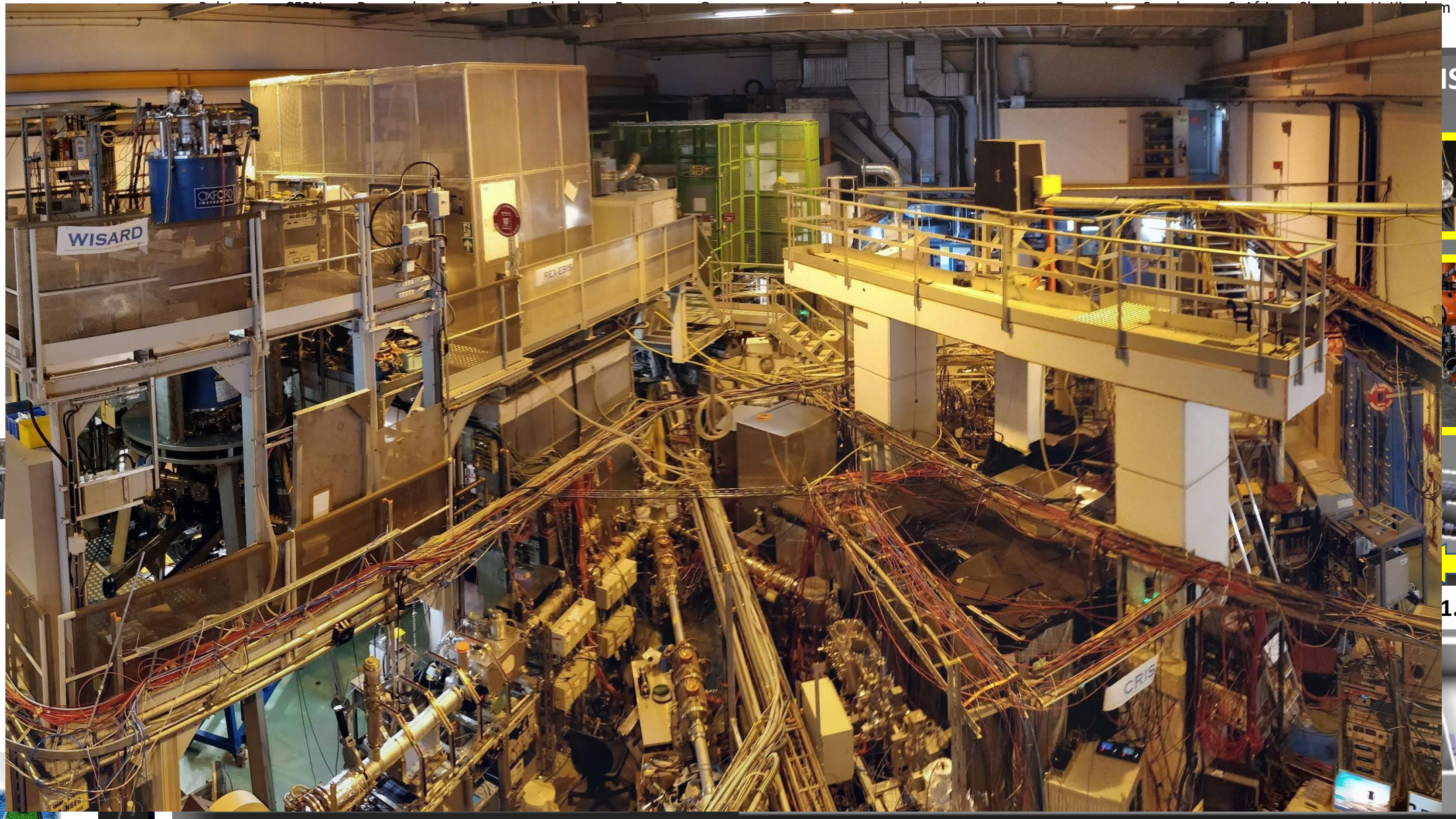
New promising probes:
 ^{68}Cu , ^{149}Gd , ^{172}Lu , ^{151}Gd , ^{197}Hg

Isotopes of this element
 **used for solid state physics or life science**

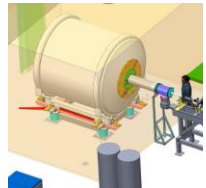
PAC → Perturbed Angular Correlations
 M → Mössbauer Effect

H																	He
Li <i>b-N</i>	Be											B	C	N	O	F <i>PAC</i>	Ne
Na <i>b-N</i>	Mg <i>b-N</i>											Al	Si	P	S	Cl	Ar
K <i>M</i>	Ca	Sr	Ti	V <i>PAC</i>	Cr	Mn	Fe <i>M</i>	Co	Ni <i>PAC</i> <i>M</i>	Cu <i>PAC</i>	Zn <i>M</i>	Ga	Ge <i>PAC</i> <i>M</i>	As <i>PAC</i>	Se <i>PAC</i>	Br <i>PAC</i>	Kr <i>PAC</i> <i>M</i>
Rb	Sr	Y	Zr	Nb	Mo <i>PAC</i> <i>M</i>	Tc <i>PAC</i> <i>M</i>	Ru <i>M</i>	Rh <i>PAC</i>	Pd	Ag	Cd <i>PAC</i>	In <i>PAC</i> <i>M</i>	Sn <i>PAC</i> <i>M</i>	Sb <i>M</i>	Te <i>M</i>	I <i>M</i>	Xe <i>M</i>
Cs <i>PAC</i> <i>M</i>	Ba <i>M</i>	La <i>M</i>	Hf <i>M</i>	Ta <i>PAC</i> <i>M</i>	W <i>M</i>	Re <i>M</i>	Os <i>M</i>	Ir <i>PAC</i> <i>M</i>	Pt <i>M</i>	Au <i>M</i>	Hg <i>PAC</i> <i>M</i>	Tl	Pb <i>PAC</i>	Bi	Po	At	Rn
Fr	Ra	Ac															
			Ce	Pr <i>PAC</i> <i>M</i>	Nd <i>M</i>	Pm <i>M</i>	Sm <i>M</i>	Eu <i>PAC</i> <i>M</i>	Gd <i>M</i>	Tb <i>M</i>	Dy <i>M</i>	Ho <i>M</i>	Er <i>M</i>	Tm <i>M</i>	Yb <i>PAC</i> <i>M</i>	Lu <i>M</i>	
			Th <i>M</i>	Pa <i>M</i>	U <i>M</i>	Np <i>M</i>	Pu <i>M</i>	Am <i>M</i>	Cm <i>M</i>	Bk	Cf	Es	Fm	Md	No	Lr	

	γ - γ & γ - e^- PAC		only e^- - γ PAC		only γ - γ PAC
	γ - γ & e^- - γ PAC		only γ - e^- PAC		



MINIBALL



ISS



ISOLTRAP



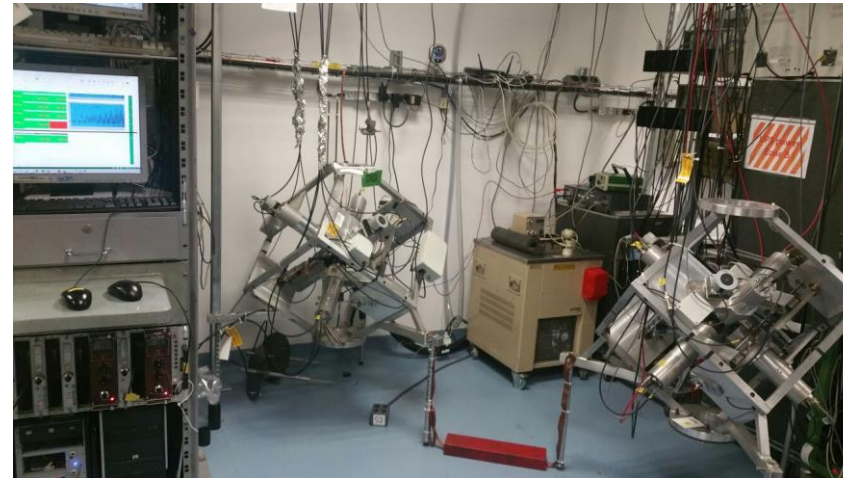
IDS



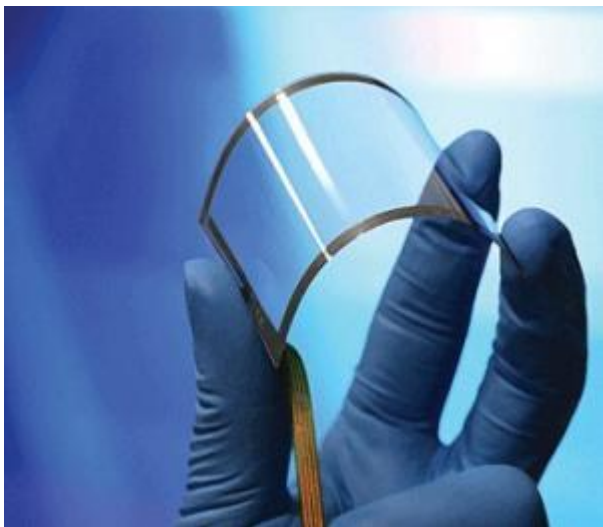
SSP

MEDICAL ISOTOPES

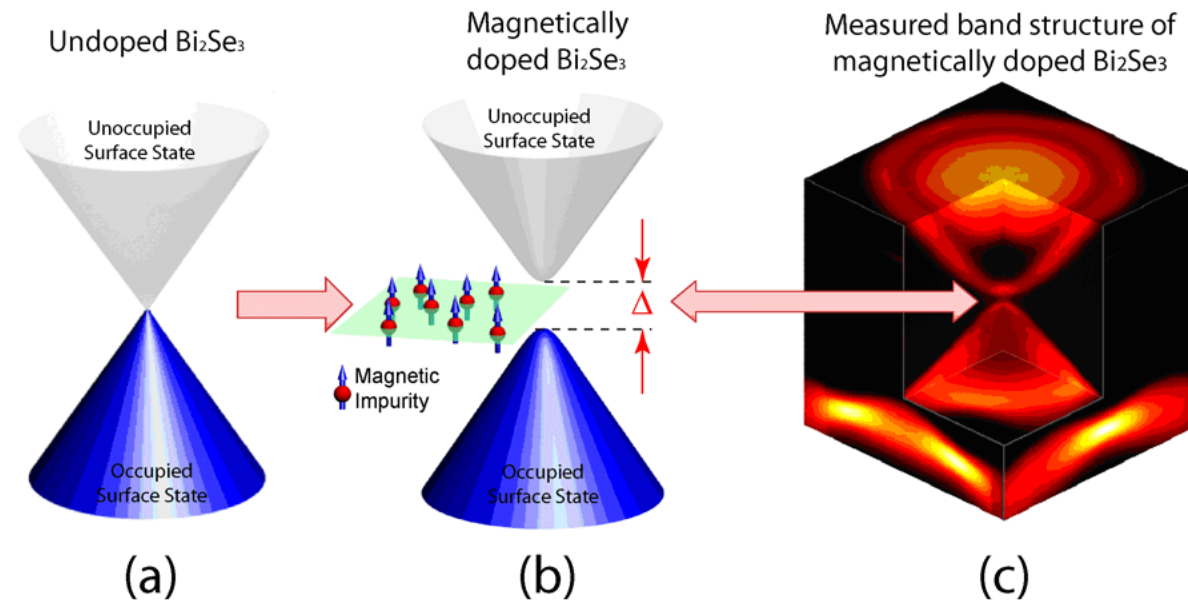
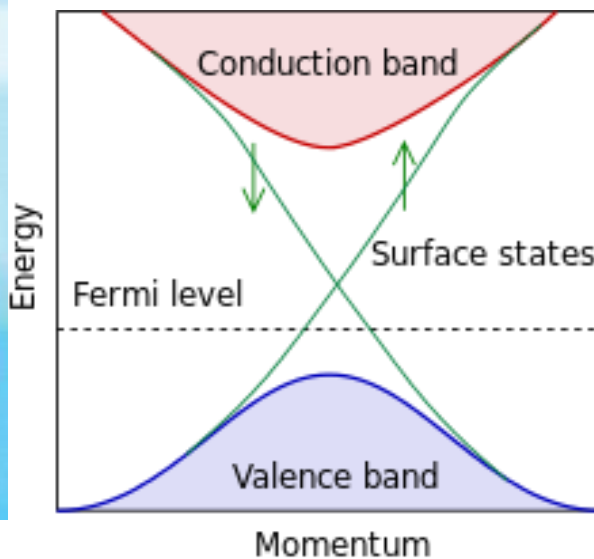
Offline labs at ISOLDE: B. 508



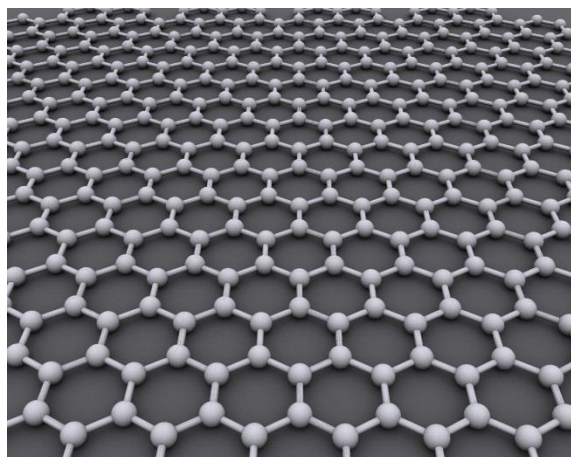
Staying relevant: Materials studied at ISOLDE



graphene



Topological Insulators



IOP Publishing

Journal of Physics

J. Phys. D: Appl. Phys. 50 (2017) 393002 (26pp)

<https://doi.org/10.1088/1361-6462/aa6600>

Topical Review

Experimentally evaluating the origin of dilute magnetism in nanomaterials

L M C Pereira

KU Leuven, Instituut voor Kern- en Stralingsfysica, 3001 Leuven, Belgium

Hyperfine techniques are particularly successful in unravelling subtle magnetic behaviour in materials

Copper Indium
Gallium Selenide
(CIGS)

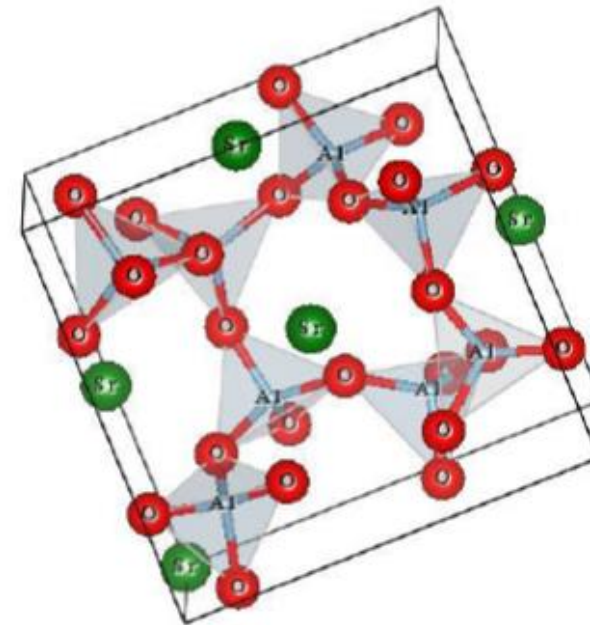
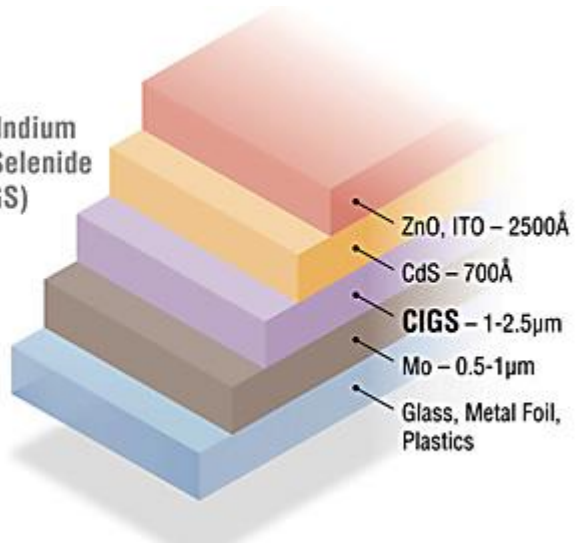


Fig. 1

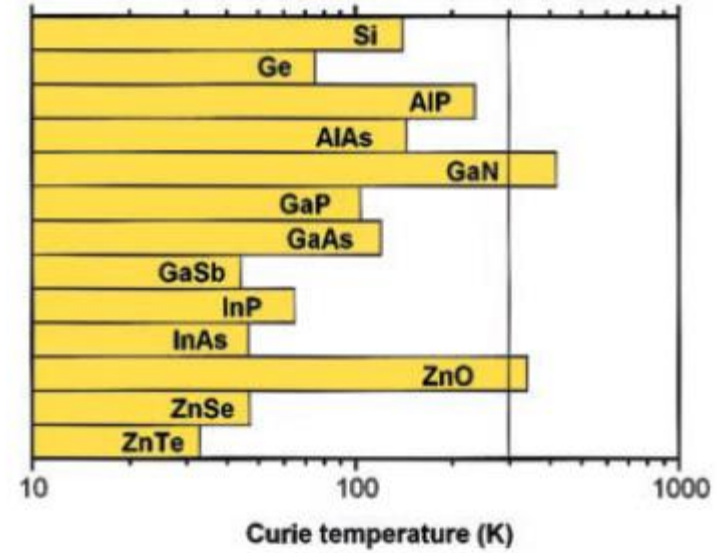
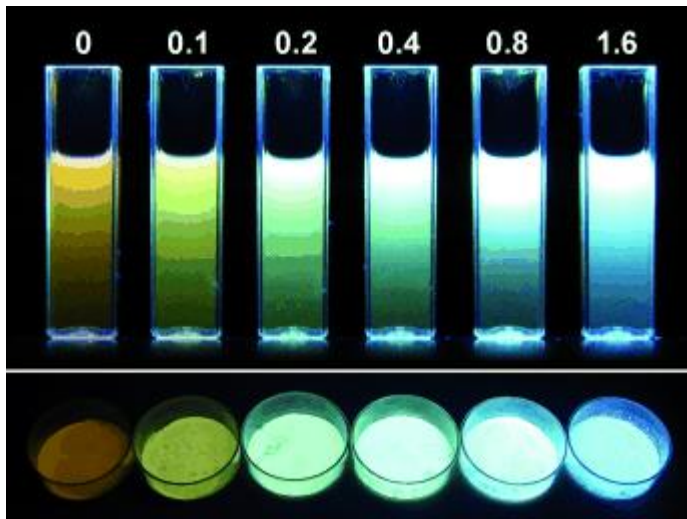


Fig. 3. Computed values of the Curie temperature T_C for various p-type semiconductors containing 5% of Mn and 3.5×10^{20} holes cm^{-3} .

Dietl *et al*, *Science* 287 (2000) 1

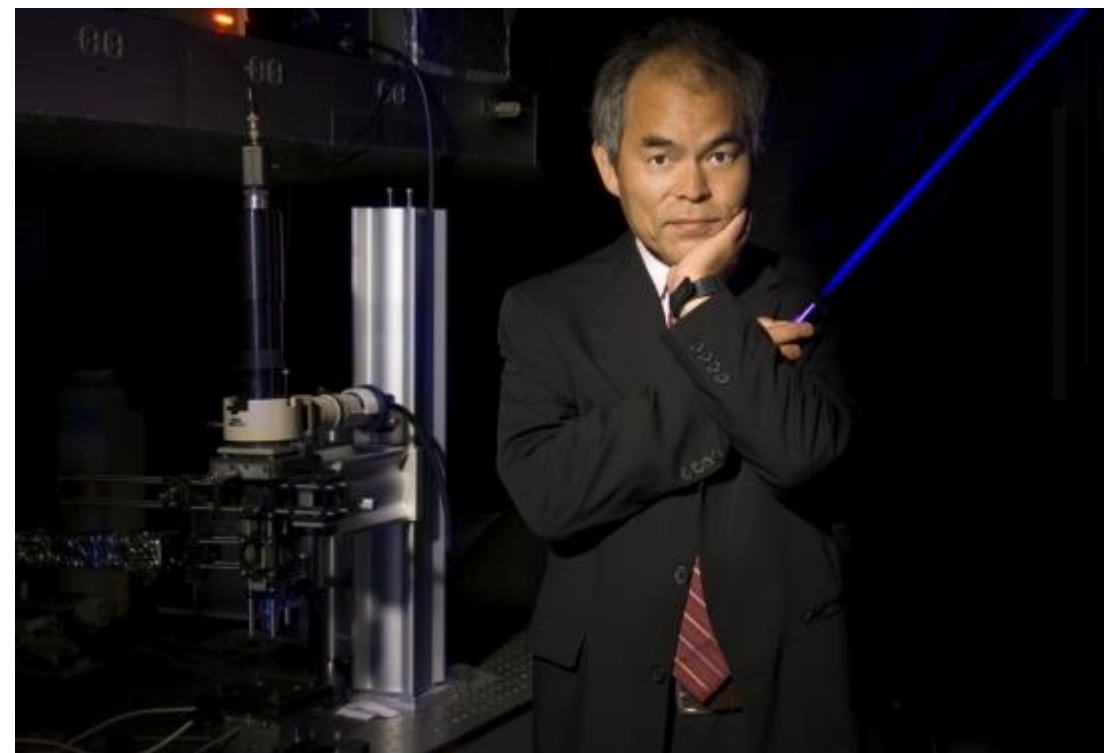
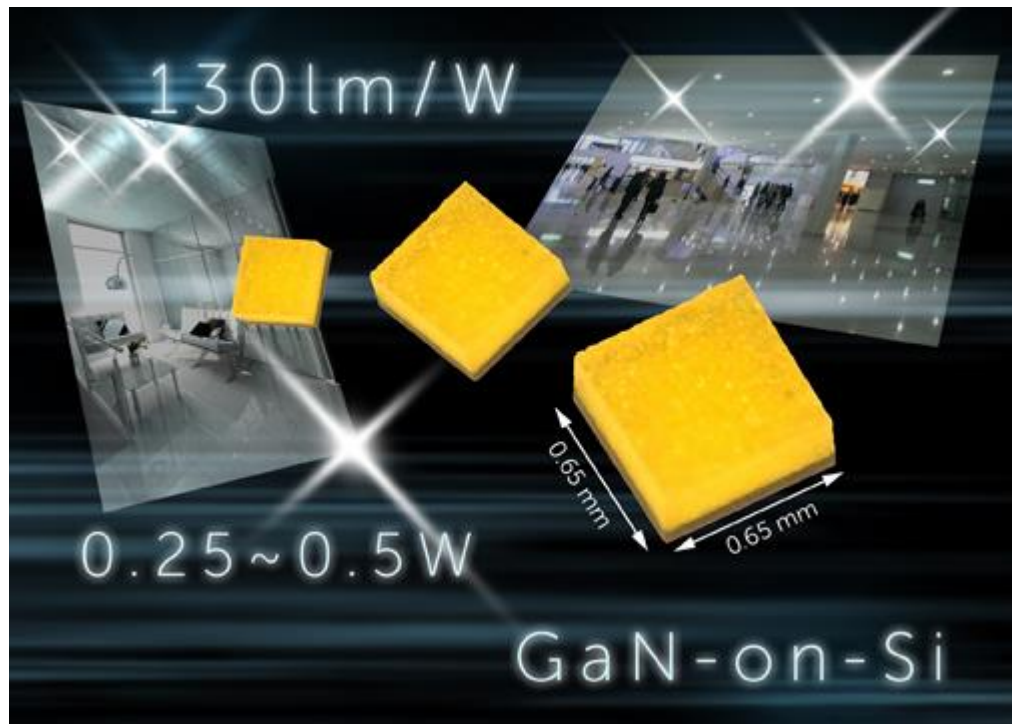


Is it possible to create magnetic semiconductors that work at room temperature?

