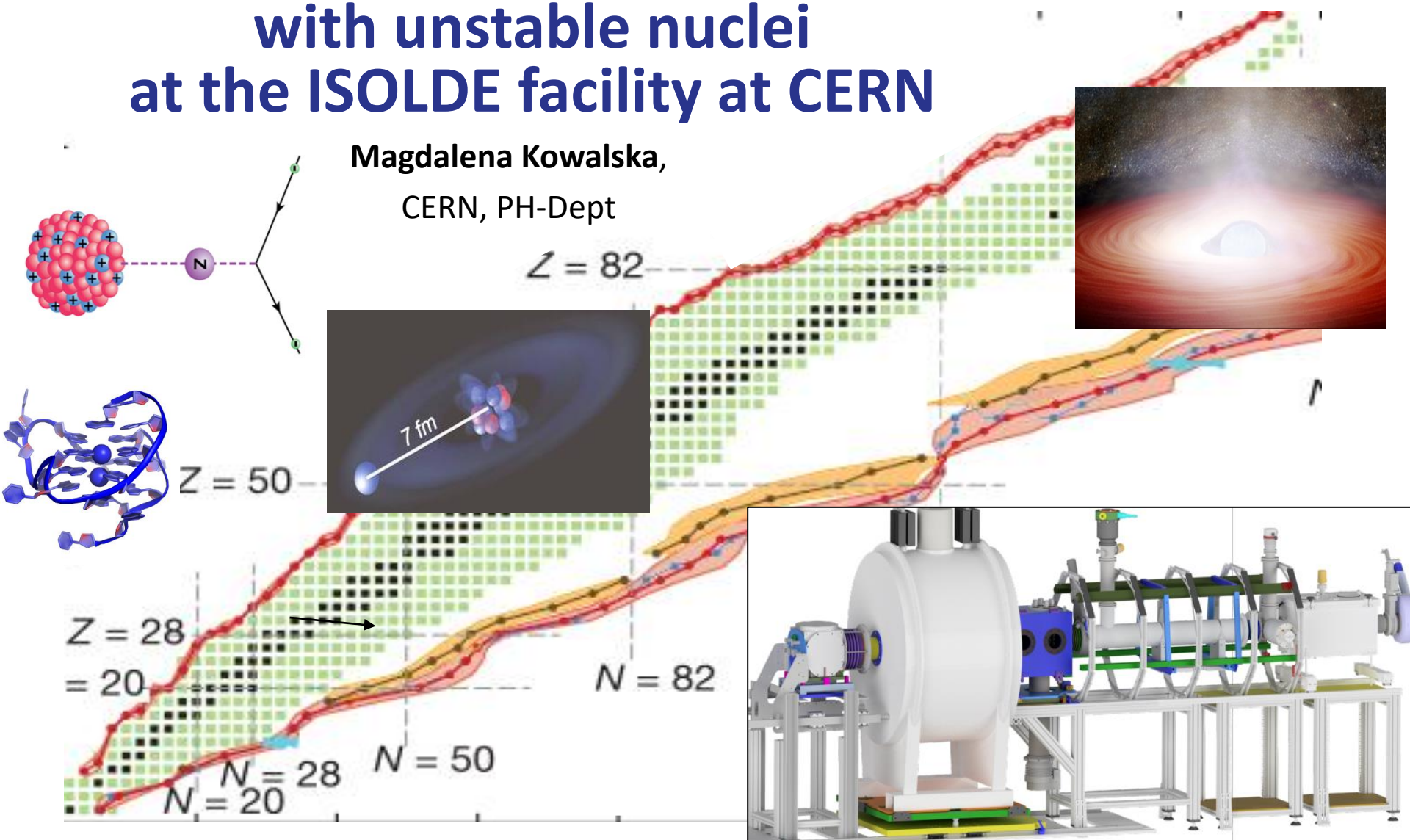
From atomic parity violation and magnetisation distribution in nuclei to biological studies with unstable nuclei at the ISOLDE facility at CERN

Magdalena Kowalska,

CERN, PH-Dept



Introduction

How is atomic parity violation linked to DNA binding ?

- Atomic parity violation (APV) experiments:
  - Provide precise low-energy tests of electroweak theory
  - Determine probability of forbidden atomic transitions
  - Compare to QED predictions

- Metal-ion binding to DNA and biomolecules:
  - Very important in living organisms
  - Narrow range of ‘healthy’ metal-ion concentration
  - Best addressed via Nuclear Magnetic Resonance
  - Compare NMR results to reference systems or quantum chemistry calculations

- Both are studied more precisely if we know/use better magnetic properties of radio- nuclei:
  - APV: distribution of magnetisation in different atomic nuclei
  - NMR: magnetic moments and relaxation times for unstable nuclei

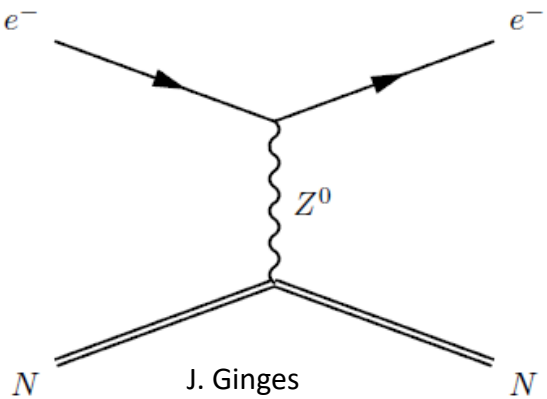
What are Atomic Parity Violation studies?

- Studies of forbidden atomic transitions, e.g. s1/2 ->s1/2 in alkali(like) atoms or ions

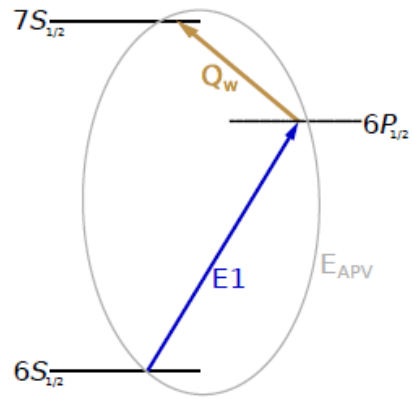
1e-11 of allowed
E1 transition

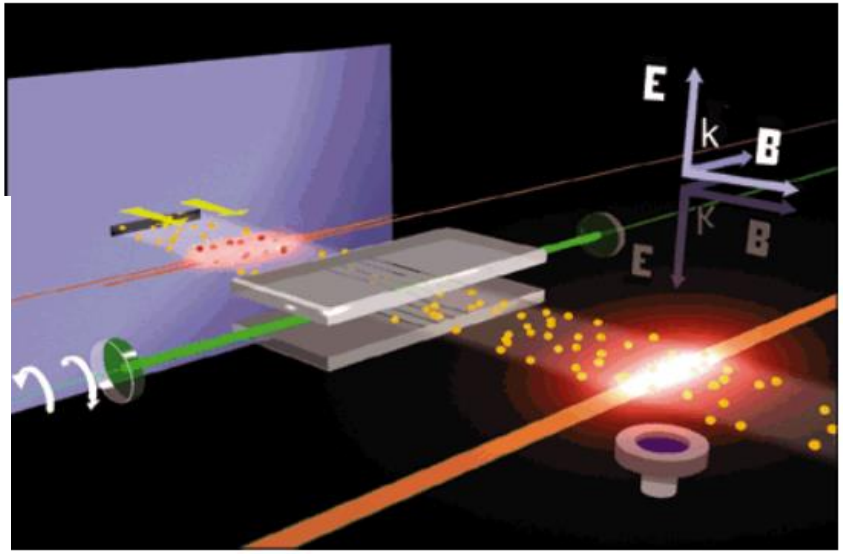
Cs 6S-7S APV amplitude,
0.35% uncertainty

Carl Wieman group (1997)



J. Ginges





T. Andrews, U Colorado

- Parity-violating weak interaction
- Experiments derive nuclear weak charge:

$$Q_W \, k_{\mathrm{PV}} / \beta$$

Vector transition polarizability
(accurate experiments available)

Atomic-structure (QED) factor

  - Leading source of uncertainty: correlations missing (nuclear structure)
  - Challenge: most sensitive to wavefunction at large and small distances from nucleus, energies test intermediate range
  - **Reliable theory benchmark needed**

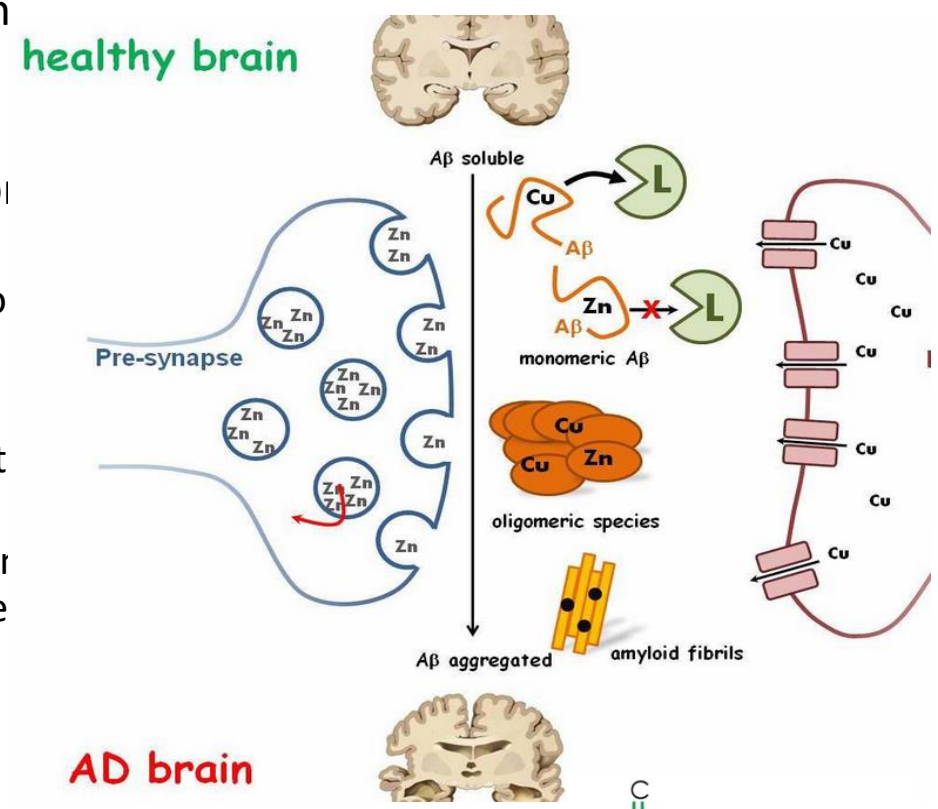
Why are metal ions important in biology?

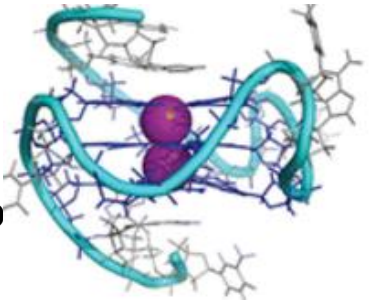
- Role of metal ions in human body depends on adopted coordination environment

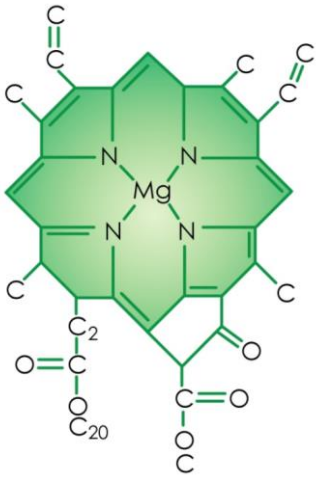
- Right concentration crucial for correct functio of cellular processes
  - Na, K: transport of sugars and amino acids into
  - Mg: RNA- and DNA-processing enzymes and ribozymes
  - Cu: present in many enzymes involved in elect transfer and activation of oxygen
  - Zn: 2nd most abundant trace element in huma catalytic and structural role, regulation of gene message transcription and translation

- Best approach metal-ion NMR
- Challenges: almost invisible signals due to small abundance, I>1/2, and small sensitivity (due to small magnetic moment)