Such devices have been demonstrated at low temperatures but not yet in a range warm enough for spintronics applications.



Next generation semiconductors : doping





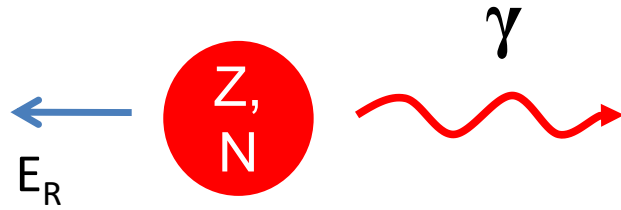
^{129}Ir

Rudolf L. Mössbauer

Nobel Prize in Physics in 1961
for his 1957 discovery of the
Mössbauer effect

1929 – 2011

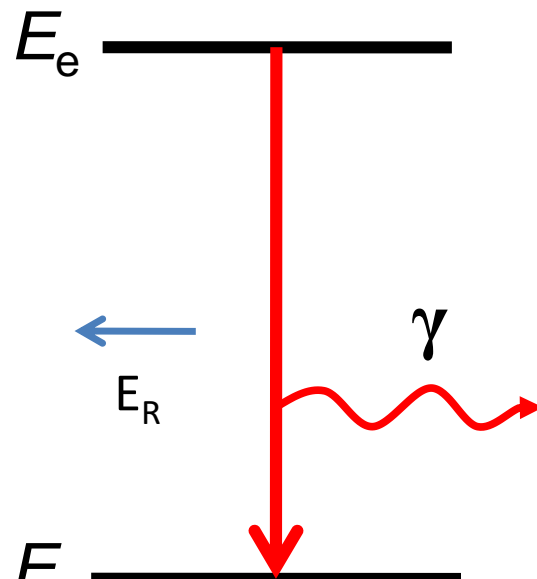
Free Nucleus



No Resonance

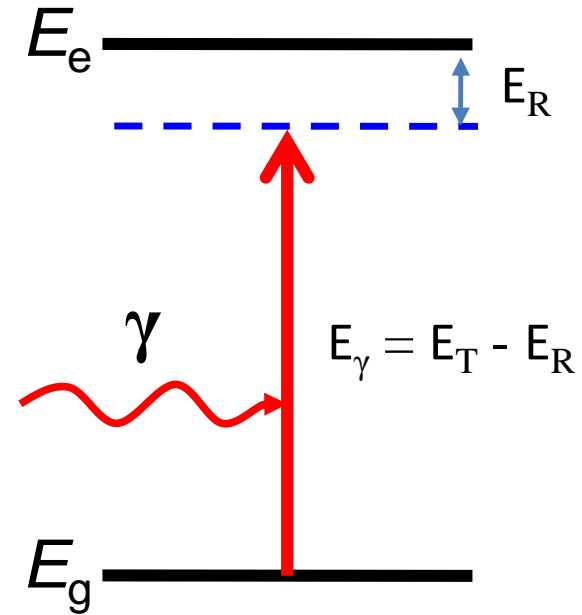
Emission

Nucleus in excited state

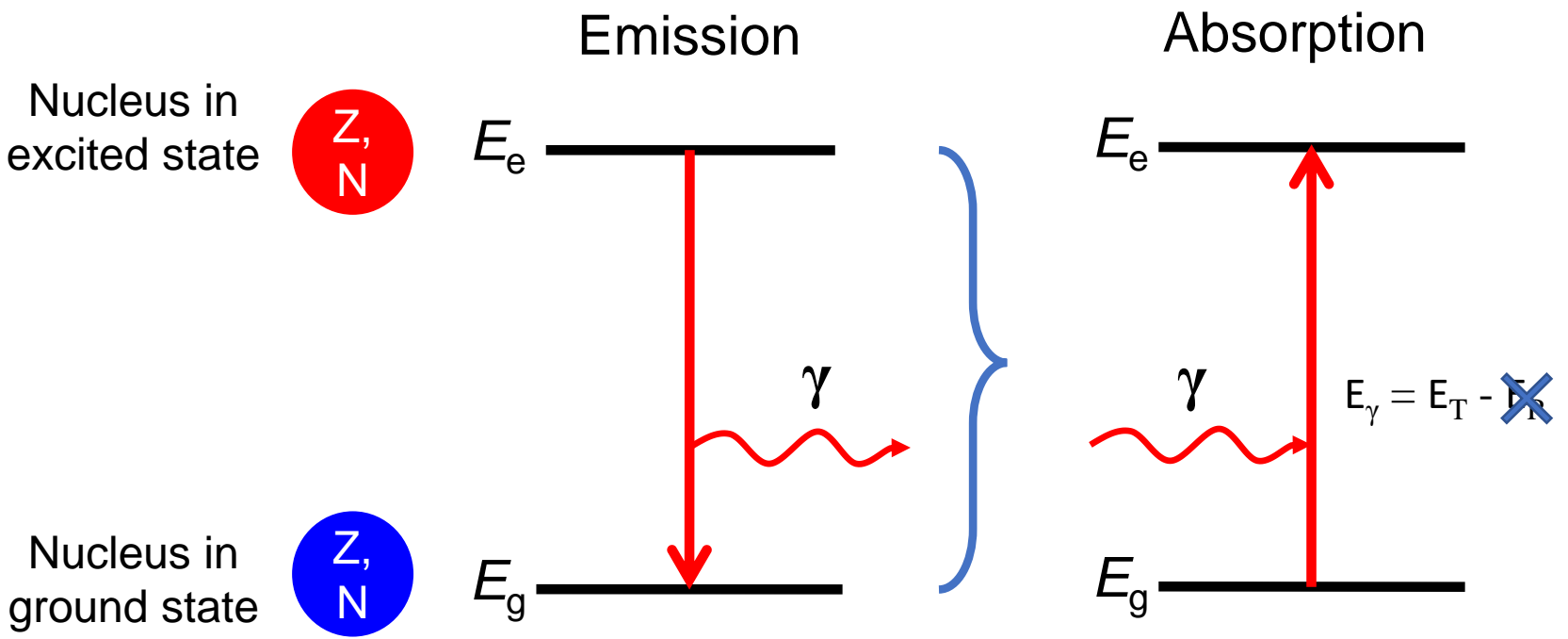
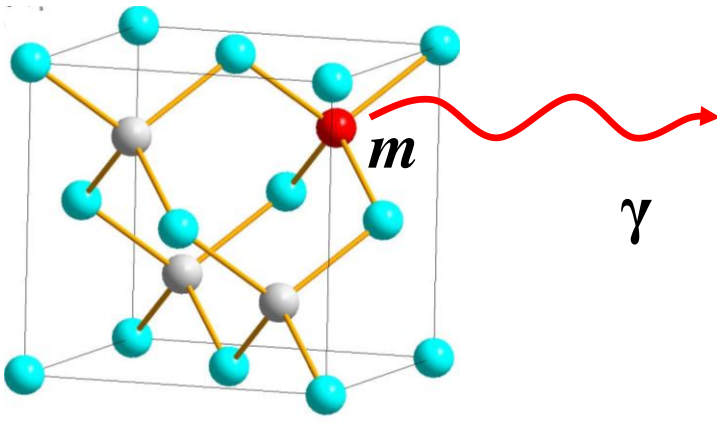


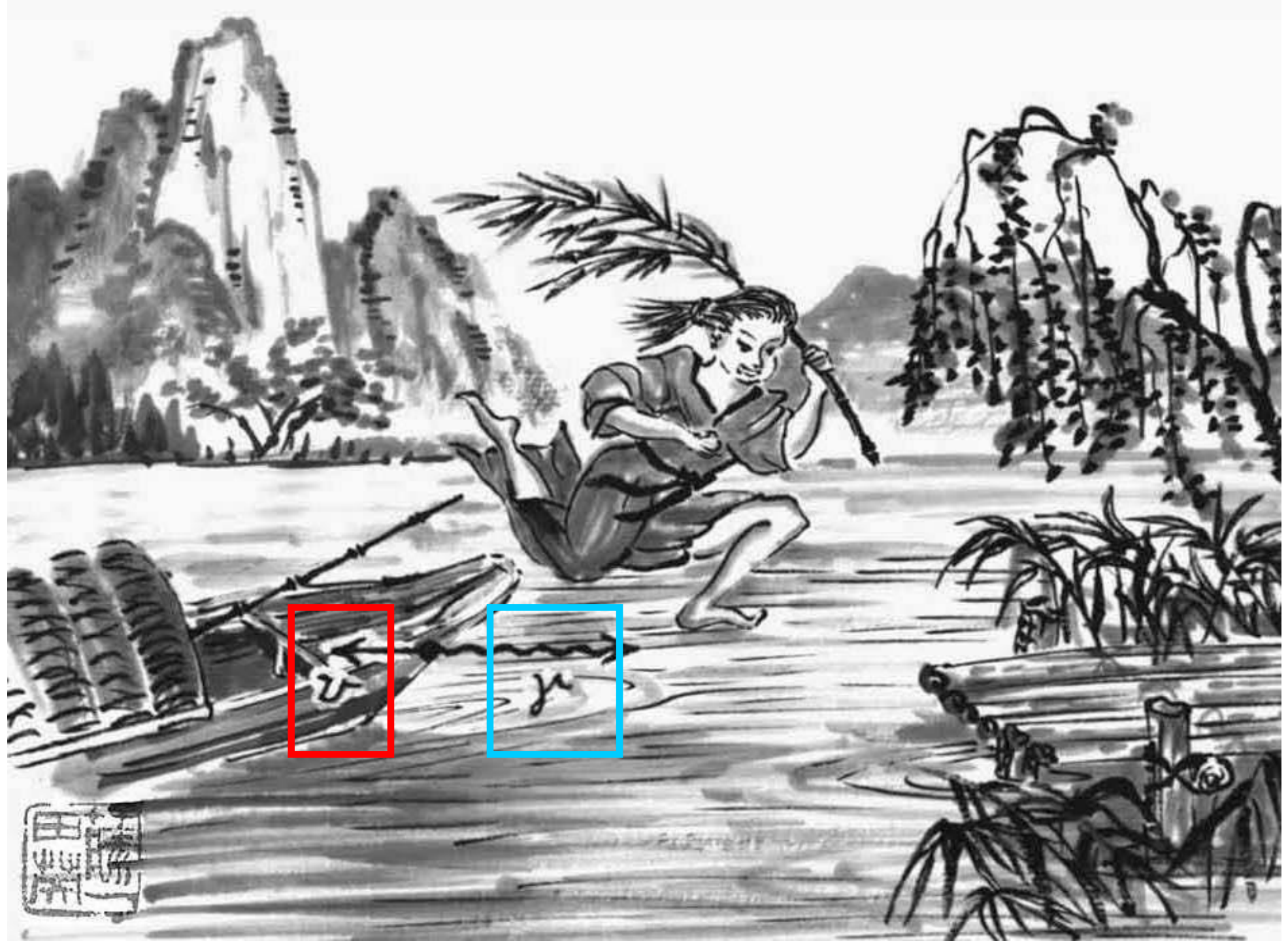
Absorption

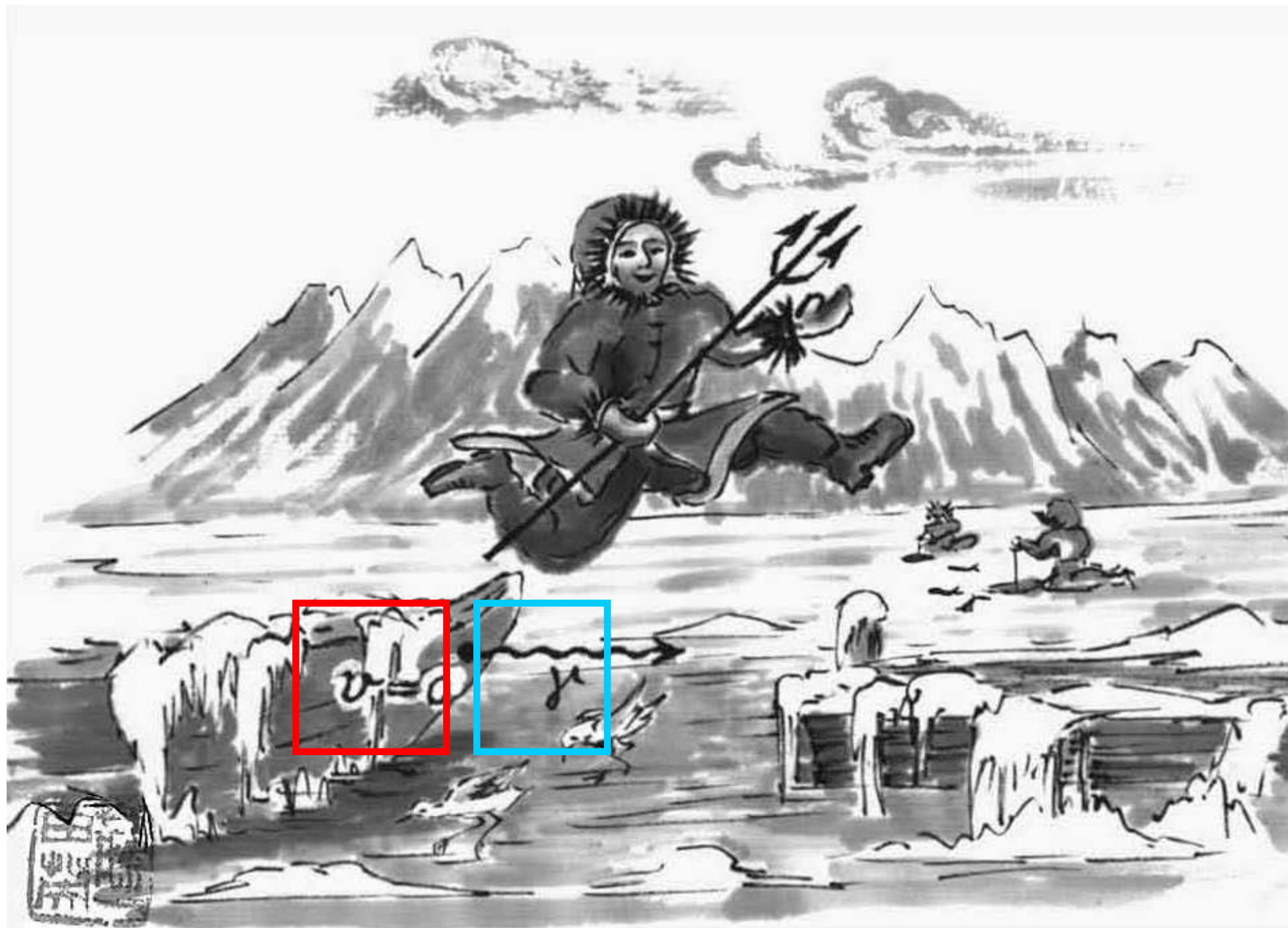
Nucleus in ground state



$$M \gg m$$

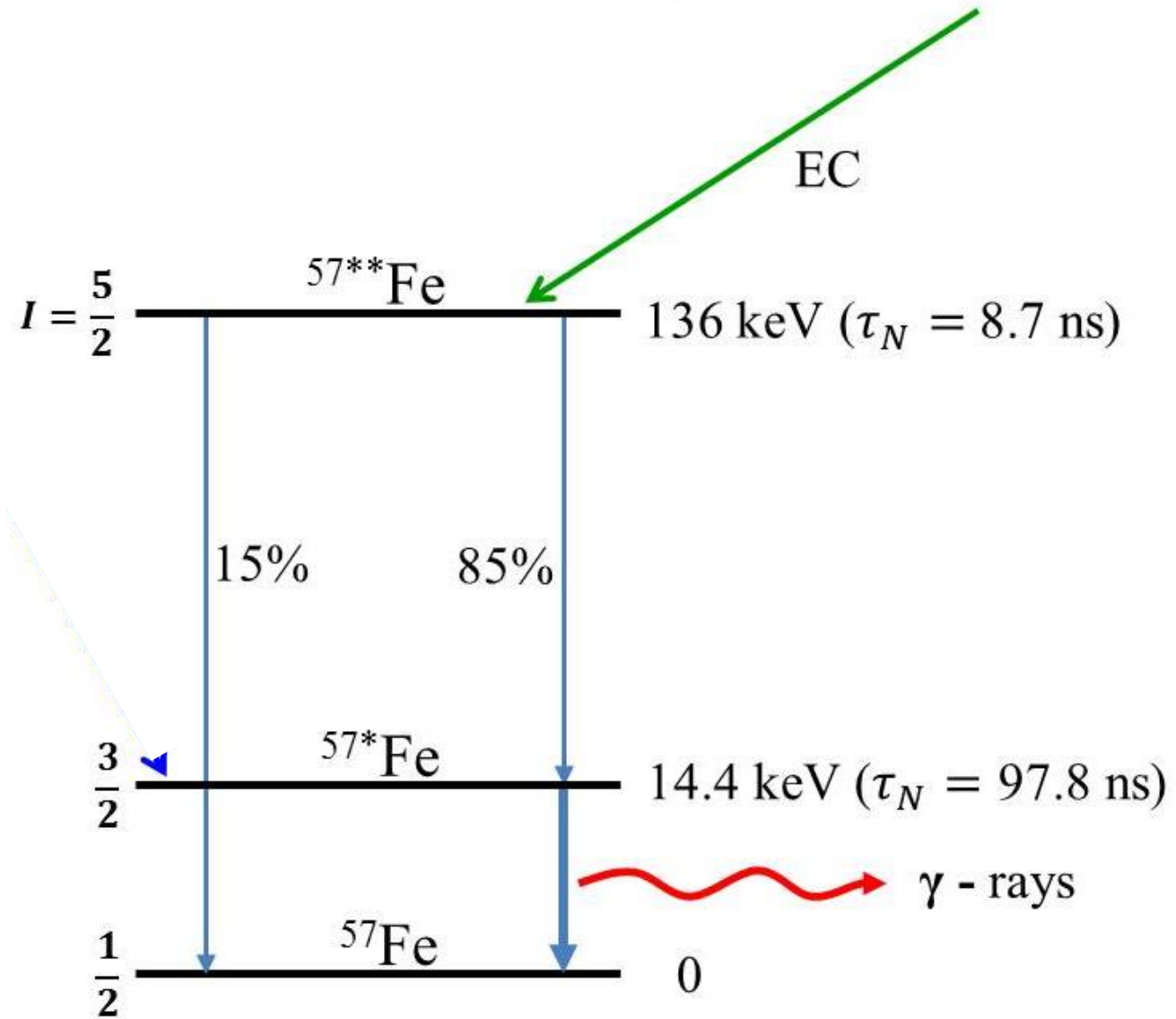






Mossbauer state ^{57}Fe via ^{57}Mn
In contrast to “standard” ^{57}Co

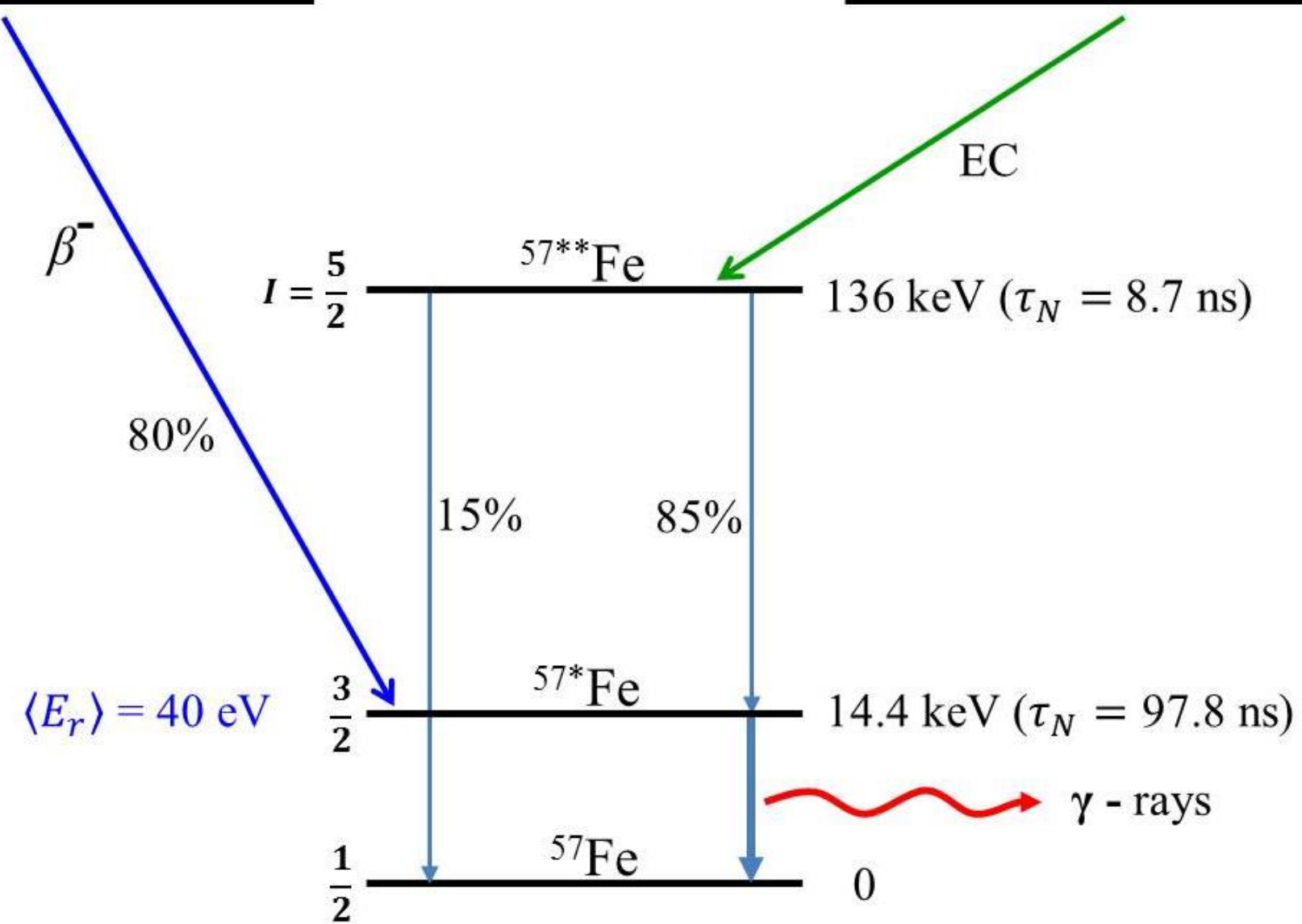
^{57}Co ($t_{1/2} = 271.74 \text{ d}$)



Mossbauer state ^{57}Fe via ^{57}Mn
In contrast to "standard" ^{57}Co

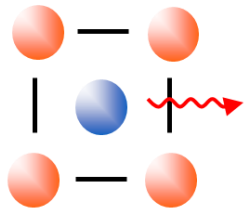
^{57}Mn ($t_{1/2} = 85.4 \text{ s}$)

^{57}Co ($t_{1/2} = 271.74 \text{ d}$)

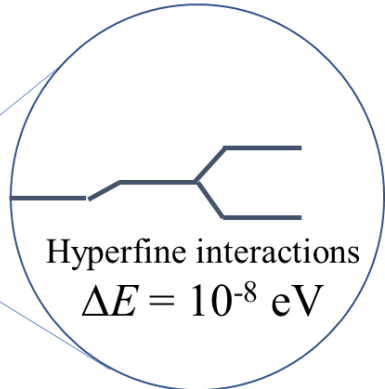
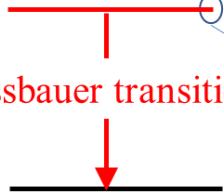


Local information....

Measure hyperfine interactions



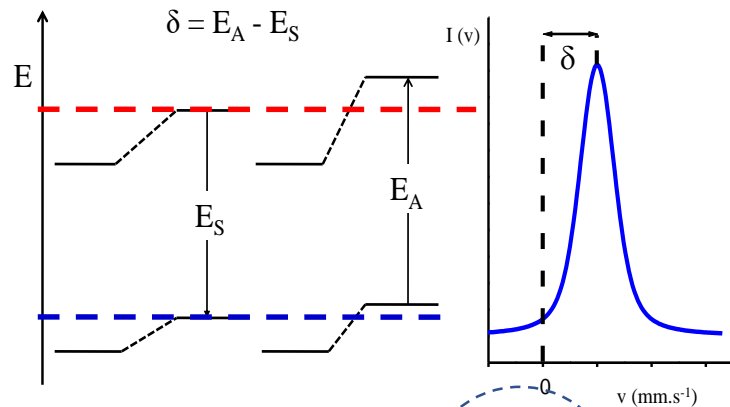
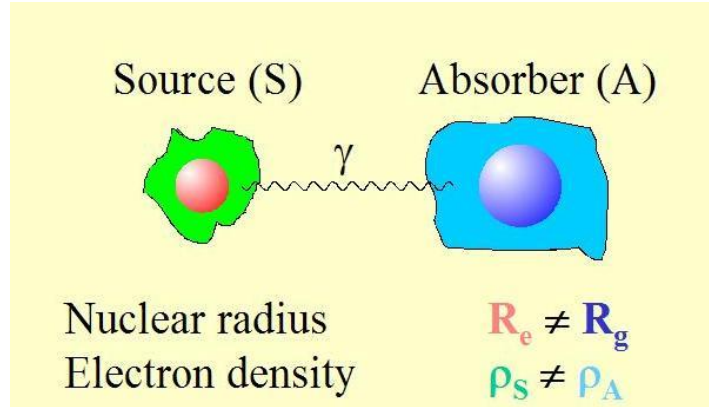
Mössbauer transition



Hyperfine interactions
 $\Delta E = 10^{-8}$ eV

Dilute Probe:
Below 10^{-3} at. %
 1×10^{18} atoms/cm³

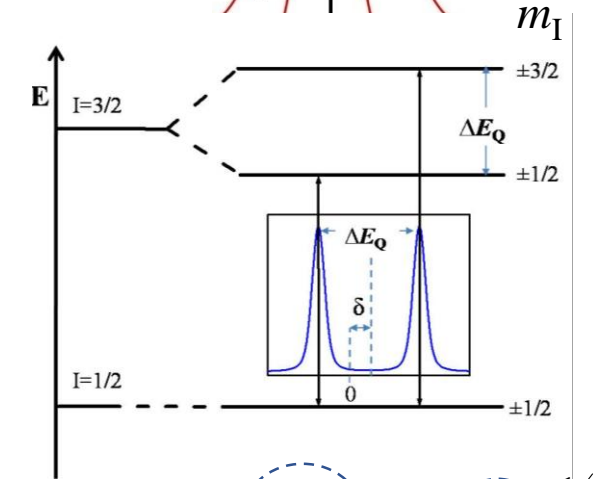
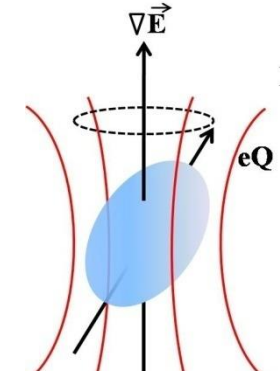
Isomer Shift



$$\delta_{IS} = \alpha [\rho_a(0) - \rho_s(0)]$$

Chemical bonding
Charge states

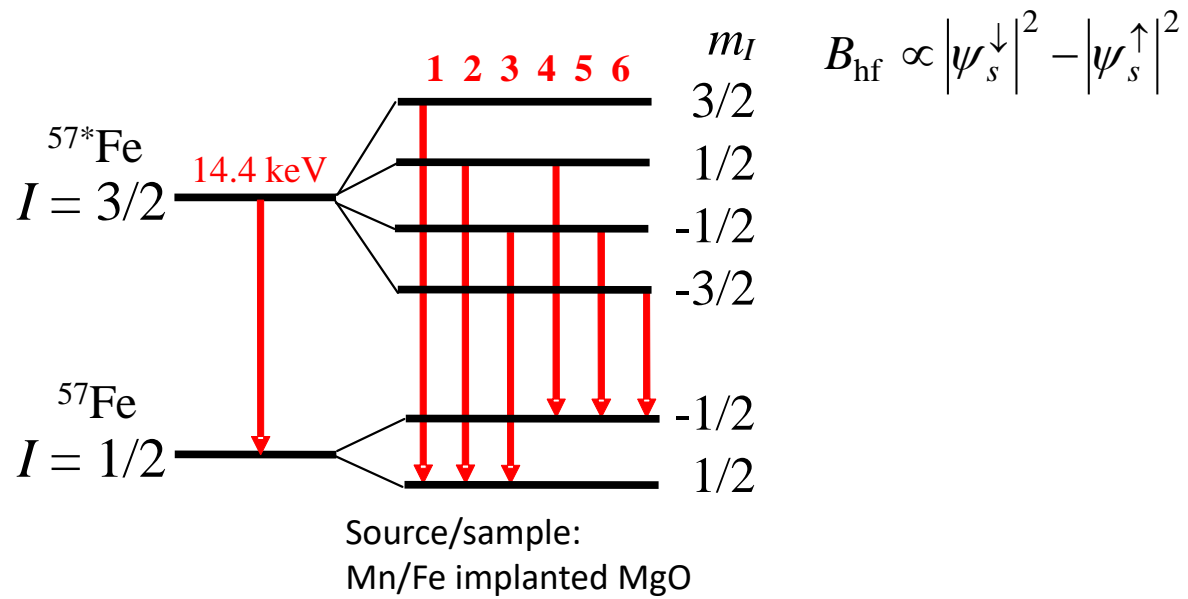
Quadrupole Splitting



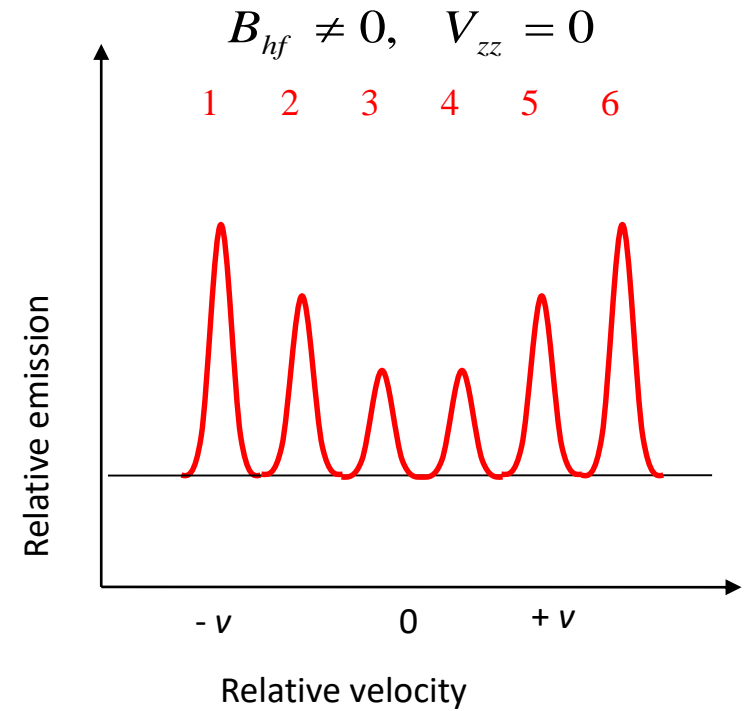
$$\Delta E_Q = \pm \frac{eQV_{ZZ}}{2} \left(1 + \frac{\eta^2}{3} \right)^{1/2}$$

Lattice asymmetry
Clustering of atoms

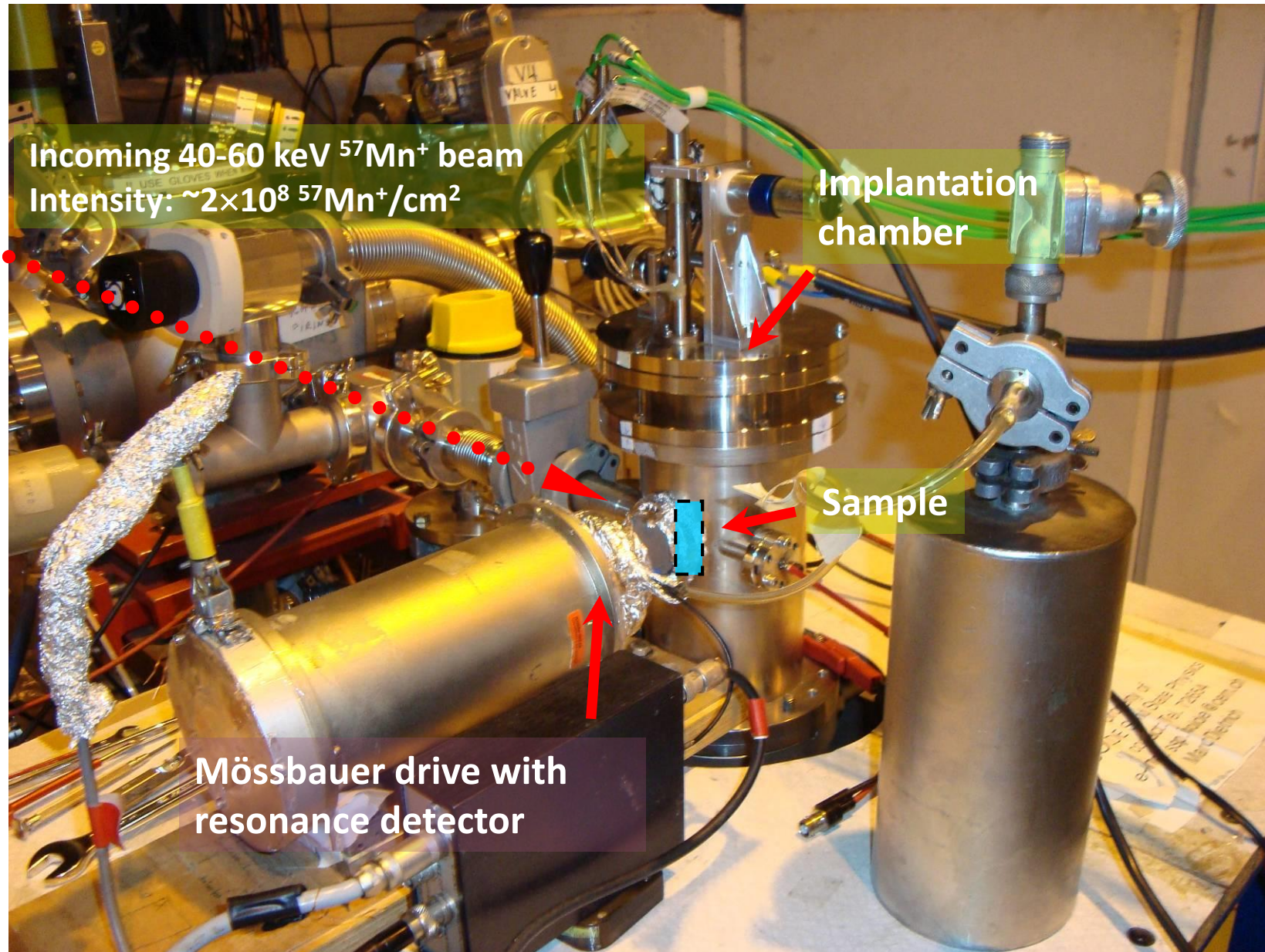
Magnetic hf. splitting of ^{57}Fe : Sextet



$$B_{\text{hf}} \propto |\psi_s^\downarrow|^2 - |\psi_s^\uparrow|^2$$



Hyperfine Interactions with Mossbauer spectroscopy



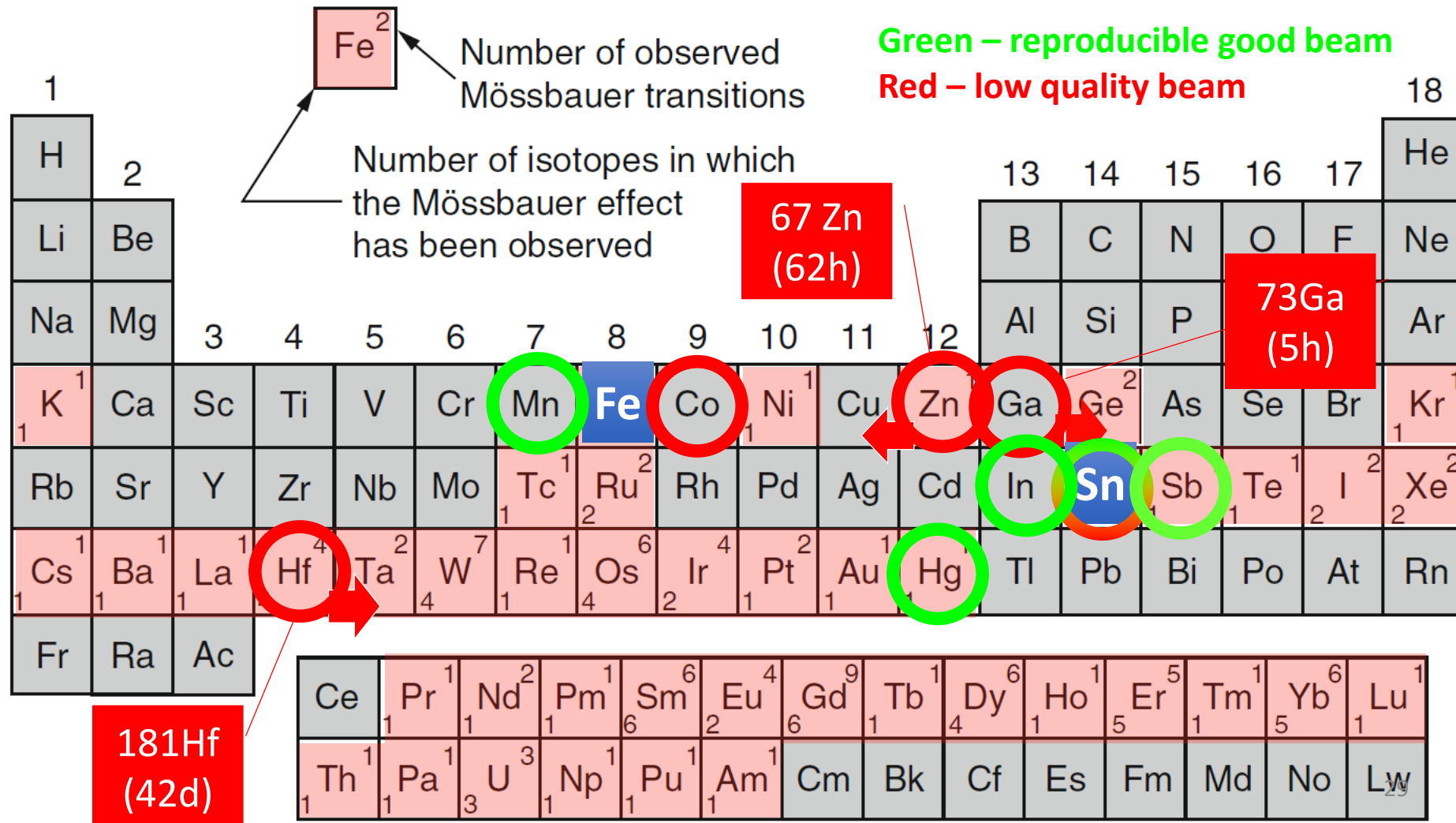
Laser Ionised ^{57}Mn beam : a new era for Mossbauer experiments at ISOLDE. 20th anniversary in 2016

- Very clean, intense beam of ^{57}Mn ($> 3 \times 10^8$ 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 ($\sim 10^{-4}\text{At}\%$)**

Mössbauer periodic table



Mössbauer Periodic Table



Fe: ZnO a ferromagnetic semiconductor? (no!)

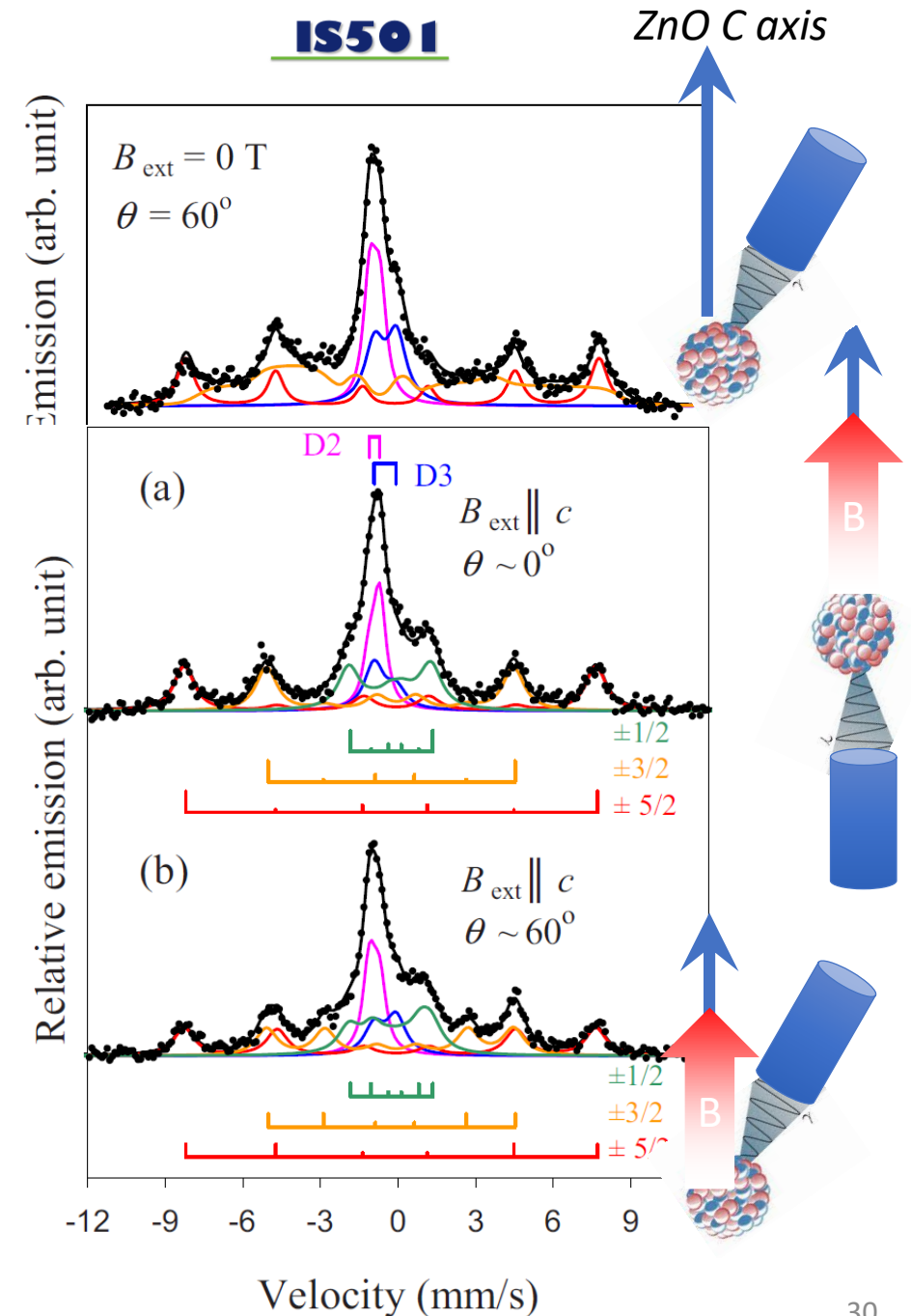
6 fold spectrum: characteristic of magnetic structure (at room temperature!!!).