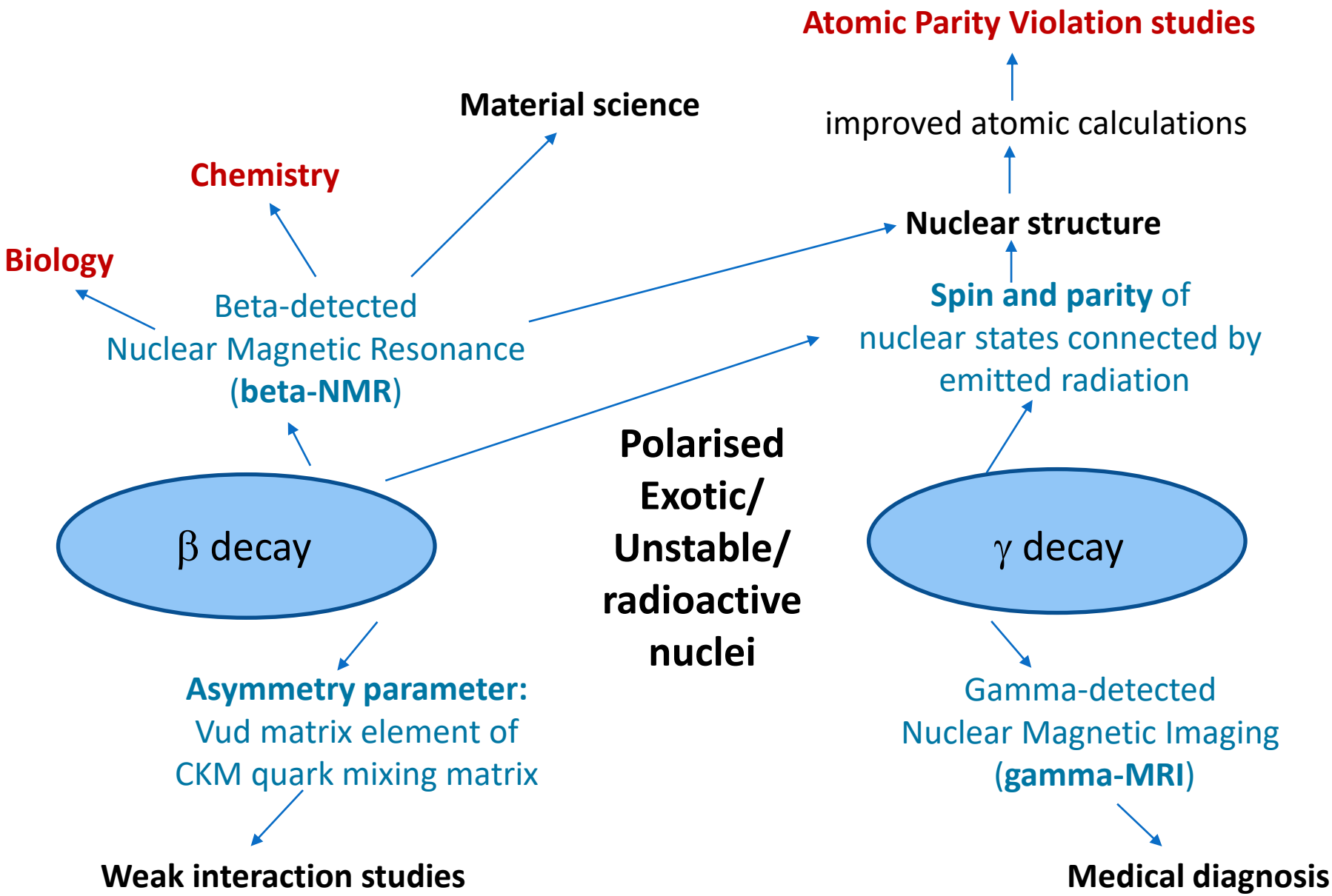
- Result: metal-ion-NMR used very rarely
- **Small amount of nuclei -> sensitive NMR appro is needed**







Why are polarised radio-nuclei the 'answer'?

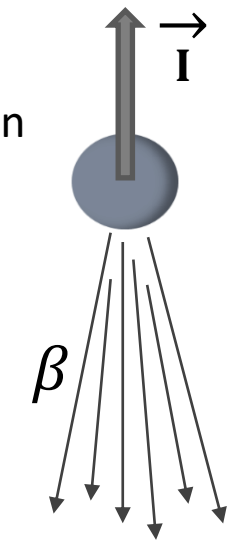


Why are polarized radio-nuclei special?

- **Their beta and gamma decay is anisotropic in space**

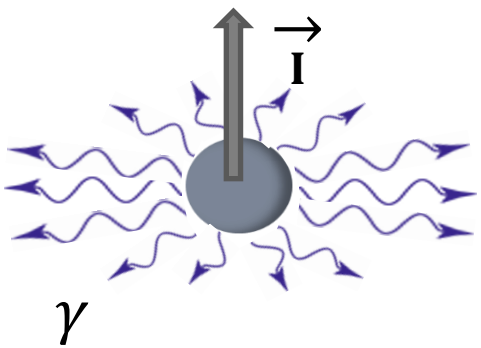
Parity non-conservation of weak interaction, Mme Wu experiment

Beta decay, I>0



B_0

Gamma decay, I>1/2



$$W(\theta_r) = 1 + a_1 \cos(\theta_r)$$

$a_1 = P\, a_\beta$

$$W(\theta_r) = a_0 + a_2 \cos(2\theta_r) + a_4 \cos(4\theta_r) + \cdots$$

depend on degree and order of spin polarization and transition details (initial spin, change of spin)

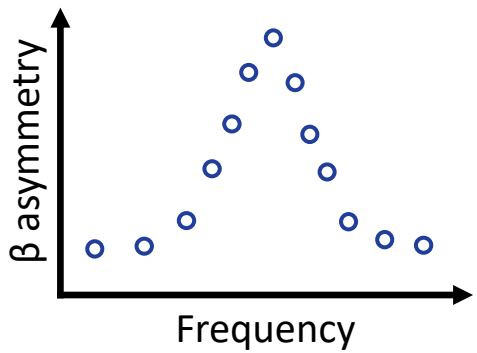
- Observed decay asymmetry can be used to:
  - Probe underlying decay mechanism
  - Determine properties of involved nuclear states
  - Derive differences in atomic and nuclear energy levels

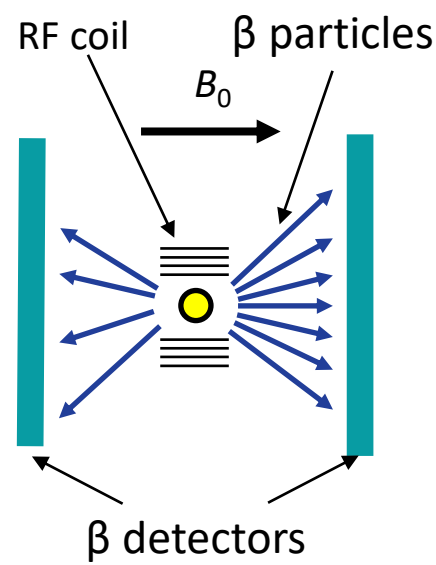
How to use polarised radio-nuclei ?

Employ radiation-detected NMR:

Up to 10 orders of magnitude more sensitive than conventional NMR:
Spin polarisation (10^5 gain over thermal equilibrium)
+ radiation detection (10^5 gain over rf pickup)

Measurement principle,
example of beta-detected NMR

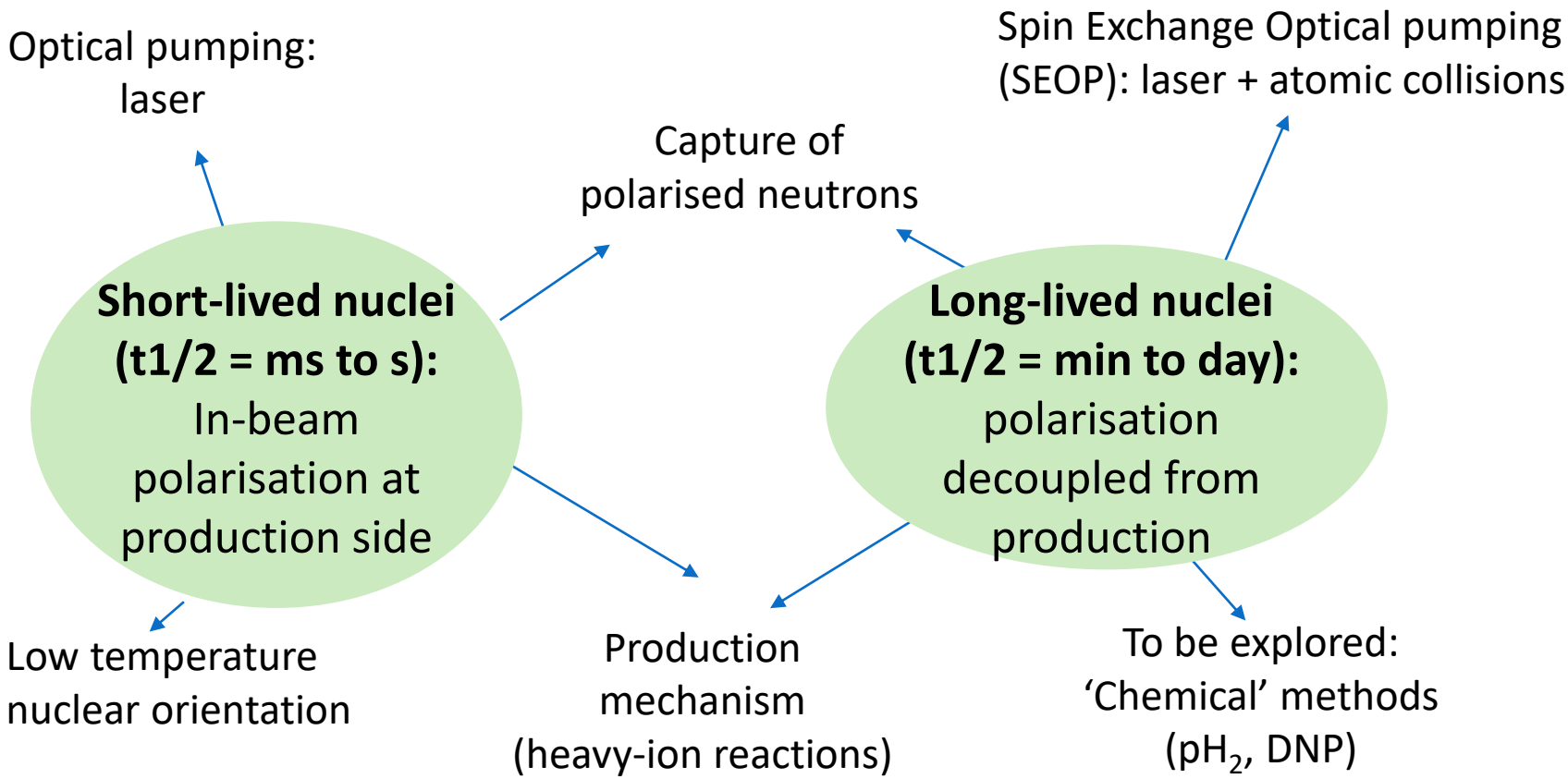




M. Jankowski

How to polarise spins of radio-nuclei?

- Criteria (element-dependent) :
  - Speed and degree of polarisation
  - Type of production site



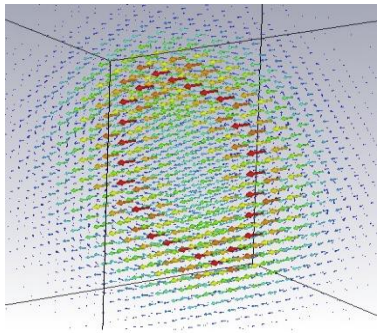
Idea

erc PreSOBEN

Measure Hyperfine Anomaly in unstable nuclei, not neglect it

What is Magnetic Hyperfine Anomaly? = Bohr-Weisskopf effect (ε)

- Effect of **finite nuclear magnetisation** on hyperfine structure
- Probes **distribution of nuclear magnetisation** and, via it, unpaired **neutrons**
- Very small effect, **down to 10^{-6}** (up to 10^{-2} in rare cases)



What do we require to determine it experimentally?

- **magnetic dipole moment** down to **10^{-5}-10^{-6} accuracy**
- **magnetic hyperfine structure constant** down to **10^{-4}-10^{-5} accuracy**

$\Rightarrow$ 2 orders of magnitude higher accuracy than previously reachable for unstable nuclei

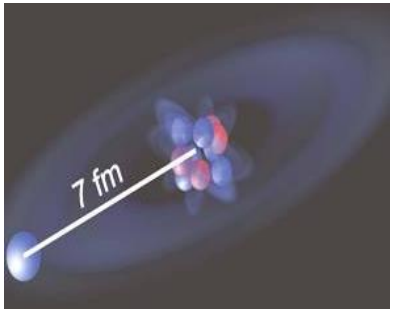
Why is hyperfine anomaly interesting?

new way to look at the nucleus

=> 1st-time access to **distribution of magnetisation (and neutrons)**

- **With consequences in different scientific areas:**

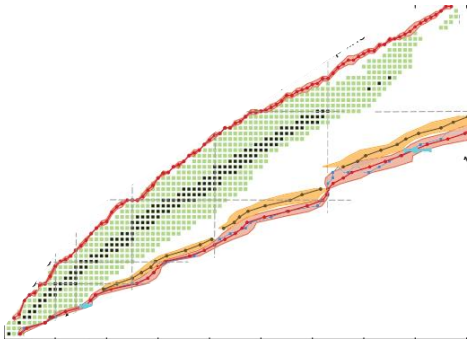
Neutron halos:
radius of halo orbit



^{11}Be

Nuclear force at large distances

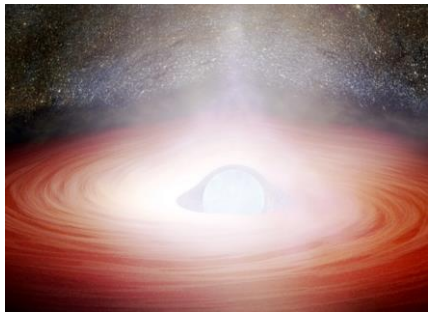
Magnetic observables in nuclear theory (with J. Dobaczewski)



^{49}K, ^{49}Ca

Limits of existence of nuclei
Nucleosynthesis path

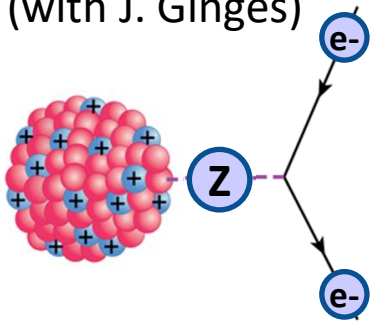
Neutron skins:
emergence
and size



^{51,53}Ca

Equation of State of neutron-rich matter

Precision atomic calculations in the region of nucleus (with J. Ginges)