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

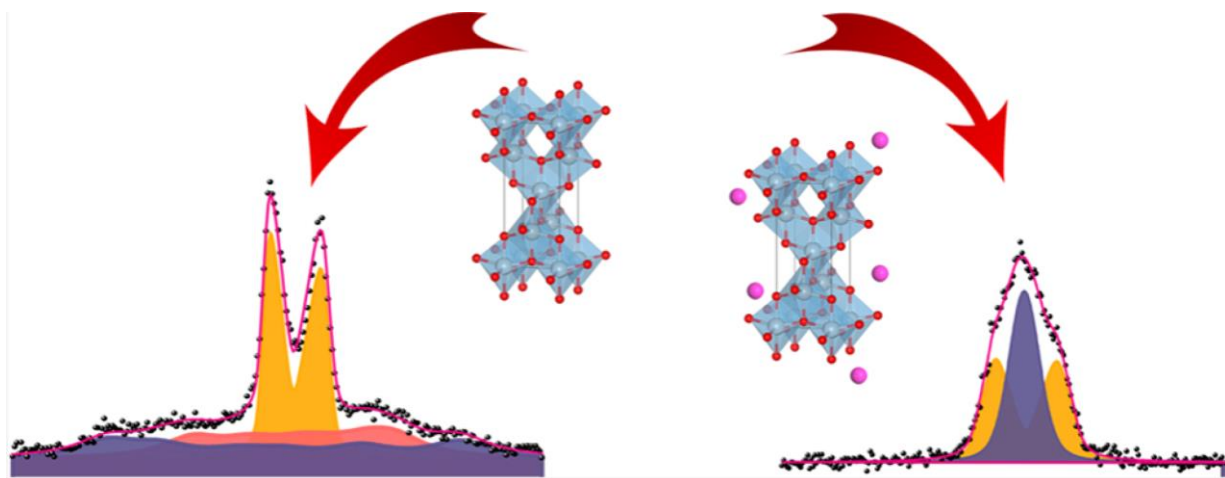
Gunnlaugsson *et al* (APL **97** 142501 2010)

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)

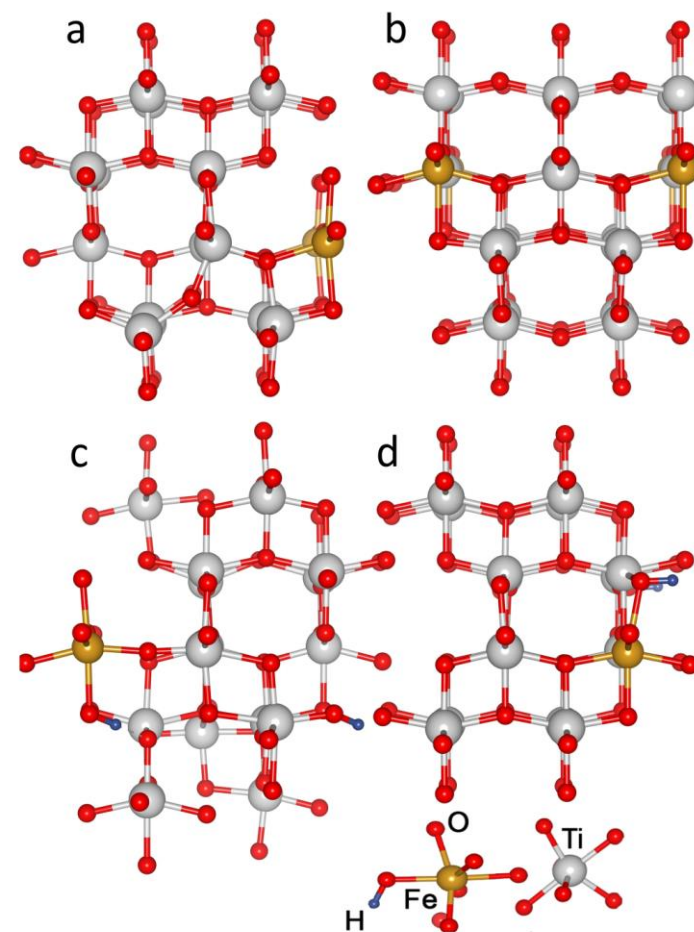


Experimental and Theoretical Study of Electronic and Hyperfine Properties of Hydrogenated Anatase (TiO_2): Defect Interplay and Thermal Stability



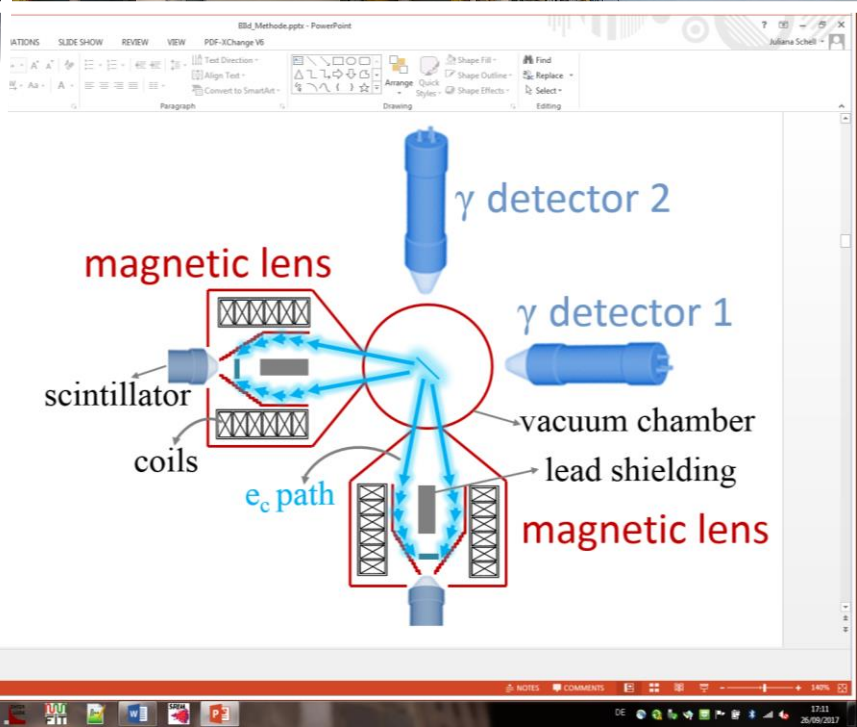
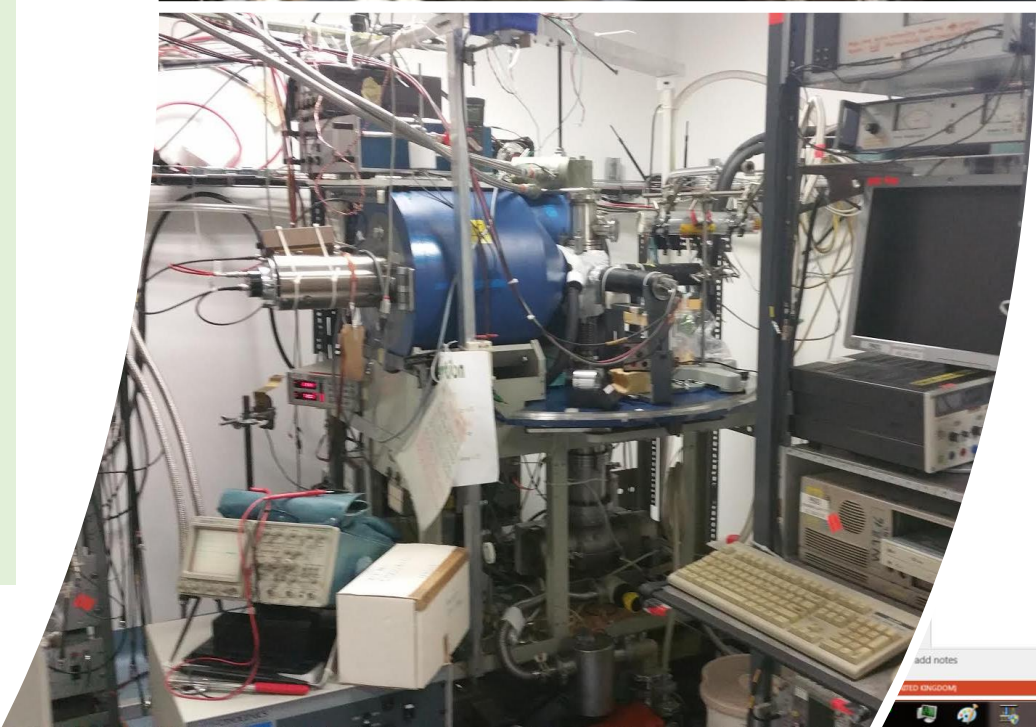
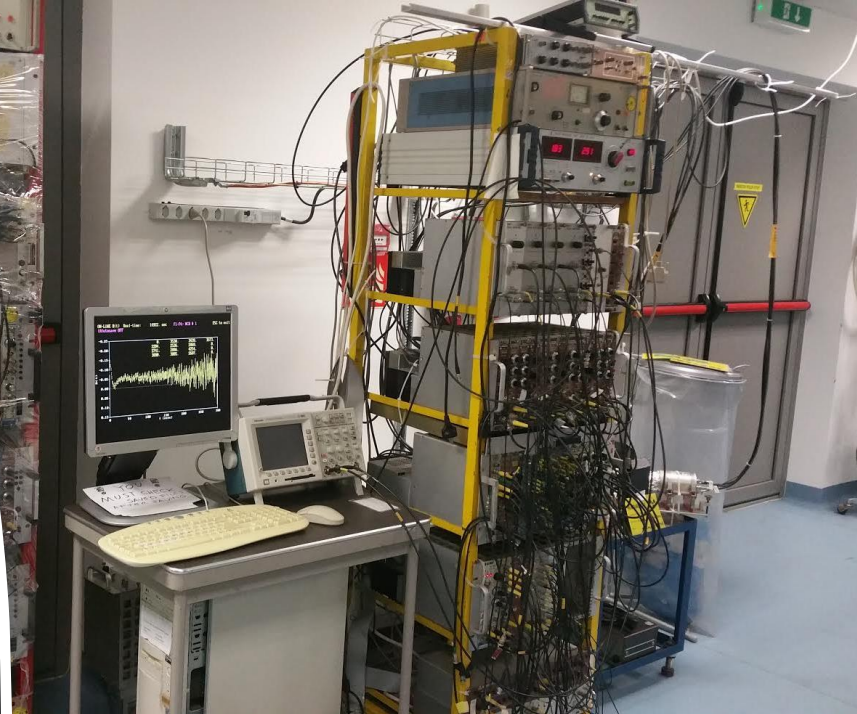
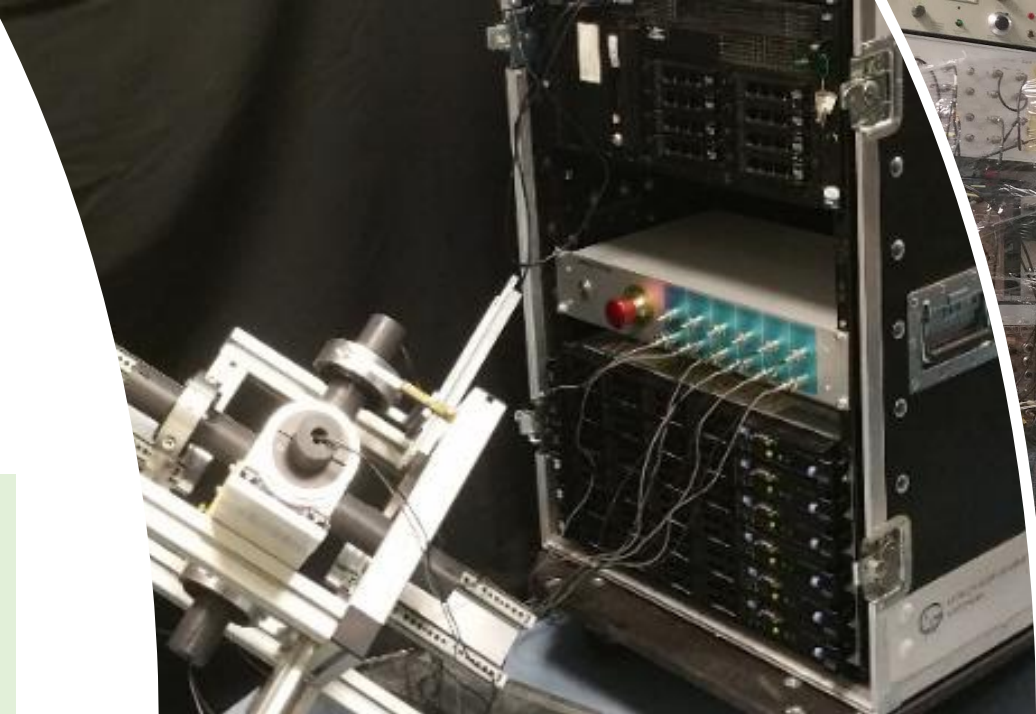
Sensitivity of Mossbauer to local interactions + *ab initio* modelling

Hydrogenated TiO_2

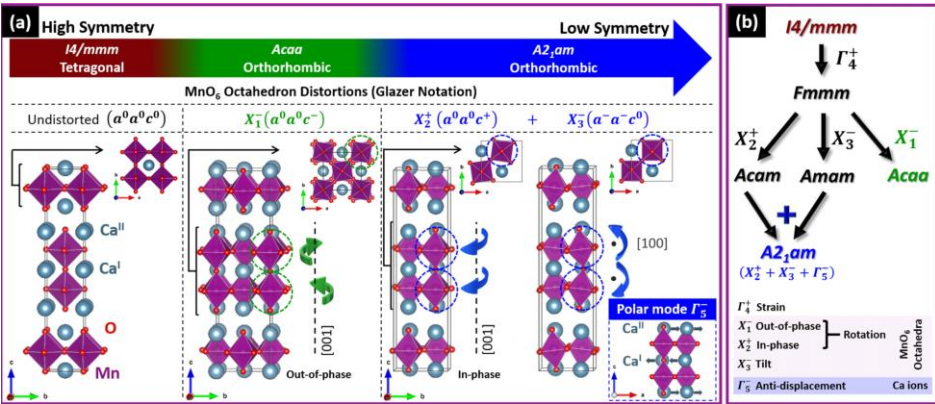


Perturbed angular correlation @ ISOLDE

- Most established technique at ISOLDE: benefitting from upgrade of spectrometers in recent years and improved relation to theory.
- Electron gamma unique to ISOLDE.
- Range of novel isotopes also only useable at ISOLDE: allows for varied programme in materials physics, biophysics and beyond



Ca₃Mn₂O₇ structural path unraveled by atomic-scale properties: A combined experimental and *ab initio* study



Probing multiferroic materials with PAC on the atomic scale: revealing the atomic changes behind the transitions from polar to ferroelectric behaviour

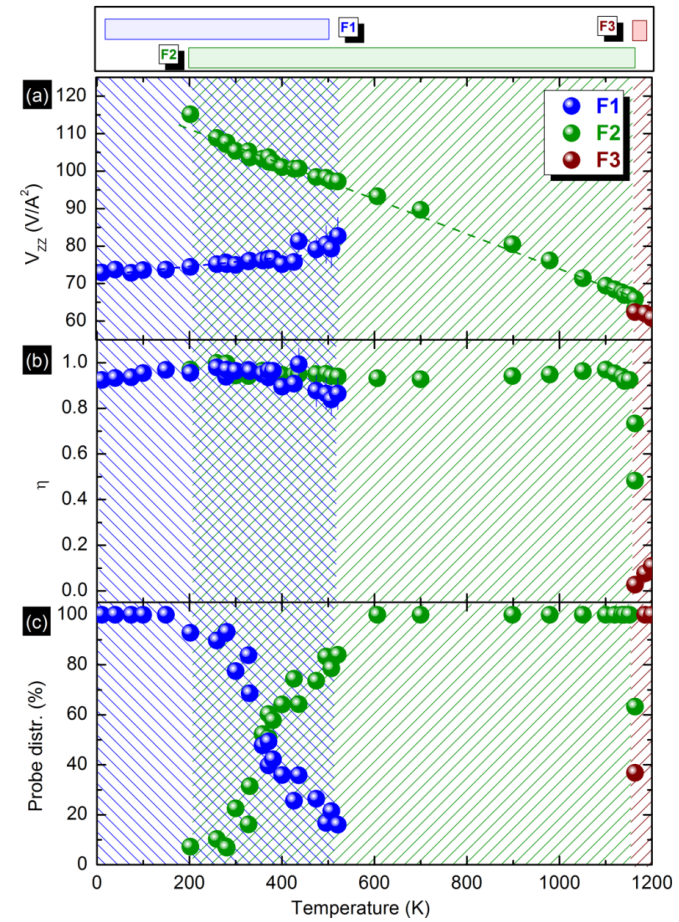
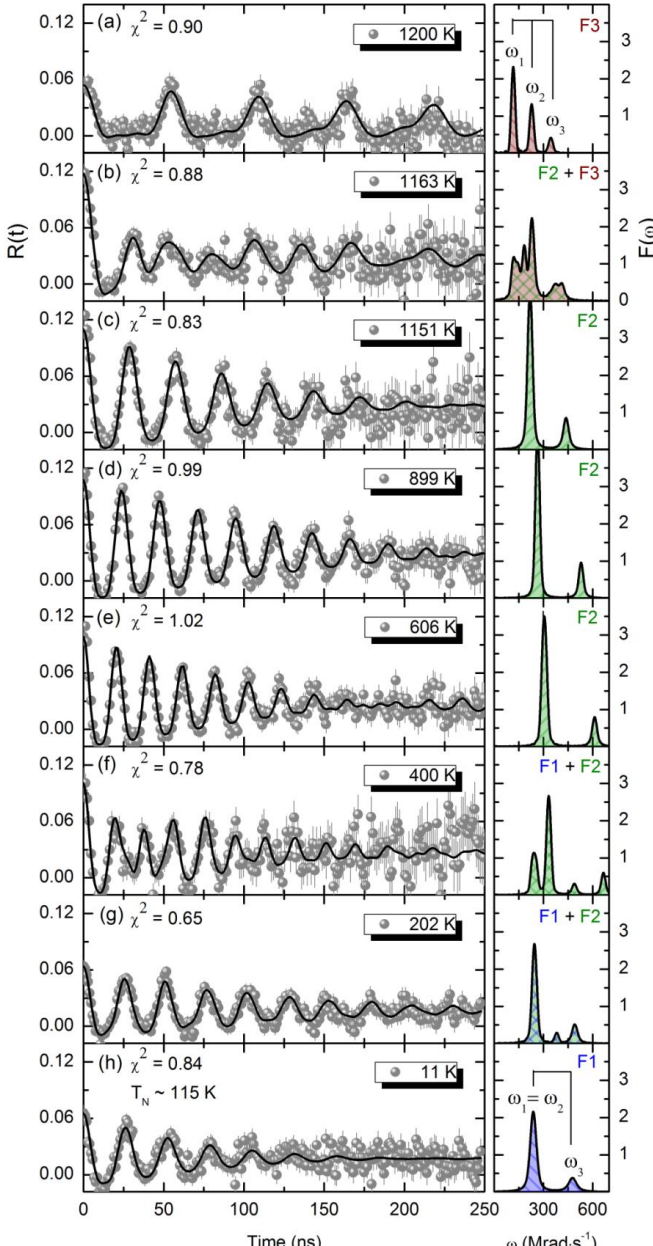
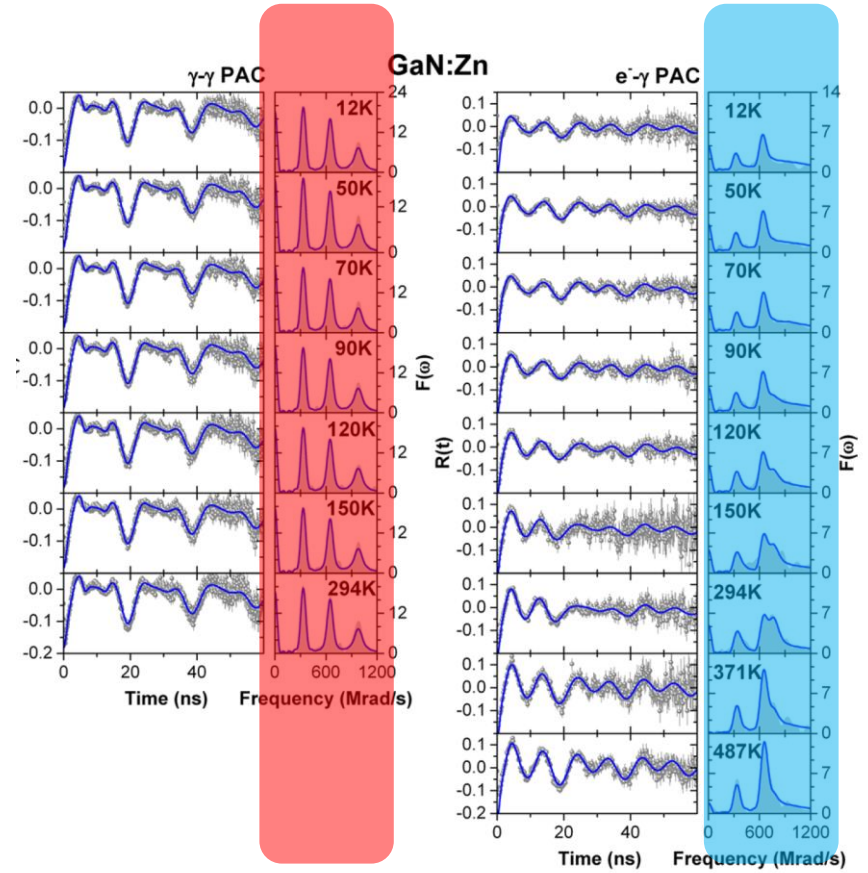
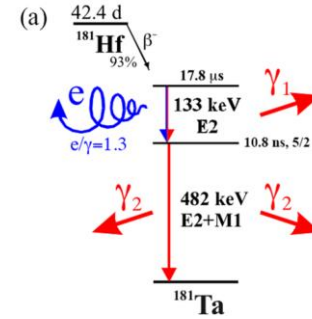
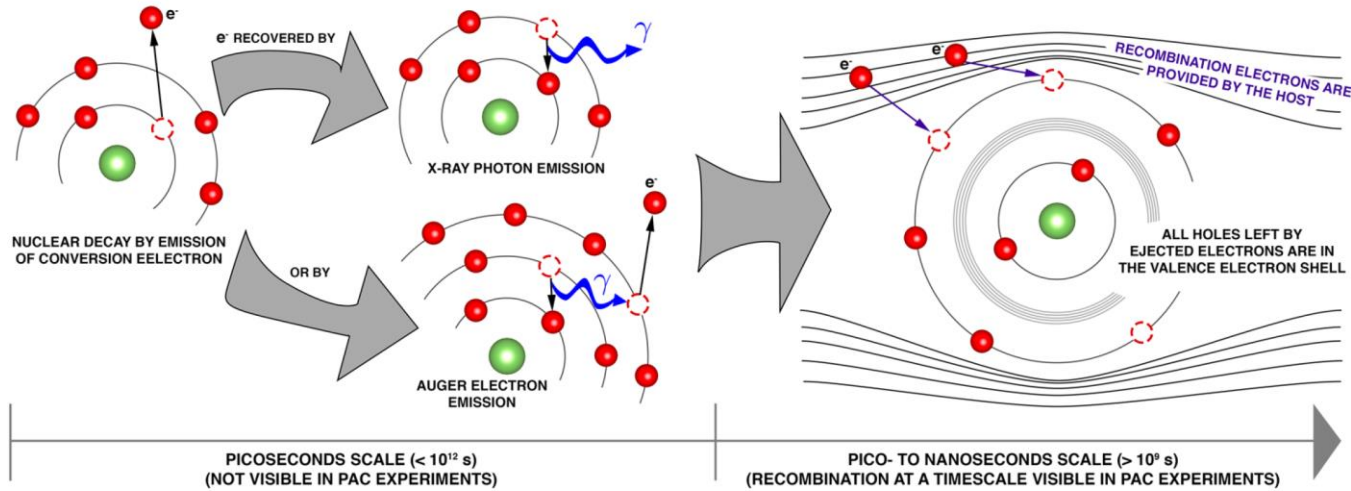


FIG. 3. Experimental EFG tensor at ¹¹¹Cd probe for the Ca₃Mn₂O₇ sample. (a) Principal component $|V_{zz}|$; (b) asymmetry parameter η ; (c) probe distribution. The dashed lines are a guide for the eyes.

Studying electronic properties in GaN without electrical contacts using γ - γ vs e^- - γ Perturbed Angular Correlations



PAC revealing bulk properties of Si and Zn-doped Ga using γ - γ and e^- - γ PAC

Biophysics: PAC of ^{111m}Cd , ^{111}Ag and ^{199m}Hg at protein metal sites

Impact factor: 21

ACCOUNTS
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Article

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Nanosecond Dynamics at Protein Metal Sites: An Application of Perturbed Angular Correlation (PAC) of γ -Rays Spectroscopy

Saumen Chakraborty,[†] Stavroula Pallada,^{‡,§} Jeppe T. Pedersen,[§] Attila Jancso,^{||} Joao G. Correia,^{‡,⊥} and Lars Hemmingsen,^{*,§}

[†]Department of Chemistry and Biochemistry, University of Mississippi, University, Mississippi 38677, United States

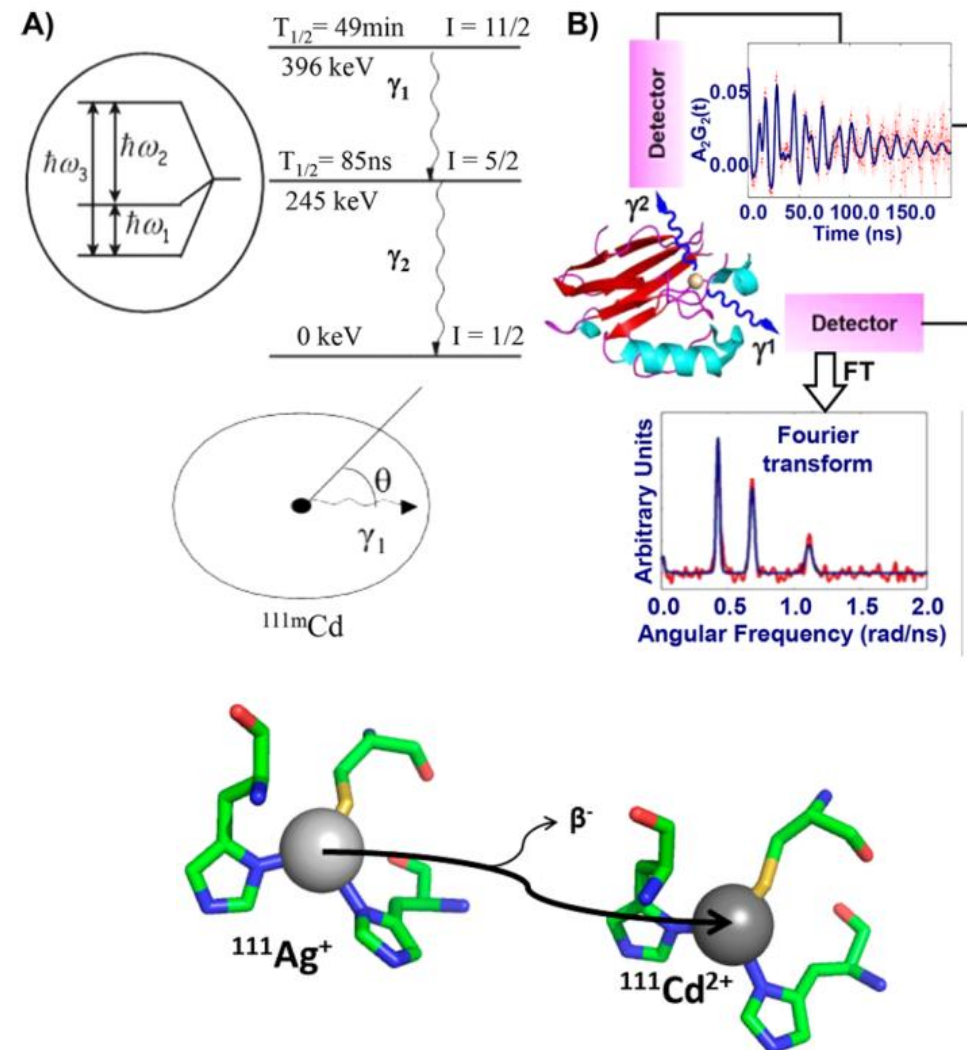
[‡]ISOLDE/CERN, PH Div, CH-1211 Geneve 23, Switzerland

[§]Department of Chemistry, University of Copenhagen, Universitetsparken 5, DK-2100 Kobenhavn Ø, Denmark

^{||}Department of Inorganic and Analytical Chemistry, University of Szeged, Dóm tér 7, H-6720 Szeged, Hungary

[⊥]Centro de Ciências e Tecnologias Nucleares, Instituto Superior Técnico, Universidade de Lisboa, 2695-066 Bobadela, Portugal

Metalloproteins are essential to numerous reactions in nature, and constitute approximately one-third of all known proteins. Their reactivity in aqueous solution depends on the exchange of water molecules. By means of PAC with several metal ion nuclear probes the dynamics of structural changes at the metal site of the proteins on the ns time scale was clearly revealed.



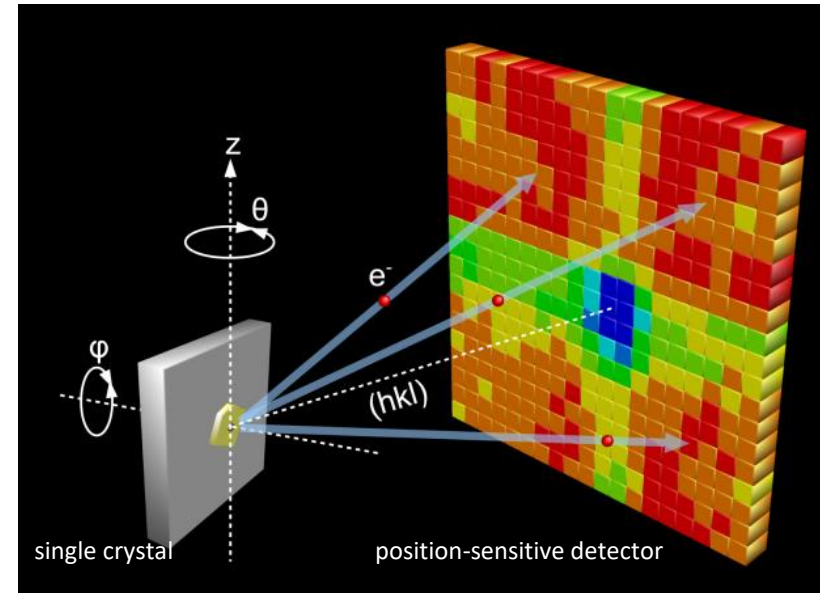
- S. Chakraborty *et al*, Acc. Chem. Res. 50 (2017) 2225

Emission Channeling method

Radioactive isotopes are implanted into a single crystal.

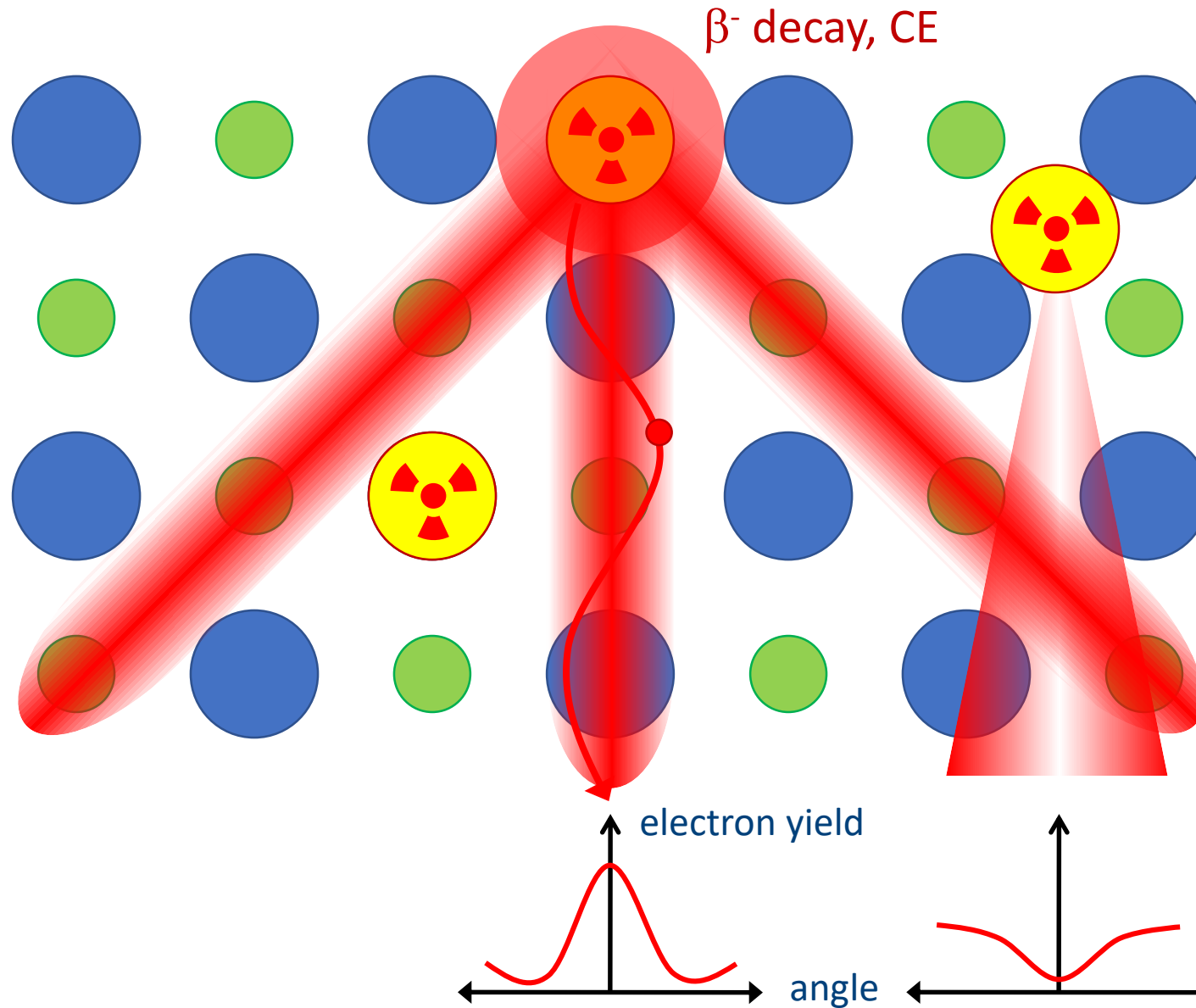
On their way out of the crystal, β^- particles emitted during probe decay experience channeling or blocking effects along major crystallographic directions.

Whether channeling or blocking is observed, depends on the lattice sites of the emitter atoms.



A position-sensitive detector at 30 cm from the sample is used to record the angular dependence of β^- emission patterns.

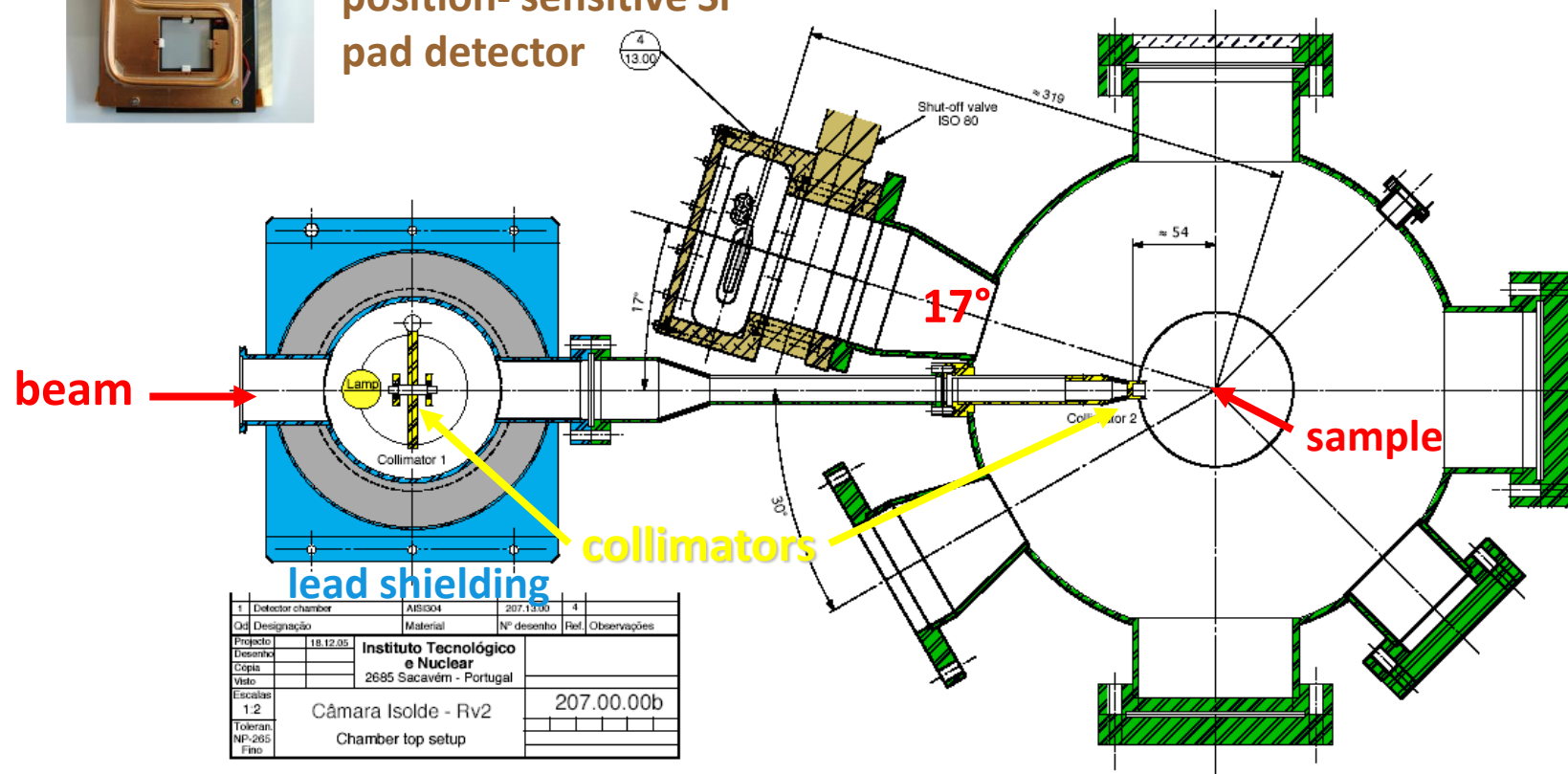
Emission channeling lattice location inside the crystal: (β^- , β^+ , c.e., α)



Emission channeling setup

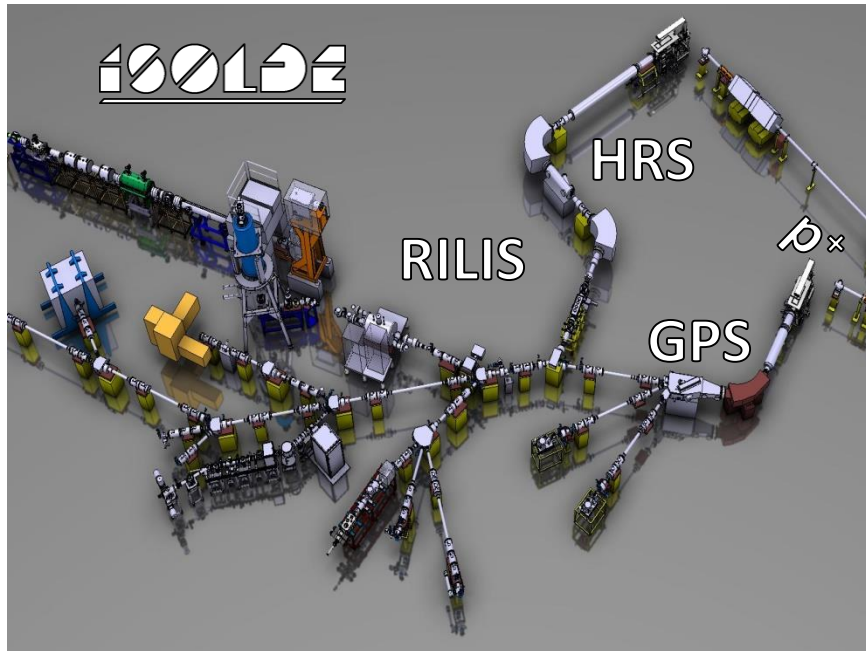


3×3 cm² cooled
position- sensitive Si
pad detector

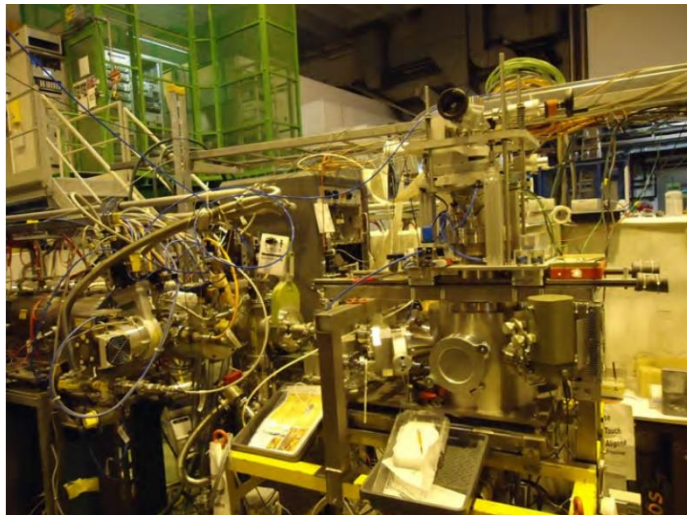


- beam collimated on sample by two apertures (last one \varnothing 1mm)
- detector at 17° backward geometry for simultaneous implantation and measurement
- 22×22 pixels of 1.3 mm position-sensitive Si pad detector, water cooled

Emission channeling at ISOLDE

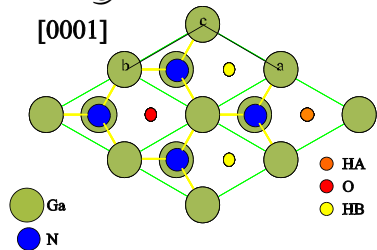
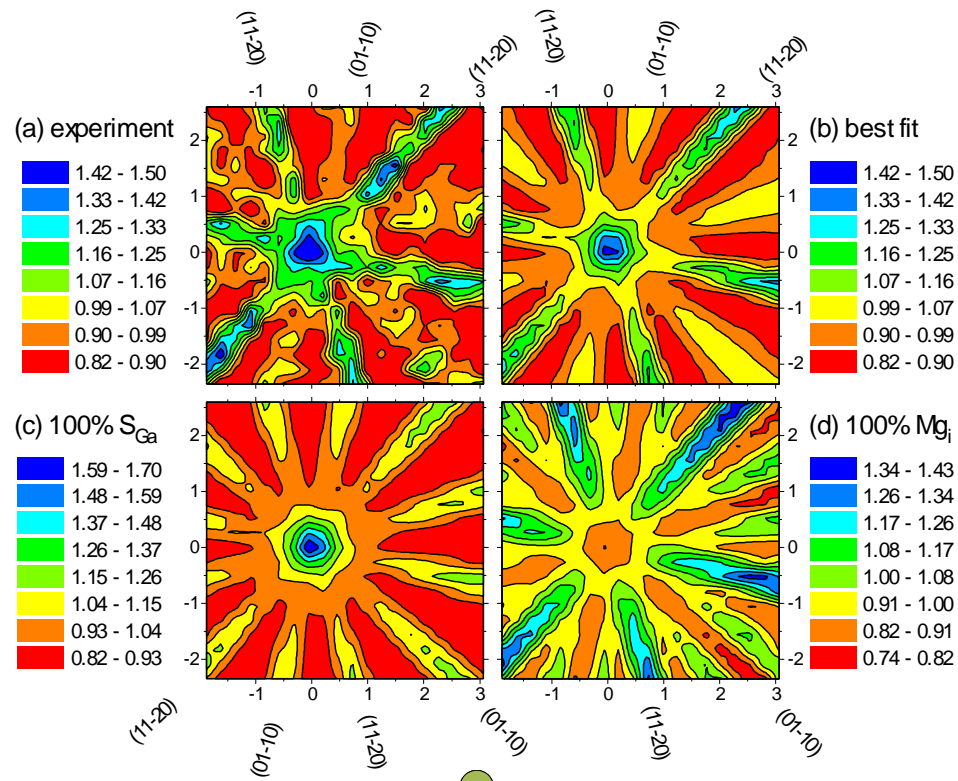


On-line setup for
Emission Channeling lattice location
with Short-Lived Isotopes (EC-SLI)
at ISOLDE GHM beam line