^{225}Rn, ^{226}Fr, ^{231}Ra

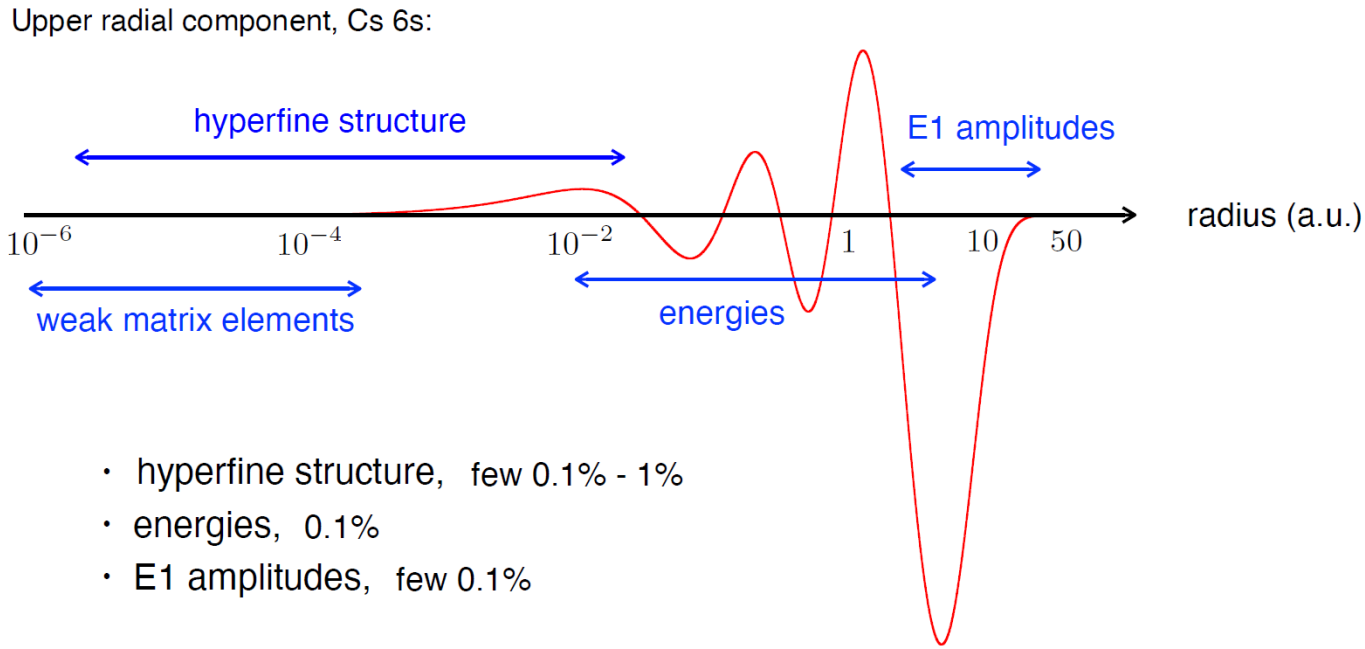
Atomic parity violation

New observable providing unique insight into different fields

Why is magnetic hyperfine anomaly interesting?

Benchmark for atomic theory:

- Test of atomic wave functions in the region of nucleus



- hyperfine structure, few 0.1% - 1%
- energies, 0.1%
- E1 amplitudes, few 0.1%

J. Ginges

- More realistic magnetization distribution in atomic calculations
- Lower uncertainty in atomic calculations used in atomic parity violation and other precision studies

Nuclear weak charge → $Q_W \, k_{\mathrm{PV}}/\beta$ → Vector transition polarizability (accurate experiments available)

↓

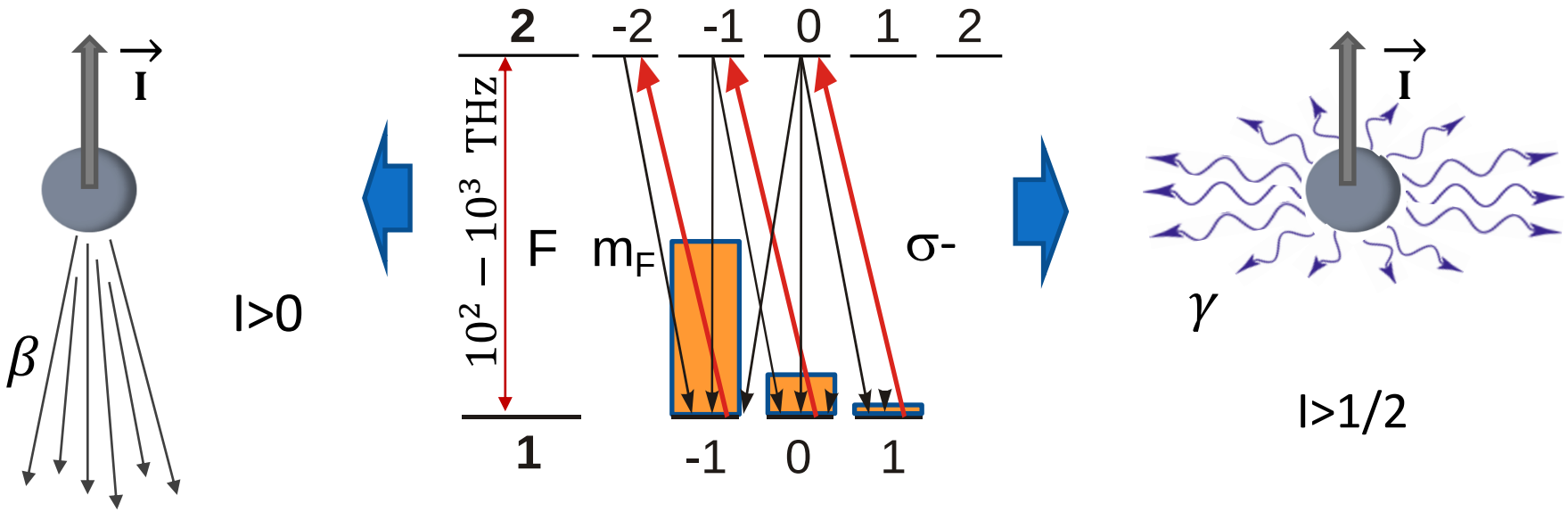
Atomic-structure factor (accurate calculation needed)

Techniques

Ingredients

PreSOBEN

- Spin polarisation and asymmetric decay: Optical pumping



- Accurate magnetic moments: Radiation-detected NMR in liquids
  - Rf-induced flip of nuclear spin in strong magnetic field
    - Resonance detection: change in decay anisotropy

betaDropNMR

- Accurate HFS constant A: Rf-laser double resonance
  - Excitation within hyperfine multiplet in no or weak magnetic field

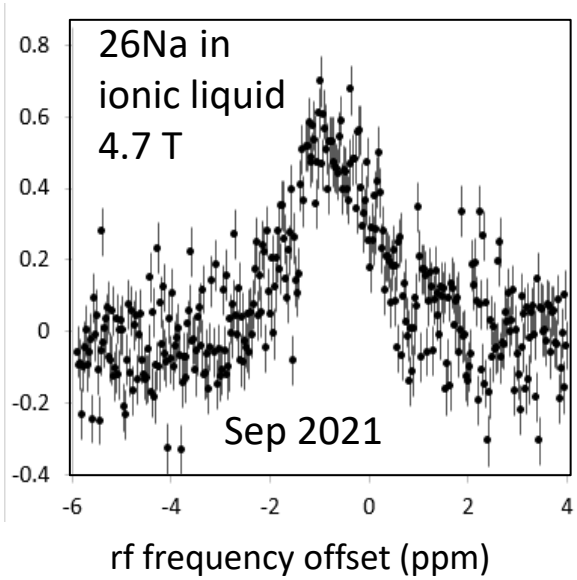
Radiation-detected NMR in liquid samples

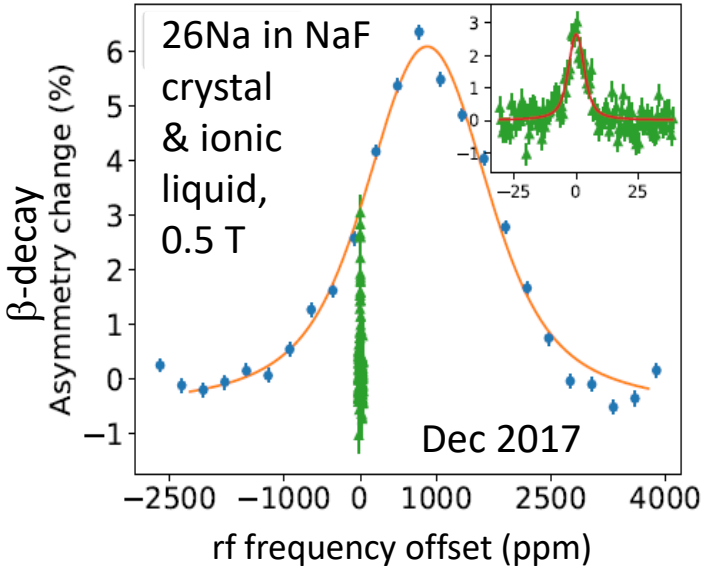
Beta-detected NMR in liquids

betaDropNMR

- Much narrower resonances than in solids: 10^2-10^3 higher precision (part-per-million)

=> **ppm magnetic moments of unstable nuclei** (combined with quantum chemistry)





Harding, …, Kowalska, Phys. Rev. X., 10, 041061 (2020)