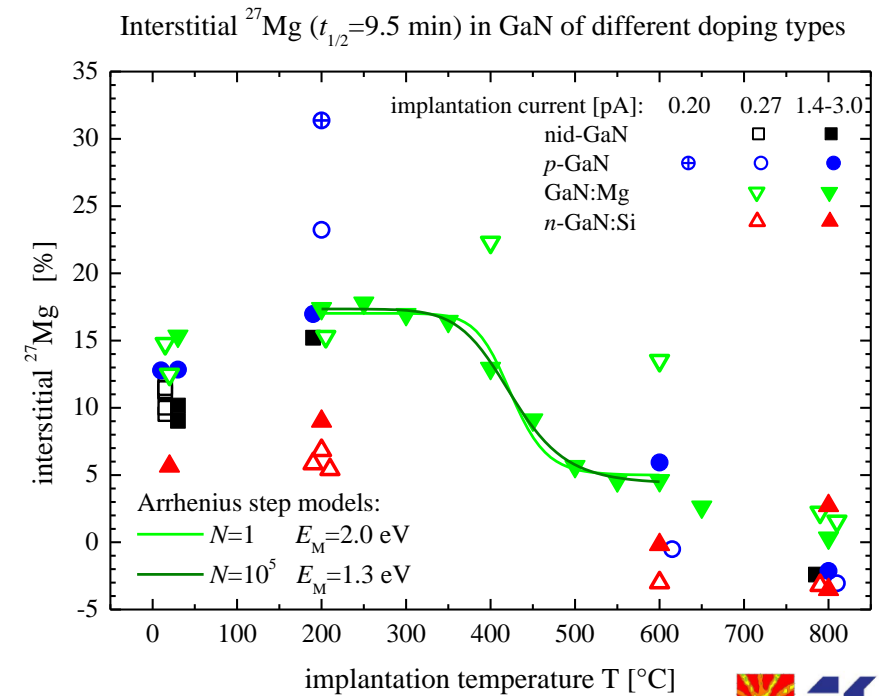


GHM

Lattice sites of ^{27}Mg in different pre-doped GaN

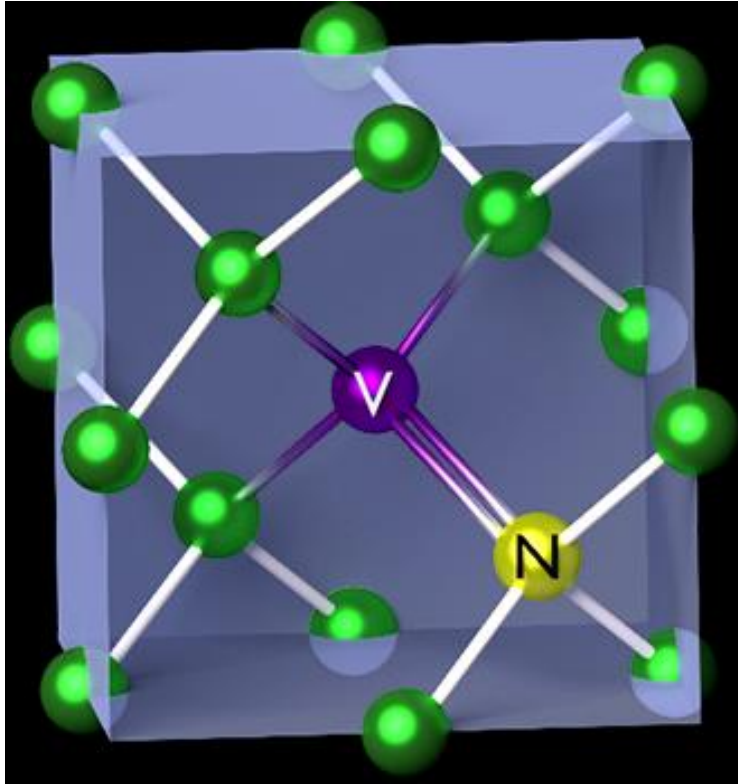


- Electron emission channeling patterns show mix of substitutional + interstitial ^{27}Mg

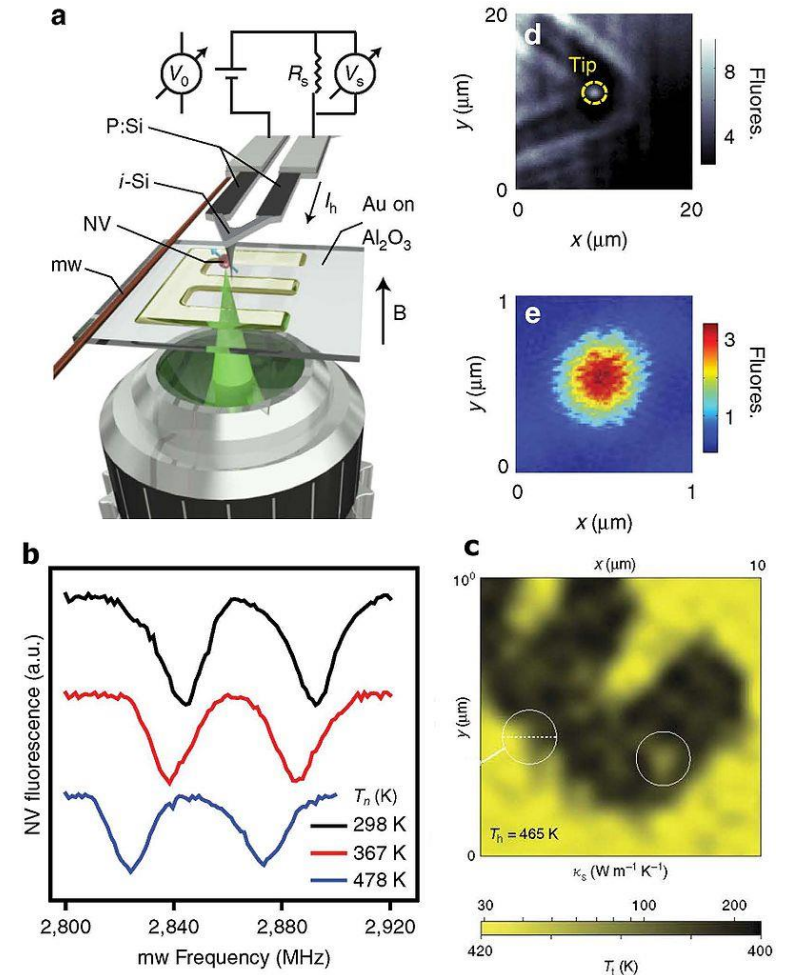


- Interstitial Mg fraction highest in $p\text{-GaN:Mg}$
- Lowest in $n\text{-GaN:Si}$
- ⇒ Direct evidence for amphoteric character of Mg that is coupled to the doping type
- Site change interstitial - substitutional Mg_{Ga}
- ⇒ Activation energy for migration of interstitial Mg: $E_M \gg 1.3 - 2.0 \text{ eV}$

N-V centres in diamond: towards quantum bits....

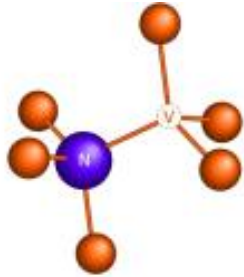


NV centre, extensively studied in the past 10 years. Has a long coherence time but low efficiency for photonic applications...already being used for metrology and sensor applications...

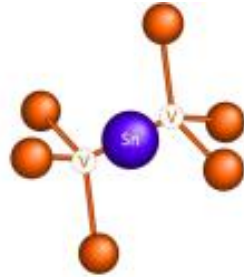


Alternative centres to N-V...

"full-vacancy",
assumed for NV

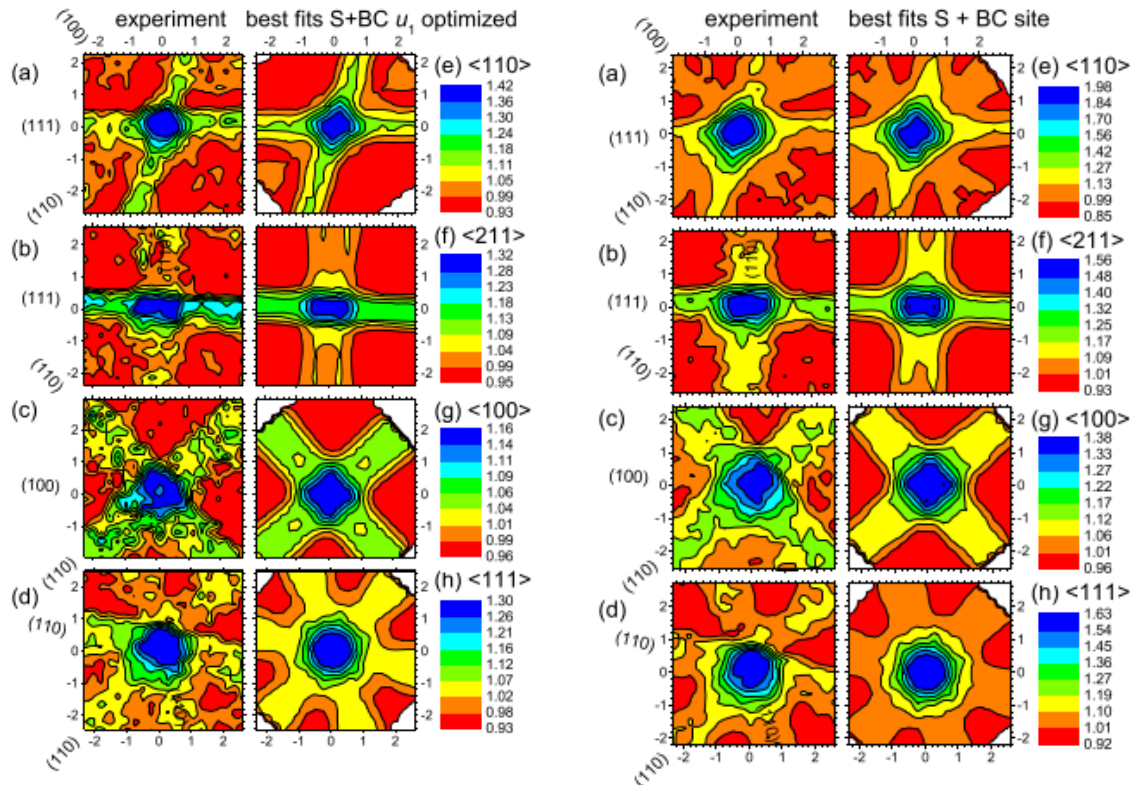


"split-vacancy" [3,4],
assumed for SiV,
GeV, SnV, PbV



Direct Structural Identification and Quantification of the Split-Vacancy Configuration for Implanted Sn in Diamond

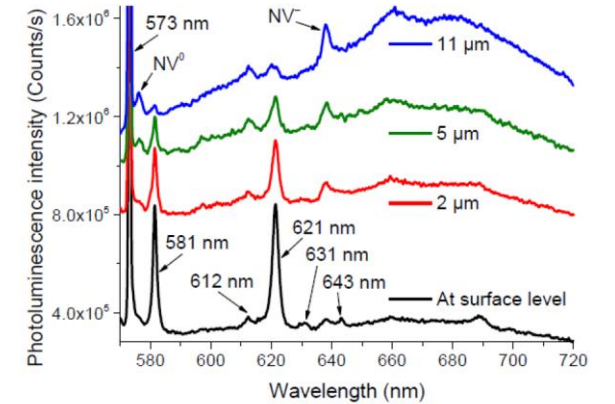
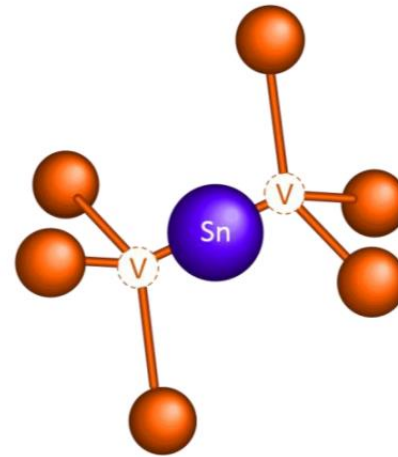
U. Wahl^{1,2,*} *et al*



As implanted

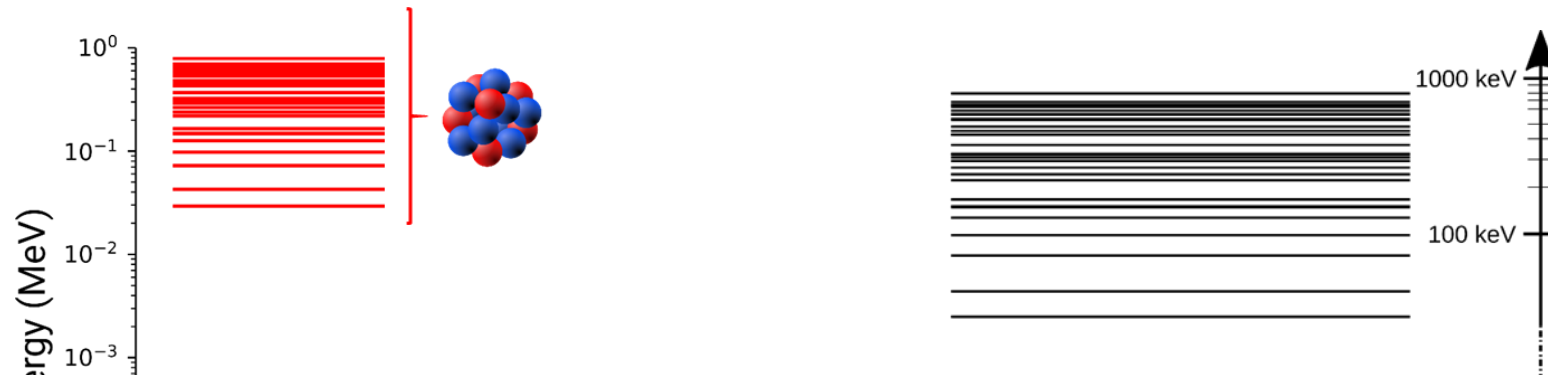
Annealed at 920C

¹²¹SnV



Observation of sharp line
possibly related to SnV in
PL ...

Slight tangent: characterization of the the low lying isomer in ^{229}Th : a nuclear clock?



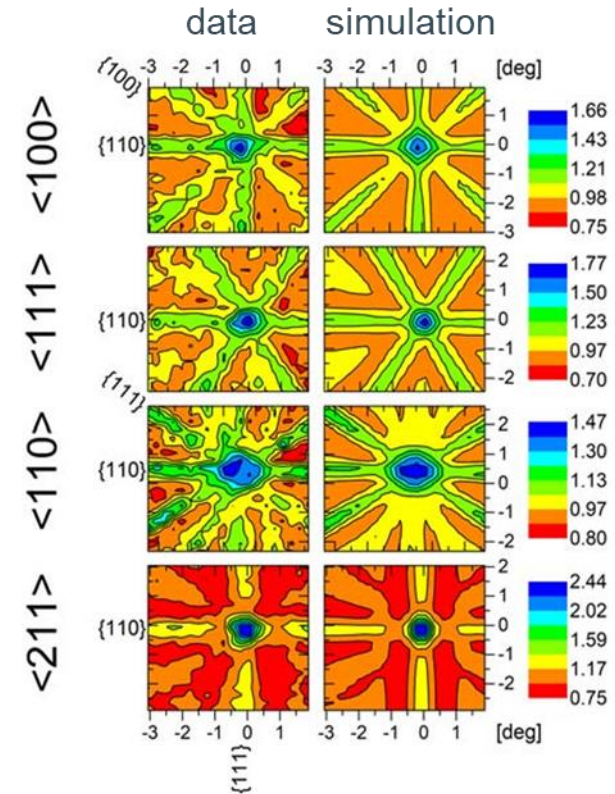
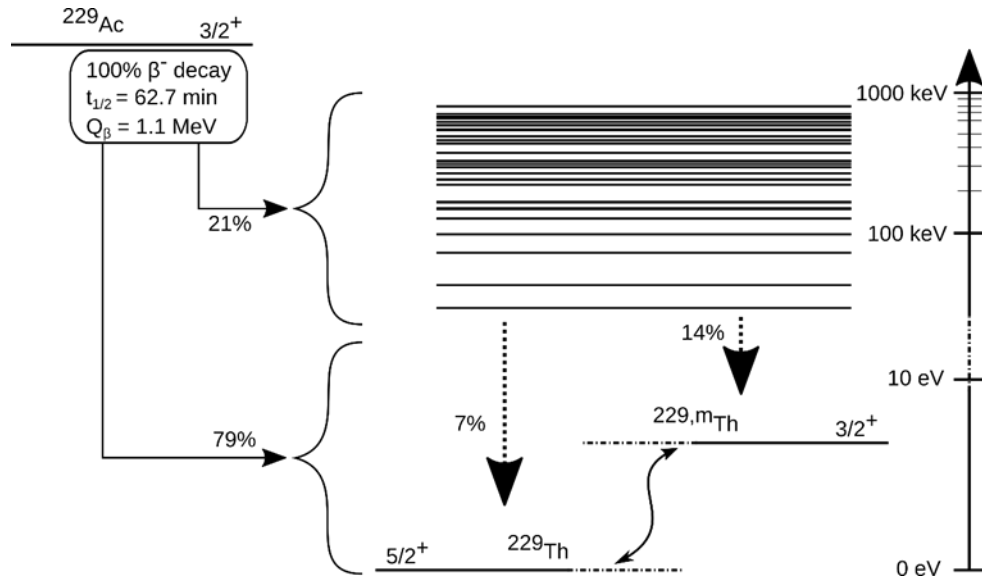
Most current work is via the α -decay of ^{233}U



Low lying isomer in ^{229}Th is within reach of laser excitation...if addressable could result in a highly accurate and stable clock... however, isomer level position still not accurately known...

- Current status – ^{229m}Th**
- Energy is poorly-defined
 - Radiative decay not yet observed
 - Internal conversion ($^{229}\text{Th}^0$): $T_{1/2,IC} = 7(1)10^{-6} \text{ s}^{(5,6)}$
 - Radiative decay ($^{229}\text{Th}^{1+}$, $^{229}\text{Th}^{2+}$, ...):
 $T_{1/2,rad} \sim 10^3 - 10^4 \text{ s}$

Novel probe of the isomer using ^{229}Ac beams at ISOLDE: combining nuclear decay spectroscopy and emission channelling



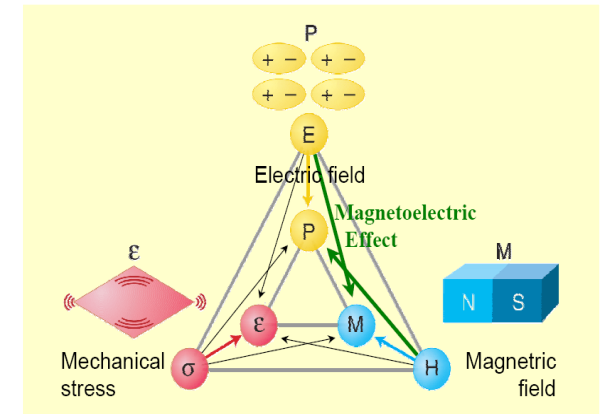
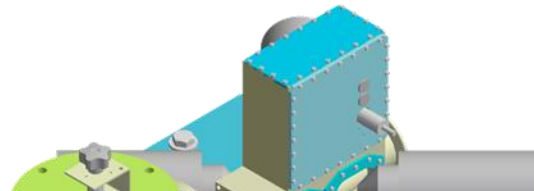
How to observe radiative emission?

Implant into wide band material e.g. CaF which blocks internal transition...

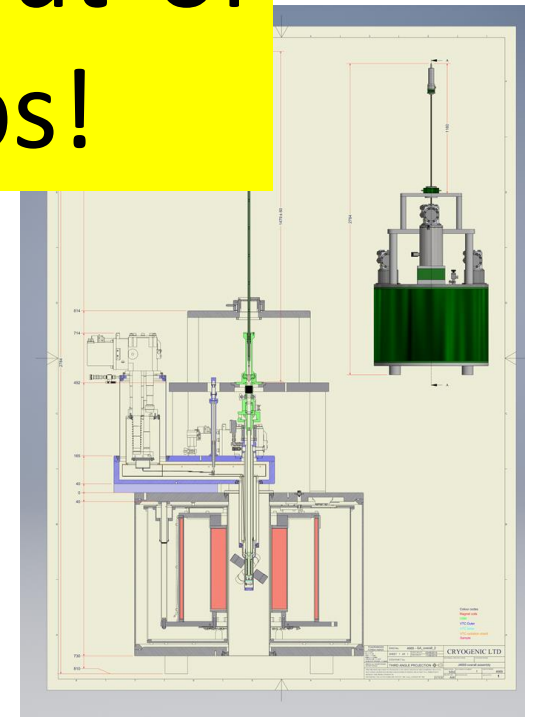
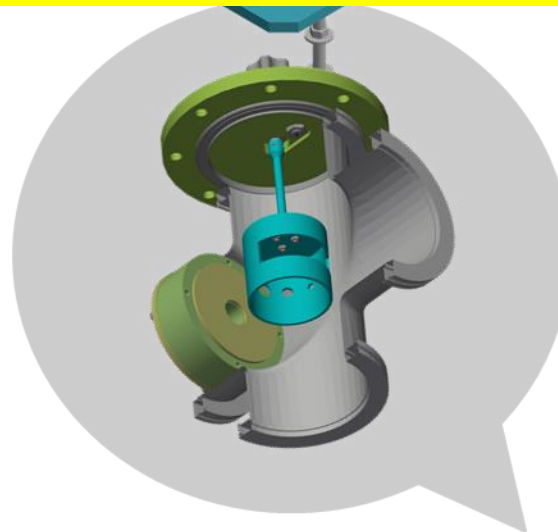
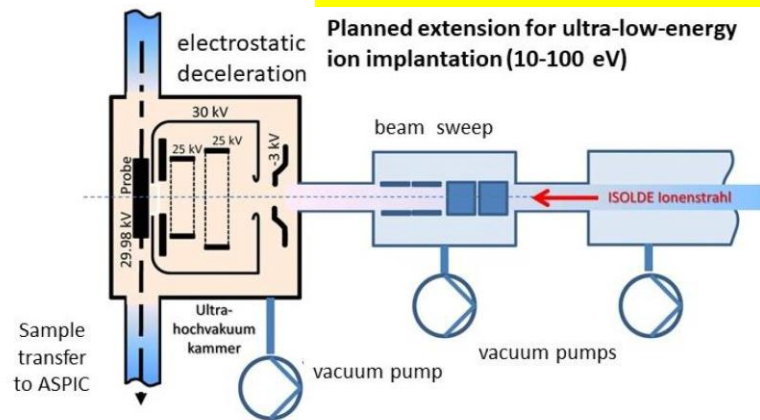
If on substitutional position can clearly study the decay properties...

Preliminary data shows 90% on sub site...to be continued next year...further studies required to control the annealing and bring isotopes to substitutional position...

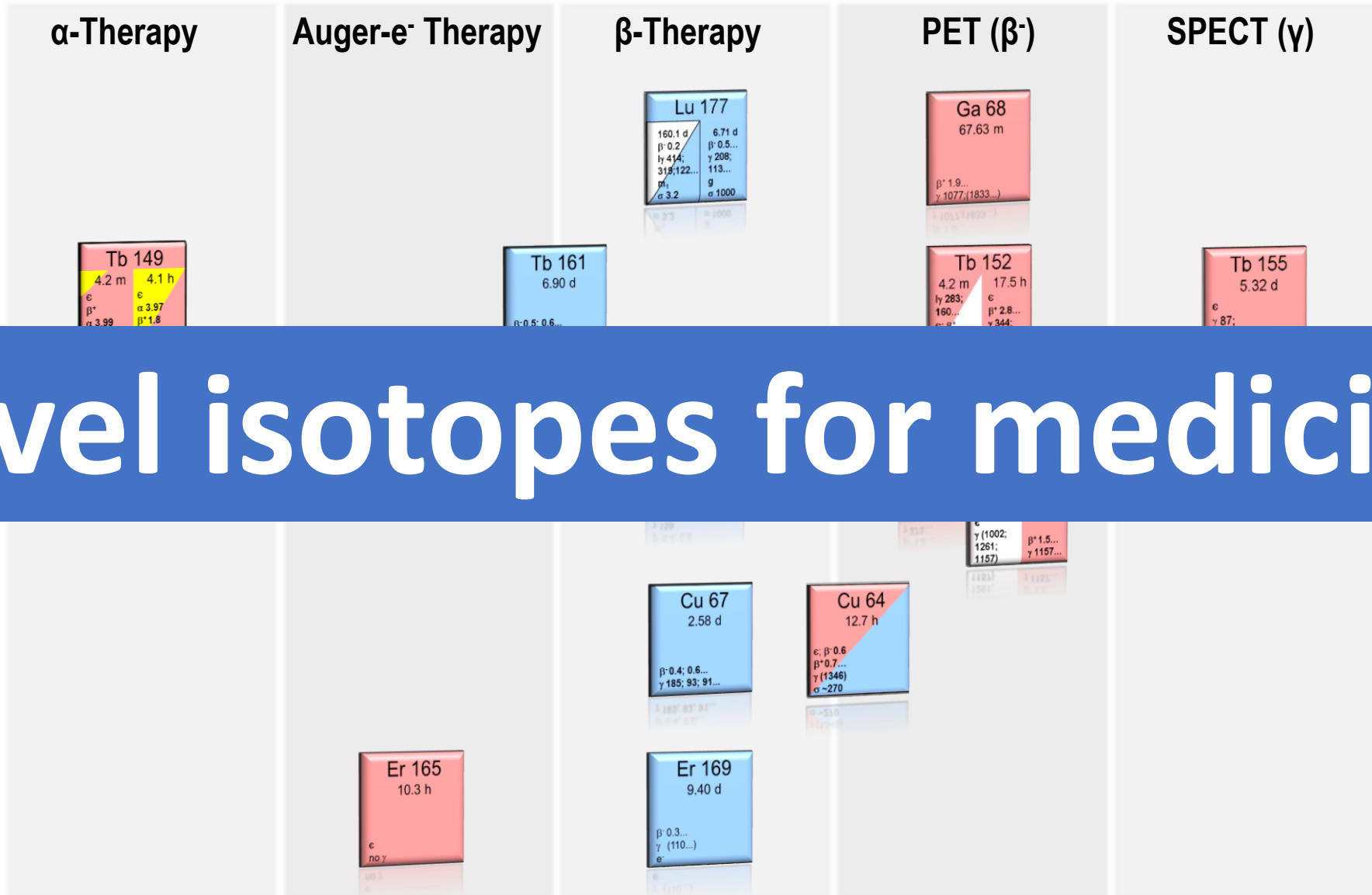
Future plans



But we are beginning to run out of space for all the proposed setups!

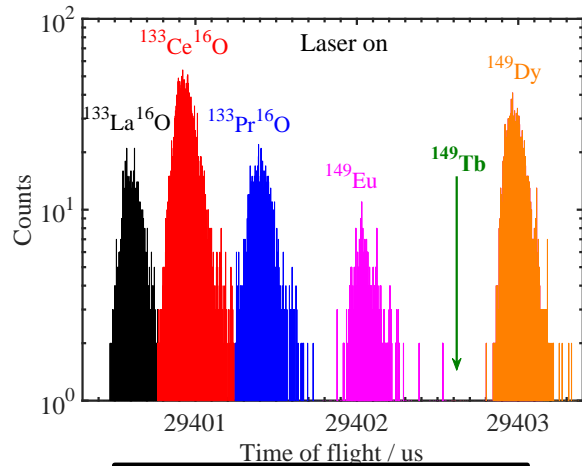
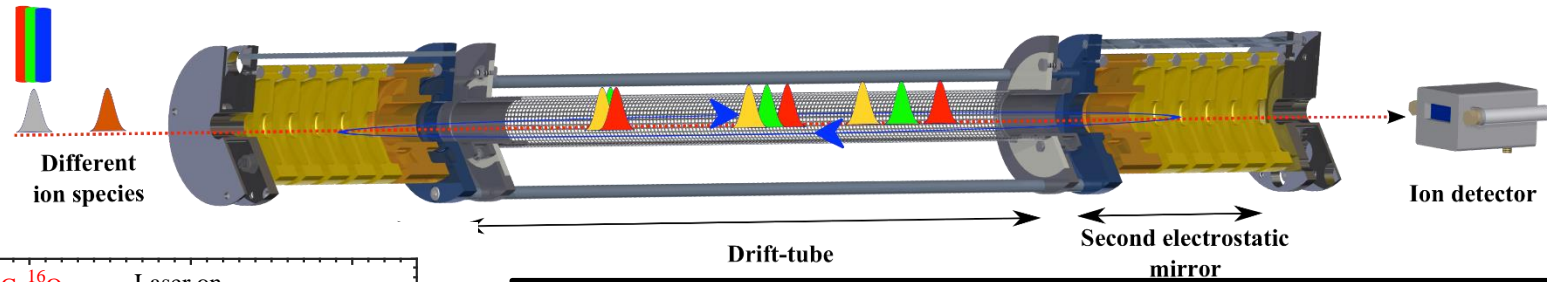


“Matched Pairs” of Radionuclides for Theragnostics

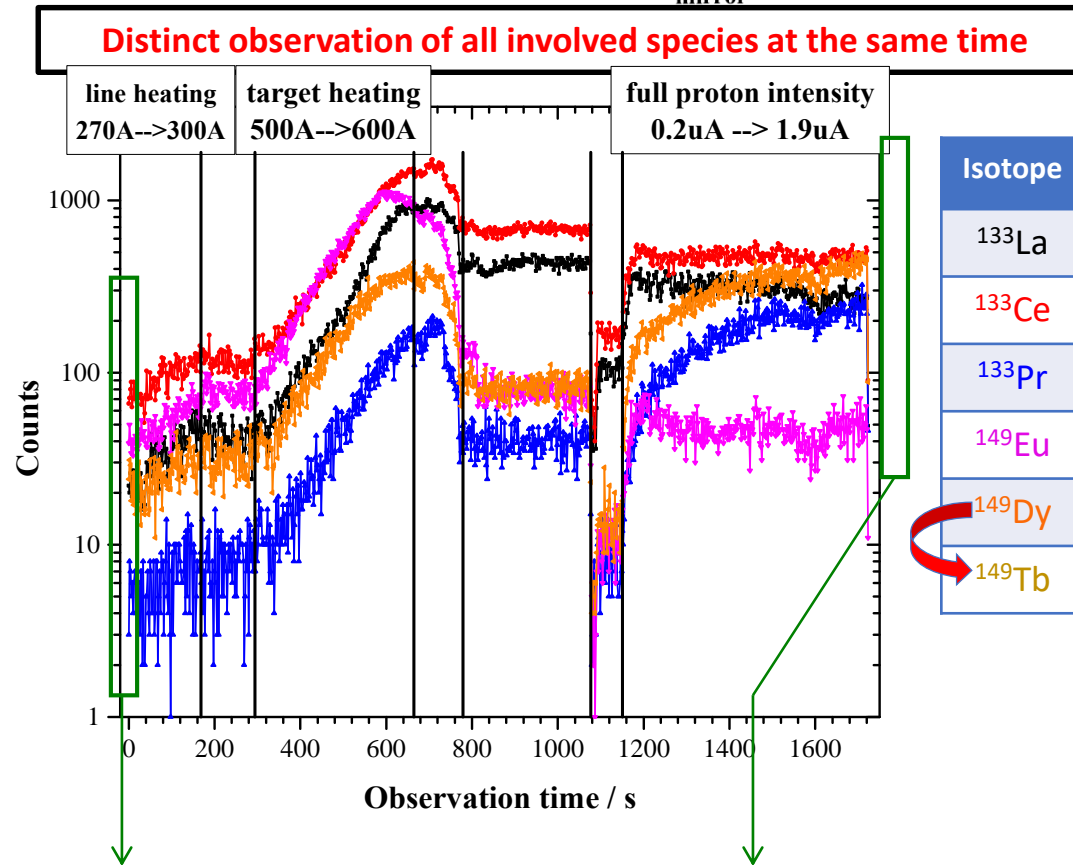
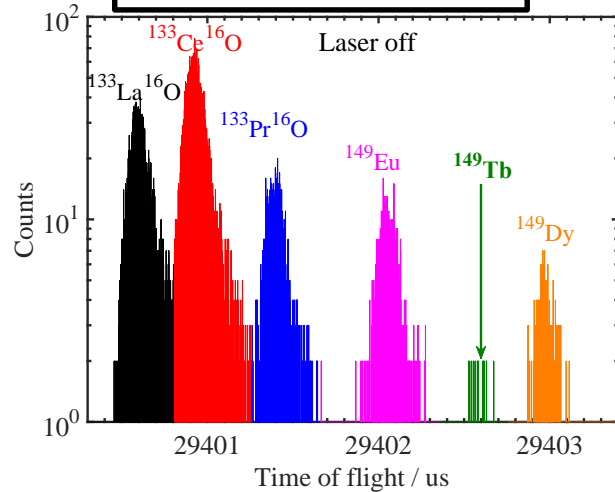


Novel isotopes for medicine

Beam optimization with ISOLTRAPs MR-ToF for Dy/Tb collections



Laser on/off ratio = 10/1



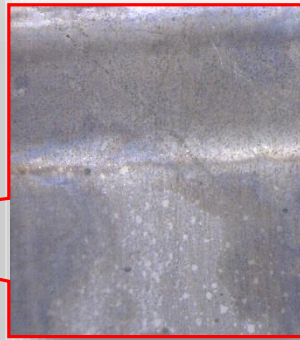
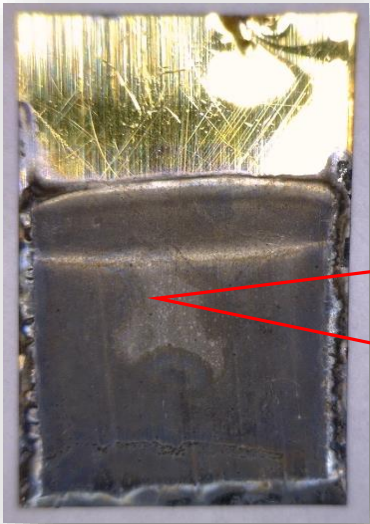
Before optimization: 6.3/1

After optimization: 2.3/1

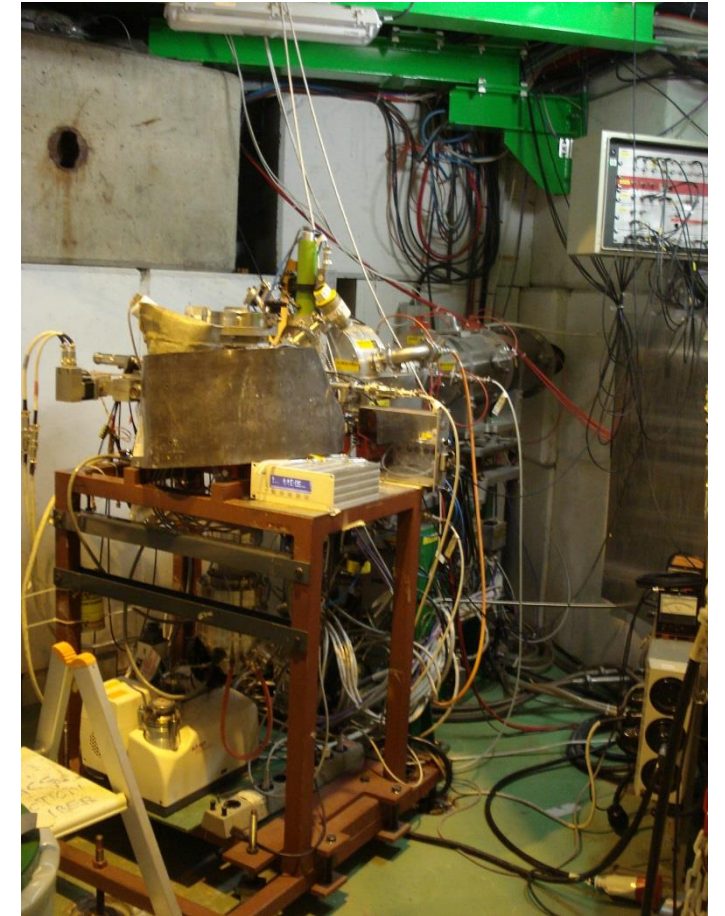
contaminants / ^{149}Dy → almost factor 3 improvement!

Implantation Foils

The Old Way

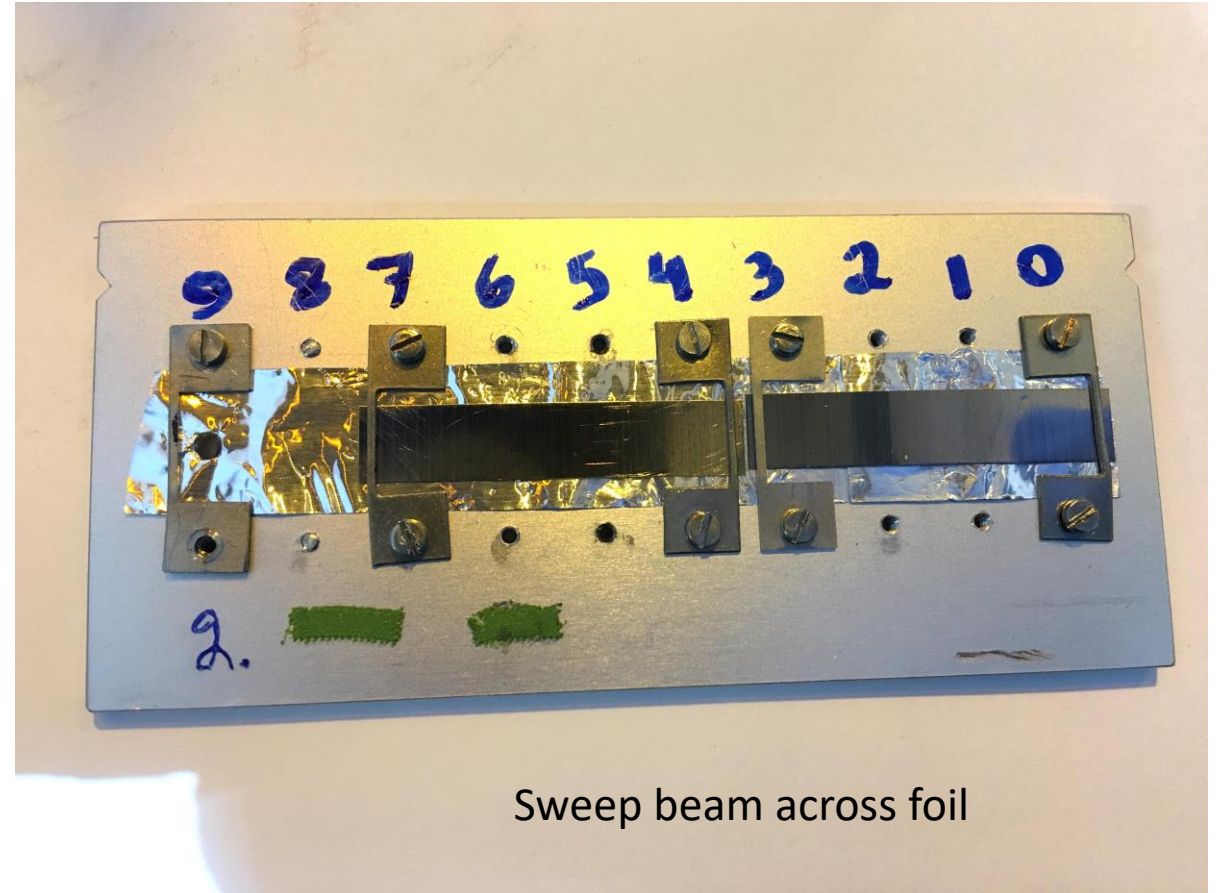
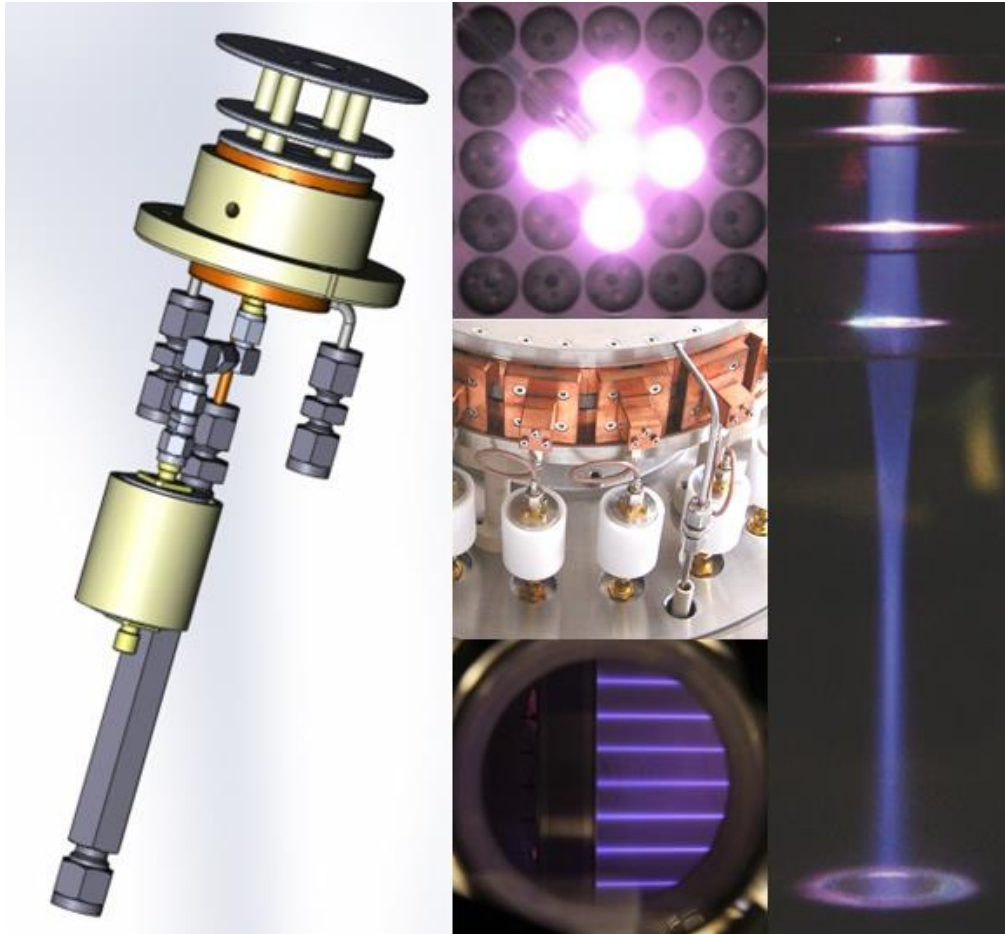


Sputtering of foils due to intense beam: implanted in Au!



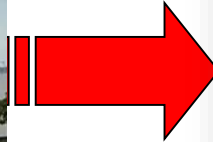
Implantation Foils

The New Way



Sweep beam across foil

Separation Method Used to Obtain ^{152}Tb and ^{149}Tb

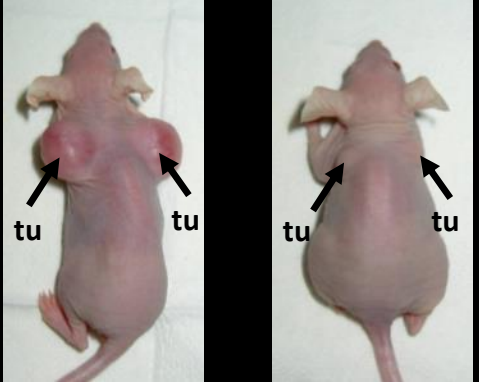


- Foil contents dissolved at 80 °C using 2x 0.5 mL dil. $\text{HNO}_3/\text{NH}_4\text{NO}_3$.
- Dissolved radionuclides loaded onto cation exchange resin.
- Column was eluted in gradients: 0.07 M to 0.13 M α -HIBA to remove Tb radionuclide.
- >100 MBq ^{149}Tb , >600 MBq ^{152}Tb was obtained in 2015
- Product labelled DOTA-compounds up to 10 MBq/nmol.



Applications of Tb-nuclides

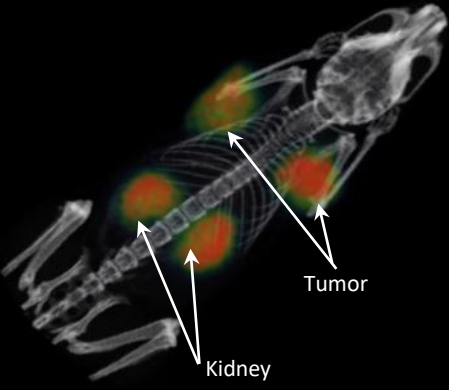
Control **Treated**



^{149}Tb -therapy with alpha particles

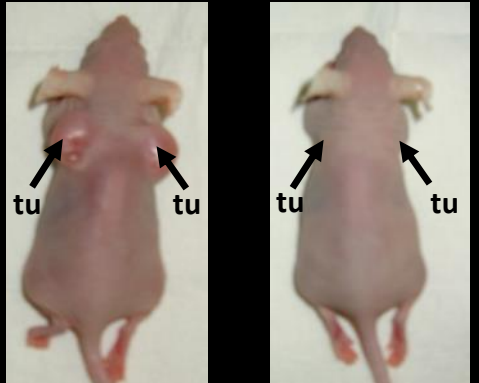
Tb 149	
4.2 m	4.1 h
€	€
β^+	α 3.97...
α 3.99	β^+ 1.8...
γ 796;	γ 352;
165...	165...