Jankowski, …, Kowalska, in preparation

rf-laser double resonance spectroscopy

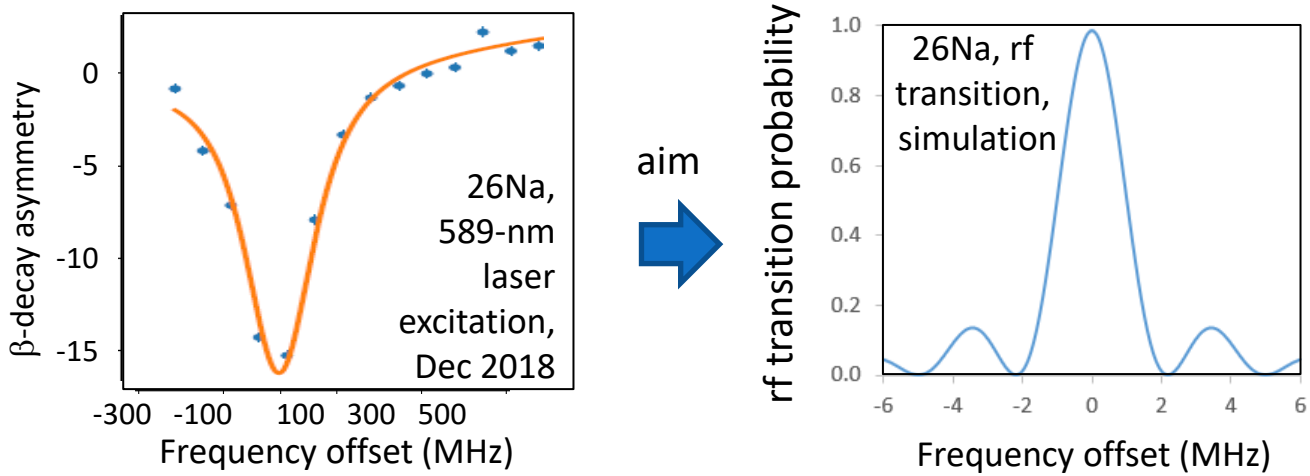
Optical pumping into defined states

- Transition to atomic excited state
- Circular or linear light polarisation

Rf excitation within hyperfine (HF) multiplet

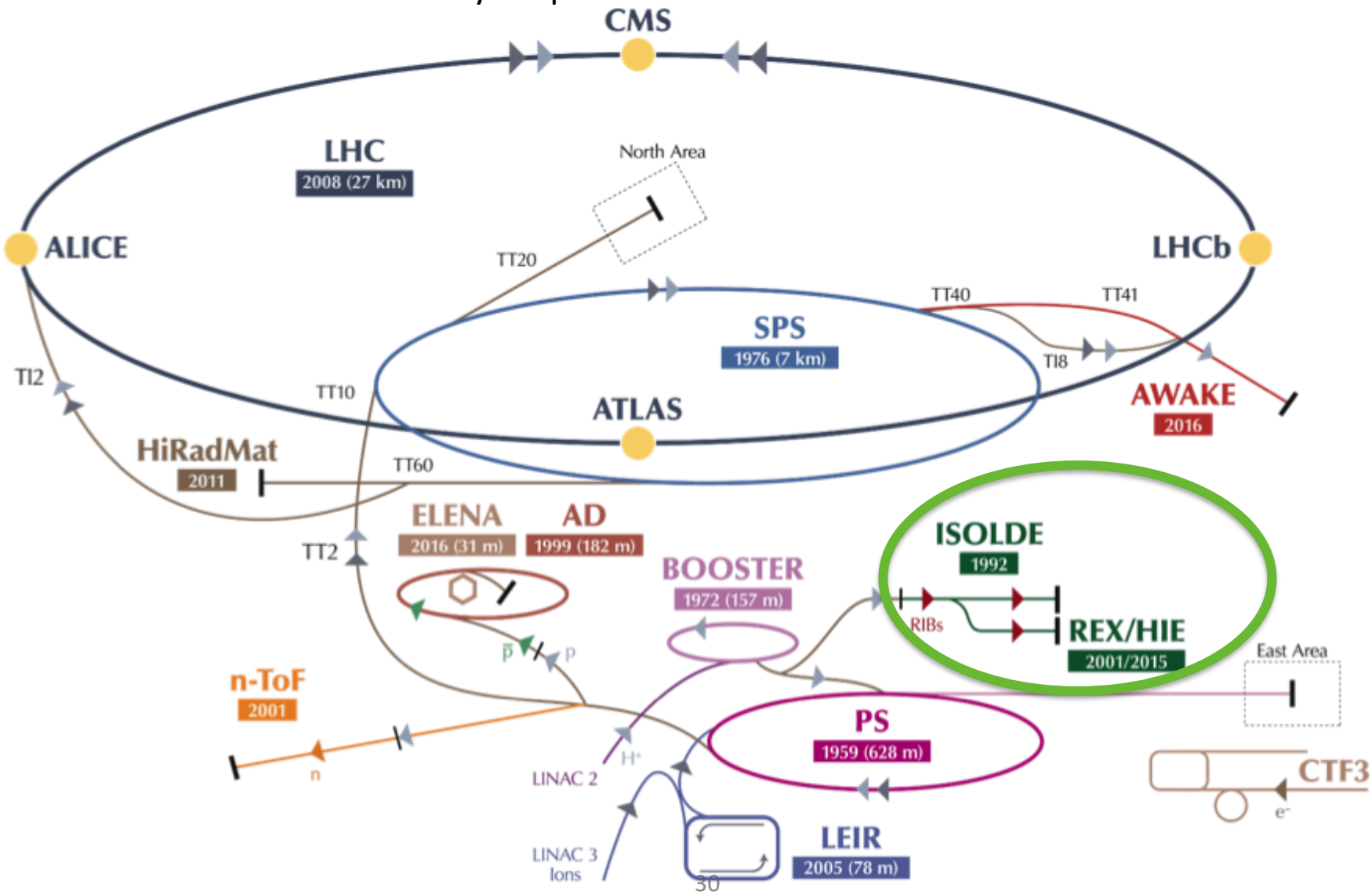
- Rf excitation => narrow resonance
- HF splitting measured directly not as a difference optical frequencies
- Detection: fluorescence or change in decay asymmetry

kHz-wide resonance => hyperfine structure constant with 10^2-10^3 higher accuracy



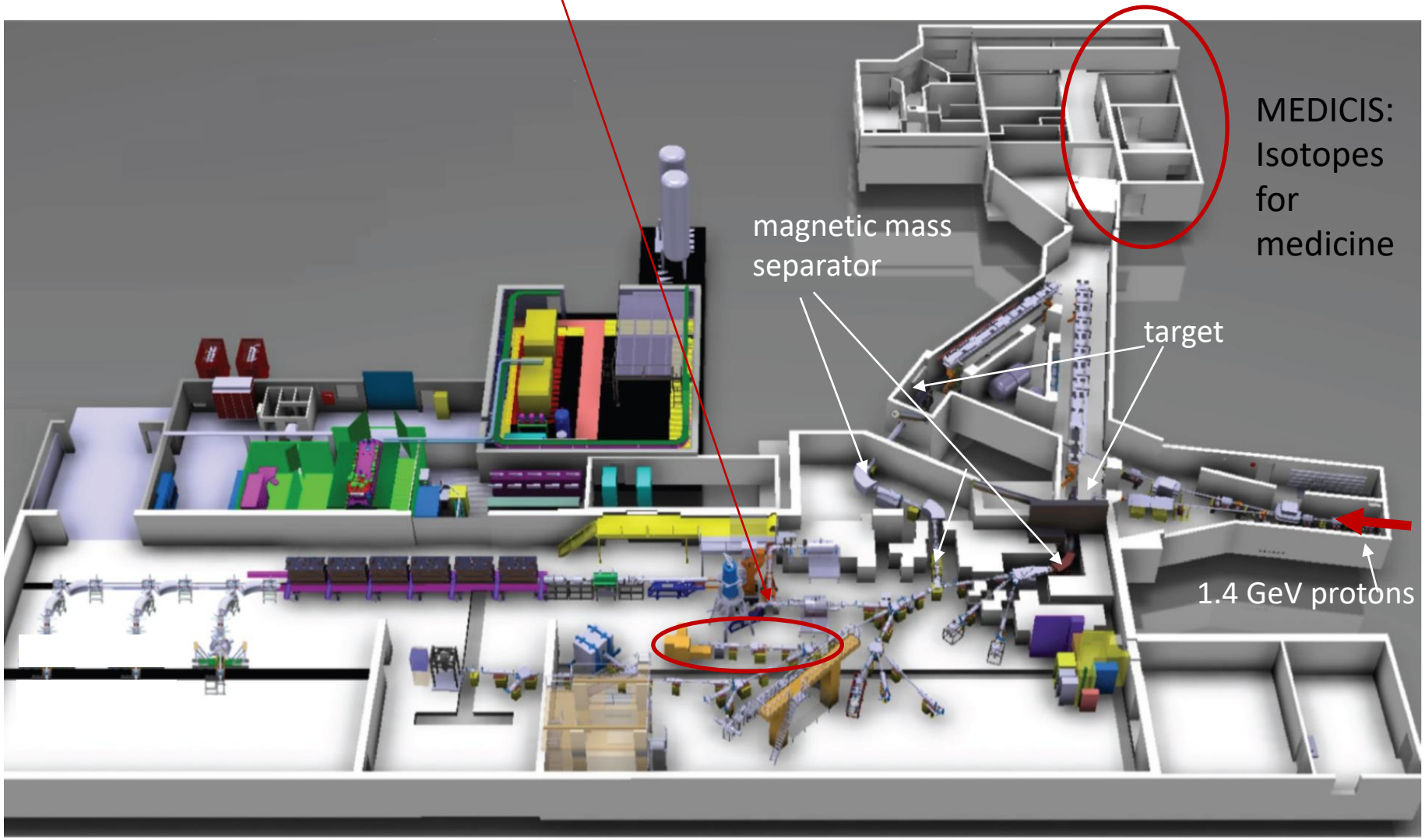
Radiation-detected NMR at CERN

- ISOLDE: CERN's laboratory for production and studies of radioactive nuclei



ISOLDE-CERN

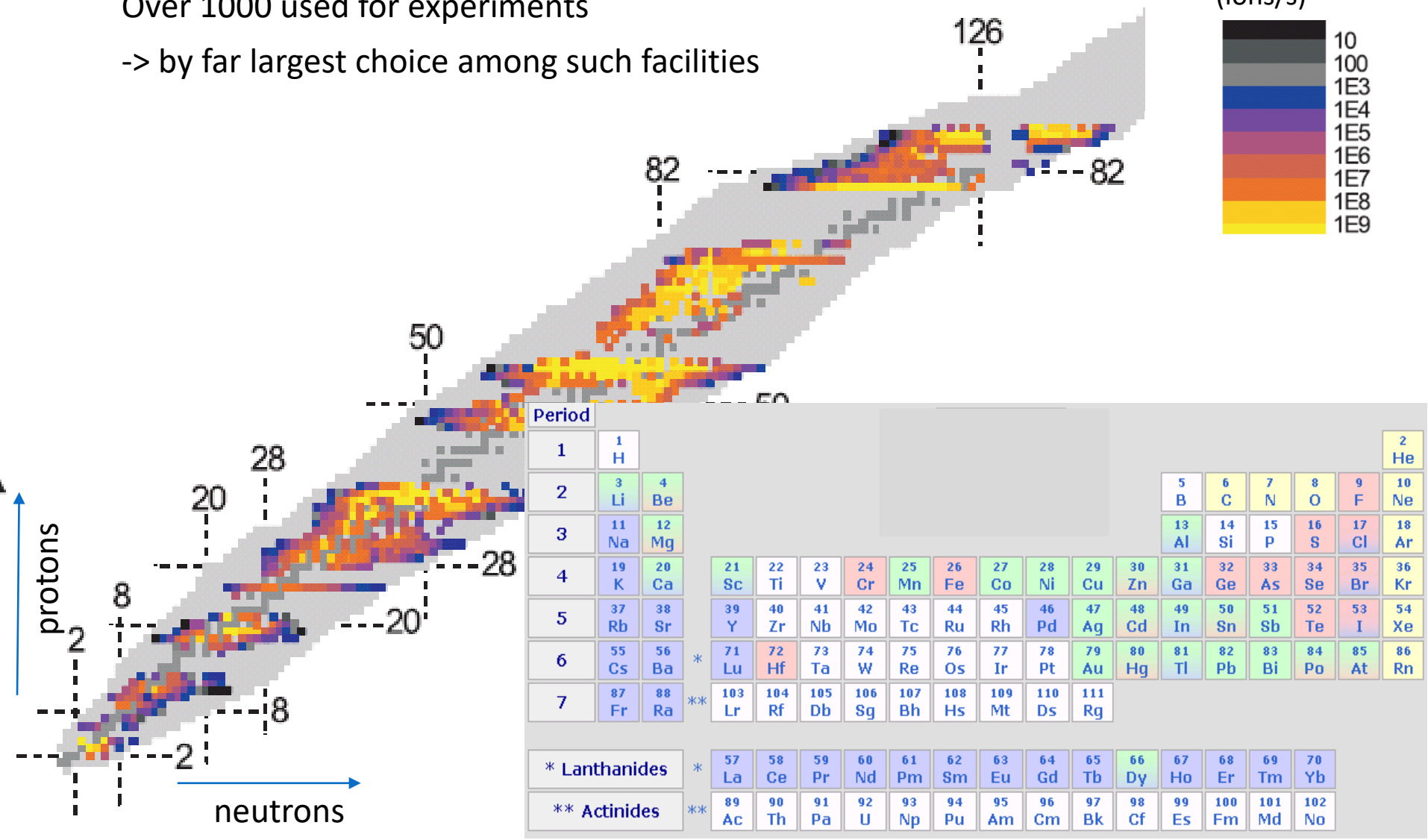
Laser-polarization and β-NMR at VITO beamline



ISOLDE radionuclei

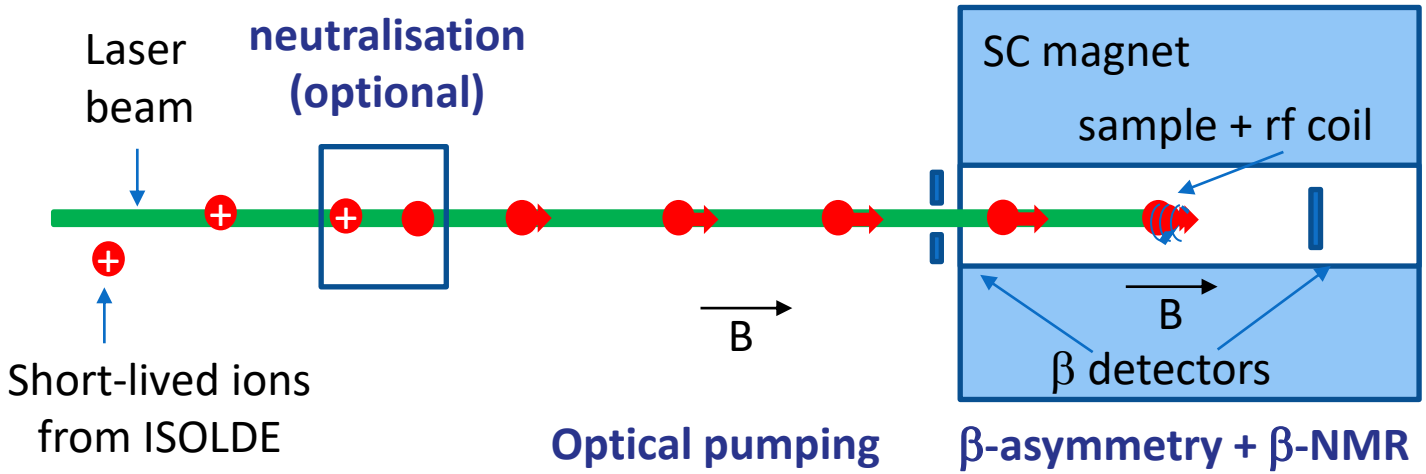
Nearly 1300 isotopes available from over 75 chemical elements
Over 1000 used for experiments