^{152}Tb -PET *in vivo* application



Tb 152	
4.2 m	17.5 h
ly 283;	€
160...	β^+ 2.8...
€; β^+ ...	γ 344;
γ 344;	586;
411...	271...

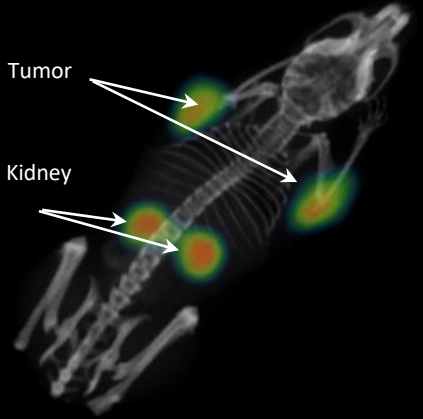
Control **Treated**



^{161}Tb -therapy with low energy beta particles

Tb 161	
6.90 d	
β^- 0.5; 0.6...	
γ 26; 49; 75...	
e^-	

^{155}Tb -SPECT *in vivo* application

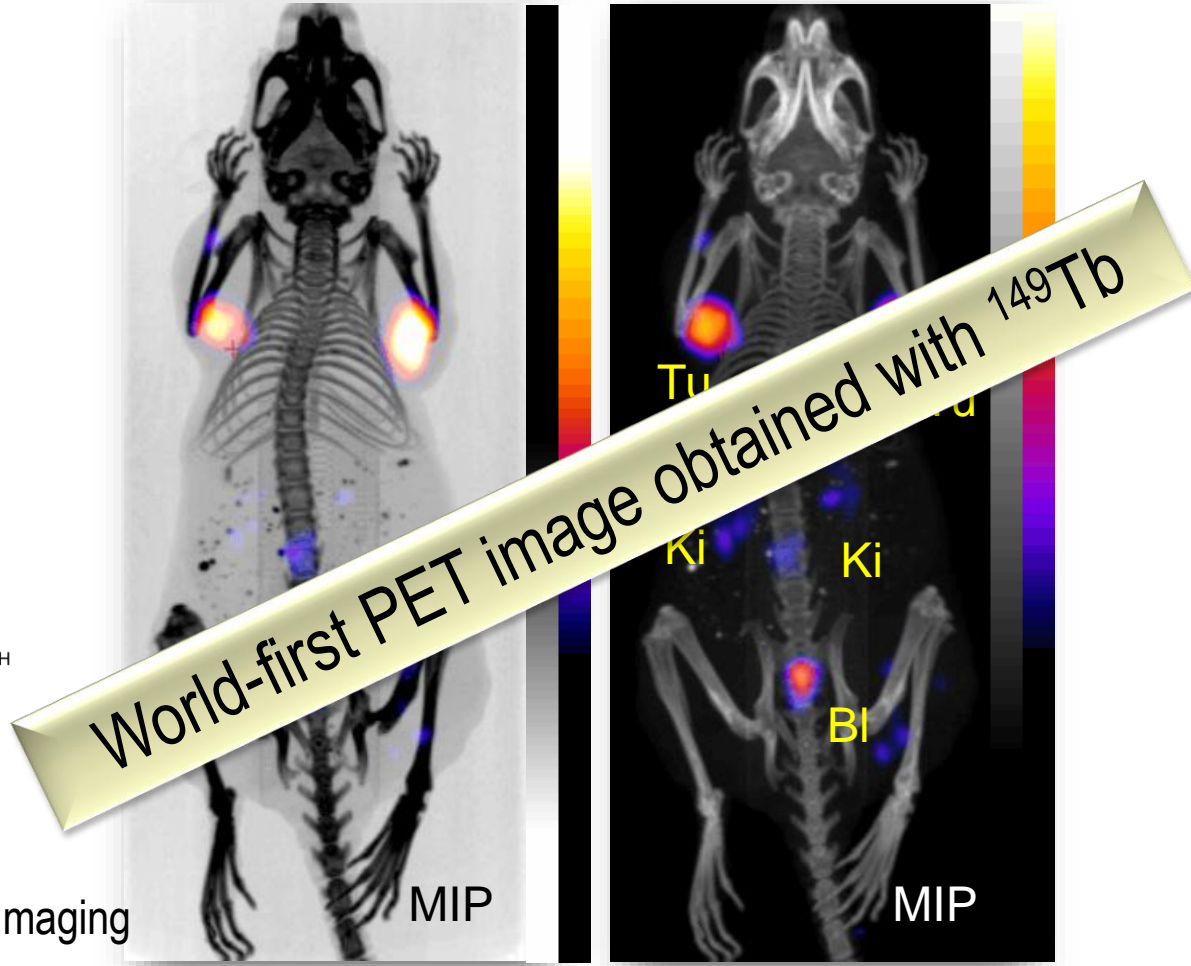
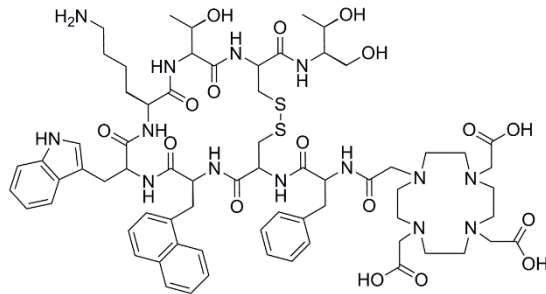


Tb 155	
5.32 d	
€	
γ 87; 105;	
180; 262...	

Müller et al. *J. Nucl Med* (2012) 53:1951-1959.

^{149}Tb : A Part Of The Future of ISOL

Tb 149
4.1 h
ϵ
α 3.97
β^+ 1.8...
γ 352;
165...



Useful for α -Therapy and PET Imaging

MIP

MIP

PET/CT scan of a AR42J tumor-bearing mouse performed 2 h after injection of ^{149}Tb -DOTANOC

Logistics: The Travel Challenge : ^{149}Tb

200 MBq



110 MBq



The Travel Challenge : ^{152}Tb : very indirectly to Lausanne



^{152}Tb -DOTATOC: First Clinical Study

First ^{152}Tb -based PET Scan of a Patient – Performed at Zentralklinik Bad Berka, Germany (Prof. Richard Baum)

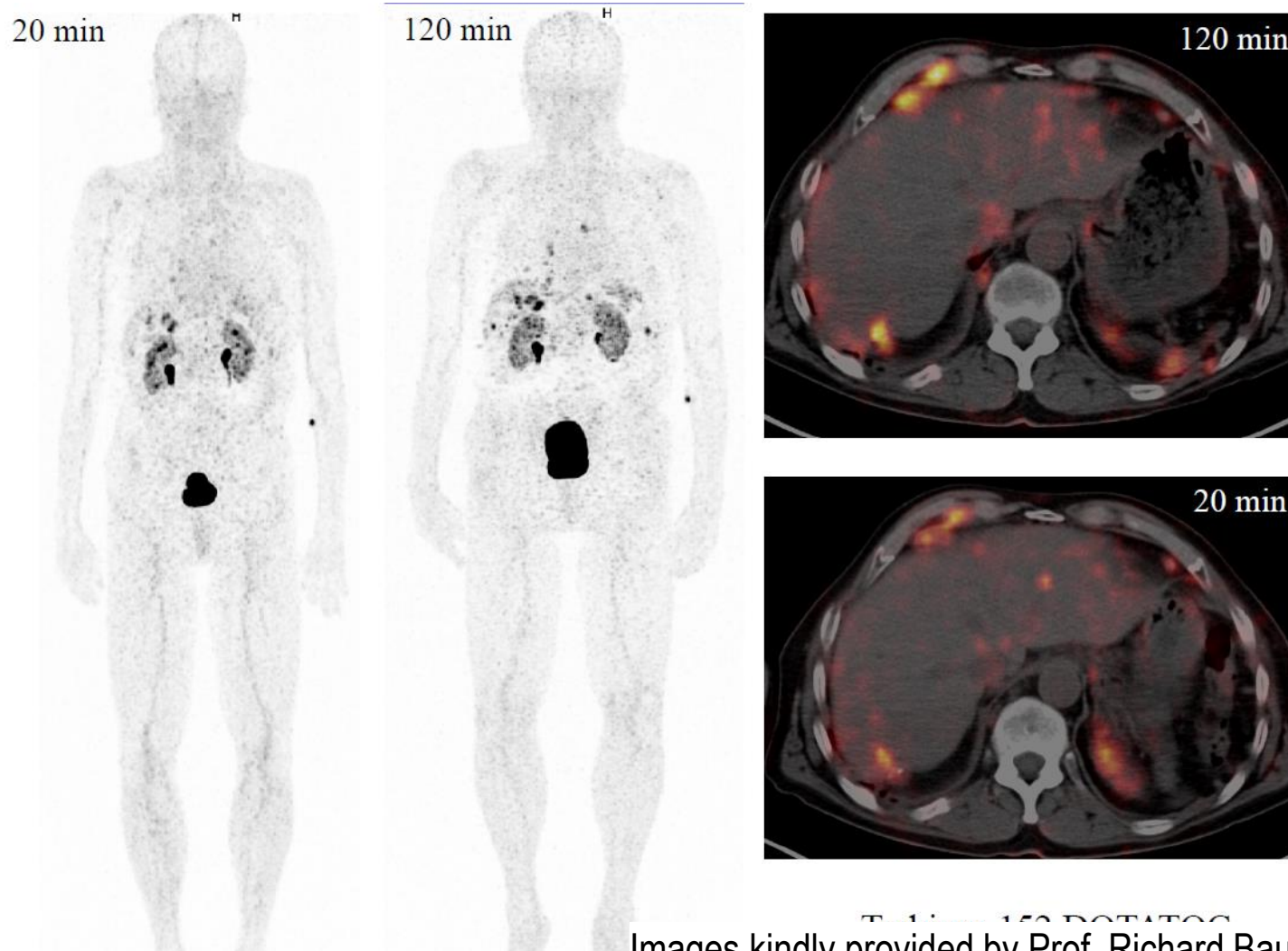
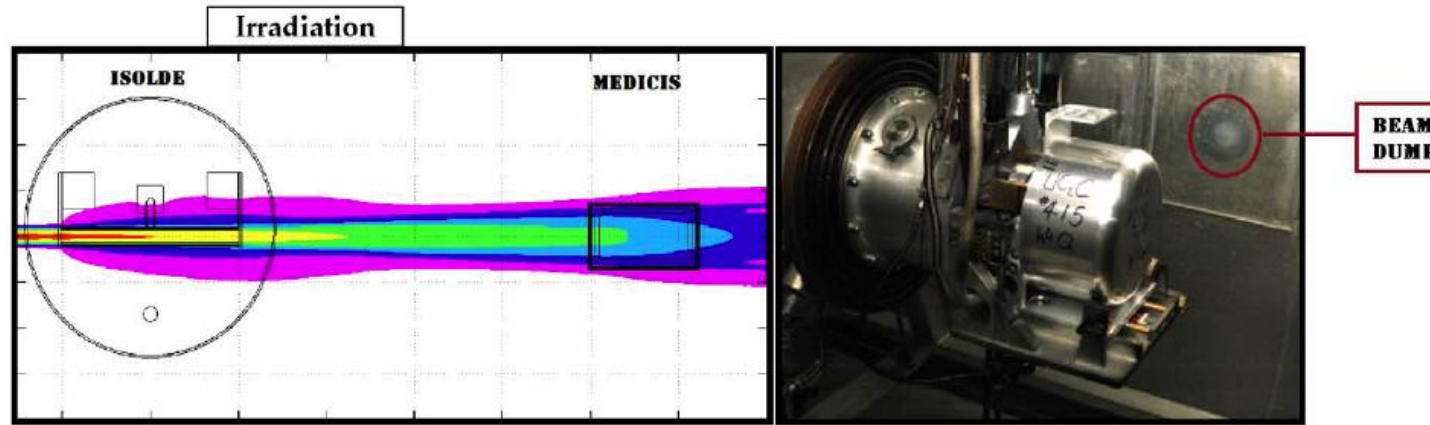


Figure 1. ^{152}Tb -DOTATOC PET scan of a patient. Images kindly provided by Prof. Richard Baum

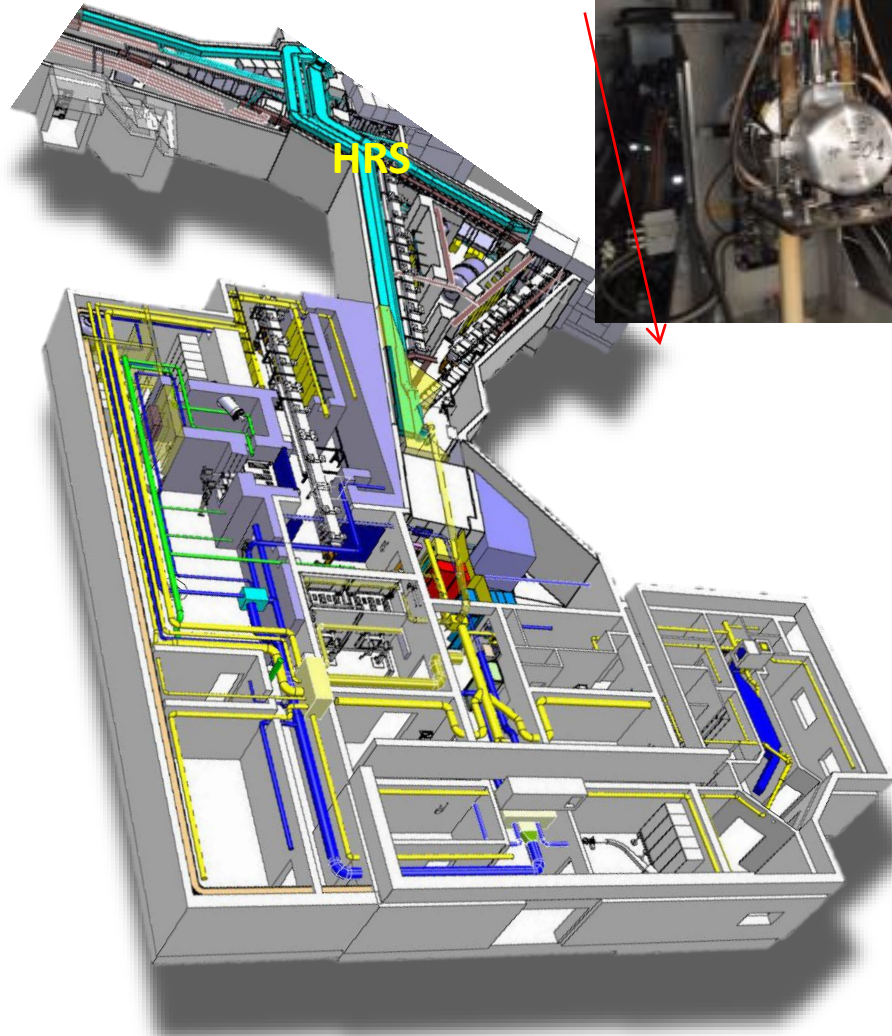
MEDICIS: a dedicated facility for production of isotopes for medicine



**90% of protons are going to the dump:
We can recycle them !**



CERN-MEDICIS: new Facility for medical isotopes (and solid state/materials?)



Dy 150 7.2 m ε; β ⁺ α 4.23 σ 387	Dy 151 17 m ε; α 4.07 γ 286; 49; 546; 176...	Dy 152 2.4 h ε α 3.63 γ 257	Dy 153 6.29 h ε; β ⁺ α 3.46; γ 81; 214; 100; 264	Dy 154 3.0 · 10 ⁶ a α 2.67	Dy 155 10.0 h β ⁺ 0.9; 1.1... γ 227	Dy 156 0.056 ε 33 σ _{n, α} < 0.009	Dy 157 6.1 h ε 326...	Dy 158 0.095 ε 33 σ _{n, α} < 0.009	Dy 159 144.4 d ε γ 58; α ⁺ σ 8000	Dy 160 2.329 α 60 σ _{n, α} < 0.0003	Dy 161 18.889 α 600 σ _{n, α} < 1E-6	Dy 162 25.475 α 170
Tb 149 4.2 m 4.1 h ε α 3.99 β ⁺ 1.8; γ 79; 126; 46...	Tb 150 5.8 m 3.67 h ε; β ⁺ α 3.17 β ⁺ 1.8; γ 27; 496...	Tb 151 25 a 17.6 h ε; β ⁺ α 4.49; β ⁺ 2.1; γ 49; 27...	Tb 152 4.2 m 17.5 h ε; β ⁺ α 3.83; β ⁺ 2.8; γ 254; 411...	Tb 153 2.34 d ε; β ⁺ α 3.41; β ⁺ 3.4; γ 212; 170; 110; 162; 83...	Tb 154 4.2 m 5.9 h 21 ε; β ⁺ α 3.41; β ⁺ 3.4; γ 212; 170; 110; 162; 83...	Tb 155 5.32 d ε α 87; 105; 160; 262	Tb 156 157 5.4 h 5.4 d ε; β ⁺ α 3.41; β ⁺ 3.4; γ 212; 170; 110; 162; 83...	Tb 157 99 a ε γ (54)	Tb 158 10.5 a 180 a ε; β ⁺ α 3.41; β ⁺ 3.4; γ 212; 170; 110; 162; 83...	Tb 159 100 α 23.2	Tb 160 72.3 d β ⁻ 0.6; 1.7... γ 879; 299; 966... σ 670	Tb 161 6.90 d β ⁻ 0.5; 0.6... γ 26; 49; 75... σ
Gd 148 74.6 a α 3.163 σ 14000	Gd 149 9.28 d ε; α 3.016 γ 150; 299; 347...	Gd 150 1.8 · 10 ⁹ a α 2.72	Gd 151 120 d ε; α 2.60 γ 154; 243; 175...	Gd 152 0.20 1.1 · 10 ¹⁴ a α 2.14; σ 700 σ _{n, α} < 0.007	Gd 153 239.47 d ε α 97; 103; 70... σ 20000 σ _{n, α} 0.03	Gd 154 2.18 α 60	Gd 155 14.80 ε 61000 σ _{n, α} 0.00008	Gd 156 20.47 α -2.0	Gd 157 15.65 α 254000 σ _{n, α} < 0.05	Gd 158 24.84 α 2.3	Gd 159 18.48 h β ⁻ 1.0... γ 384; 58...	Gd 160 21.86 α 1.5

CERN to produce radioisotopes for health

A new project called CERN MEDICIS aims to produce novel isotopes as diagnostic agents and treatments for brain and pancreatic cancers, explain **Leo Buehler, Thomas Cocolios, John Prior and Thierry Stora**.

Accelerators and their related technologies have long been developed at CERN to undertake fundamental research in nuclear physics, probe the high-energy frontier or explore the properties of antimatter. Some of the spin-offs of this activity have become key to society. A famous example is the World Wide Web, while another is medical applications such as positron emission tomography (PET) scanner prototypes and image reconstruction algorithms developed in collaboration between CERN and Geneva University Hospitals in the early 1990s. Today, as accelerator physicists develop the next-generation radioactive beam facilities to address new questions in nuclear structure – in particular HIE-ISOLDE at CERN, SPIRAL 2 at GANIL in France, ISOL@Myrrha at SCK-CEN in Belgium and SPES at INFN in Italy – medical doctors are devising new approaches to diagnose and treat diseases such as neurodegenerative disorders and cancers.

The bridge between the radioactive-beam and medical communities dates back to the late 1970s, when radioisotopes collected from a secondary beam at CERN's Isotope mass Separator On-Line facility (ISOLDE) were used to synthesise an injectable radiopharmaceutical in a patient suffering from cancer. ^{107}Tm -citrate, a radiolanthanide associated to a chelating chemical, was used to perform a PET image of a lymphoma, which revealed the spread-out cancerous tumours. While PET became a reference protocol to provide quantitative imaging information, several other pre-



Clockwise from top left: Storage shelves for ISOLDE and CERN-MEDICIS targets after their operation, showing the robot for remote handling. A "fresh" target unit stands on the CERN-MEDICIS supply point, ready for the robot pick-up and transportation to the irradiation point. A rail conveyor system end-station for target transportation, showing the inspection camera and two modern target units. The MEDICIS building at CERN, next to ISOLDE. (Image credits: Yury Gavrikov.)

cells, killing them with minimal damage to healthy tissue.

CERN-MEDICIS aims to further advance this area of medicine. New isotopes with specific types of emission, tissue penetration and half-life will be produced and purified based on expertise acquired during the past 50 years in producing beams of radioisotope ions for ISOLDE's experimental programme. Diagnosis by single photon emission computed tomography (SPECT), a form of scintigraphy, covers the vast majority of worldwide isotope consumption based on the gamma-emitting $^{99\text{m}}\text{Tc}$, which is used for functional probing of the brain and various other organs. PET protocols are increasingly used based on the positron emitter ^{18}F and, more recently, a ^{68}Ga compound. Therapy, on the other hand, is mostly carried out with beta emitters such as ^{131}I , more recently with ^{177}Lu , or with ^{223}Ra for the new application of targeted alpha therapy (see p35). Other isotopes also offer clear benefits, such as ^{166}Tb , which is the lightest alpha-emitting radiolanthanide and also combines positron-emitting properties.

Driven by ISOLDE

With 17 Member States and an ever-growing number of users, ISOLDE is a dynamic facility that has provided beams for around 300 experiments at CERN in its 50 year history. It allows researchers to explore the structure of the atomic nucleus, study particle physics at low energies, and provides radioactive probes for solid-state and biophysics. Through 50 years of collaboration between the technical teams and the users, a deep bond has formed, and the facility evolves hand-in-hand with new technologies and research topics.

CERN MEDICIS is the next step in this adventure, and the user community is joining in efforts to push the development of the machine in a new direction. The project was initiated six years ago by a relatively small collaboration involving CERN, KU Leuven, EPFL and two local University Hospitals (CHUV in Lausanne and HUG in Geneva). One year later, in 2011, CERN decided to

Summary

- Nuclear solid state physics allows for unique experiments to be performed which can reliably and unambiguously study at the local level electrical, magnetic and structural properties of materials.
- ISOLDE with the largest number of beams available in the world has had so-called “applications” at its core since the early 1970s.
- These techniques have now also been extended towards biological systems.
- Also core to the science programme at ISOLDE is the development of novel isotopes for medicine. ISOLDE develops the isotopes and MEDICIS will then allow such isotopes to be used for systematic trials.
- Although pressure for beamtime is intense, the current generation of RIB facilities emphasise the science case for nuclear applications and the field is growing.
- ISOLDE is now exploring the concept of a new experimental hall to allow for more experimental campaigns in these areas to realise the field’s ultimate potential.

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The solid state physics programme at ISOLDE: recent developments and perspectives

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