-> by far largest choice among such facilities

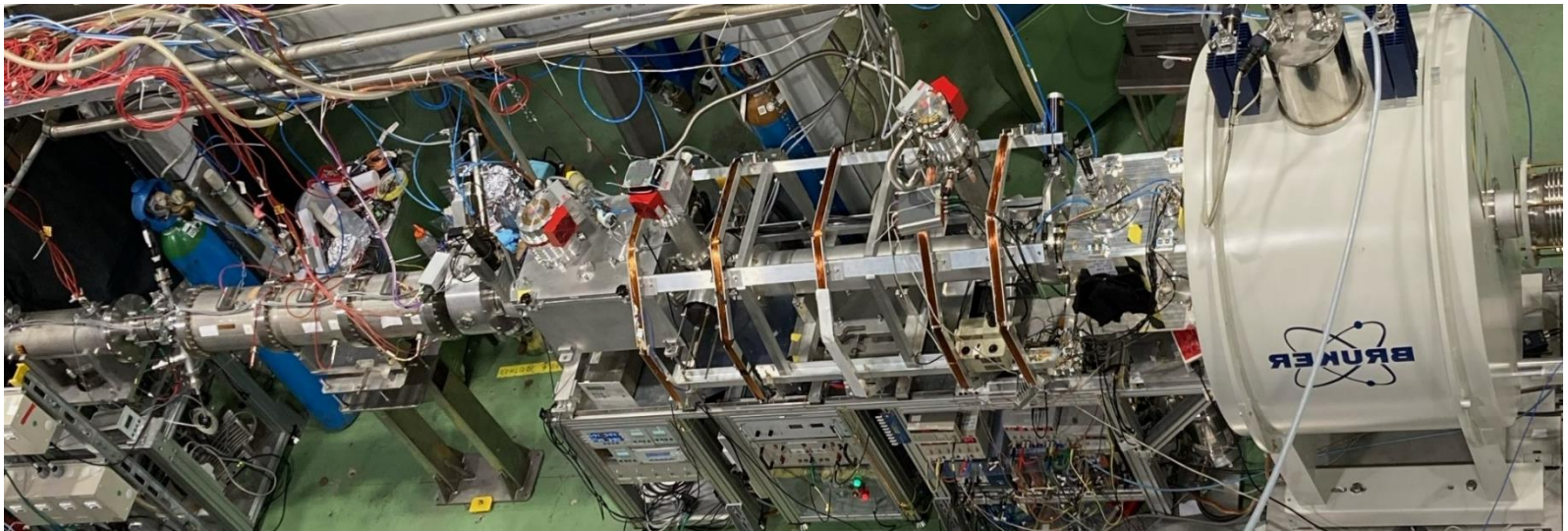


β-NMR on optically-pumped short-lived nuclei

- Experimental setup at ISOLDE
  - Polarisation online via optical-pumping (e.g. on alkali, alkali earths, excited noble gases)
  - Major upgrades during CERN Long Shutdown 2019-2020



betaDropNMR



Design:
S. Warren,
N. Azaryan,
J. Croese

J. Croese et al.,
Nucl. Inst. Meth. A (2022)
M. Jankowski et al.,
in preparation

Results

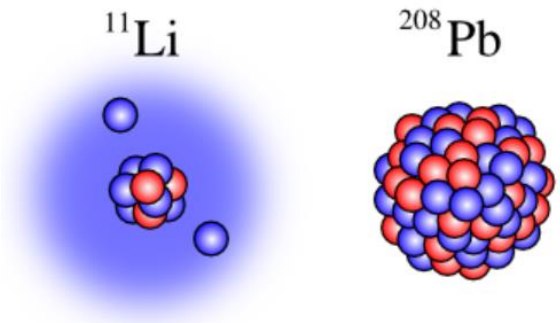
ppm magnetic moments of unstable nuclei

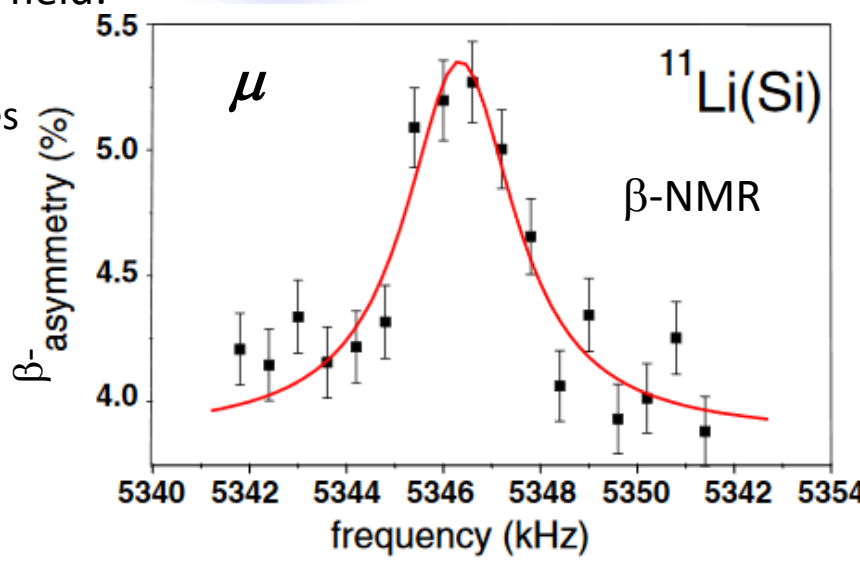
Nuclear magnetic dipole moments:

- Experiments:
  - stable isotopes: ppm precision from NMR
  - short-lived nuclei: 10^{-3} – 10^{-4} precision
    - ✓ HFS from laser spectroscopy
    - ✓ β-NMR in solid hosts

- Calculations of shielding by electrons in magnetic field:
  - All nuclei => till recently: per-mill level
  - Since recently: ab initio, coupled cluster approaches

- Per-mill accuracy
  - Enough to compare with nuclear-structure theory
  - Not enough for fundamental tests
  - Not enough to study the 'magnetic radii' of nuclei
  - Not enough to combine β-NMR with NMR





E. Arnold et al., Phys. Lett. B 197, 311 (1987)
R. Neugart et al., Phys. Rev. Lett. 101, 132502 (2008)

ppm magnetic moments of unstable nuclei

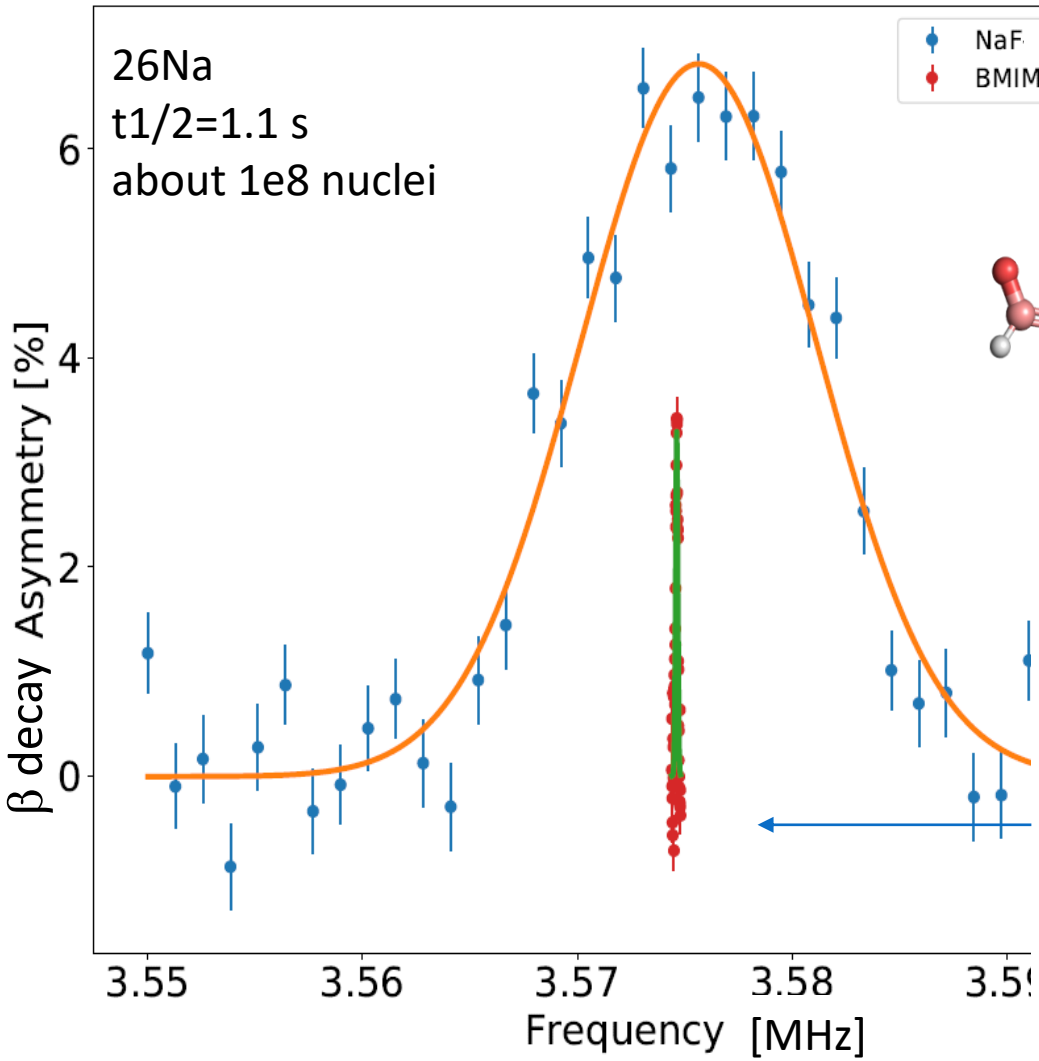
Two orders of magnitude improvement over literature thanks to:

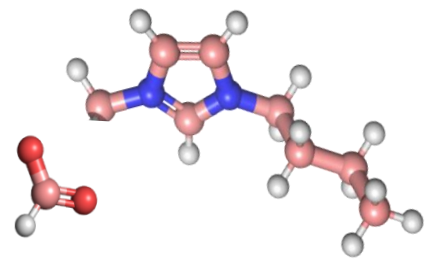
- Extremely narrow resonances => liquid samples
- In-situ NMR measurement of stable reference => vacuum-compatible 1H NMR probe
- Increased field stability => 1H NMR feedback loop
- Increased field homogeneity => shimming coils
- ppm NMR shielding and reference moment => ab initio calculations (A. Antusek)

R. Harding et al., Phys. Rev. X 10, 041061 (2020)

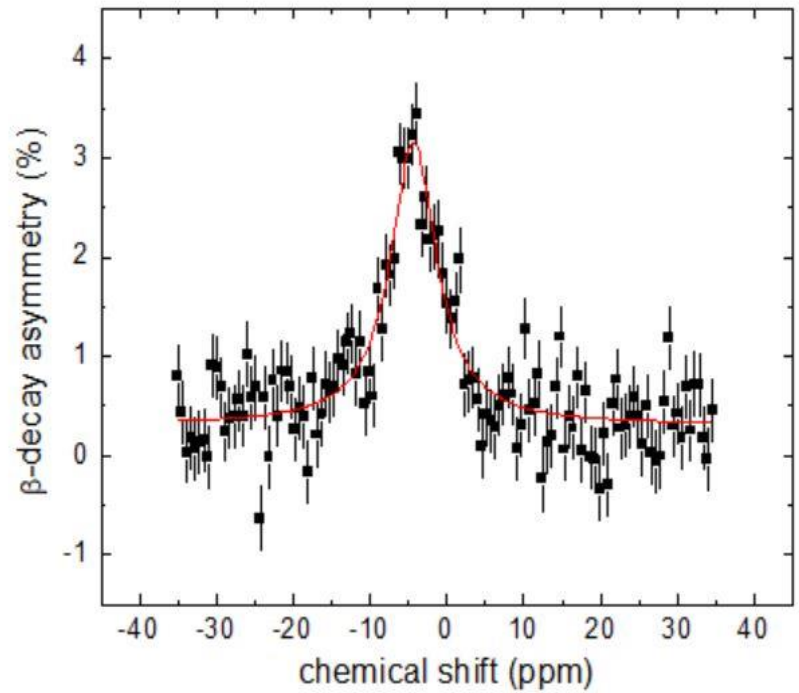
ppm precision: β-NMR in liquids

Molecular tumbling in liquids => over 100 x narrower resonances than in solid hosts





vacuum-compatible liquid hosts: ionic liquids

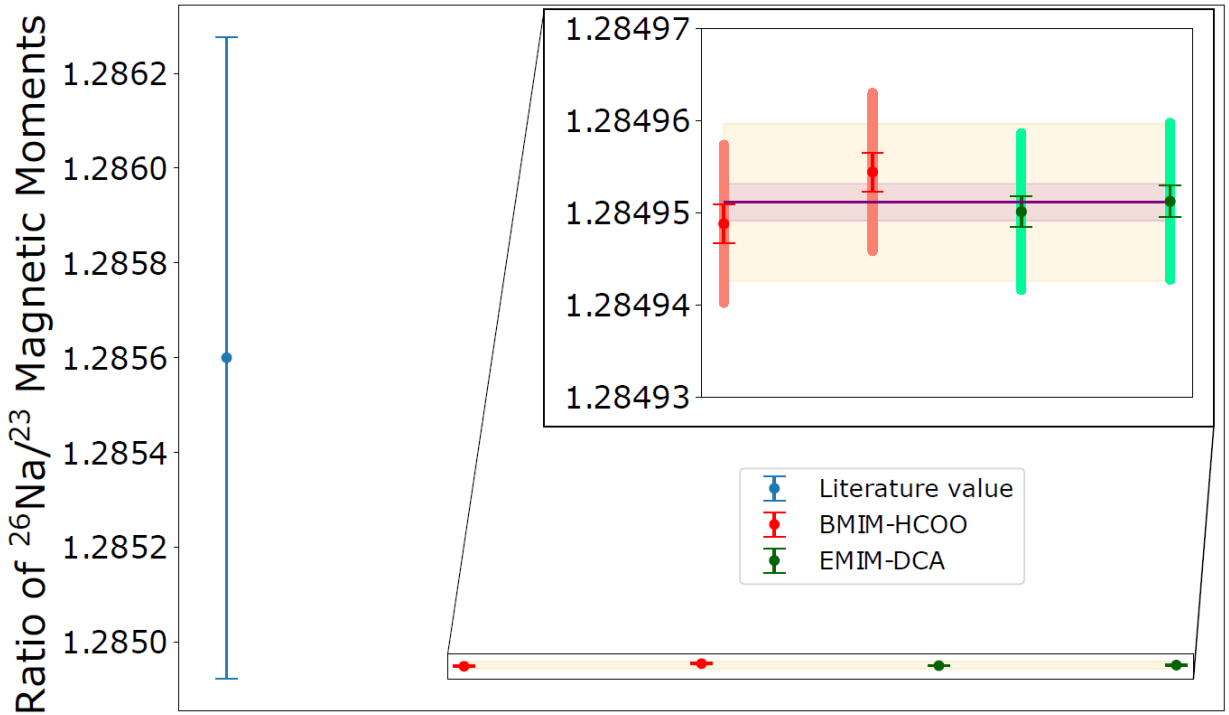


R. Harding et al., Phys. Rev. X 10, 041061 (2020)

ppm accuracy in frequency ratio & reference

- ^{26}Na relative to stable 23Na

Accurate frequency ratio:



Accurate reference:

μ(23Na) /μ_N	old reference	This work
ABMR	+2.217522(2)	2.217495(2)
NMR	+2.2176556(6)	2.217500(7)

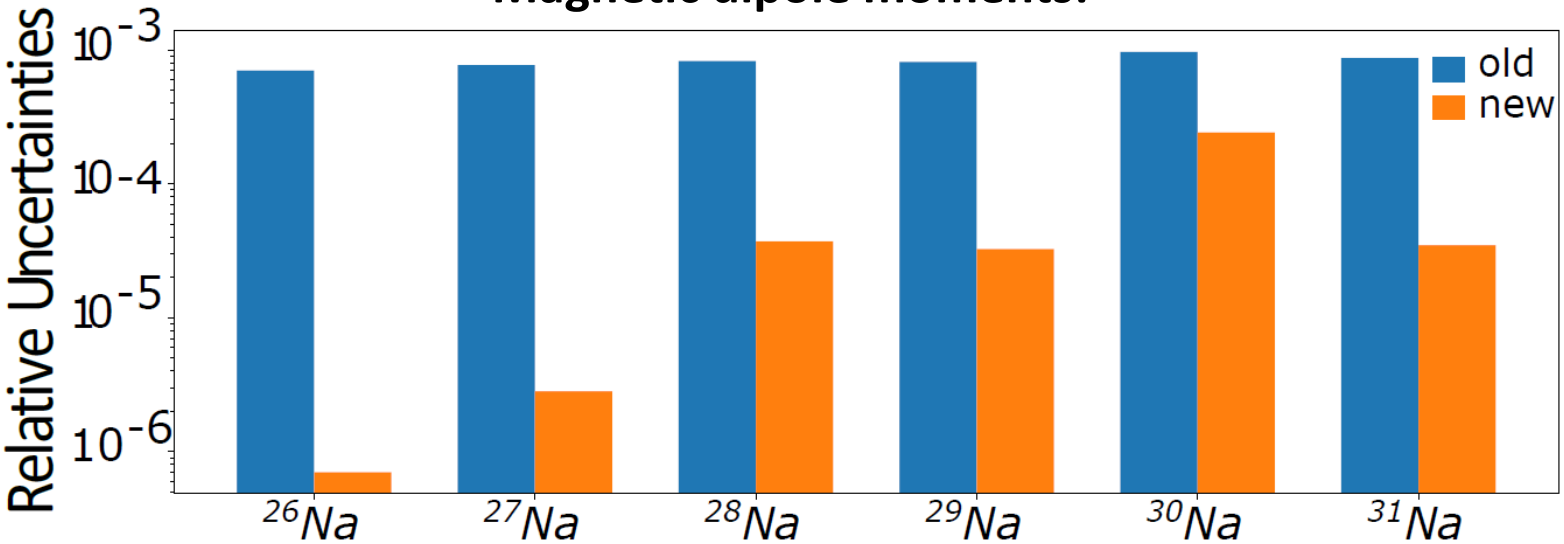
A. Antusek, Bratislava

R. Harding et al., Phys. Rev. X 10, 041061 (2020)

Moments of radio-nuclei with ppm accuracy

- 2 orders of magnitude more precise than previously: ppm accuracy
- Improved precision and accuracy for 27-31Na using 26Na moment as reference (β-NMR in solid hosts)

Magnetic dipole moments:

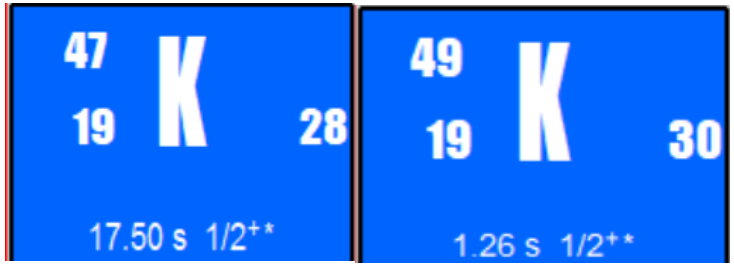


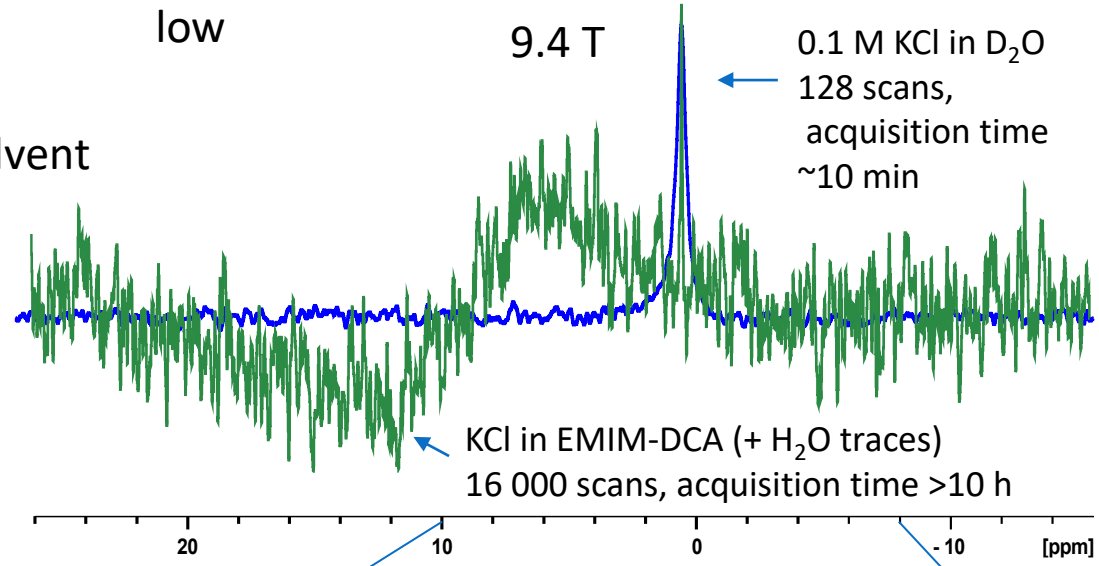
Direct comparison to conventional NMR
Experimental approach – speeds up β-NMR measurements

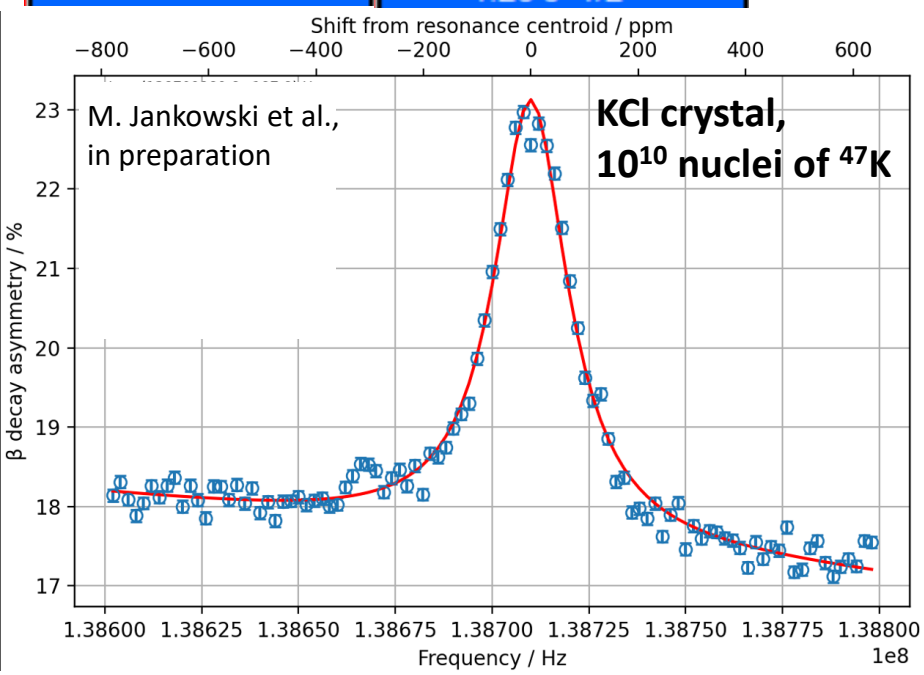
R. Harding et al., submitted to Phys. Rev. X; arXiv:2004.02820

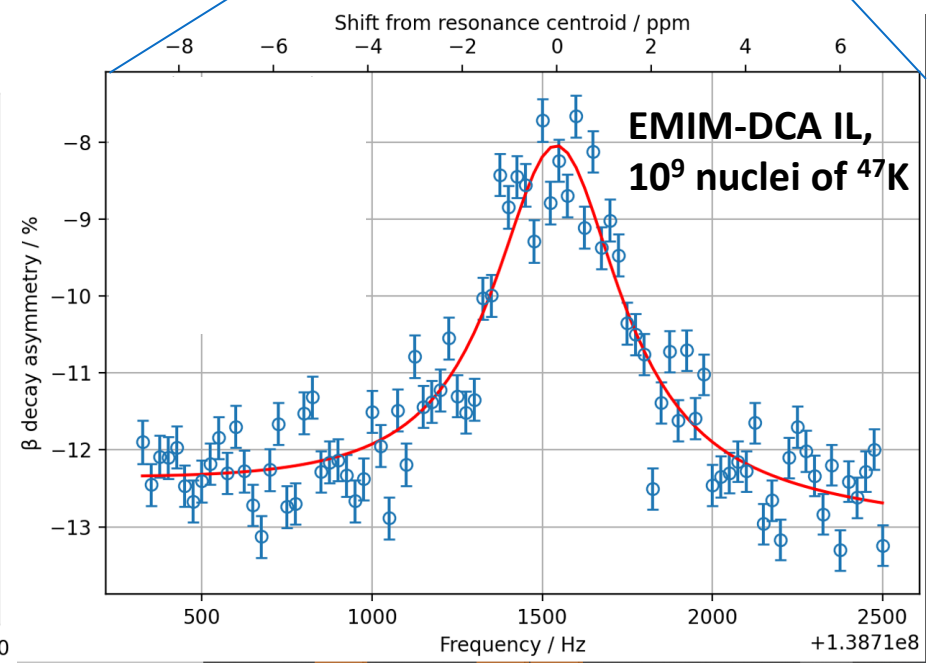
Liquid β-NMR on I=1/2 potassium nuclei

- Stable K NMR: usually ^{39}K (I=3/2), receptivity and Q line broadening
- In ionic liquids and deep eutectic solvent (glycholine) -> almost no signal
- β-NMR:

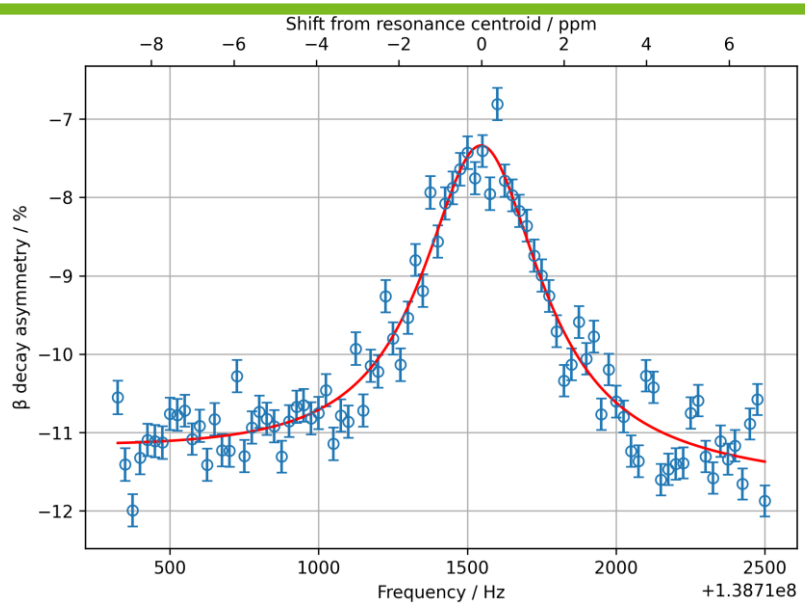








1st hyperfine anomalies for short-lived nuclei



Literature[1] stable MNR:

$$\frac{\nu(^{39}K,\ H_2O)}{\nu\ (D_2O)} = 0.303\ 984\ 85(9)$$

$$\boxed{\frac{\nu(^{47}K, EMIM\ DCA)}{\nu\ (^{39}K,\ H_2O)} = 14.83852(3)}$$

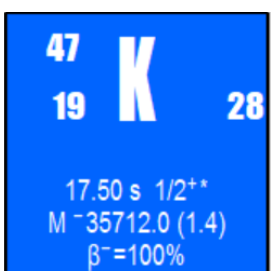
COLLAPS HFS measurements[2]:

$$\frac{A(^{47}K)}{A\ (^{39}K)} = 14.785(1)$$

$$^{39}\Delta^{47} = 0.364\ (9)\ \%$$

Preliminary Experimental result:

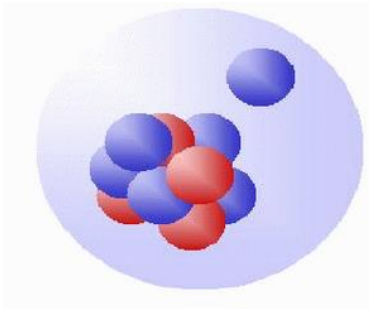
$$\frac{\nu(^{47}K, EMIM\ DCA)}{\nu\ (D_2O)} = 4.501\ 684\ (9)$$



Atomic theory (Jacinda Ginges, Georgy Sanamyan)
+
Density Functional Theory (Jacek Dobaczewski)

work ongoing…

Initial calculations look extremely promising!



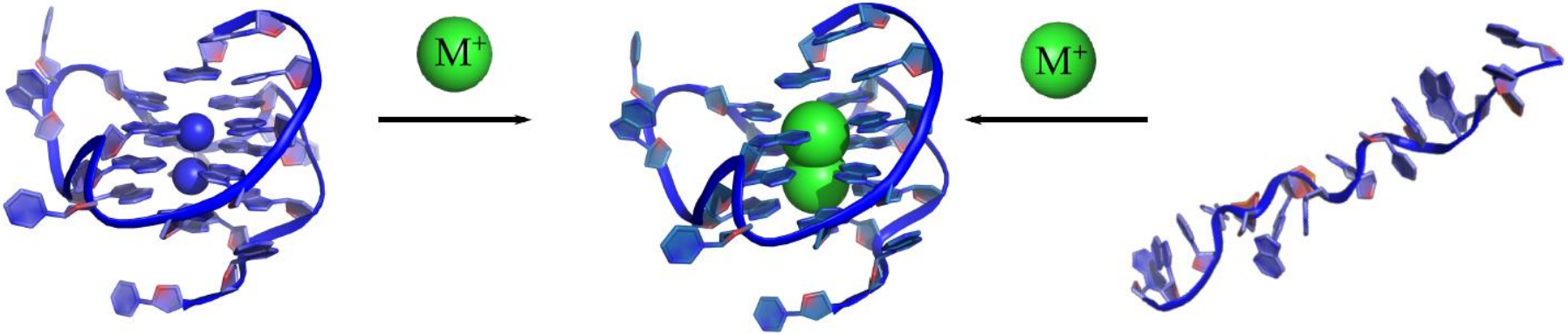
Next case: 11Be – ‘halo nucleus’ where magnetisation is carried by halo neutron -> determination of neutron radius

β-NMR and DNA G-Quadruplexes

- DNA G-quadruplexes:
  - present e.g in telomers, crucial: binding to alkali metals

β-NMR advantages:

Sensitivity: metal ions are easily visible, cleaner spectra
Smaller quadrupole moments -> longer relaxation and narrower spectra
Real-time: folding intermediates



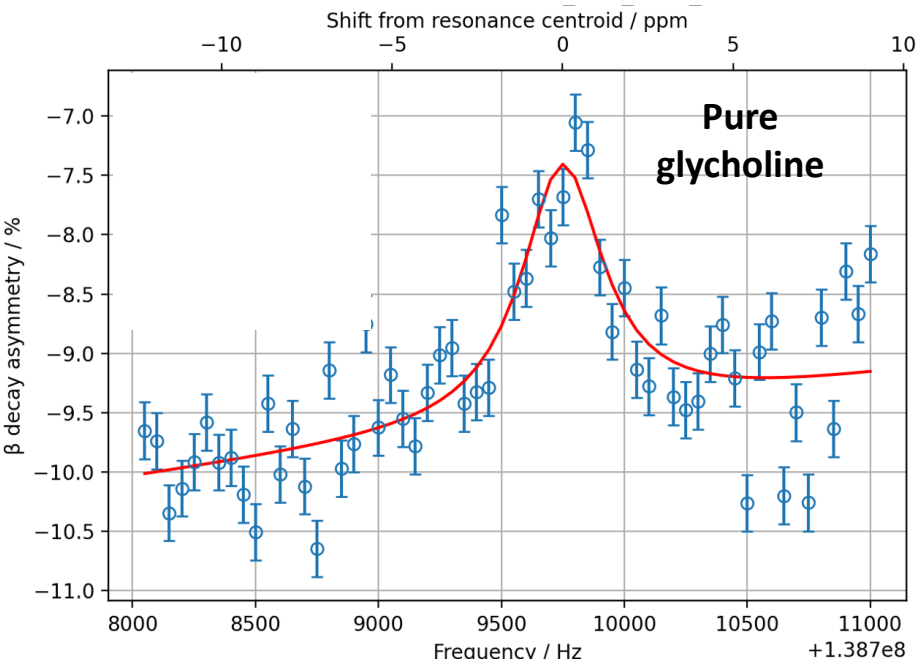
B. Karg

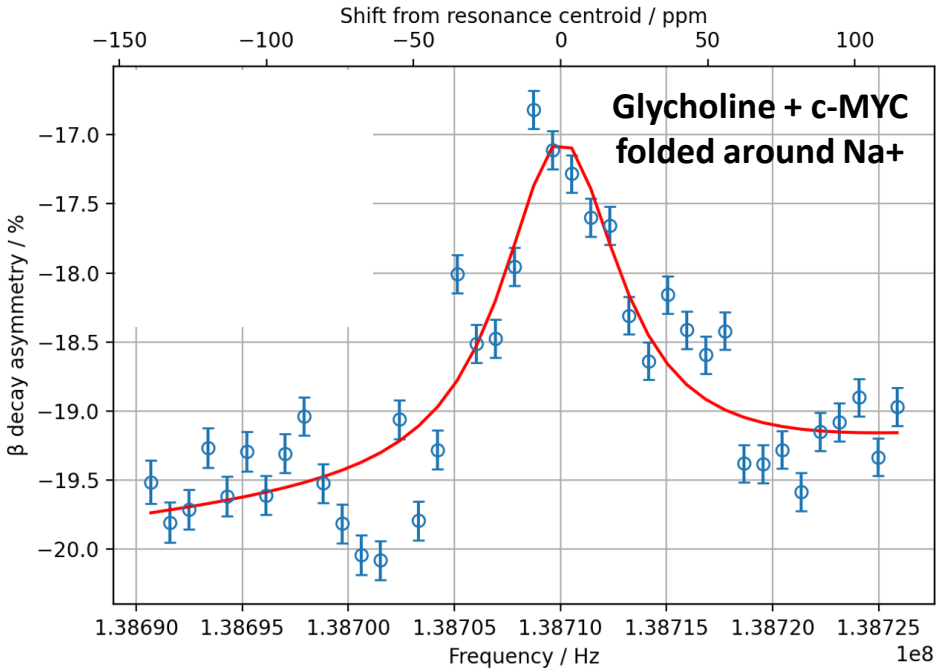
Potassium binding to DNA G-quadruplexes

B. Karg

- Suitable vacuum-compatible solvent to fold G-quadruplex:
  - Ionic liquids not suitable
  - Deep Eutetic Solvent glycholine (glycerol + choline chloride) shown to fold GQ

- β-NMR experiment in summer 2022: ^{47}K implanted into glycholine + DNA

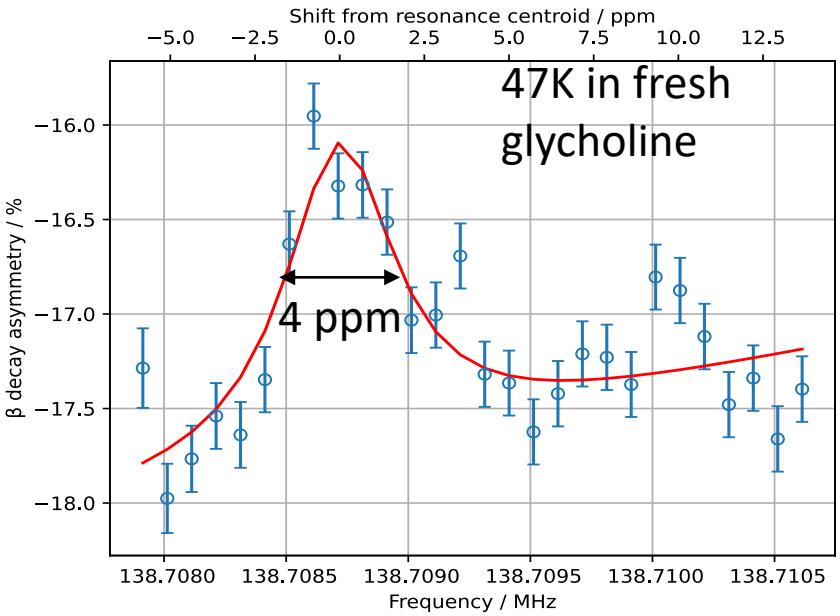


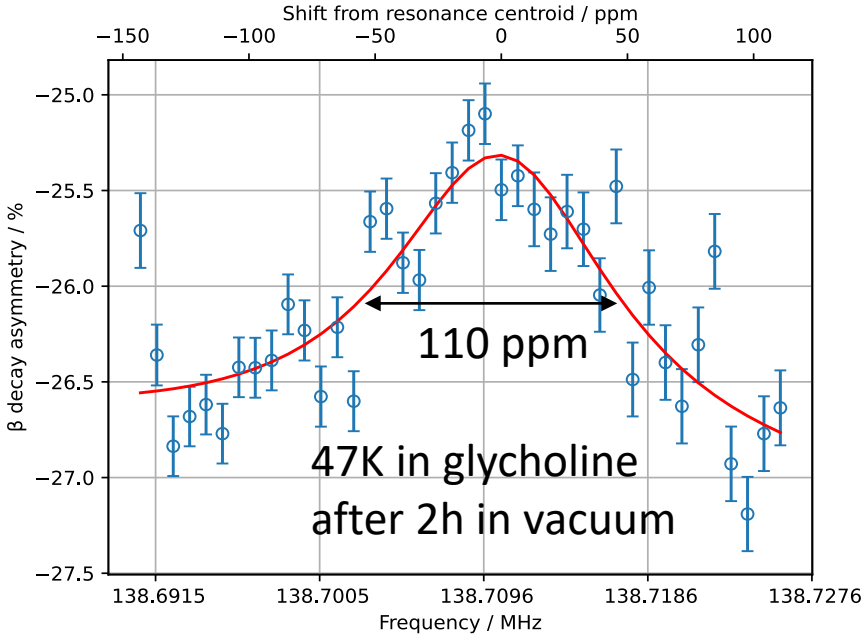


In presence of DNA: K resonance shifted and broadened: implanted K replaces Na inside G-quadruplex?

Potassium binding to DNA G-quadruplexes

- Experimental challenge:
  - Pure glycholine resonances broaden after exposed to vacuum for several hour
  - Solid-like behaviour



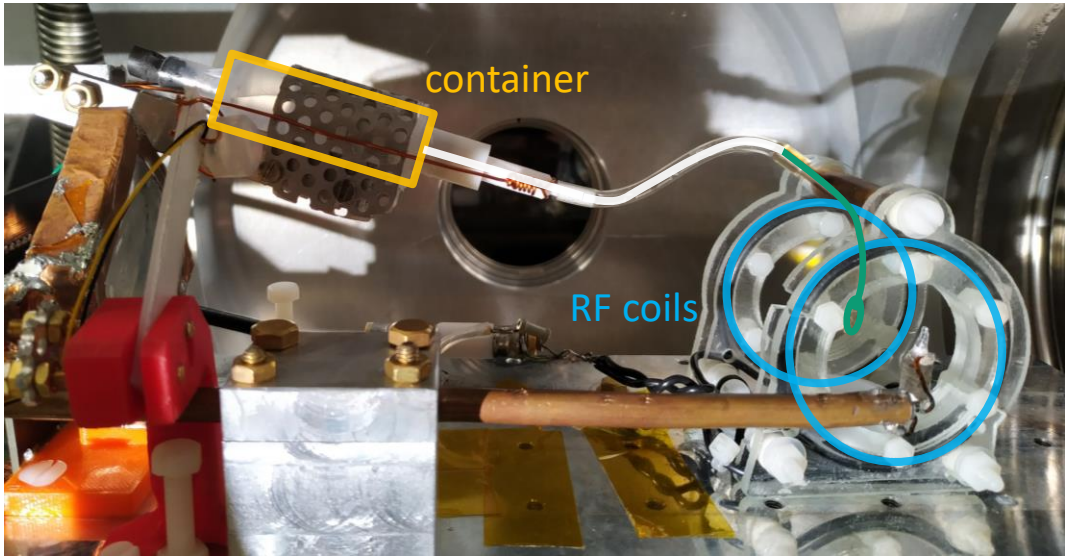


→ Solution: provide regularly new liquid

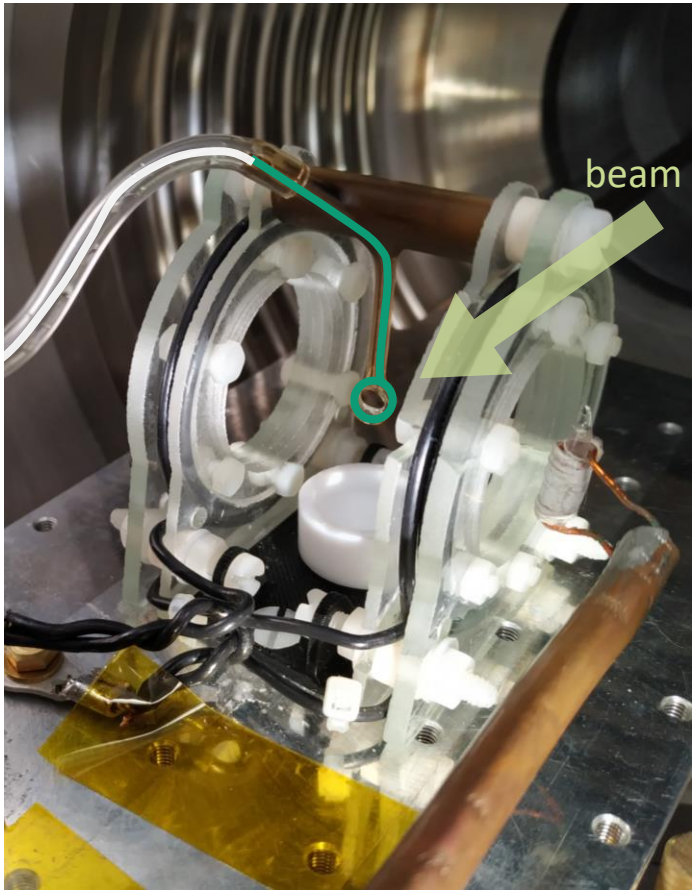
B. Karg, M. Jankowski

Liquid dispenser system at high vacuum

- Fresh droplet → avoid peak broadening
  - Container with liquid sample inside beamline, but open from outside



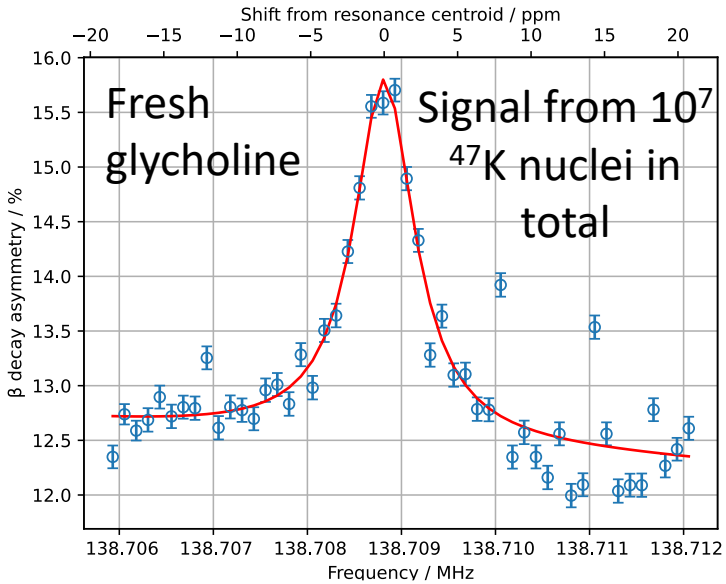
Photos: M. Jankowski

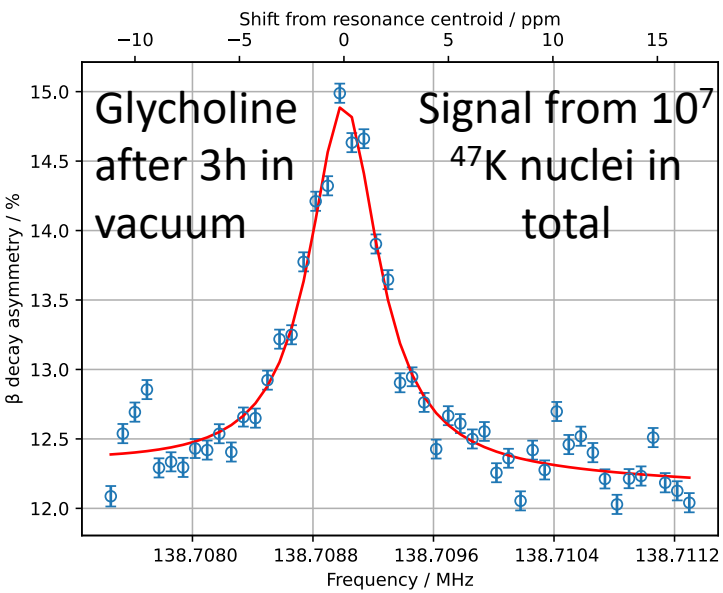


T. Treczoks, N. Azaryan

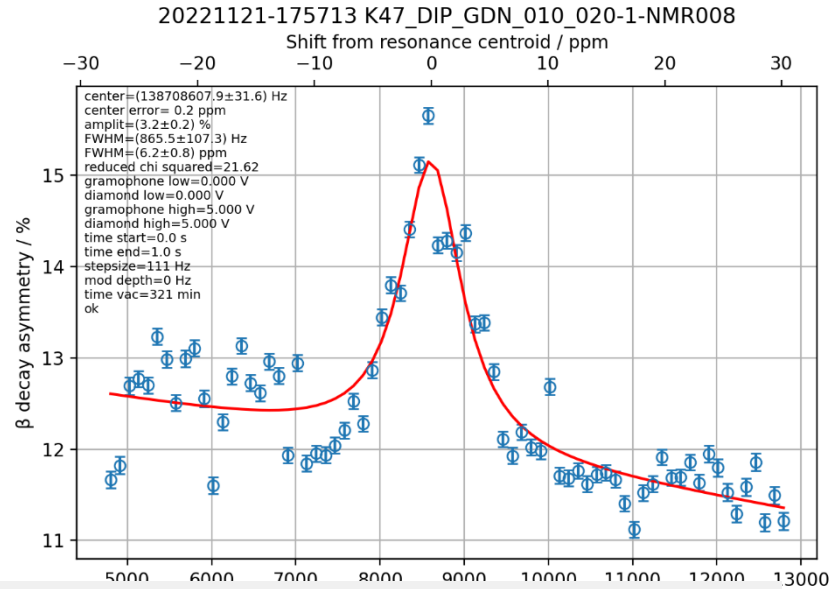
Potassium binding to DNA G-quadruplexes

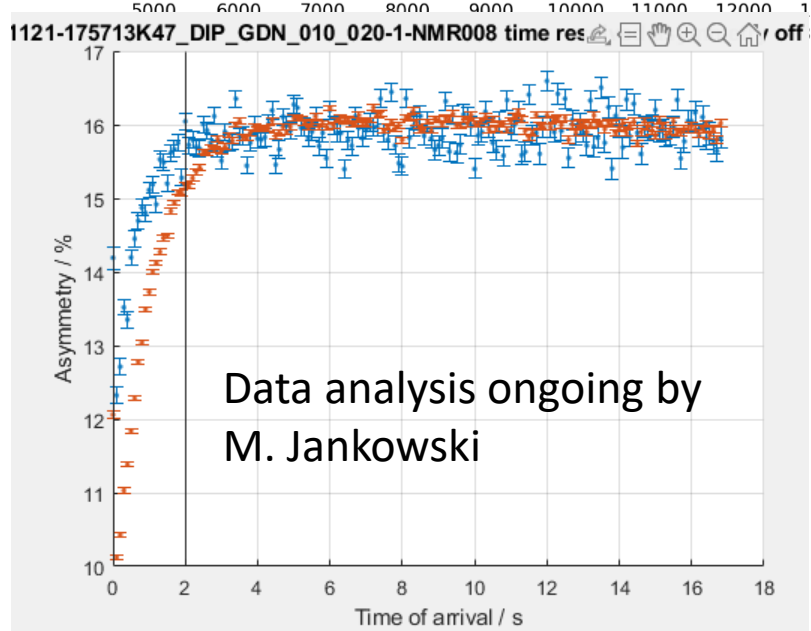
- Beamtime in November 2022





Sample with DNA pre-folded with ^{23}Na

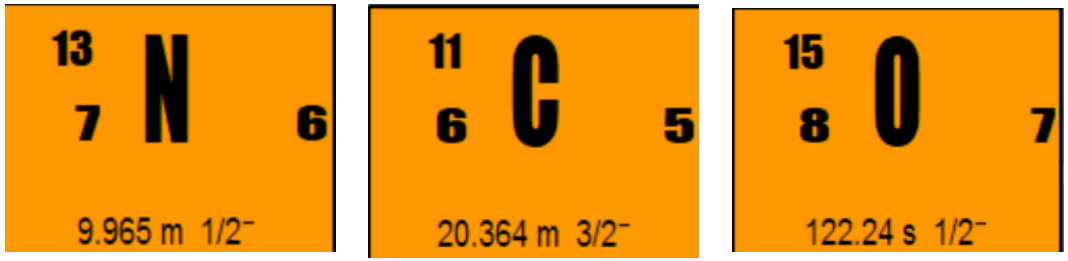




Data analysis ongoing by M. Jankowski

β-ZULF-NMR on long-lived PET nuclei

- RD-ZULF-NMR: radiation-detected + zero-to-ultralow-field NMR:
  - Combine ZULF-NMR portability with RD-NMR sensitivity
  - Design of proof-of-principle experiment ongoing
  - Suitable candidates:



Isotope production as aqueous solution (like for PET)

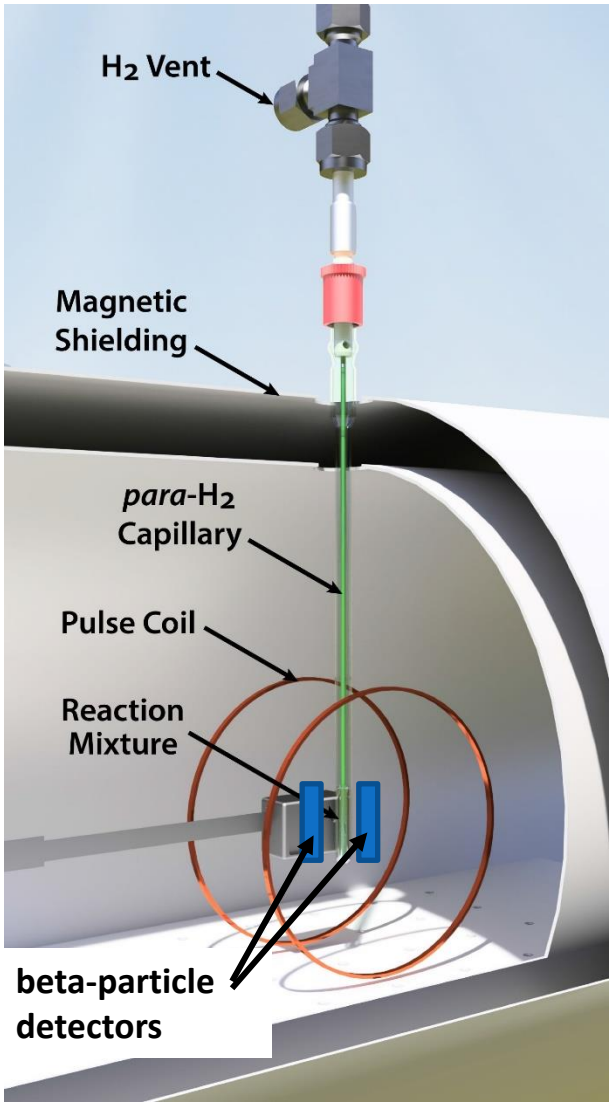
Parahydrogen prepared from small H2 bottle

pH_2 hyperpolarising chemical reaction inside ZULF apparatus

Magnetic field pulse and signal acquisition in beta-decay asymmetry

In collaboration with U Mainz: D. Budker, D. Barskyi and HUG cyclotron team (A. Grotzky, V. Garibotto)

CERN Medical Applications Fund + ERC Proof of Concept



Summary

- Common point of atomic parity violation and metal ions in biology -> polarised unstable nuclei

- Polarised unstable nuclei:
  - Asymmetric emission of radiation
  - Polarisation
  - Sensitive Nuclear Magnetic Resonance

- Techniques:
  - Beta-NMR at ISOLDE-CERN

- Results:
  - Precise magnetic moments
  - Distribution of magnetisation inside nuclei (-> neutron-orbit radius)
  - Interaction of metal ions with DNA

- New ideas:
  - beta-NMR on PET isotopes

Acknowledgements

ISOLDE-CERN team:

N. Azaryan, M. Bissell, K. Dziubinska-Kuehn, **M. Jankowski**, **M. Chojnacki, B. Karg,** K. Kulesz, **W. Lindberg**, **I. Michelon, M. Pesek, M. Piersa-Silkowska**, S. Warren, **T. Treczoks**

Collaborators:

Experiment: L. Vazquez, CERN; M. Baranowski& M. Kozak, Poznan; M. Madurga, Knoxville; A. Korgul, Warsaw, R. van de Grote, Leuven; D. Zakoucky, Rez, J Gravier, M Pupier, UNIGE

Theory: A. Antusek, Bratislava; J. Ginges, Brisbane; J. Dobaczewski, York; K. Pachucki, Warsaw; S. Pastore, Washington; A. Wesolowski, UNIGE

Thank you for your attention

Funding: