National Physical Laboratory

Development of standards for alpha emitting radionuclides for nuclear medicine

Ra-223 and Th-227

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NPL Radioactivity Group

CIRMS 2017

Outline

- Application of ^{223}Ra to palliative treatment of skeletal metastases associated with prostate cancer.
- Application of ^{227}Th Targeted Thorium Conjugates (TTC) utilizing mAbs
- Introduction to Primary Standards of radioactivity
- Introduction to clinical measurement methods
  Dose Calibrators
- Comparison with published nuclear data

^{223}Ra and ^{227}Th : Scope of projects

Primary standardisation of radioactivity of ^{223}Ra and ^{227}Th.

Instigation of a new service for NPL to provide rapid traceable calibrations to NPL primary standards.

Publication of calibration factors for radionuclide calibrators used in nuclear medicine clinics, enabling accurate assay of administered activities.

Publication of new nuclear decay data

(γ-emission intensities, half lives…)

Xofigo®
radium Ra 223 dichloride
INJECTION

NPL
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$^{223}RaCl_2$ (Xofigo) is the first α-emitting radioactive palliative therapeutic agent to be approved by the FDA following successful clinical trails (ALSYMPCA) for patients with castration-resistant prostate cancer and symptomatic bone metastases.

The EC granted a marketing authorisation valid throughout the European Union for Xofigo on 13 November 2013

^{223}Ra

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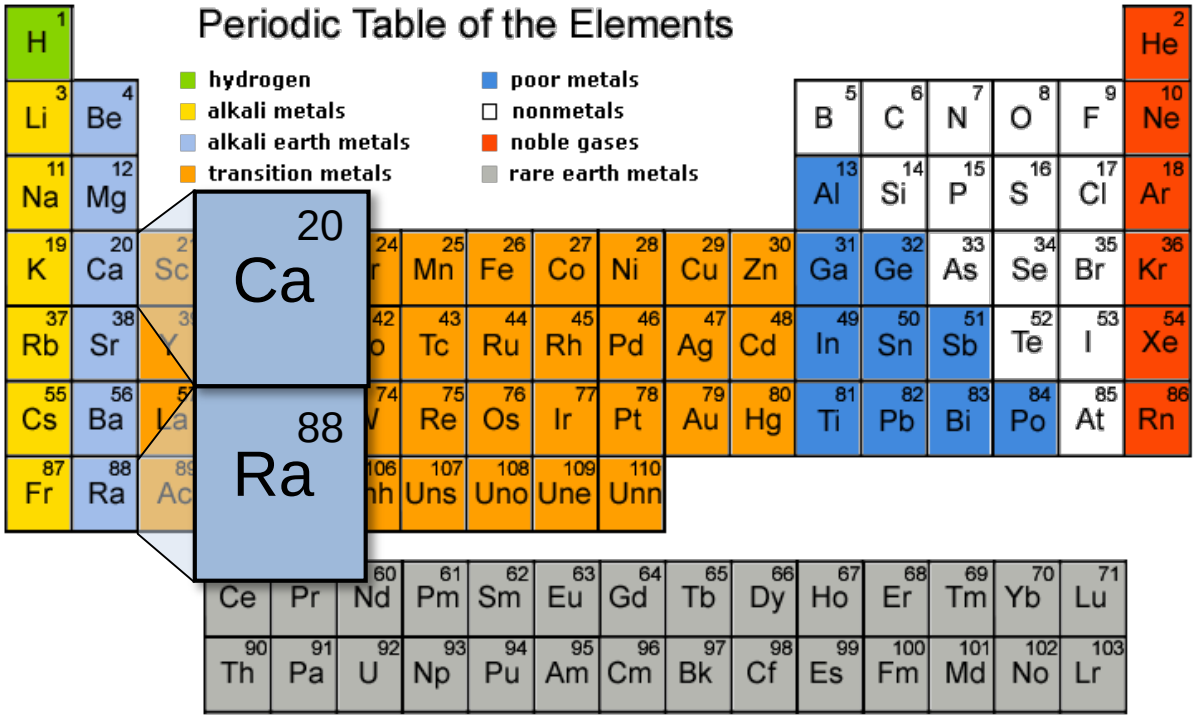
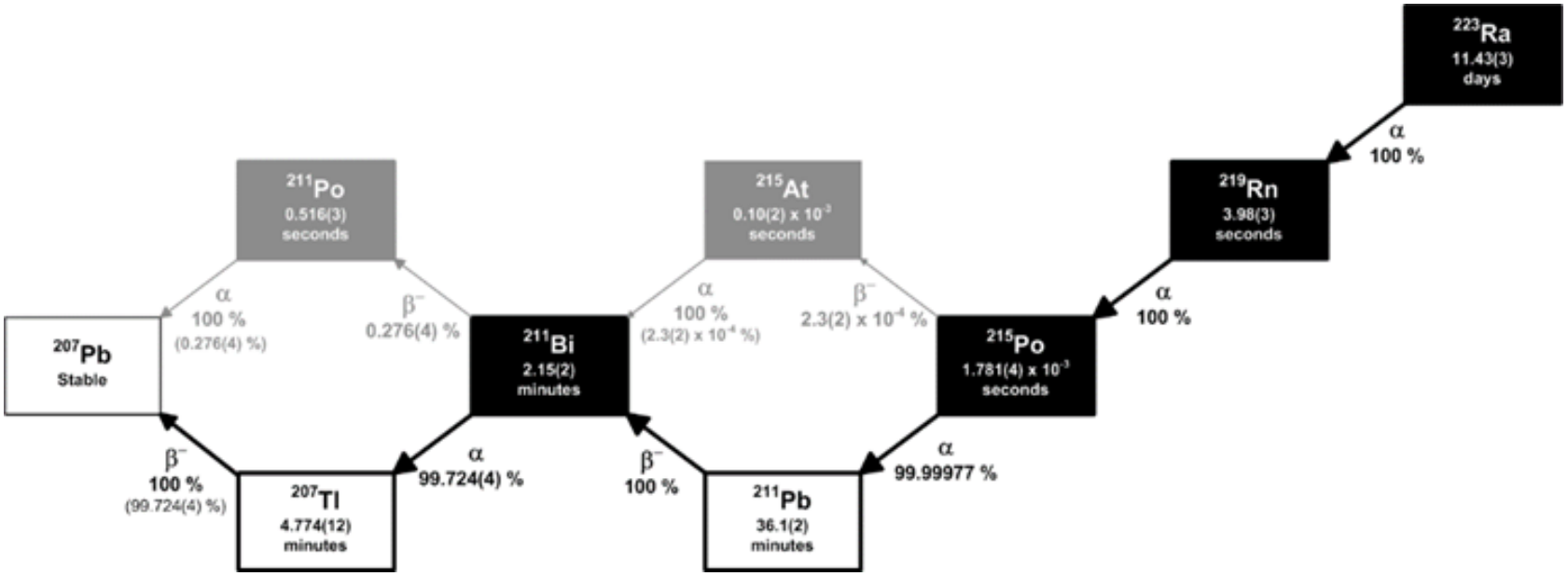
- Radium belongs to the same group of elements as Calcium
- Radium is a calcium-mimetic element
- Taken up in newly forming bone in the human skeleton



^{223}Ra decay



Ra-223 lies in the decay chain of U-235, and is produced by separation and purification from an Actinium-Thorium-Radium generator

Ra-223 - Targeted alpha therapy

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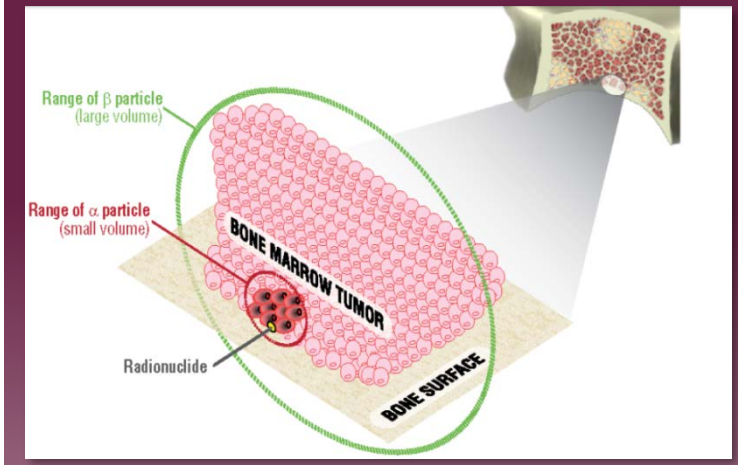
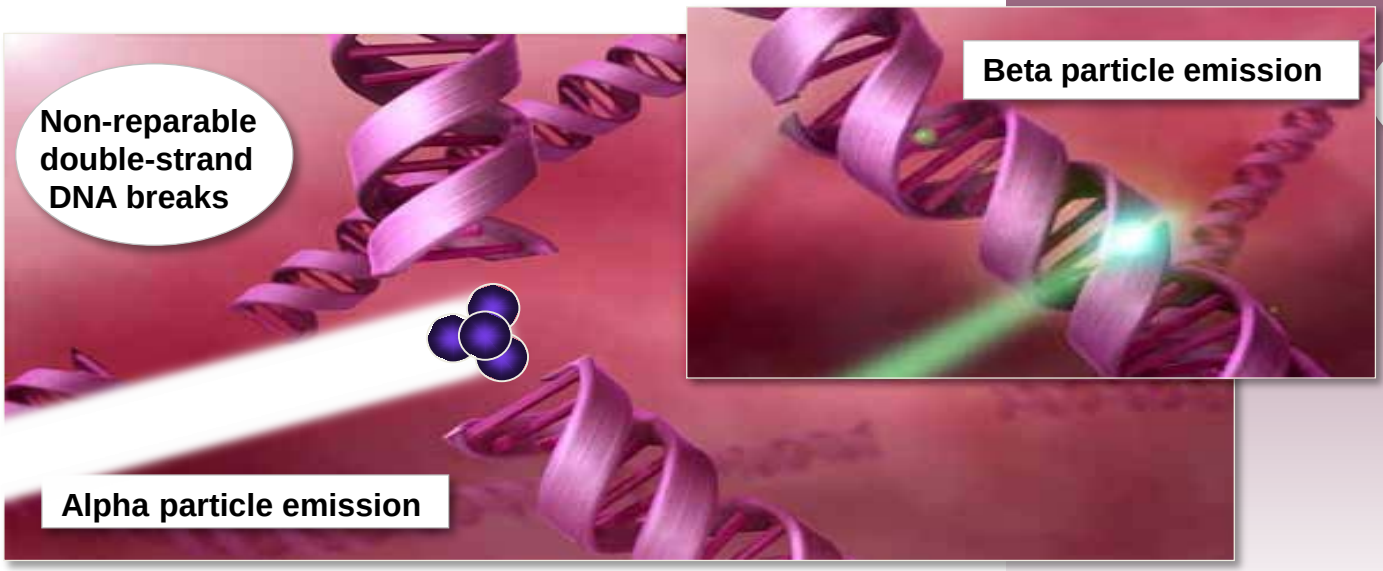
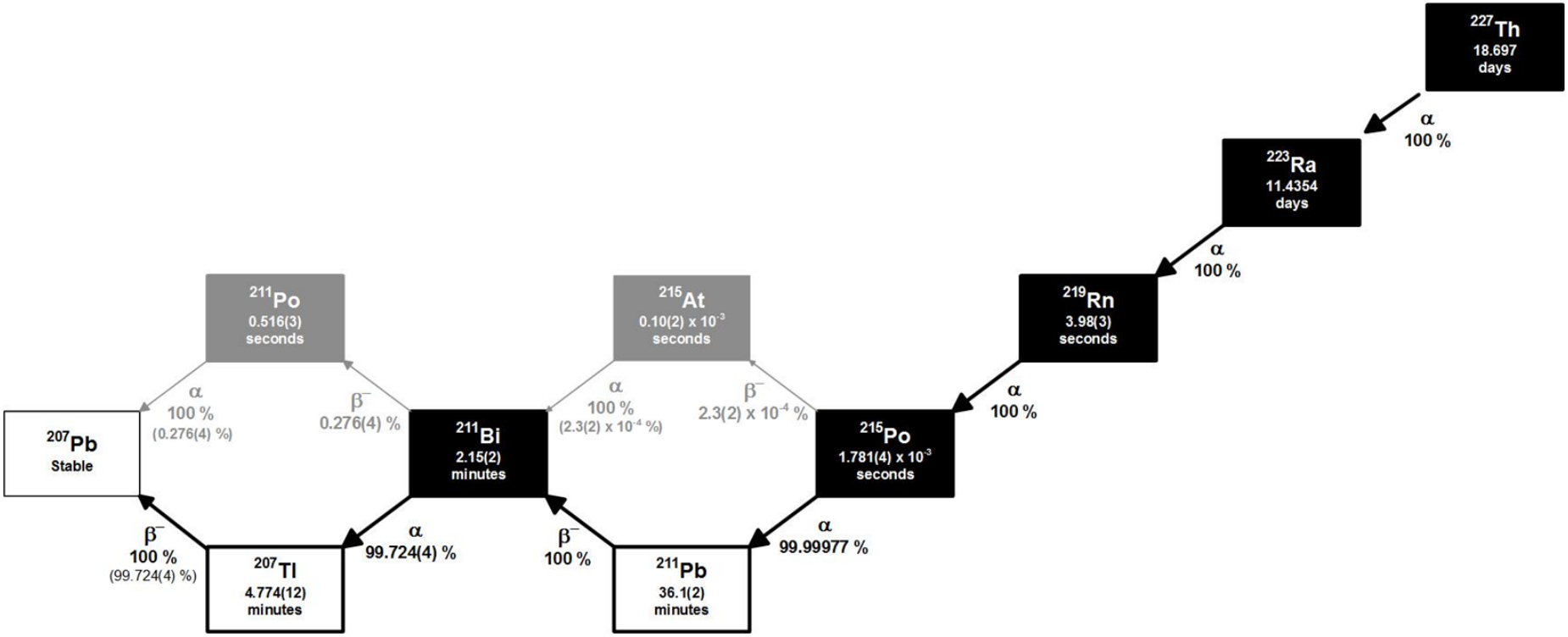
- Radium-223 selectively targets bone, specifically bone metastases
- It emits high-energy ionizing alpha particles which cause lethal, double-strand DNA breaks in adjacent cells
- This results in a highly localized anti-tumor effect in bone metastases





Th-227 decay



- However Radium-223 is not suitable for targeting tumours outside the bone
- Thorium-227 has broader application due to the availability of chelates which can be attached to targeting proteins such as antibodies for delivery to tumour cells.

What Makes Thorium-227 Unique?

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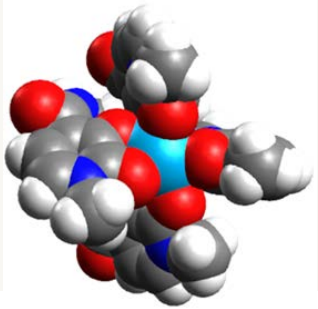
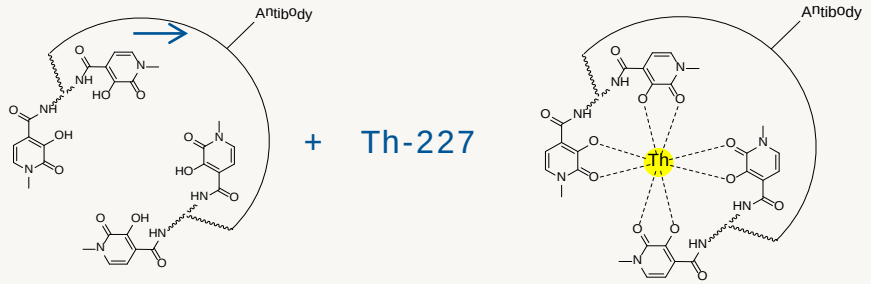
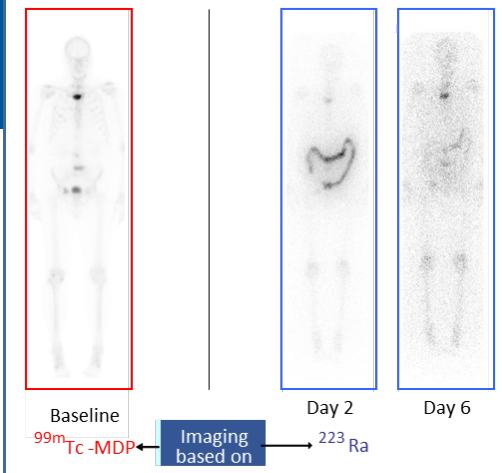




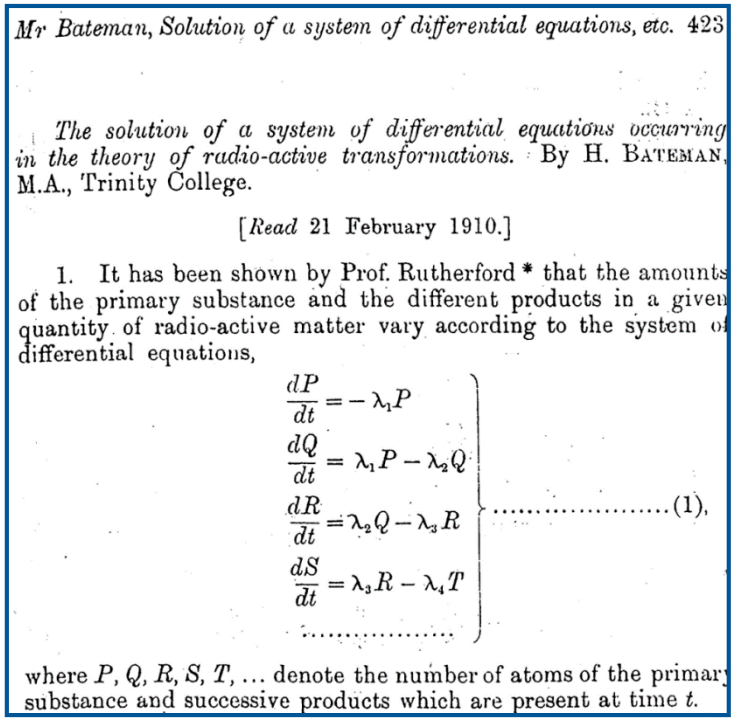
Thorium-227, suitable for antibody-targeted therapy

- Half-life ideal for manufacture and commercial distribution
- Th(IV) forms highly stable complexes at ambient temperature
- Optimal physical half-life for tumor delivery by mAbs



- *Rapid clearance into gut (no liver)*
- *Spares kidney- radiation dose low*
- *Held in gut content - no mucositis*
- *The same clearance pattern has been confirmed in primates*

Bateman Equations (Bateman, Proc. Camb. Phil. Soc. 1910)



Mr Bateman, Solution of a system of differential equations, etc. 423

The solution of a system of differential equations occurring in the theory of radio-active transformations. By H. Bateman, M.A., Trinity College.

[*Read* 21 February 1910.]

1. It has been shown by Prof. Rutherford * that the amounts of the primary substance and the different products in a given quantity of radio-active matter vary according to the system of differential equations,

$$\left.\begin{aligned} \frac{dP}{dt} &= -\lambda_1 P \\ \frac{dQ}{dt} &= \lambda_1 P - \lambda_2 Q \\ \frac{dR}{dt} &= \lambda_2 Q - \lambda_3 R \\ \frac{dS}{dt} &= \lambda_3 R - \lambda_4 T \\ &\cdots\cdots\cdots \end{aligned}\right\} \cdots\cdots\cdots\cdots\cdots\cdots (1),$$

where $P, Q, R, S, T, \ldots$ denote the number of atoms of the primary substance and successive products which are present at time t.

$$\frac{dN_1}{dt} = -\lambda_1 N_1 ,$$

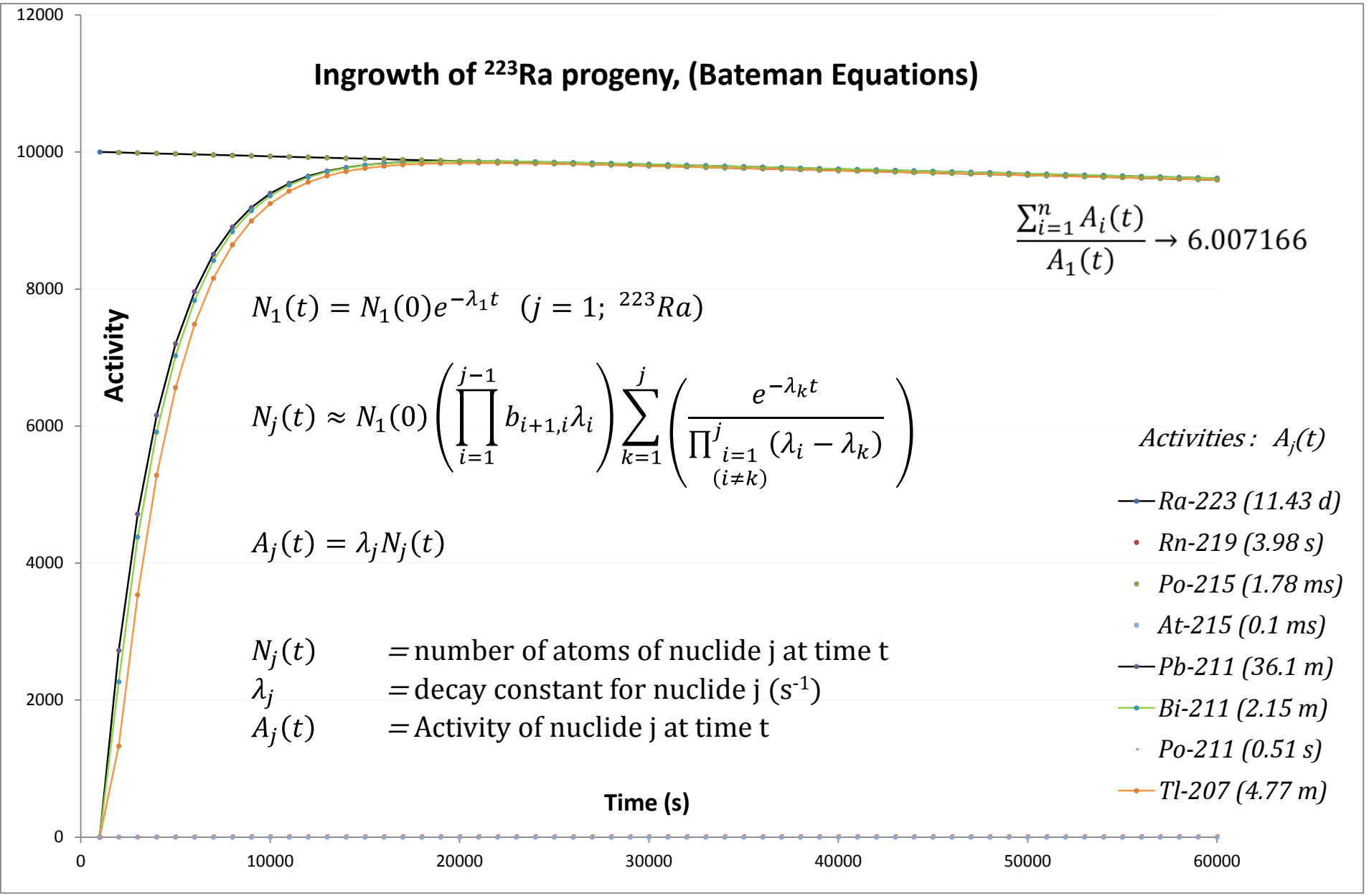
$$\frac{dN_j}{dt} = \sum_{i=1}^{j-1} \lambda_i b_{ji} N_i - \lambda_j N_j \quad (j = 2,\ldots,n)$$

Bateman did not consider “branching”

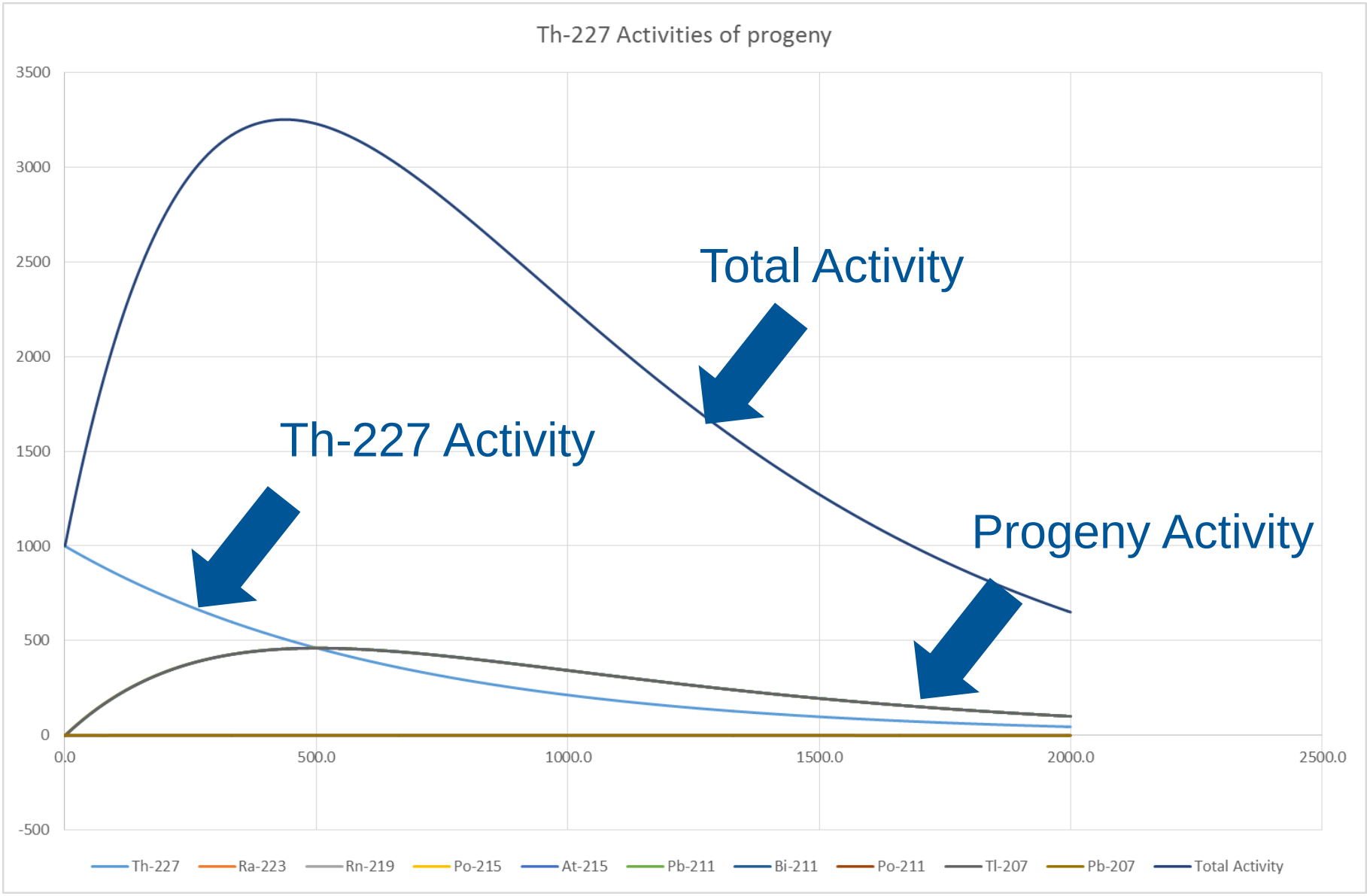
Modify differential equations to yield (for n decay products):

Requires algebraic solution involving relative probabilities for each branch decay, as solutions for j > 2 rapidly become cumbersome

Ingrowth/Decay of Ra-223



Ingrowth/Decay of Th-227



Why is this a problem ?

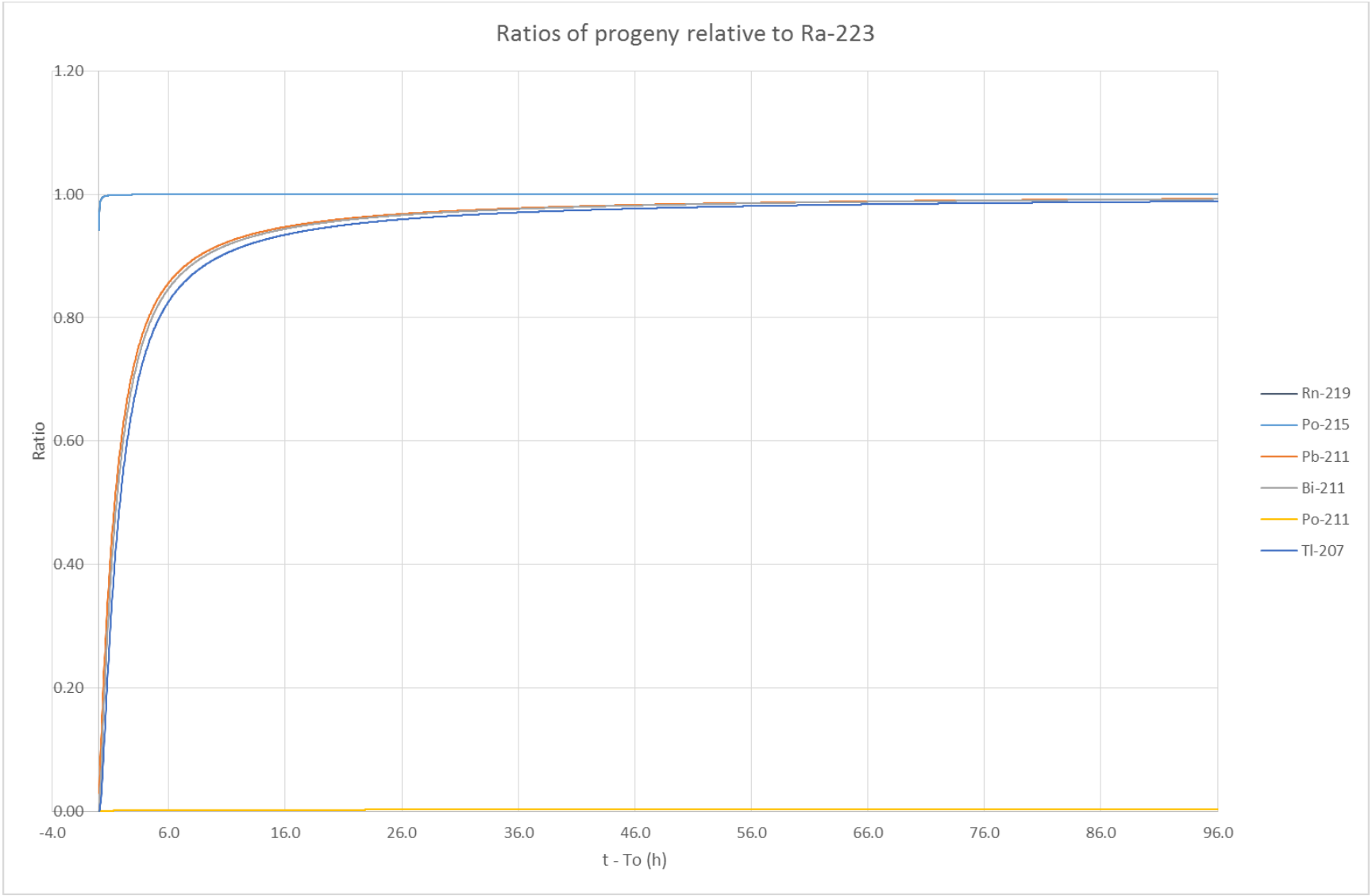
- Usual Exponential decay corrections do not apply

  The decay rates are often INCREASING as progeny grow in.

- You MUST know know/determine the effective separation time, where you have “pure” Th-227. You can then make corrections for decay/ingrowth.

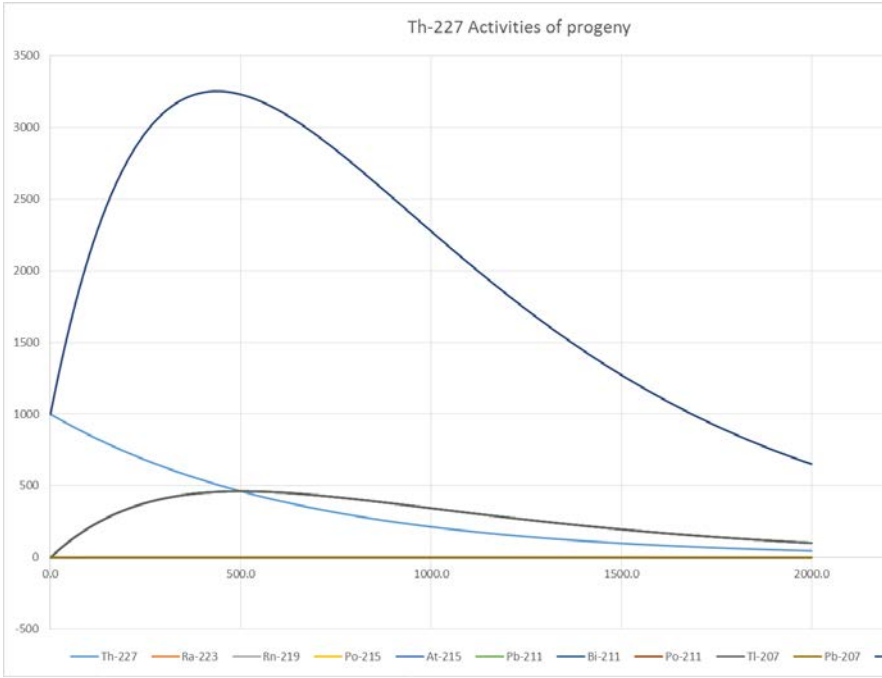
- Many others problems …

Th-227 doesn't really decay to Ra-223



Time dependent Dial Factors for Th-227

- Dose calibrators measure a single quantity: Current induced in re-entrant ionisation chamber
- This current it converted into a reading in MBq for the isotope, by altering the dial factor, which alters the gain of the instrument appropriately.



Capintec Response Curve

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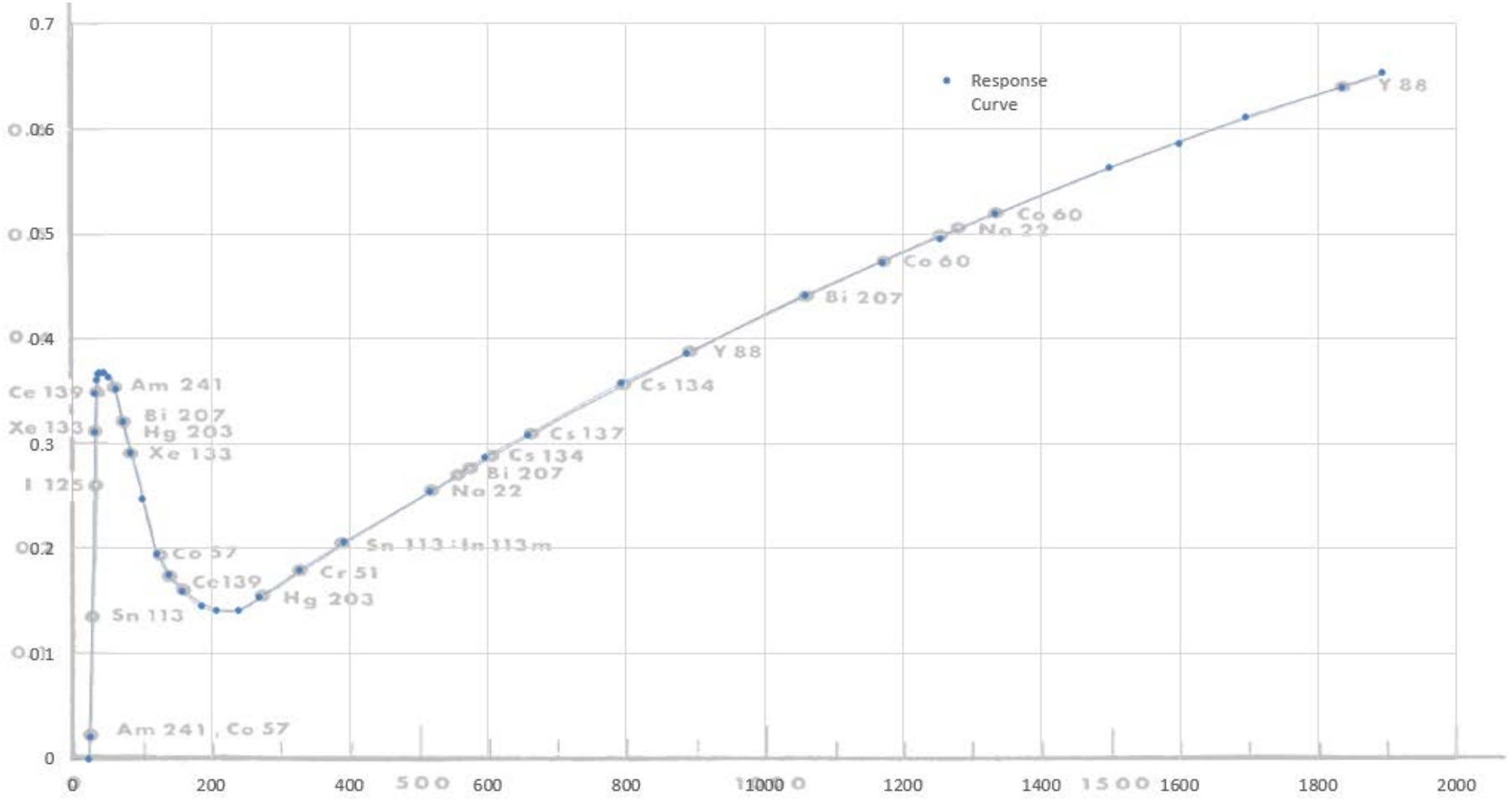
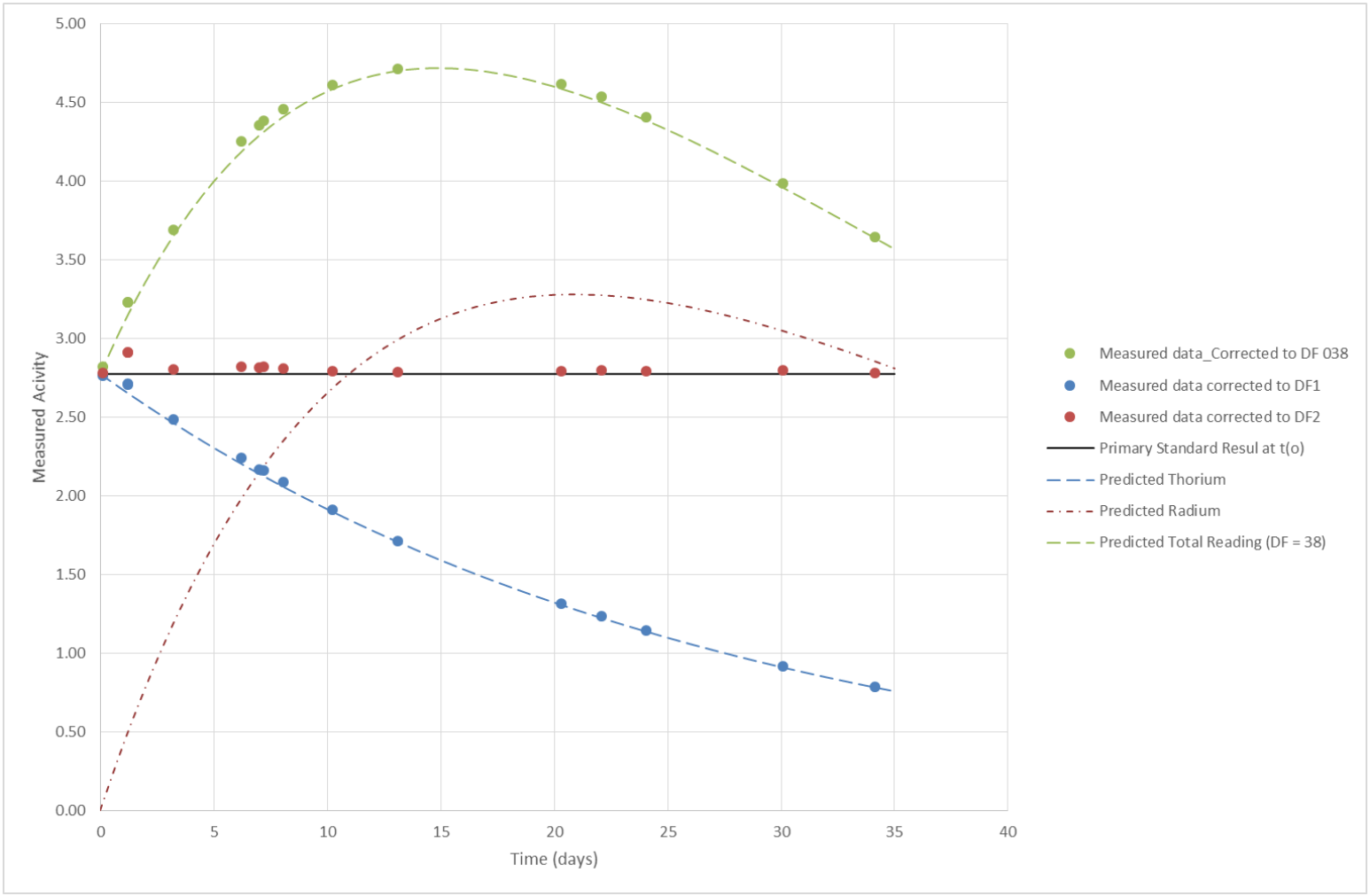


Analysis of a Radioisotope Calibrator

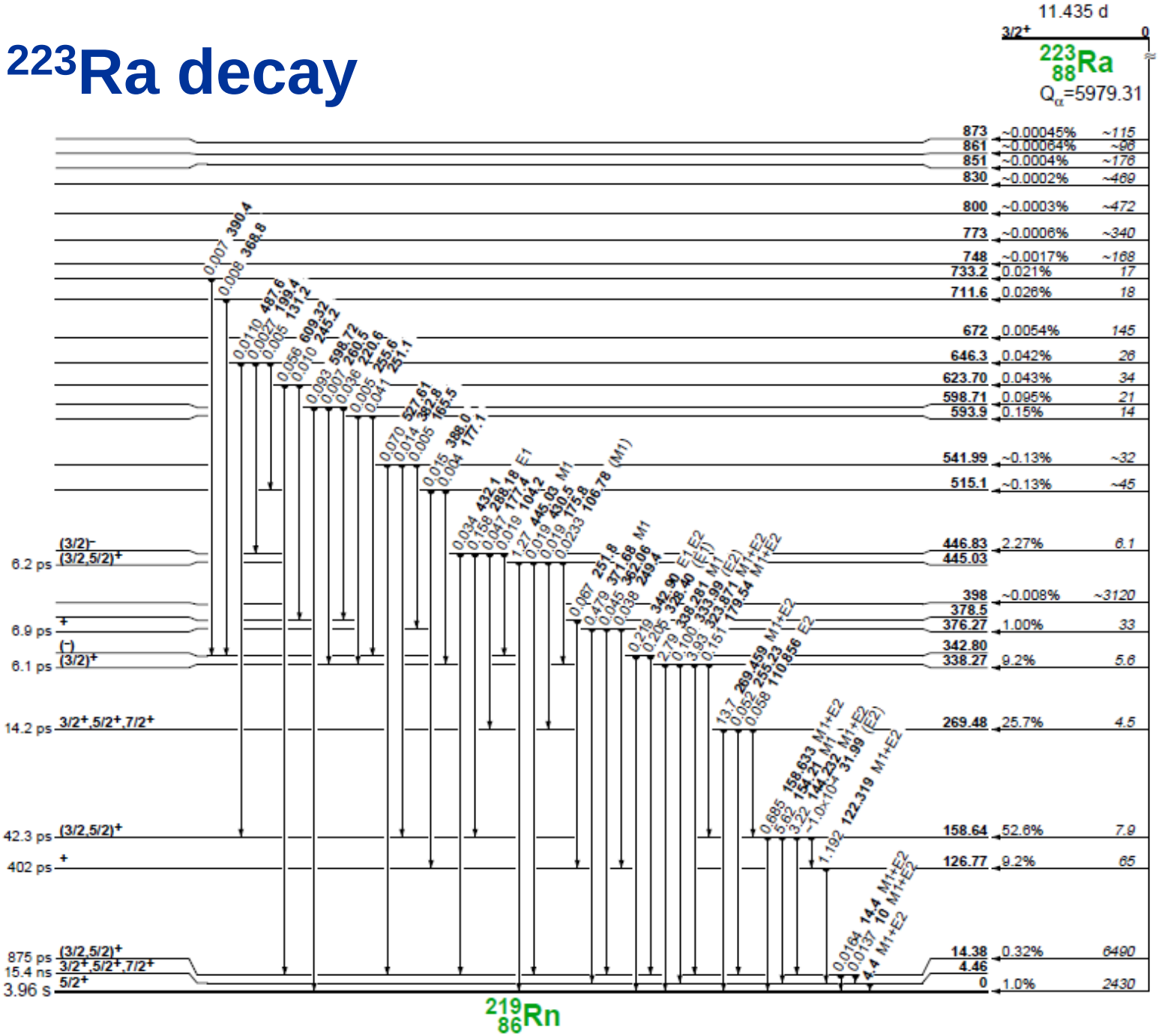
Arata Suzuki, Marcia N. Suzuki and Arthur M. Weis

J. Nucl. Med. Technol. 1976;4:193-198.

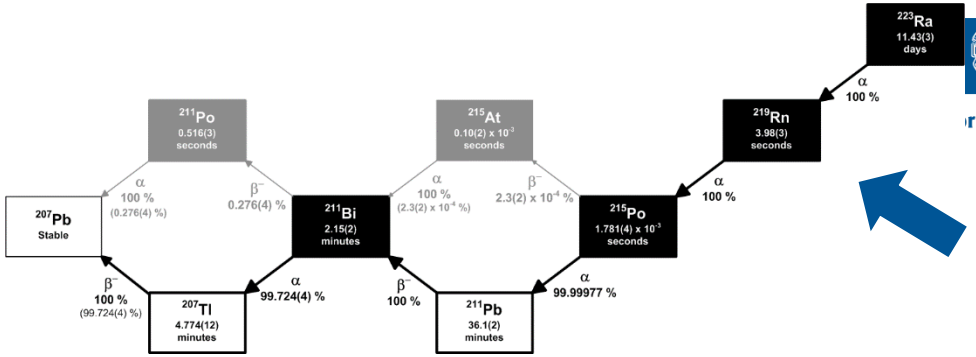
Real source: (traceable to NPL primary standard)

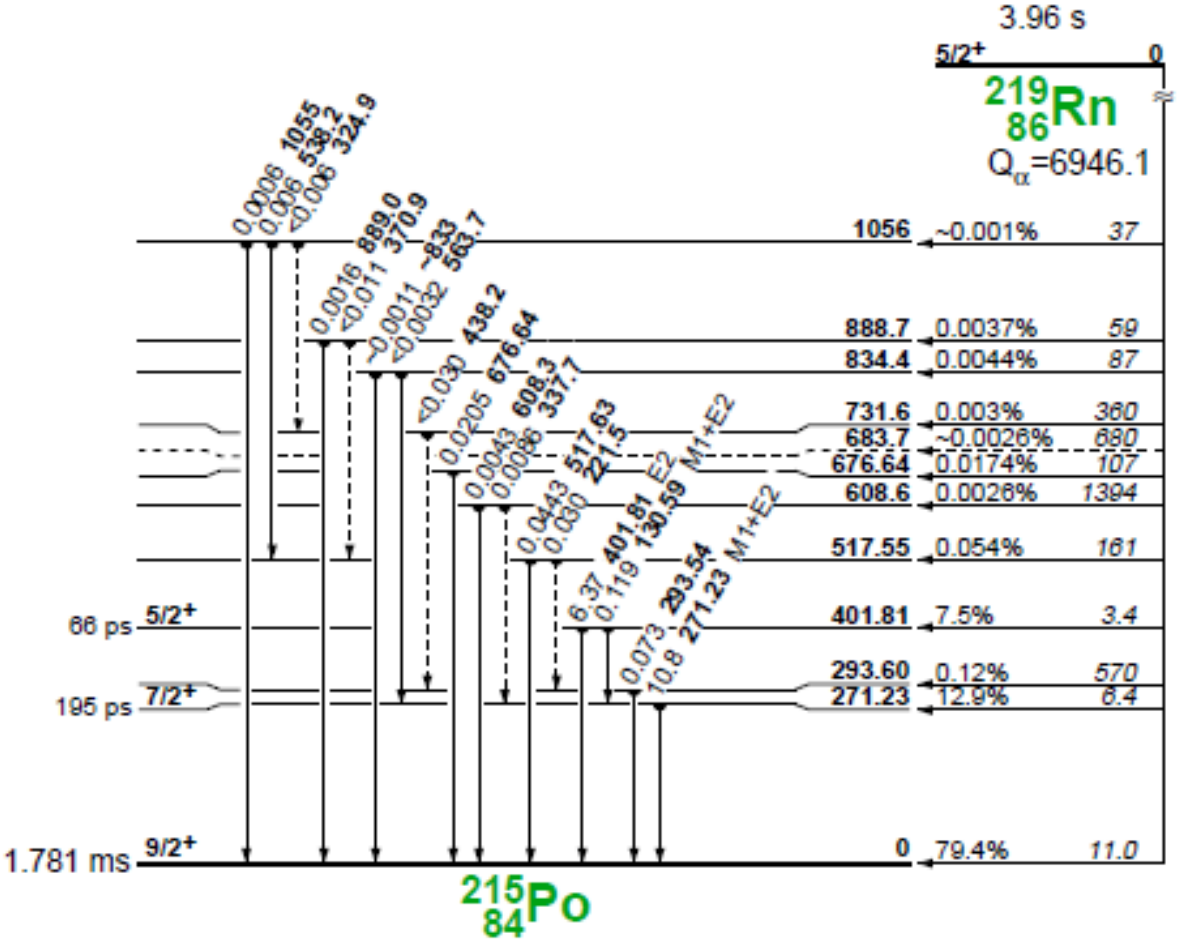


^{223}Ra decay

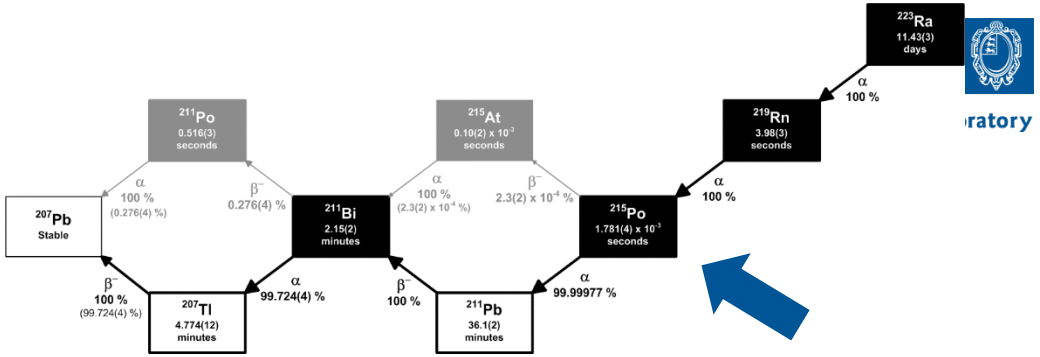

11.435 d
3/2+
0
223 88 Ra
Qα=5979.31
873 ~0.00045% ~115
861 ~0.00064% ~96
851 ~0.0004% ~176
830 ~0.0002% ~469
800 ~0.0003% ~472
773 ~0.0006% ~340
748 ~0.0017% ~168
733.2 0.021% 17
711.6 0.026% 18
672 0.0054% 145
646.3 0.042% 26
623.70 0.043% 34
598.71 0.095% 21
593.9 0.15% 14
541.99 ~0.13% ~32
515.1 ~0.13% ~45
446.83 2.27% 6.1
445.03
398 ~0.008% ~3120
378.5
376.27 1.00% 33
342.80
338.27 9.2% 5.6
269.48 25.7% 4.5
158.64 52.6% 7.9
126.77 9.2% 65
14.38 0.32% 6490
4.46
0 1.0% 2430
(3/2)−
(3/2,5/2)+
6.2 ps
+
6.9 ps
(−)
(3/2)+
6.1 ps
3/2+,5/2+,7/2+
14.2 ps
(3/2,5/2)+
42.3 ps
+
402 ps
(3/2,5/2)+
875 ps
3/2+,5/2+,7/2+
15.4 ns
5/2+
3.96 s
219 86 Rn

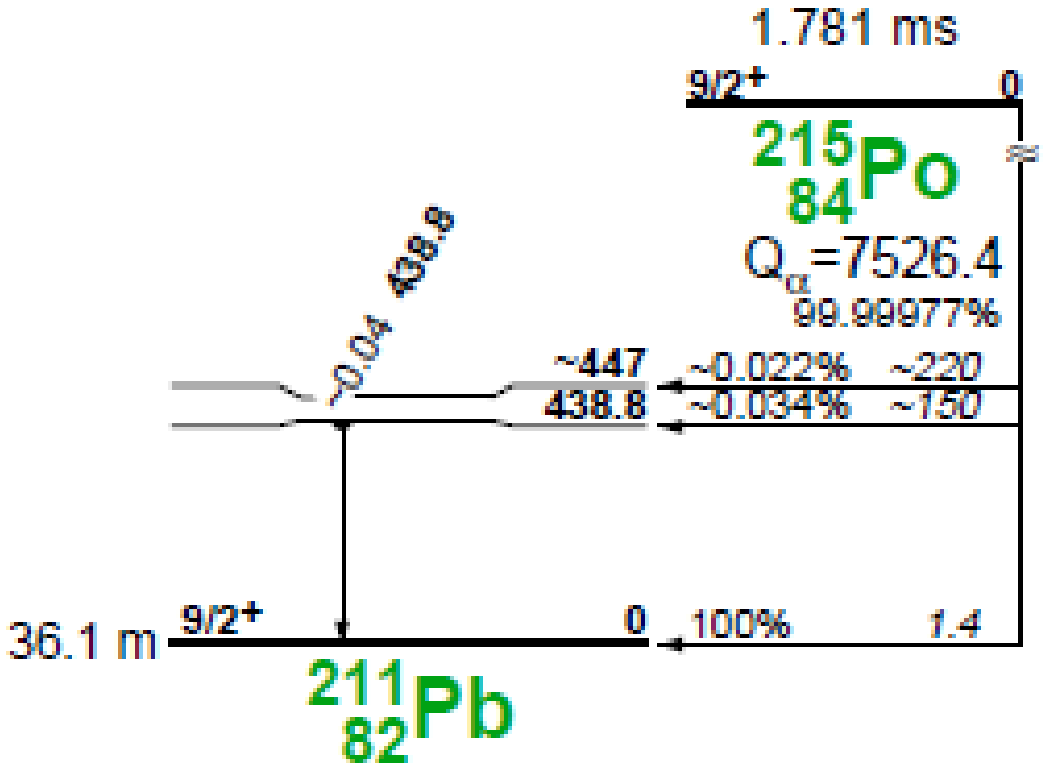
^{219}Rn decay


223Ra
11.43(3) days
α
100 %
219Rn
3.98(3) seconds
α
100 %
215Po
1.781(4) x 10-3 seconds
α
99.99977 %
211Pb
36.1(2) minutes
β−
100 %
215At
0.10(2) x 10-3 seconds
α
100 %
(2.3(2) x 10-4 %)
β−
2.3(2) x 10-4 %
211Bi
2.15(2) minutes
α
99.724(4) %
207Tl
4.774(12) minutes
β−
100 %
(99.724(4) %)
207Pb
Stable
α
100 %
(0.276(4) %)
β−
0.276(4) %
211Po
0.516(3) seconds

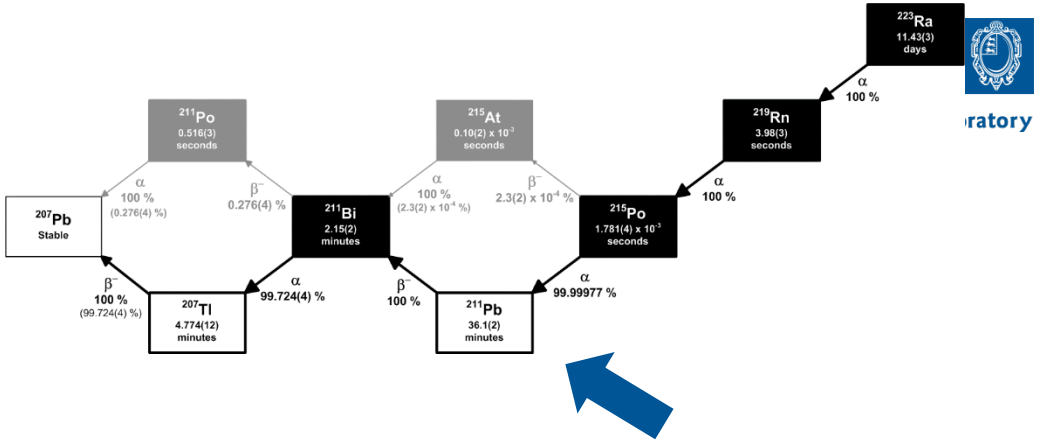

3.96 s
5/2+
0
219 86Rn
Qα=6946.1
1056
-0.001%
37
888.7
0.0037%
59
834.4
0.0044%
87
731.6
0.003%
360
683.7
-0.0026%
680
676.64
0.0174%
107
608.6
0.0026%
1394
517.55
0.054%
161
401.81
7.5%
3.4
293.60
0.12%
570
271.23
12.9%
6.4
0
79.4%
11.0
66 ps
5/2+
195 ps
7/2+
1.781 ms
9/2+
215 84Po

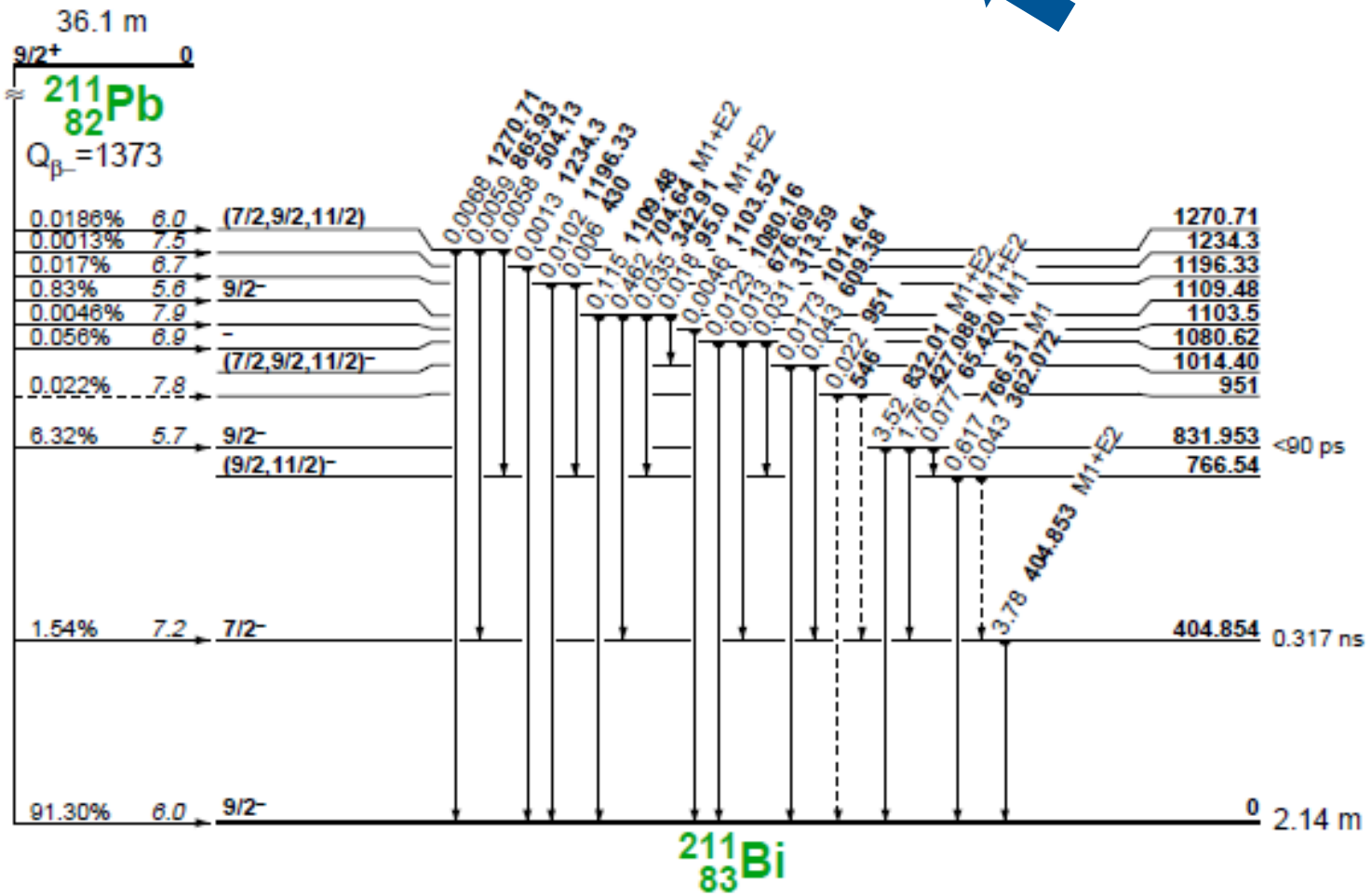
^{215}Po decay


223Ra
11.43(3)
days
α
100 %
219Rn
3.98(3)
seconds
α
100 %
215Po
1.781(4) x 10-3
seconds
215At
0.10(2) x 10-3
seconds
α
100 %
(2.3(2) x 10-4 %)
β-
2.3(2) x 10-4 %
211Bi
2.15(2)
minutes
α
99.724(4) %
β-
100 %
(99.724(4) %)
207Tl
4.774(12)
minutes
211Pb
36.1(2)
minutes
β-
100 %
α
99.99977 %
211Po
0.516(3)
seconds
α
100 %
(0.276(4) %)
β-
0.276(4) %
207Pb
Stable

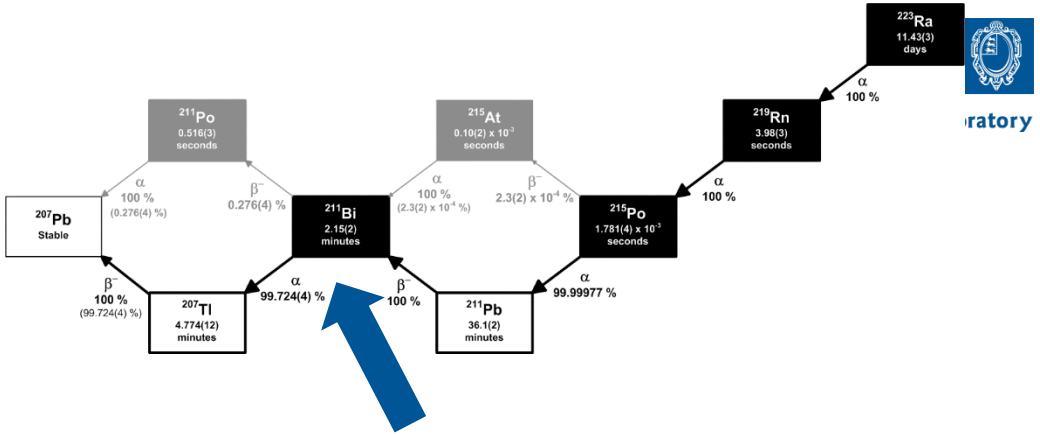

1.781 ms
9/2+
0
215 84 Po
Qα=7526.4
99.99977%
~447
~0.022%
~220
438.8
~0.034%
~150
0.04
438.8
36.1 m
9/2+
0
100%
1.4
211 82 Pb

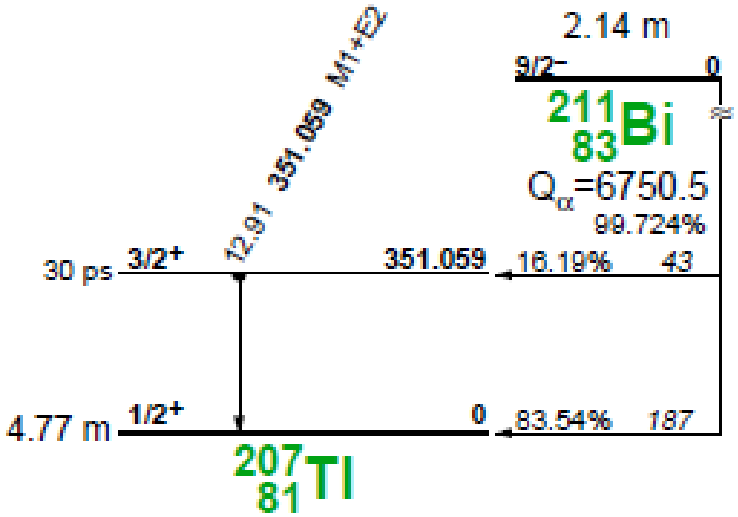
^{211}Pb decay

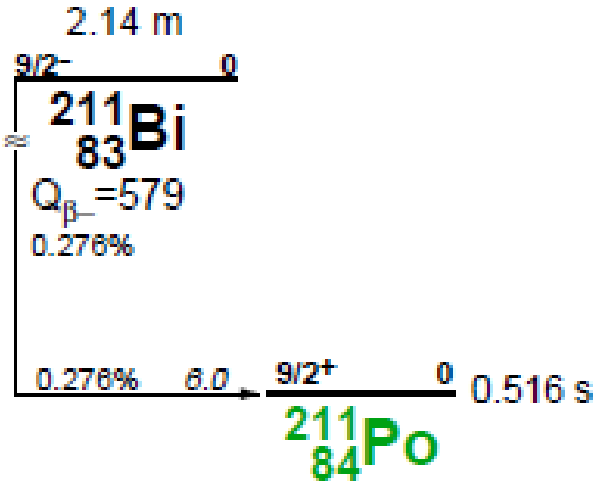

223Ra
11.43(3) days
α
100 %
219Rn
3.98(3) seconds
α
100 %
215Po
1.781(4) x 10-3 seconds
α
99.99977 %
211Pb
36.1(2) minutes
β−
100 %
215At
0.10(2) x 10-3 seconds
α
100 %
(2.3(2) x 10-4 %)
β−
2.3(2) x 10-4 %
211Bi
2.15(2) minutes
α
99.724(4) %
207Tl
4.774(12) minutes
β−
100 %
(99.724(4) %)
207Pb
Stable
α
100 %
(0.276(4) %)
β−
0.276(4) %
211Po
0.516(3) seconds
α
100 %


36.1 m
9/2+
0
211 82 Pb
Qβ−=1373
0.0186% 6.0
0.0013% 7.5
0.017% 6.7
0.83% 5.6
0.0046% 7.9
0.056% 6.9
0.022% 7.8
6.32% 5.7
1.54% 7.2
91.30% 6.0
(7/2,9/2,11/2)
9/2−
−
(7/2,9/2,11/2)−
9/2−
(9/2,11/2)−
7/2−
9/2−
1270.71
1234.3
1196.33
1109.48
1103.5
1080.62
1014.40
951
831.953
766.54
404.854
0
<90 ps
0.317 ns
2.14 m
211 83 Bi

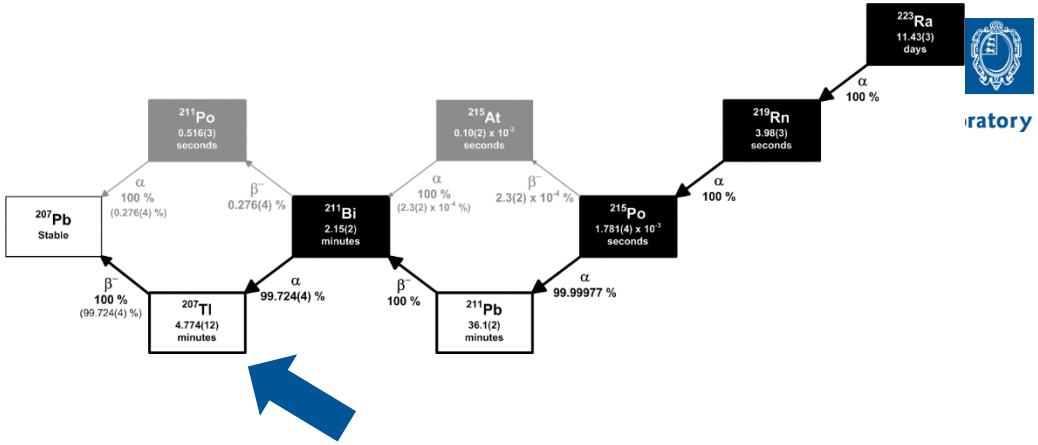
^{211}Bi decay

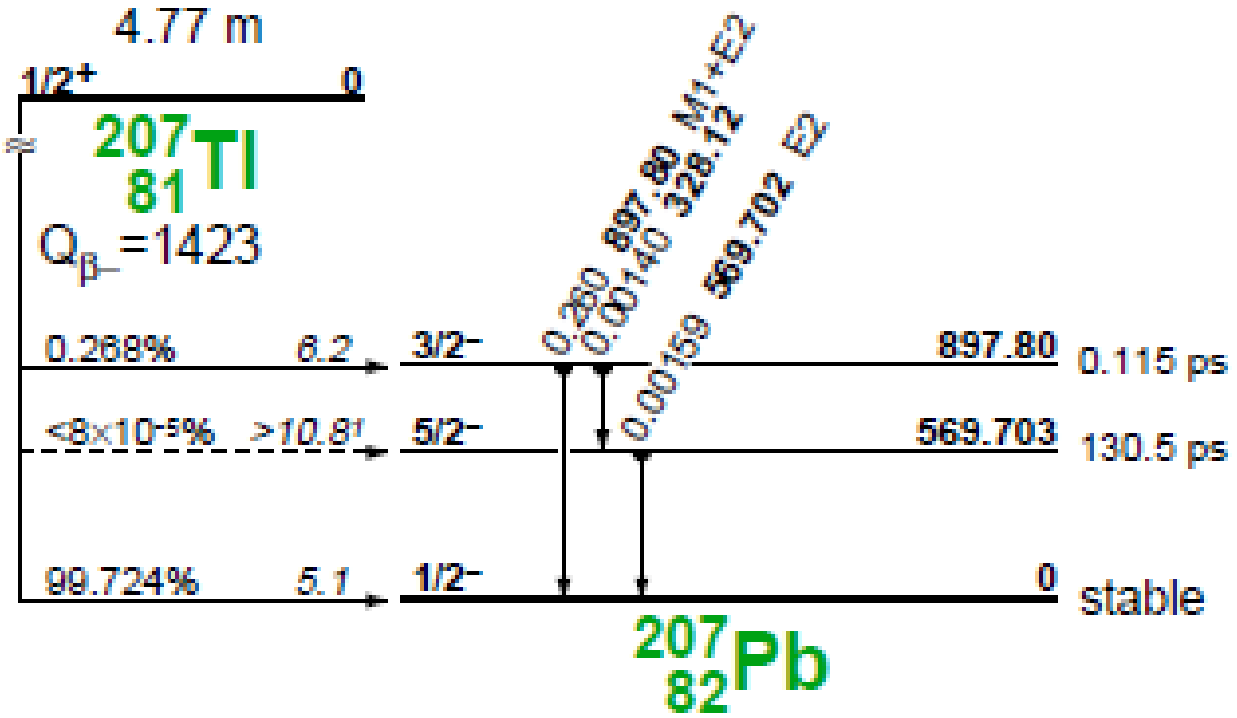

223Ra
11.43(3) days
α 100 %
219Rn
3.98(3) seconds
α 100 %
215Po
1.781(4) x 10-3 seconds
α 99.99977 %
β- 100 %
211Pb
36.1(2) minutes
215At
0.10(2) x 10-3 seconds
α 100 % (2.3(2) x 10-4 %)
β- 2.3(2) x 10-4 %
211Bi
2.15(2) minutes
α 99.724(4) %
β- 0.276(4) %
211Po
0.516(3) seconds
α 100 % (0.276(4) %)
β- 100 % (99.724(4) %)
207Tl
4.774(12) minutes
207Pb
Stable


2.14 m
9/2−
0
211 83 Bi
Qα=6750.5
99.724%
12.91
351.059
M1+E2
30 ps
3/2+
351.059
16.19%
43
4.77 m
1/2+
0
83.54%
187
207 81 Tl


2.14 m
9/2−
0
211 83 Bi
Qβ−=579
0.276%
0.276%
6.0
9/2+
0
0.516 s
211 84 Po

^{207}Tl decay


223Ra
11.43(3) days
α 100 %
219Rn
3.98(3) seconds
α 100 %
215Po
1.781(4) x 10-3 seconds
α 99.99977 %
211Pb
36.1(2) minutes
β- 100 %
215At
0.10(2) x 10-3 seconds
α 100 % (2.3(2) x 10-4 %)
β- 2.3(2) x 10-4 %
211Bi
2.15(2) minutes
α 99.724(4) %
β- 0.276(4) %
211Po
0.516(3) seconds
α 100 % (0.276(4) %)
207Tl
4.774(12) minutes
β- 100 % (99.724(4) %)
207Pb
Stable


4.77 m
1/2+
0
207 81 Tl
Qβ- =1423
0.268%
6.2
3/2−
<8×10-5%
>10.8
5/2−
99.724%
5.1
1/2−
0.260
897.80 M1+E2
0.00140
328.12
0.00159
569.702 E2
897.80
0.115 ps
569.703
130.5 ps
0
stable
207 82 Pb

The 4πβ–γ coincidence method

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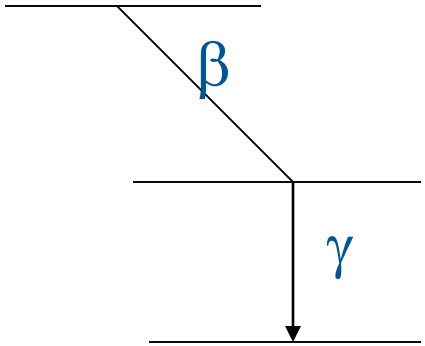
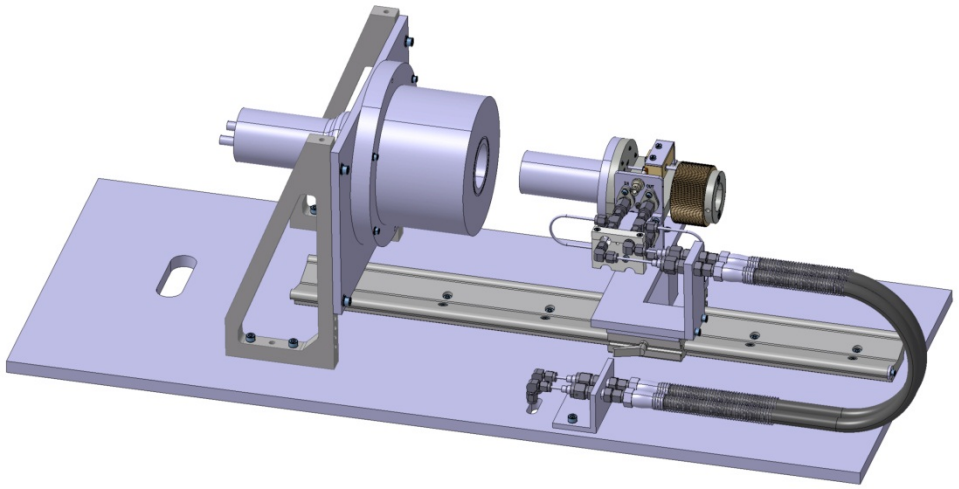
Count Rates

$N_\beta = N_o \varepsilon_\beta$

$N_\gamma = N_o \varepsilon_\gamma$

$N_c = N_o \varepsilon_\beta \varepsilon_\gamma$



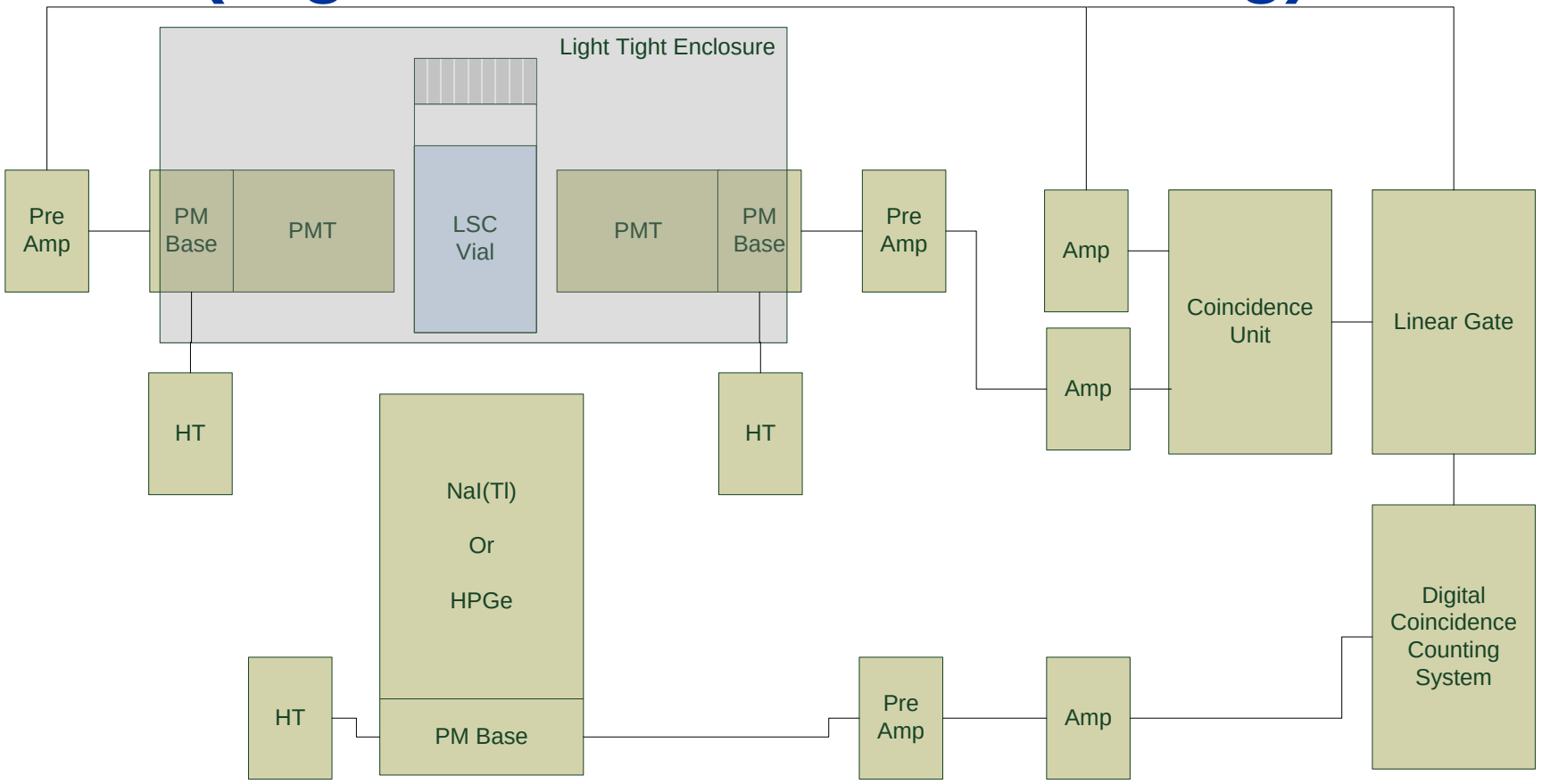


Efficiencies: $\varepsilon_\beta = N_c/N_\gamma$

$\varepsilon_\gamma = N_c/N_\beta$

$$Activity: N_o = \frac{N_\beta N_\gamma}{N_c}$$

4π(LS)-γ coincidence counting (Digital Coincidence Counting)



“Simplified” LS Counter rate ^{223}Ra + progeny in equilibrium

$$N_{LS} = N_0 \sum_r a_r \left[\varepsilon_{LS_r} + \left(1-\varepsilon_{LS_r}\right) \left[\left(\frac{1}{1+\alpha_r}\right)\varepsilon_{LS\gamma_r} + \left(\frac{\alpha_{Kr}}{1+\alpha_{Kr}}\right) \left(\varepsilon_{LSce_{Kr}} + \left(1-\varepsilon_{LSce_{Kr}}\right) \left\{ \begin{array}{l} \omega_K \varepsilon_{LSX_K} + \left(1-\omega_K\right)\varepsilon_{LSA_K} \\ + \left(1-\left(\omega_K \varepsilon_{LSX_K} + \left(1-\omega_K\right)\varepsilon_{LSA_K}\right)\right)\eta_{KL}\varepsilon_{LSL} \\ + \dfrac{\alpha_{Tr}-\alpha_{Kr}}{1+\alpha_{Tr}}\left(\varepsilon_{LSce_{L+}} + \left(1-\varepsilon_{LSce_{L+}}\right)\varepsilon_{LS_L}\right) \end{array} \right) \right) \right] \right]$$

where:

$$\sum_r a_r = 6.00716$$

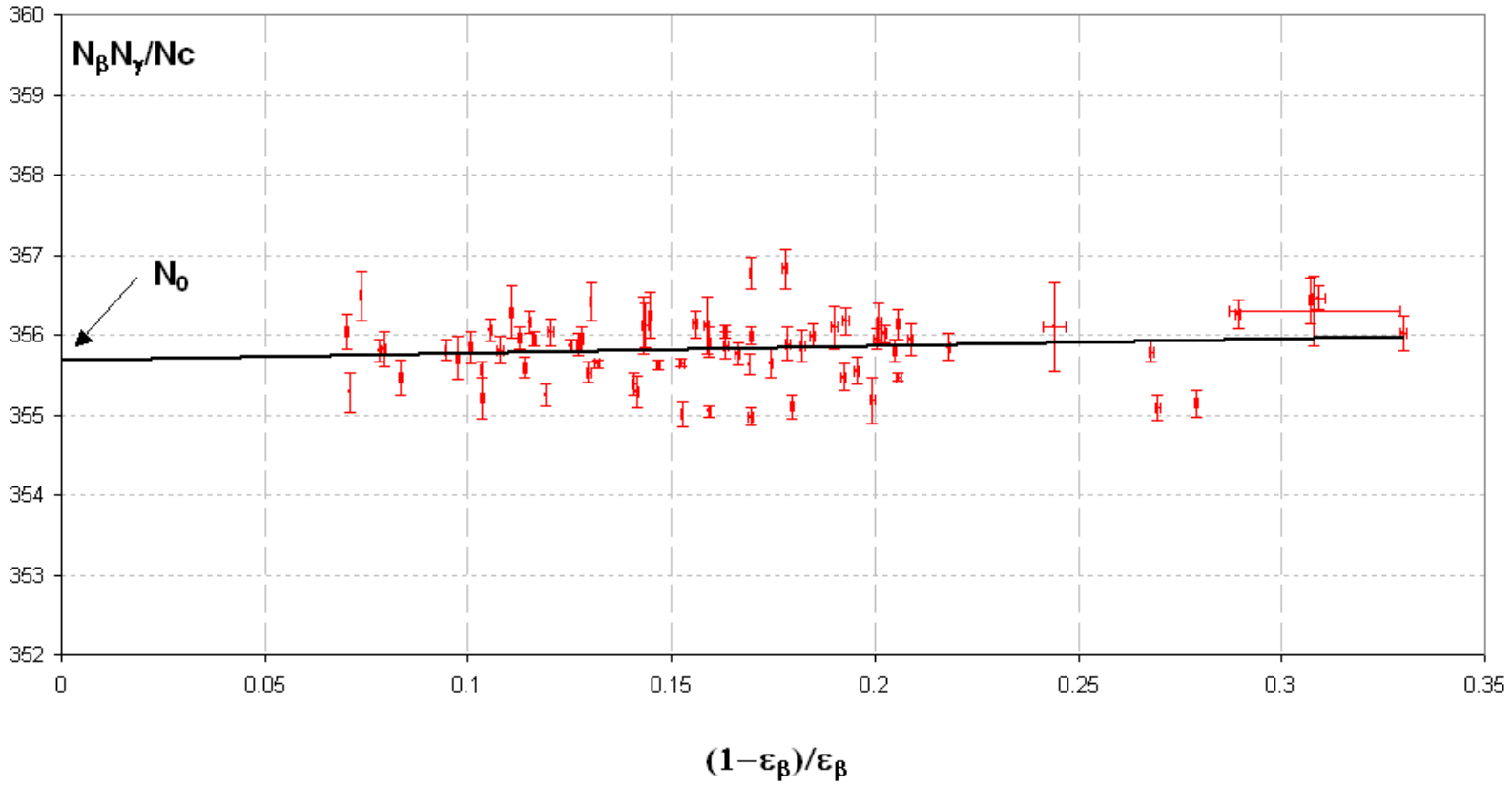
$$\varepsilon_{LS_L} = \omega_L \varepsilon_{LSX_L} + \left(1-\omega_L\right)\varepsilon_{LSA_L}$$

$$\varepsilon_{LSce_{L+}} = L, M, N, O \text{ terms}$$

Efficiency Extrapolation

National Physical Laboratory

$$\frac{N_\beta \, N_\gamma}{N_c} = No \left[\varepsilon_\beta + f \left(\frac{1 - \varepsilon_\beta}{\varepsilon_\beta} \right) \right]$$



4π(LS)-γ coincidence counting

NPL National Physical Laboratory

- The “trick” is to monitor counting efficiencies with appropriate gamma “gates”, in order to effectively and simultaneously trace efficiencies of the multitude of α and β transitions, avoiding non-linearities where possible.

- Multiple gamma gates selected

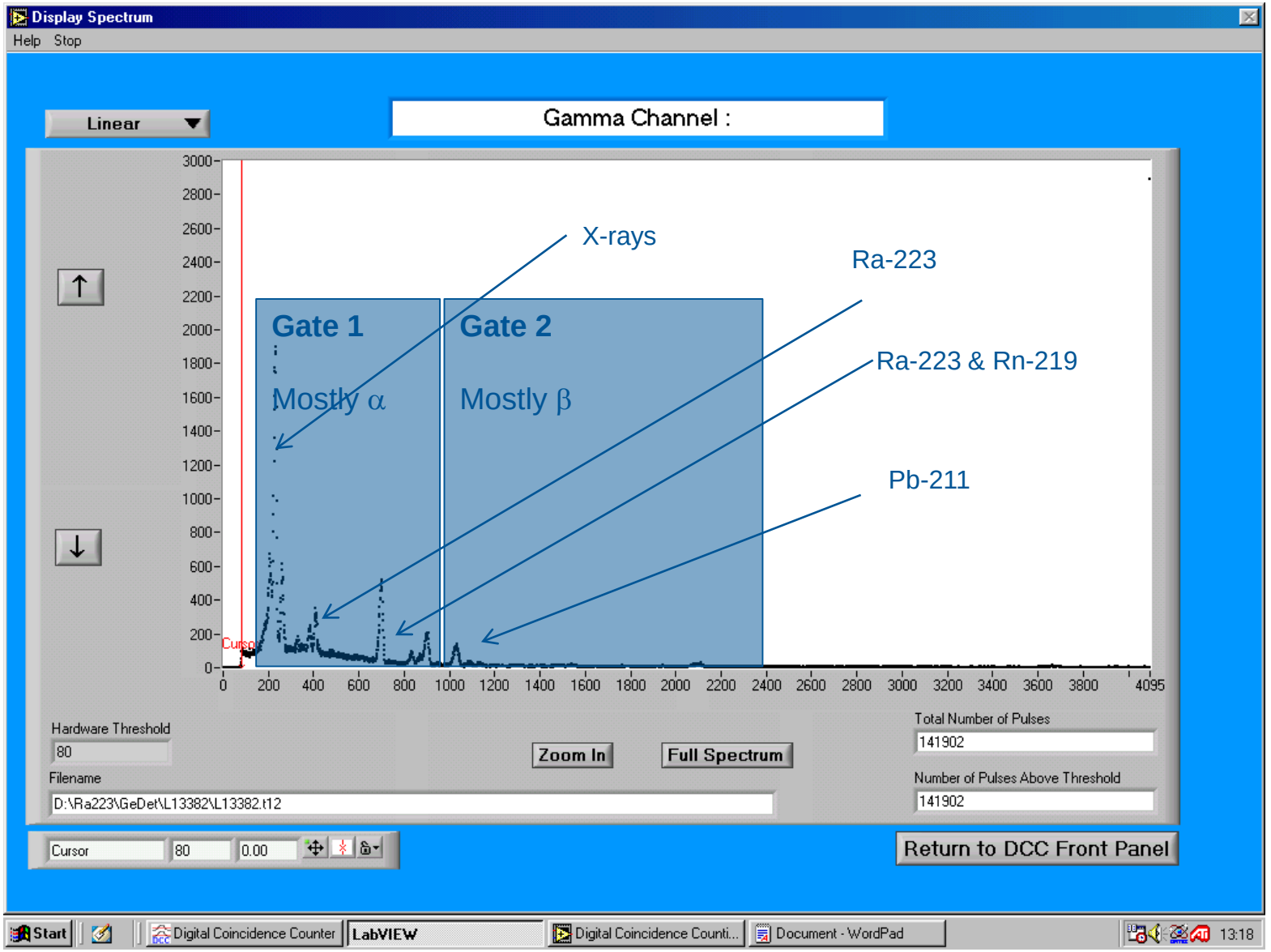
  Digital Coincidence Counting

  Multiple dimensional extrapolation, extrapolation of 3-D hyper-surface

Keightley and Park *“Digital coincidence counting for radionuclide standardization”* Metrologia 44 (2007) S32-S35

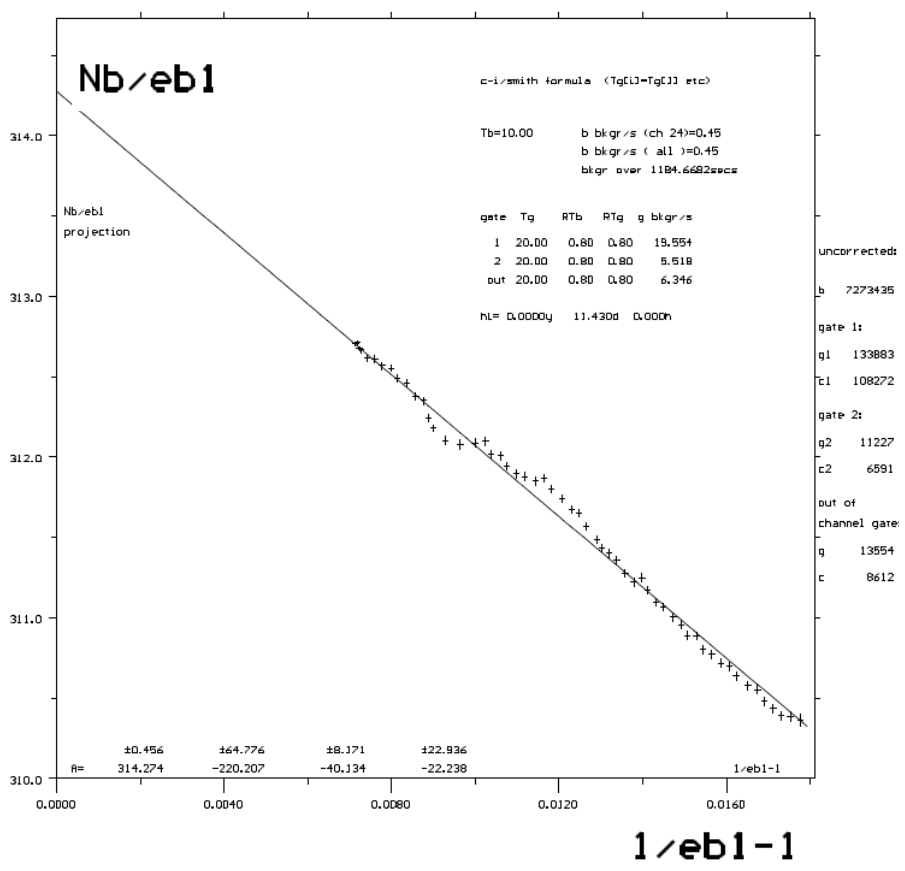
Multiple Dimensional Extrapolations (^{223}Ra)

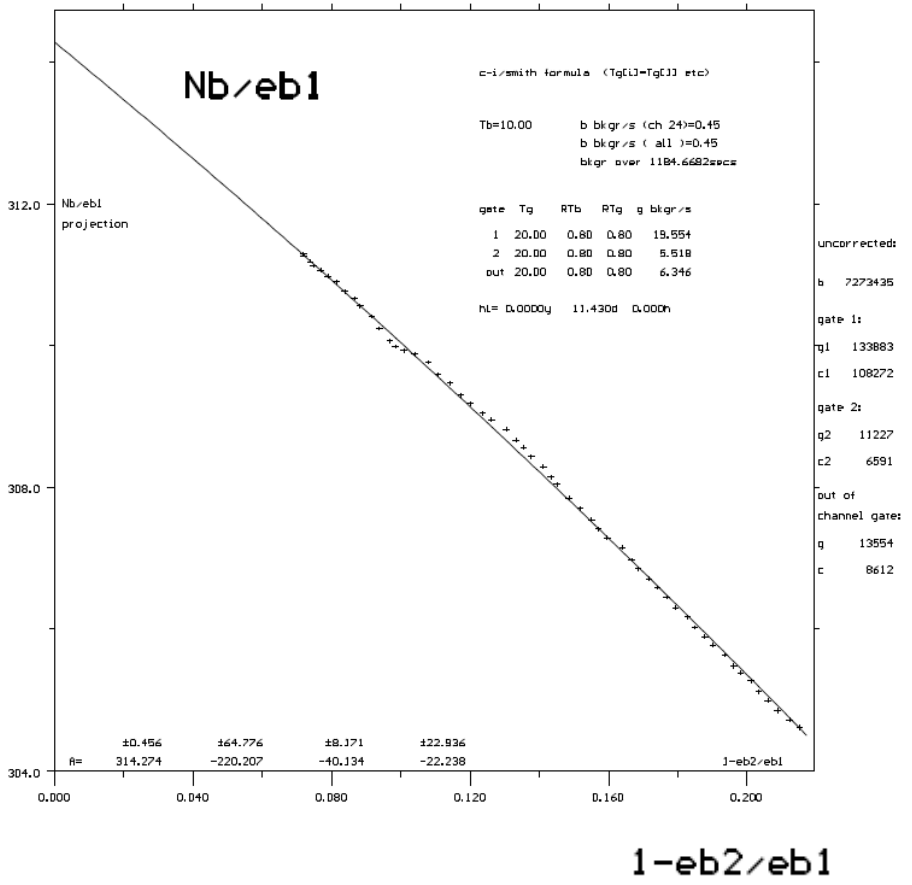
National Physical Laboratory



Multiple Dimensional Extrapolations (^{223}Ra)

National Physical Laboratory



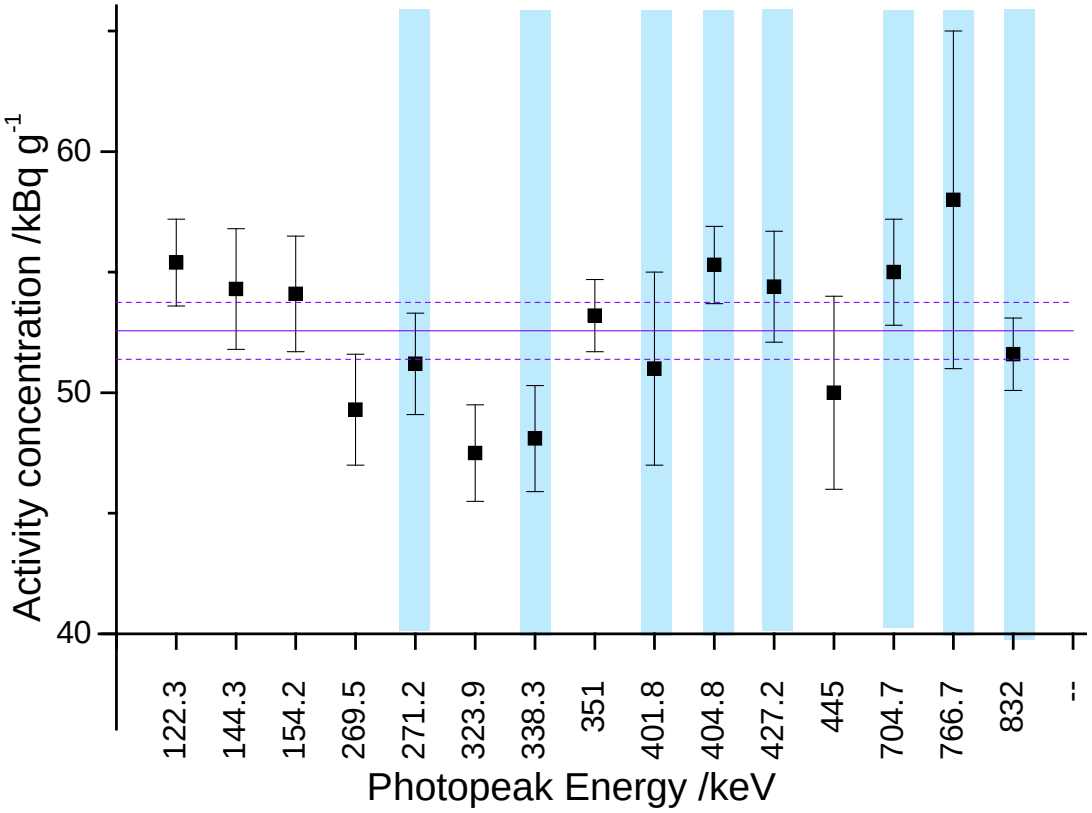


$\varepsilon 1 \in [0.993, 0.983]$

$\varepsilon 2 \in [0.922, 0.771]$

Ra-223

High resolution gamma spectrometry



- Purple line shows weighted mean; dotted line represents uncertainty
- Decay products highlighted in blue; values in agreement with direct measurement of ^{223}Ra

- HOWEVER, 18% spread on data, due to poorly known photon emission intensities.

Nuclear data – ^{223}Ra

- Known issues with current recommended γ-ray intensities
  - Large spread (18 %) in activities from main γ rays
  - 6 % relative difference of normalisation factor from new measurements
  - Large uncertainty on recommended half-life

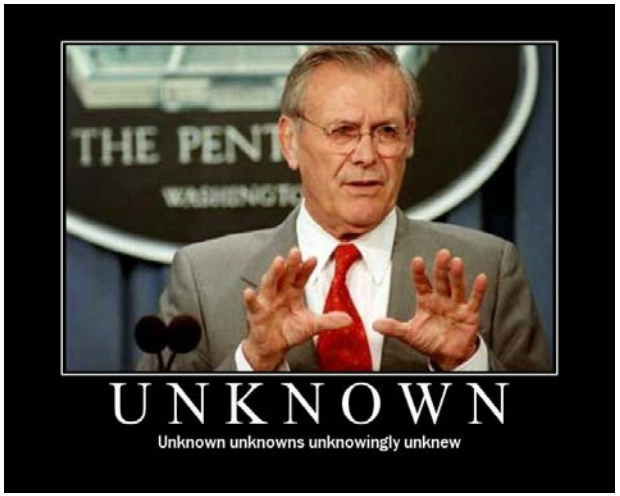
- New half-life and intensities published by PTB, NIST, NPL
  - All in good agreement
  - I've used the NPL values (for convenience)

Zero time of ^{227}Th: Outline of the problem

- For an absolute standardisation we need ^{227}Th chemically separated from decay progeny
- Accurate zero time for ^{227}Th is required for ingrowth corrections for the absolute measurements.
- Many unknowns….

  When is the zero time of a chemical separation? Is it the mid-point?

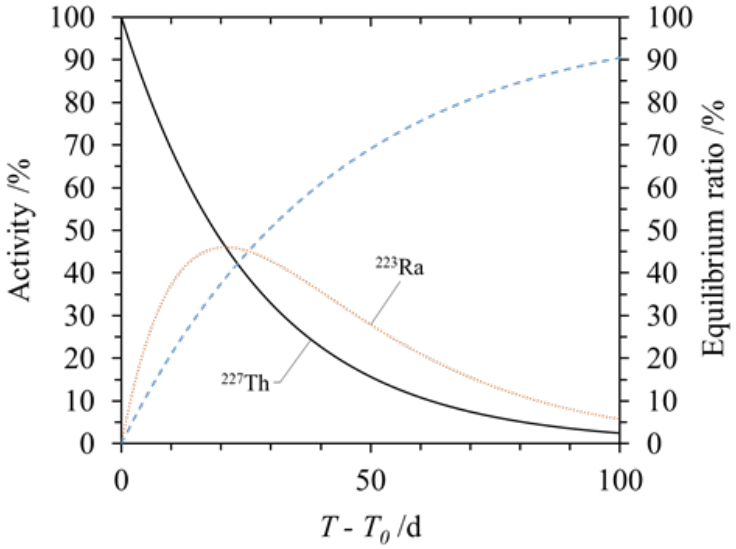
  How efficient was the chemical separation? Were all the decay progeny removed? Were they removed by the same amount? Etc…



- Ingrowth continues during chemical separation
  - Is there a moment in time when there is zero activity of decay progeny?

Zero time: What to do then?

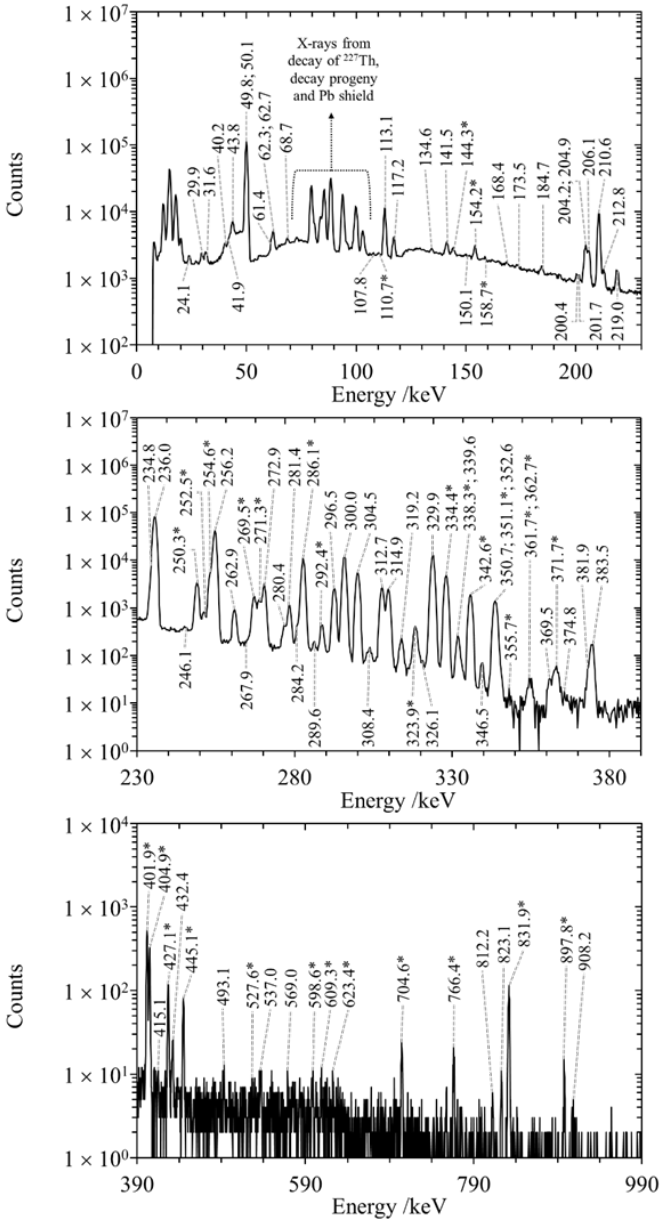
- Measure it!
- ‘Simple’ process of determining the activity of parent and daughter(s) at a moment in time.
  - Use activity ratio to derive time elapsed since the zero time.
  - Bateman equations.



- Measured zero time is considered to be the effective zero time
  - Might not match the time of the chemical separation depending on efficacy of method
  - Assumes that, at some point, the sample contained no decay progeny.
- A good idea to confirm the separation efficacy if possible!

Zero time: measurement

- ^{227}Th and decay progeny are γ-ray emitters
- Hundreds of γ-ray emissions to choose from
  - A fraction of these are useful
- ‘Easy’ to measure activity ratios using a HPGe γ-ray spectrometer
- Unfortunately, the nuclear data is ‘not the best’



Nuclear data – ^{227}Th

- DDEP evaluation withdrawn from website.
  - Nuclear data taken from ENSDF evaluation

- Recommended $T_{1/2}(^{227}Th)$ = 18.697 (7) days
  - Only two independent measurements used in evaluation.
  - All other published values rejected (for good reasons)

- Poorly defined decay scheme

- γ-ray emission intensities from three measurements
  - 'Best' ones are from a private communication!
  - Room for improvement on the uncertainties of relative intensities
  - Normalisation factor has 8.5 % uncertainty

Zero time: Selection of γ-ray emissions

- Ideal criteria
  - Above 100 keV
  - High emission intensity
  - Have similar energies
  - No interferences
  - Not in a multiplet

- Some criteria difficult to achieve for ^{227}Th and ^{223}Ra
  - Highly converted
  - Lots of γ-rays that either interfere or form a multiplet

- Cannot use γ-rays from ^{211}Pb, ^{211}Bi, ^{211}Po or ^{207}Tl
  - Delay in reaching equilibrium

Zero time: Selected γ-ray emissions for ^{227}Th

- For ^{227}Th
  - 49.8 keV & 50.1 keV doublet
    - Small problems in consistent fitting due to the change in the Compton continuum due to the ingrowth of decay progeny.
    - Shouldn't be a large effect
    - Below 100 keV

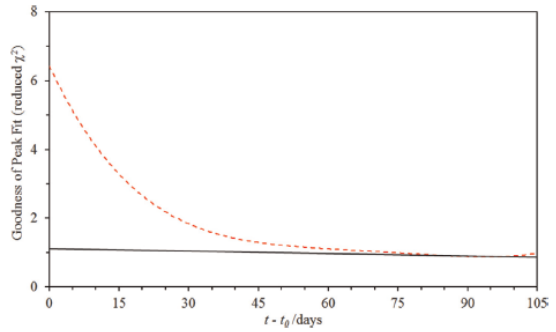
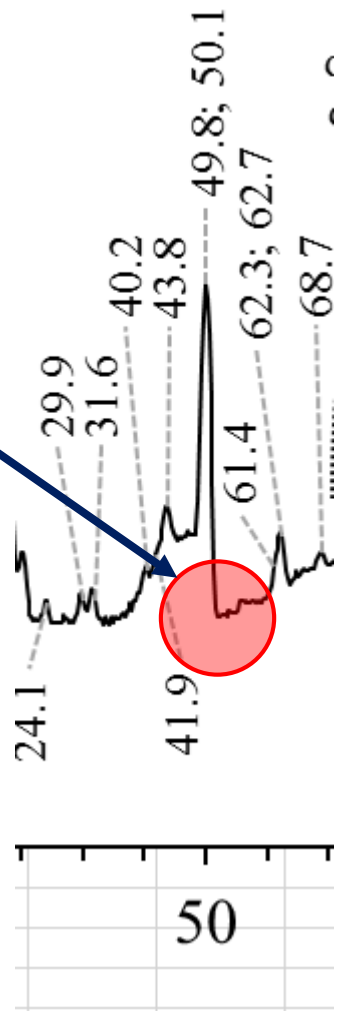


Fig. 4. Goodness of the peak fit of the 50.1 keV (dashed line) and the 236.0 keV doublet (solid line) as calculated by the peak fitting software.

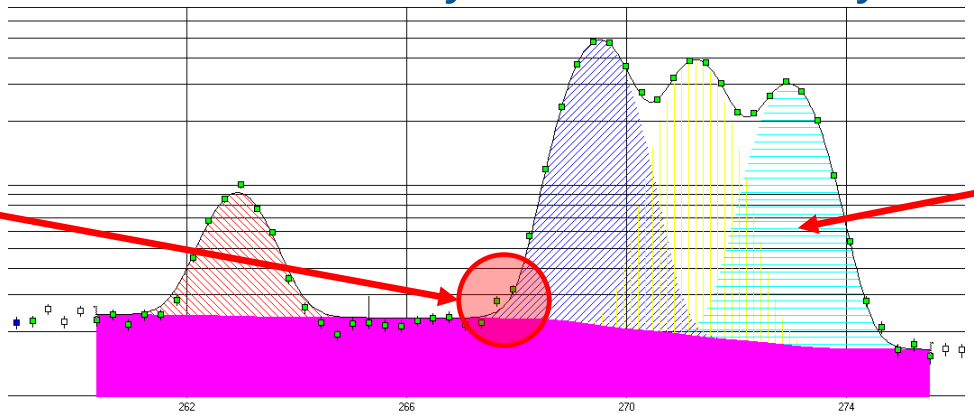


  - 234.8 keV & 236.0 keV doublet
  - Possibly 300.0 keV

Zero time: Selected γ-ray emissions for decay progeny

- For decay progeny
  - 154.2 keV from ^{223}Ra
    - No interferences
    - No multiplet
    - Poor statistics in the early phase of measurements
  - 269.5 keV & 271.2 Kev doublet from ^{223}Ra and ^{219}Rn
    - Improved statistics in the early phase
    - Extra care needed as they are bracketed by ^{227}Th emissions

Possible ^{227}Th γ ray here



274 keV ^{227}Th γ ray

  - No other suitable γ-rays available

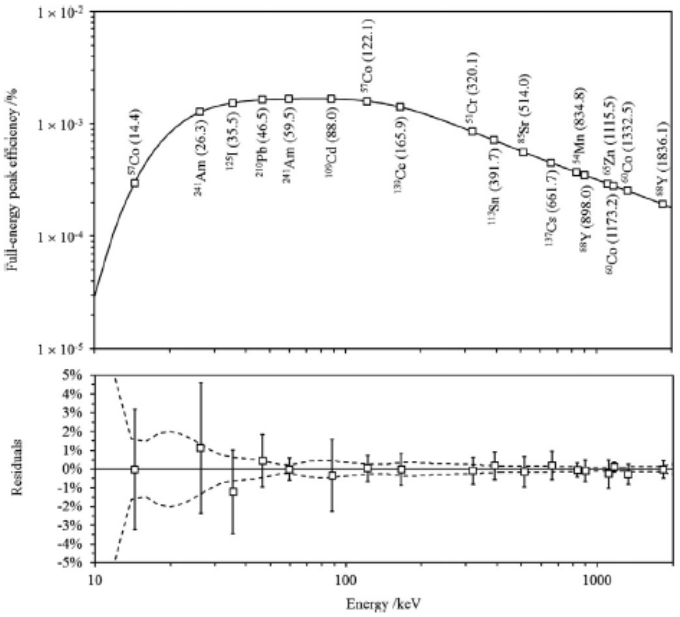
Zero time: Selected nuclear data

Radionuclide	T1/2 /days	Source
^{227}Th	18.697 (7)	ENSDF
^{223}Ra	11.4354 (17)	NPL

Radionuclide	Energy /keV	Iγ /%	Source
^{227}Th	49.8 + 50.1	8.81 (85)	ENSDF
^{227}Th	234.8 + 236.0	13.4 (11)	ENSDF
^{223}Ra	154.2	6.02 (3)	NPL
^{223}Ra + ^{219}Rn	269.5 + 271.3	24.12 (9)	NPL

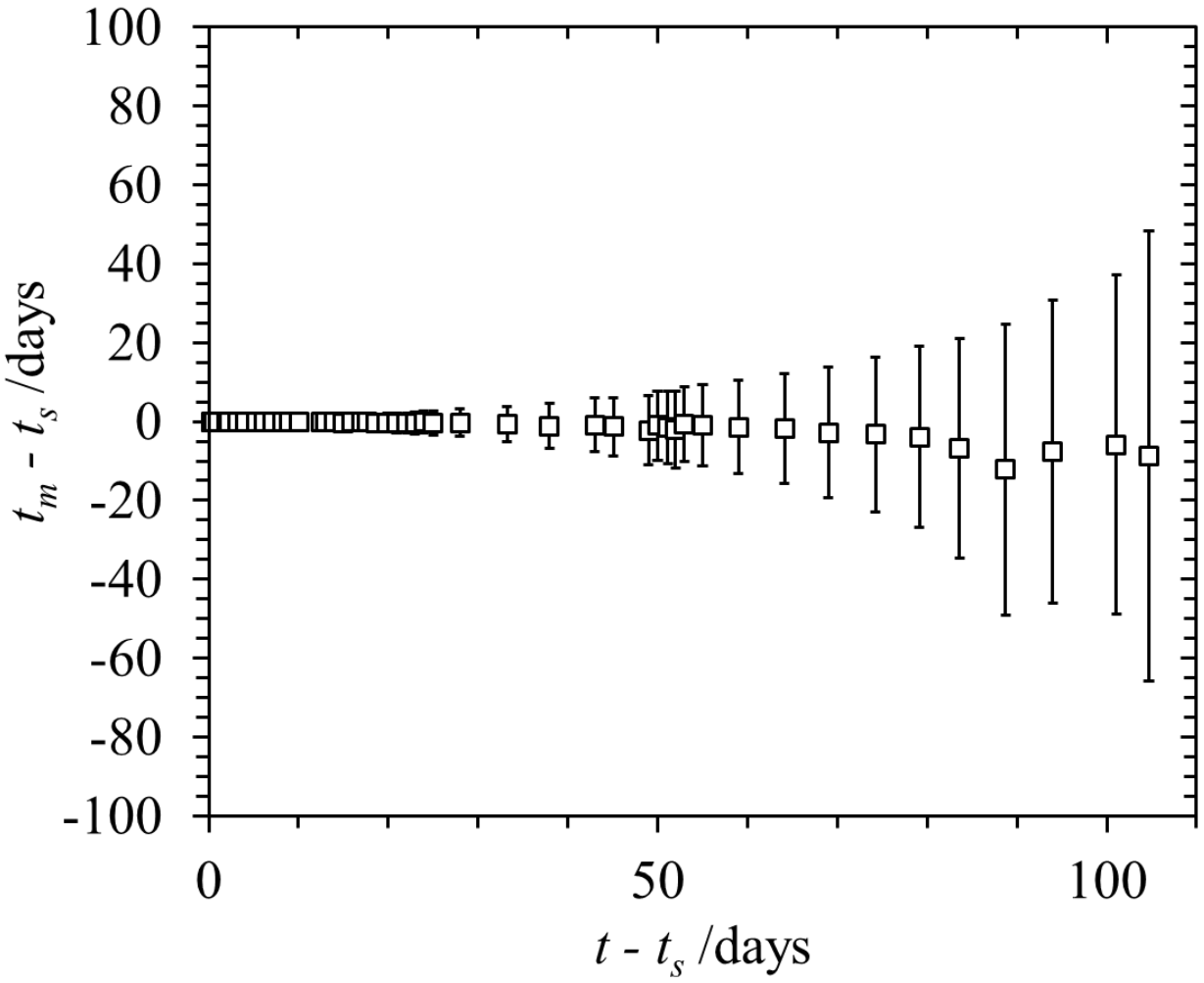
HPGe measurements

- A single calibrated (for the matched sample geometry) HPGe detector used
- A series of 360 x 5000 s measurements over a period of 105 days
- 56 of these used for zero time measurement
- Corrections for dead-time, pulse-pile up and self-absorption made
- Sample-to-detector window ~ 30 cm
  - No TCS corrections made

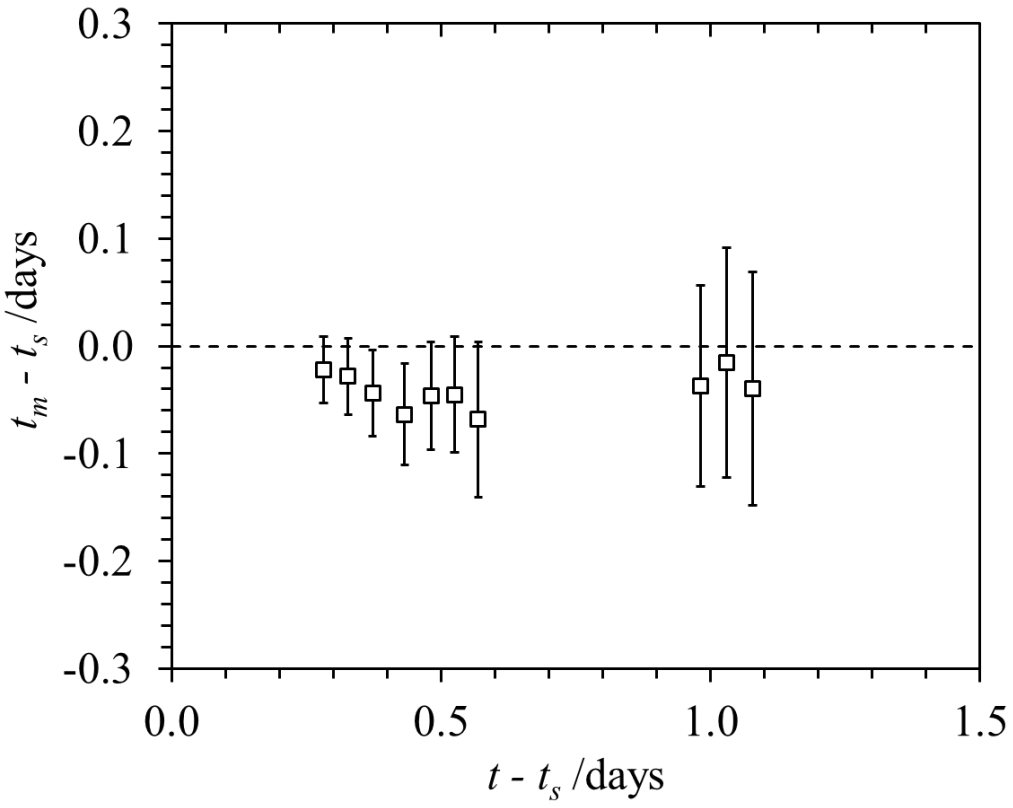


Results for 105 days

- Ratio of ^{223}Ra(154.2 keV) activity against weighted mean of ^{227}Th doublets



Results from first 1.5 days



- Weighted mean result is 08:23 ± 44 min
- Consistently lower than mid-point of chemical separation

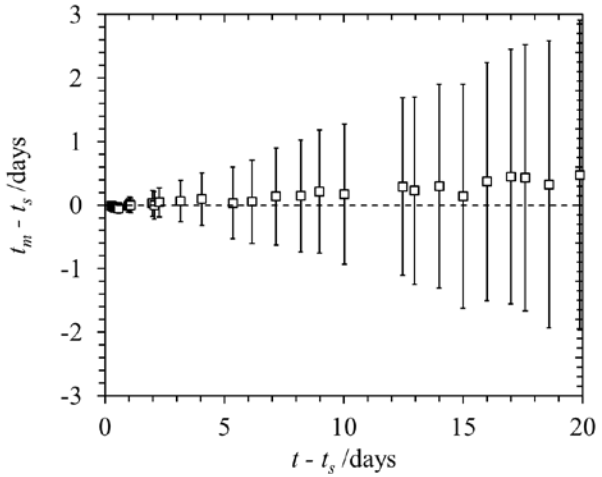
Large uncertainties from ^{227}Th γ-ray intensities and ^{223}Ra statistics dominate

Can't say that separation mid-point not the zero time

Results for each ^{227}Th doublet

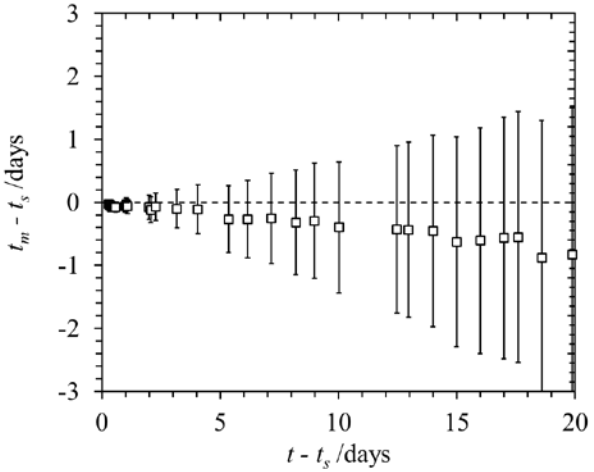
- All is not quite as it seems….

50 keV doublet



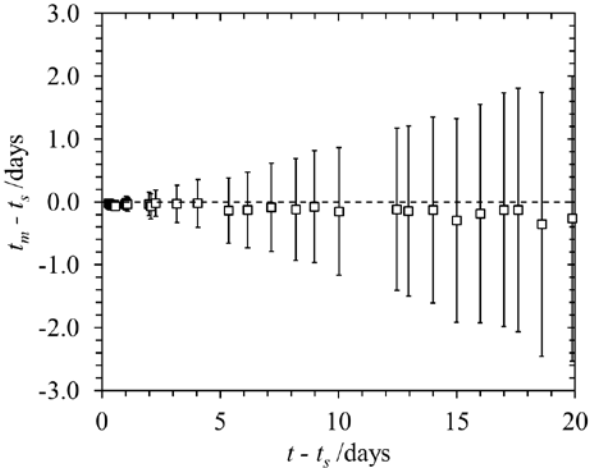
08:46 ± 48 min

236 keV doublet



08:06 ± 45 min

Combined

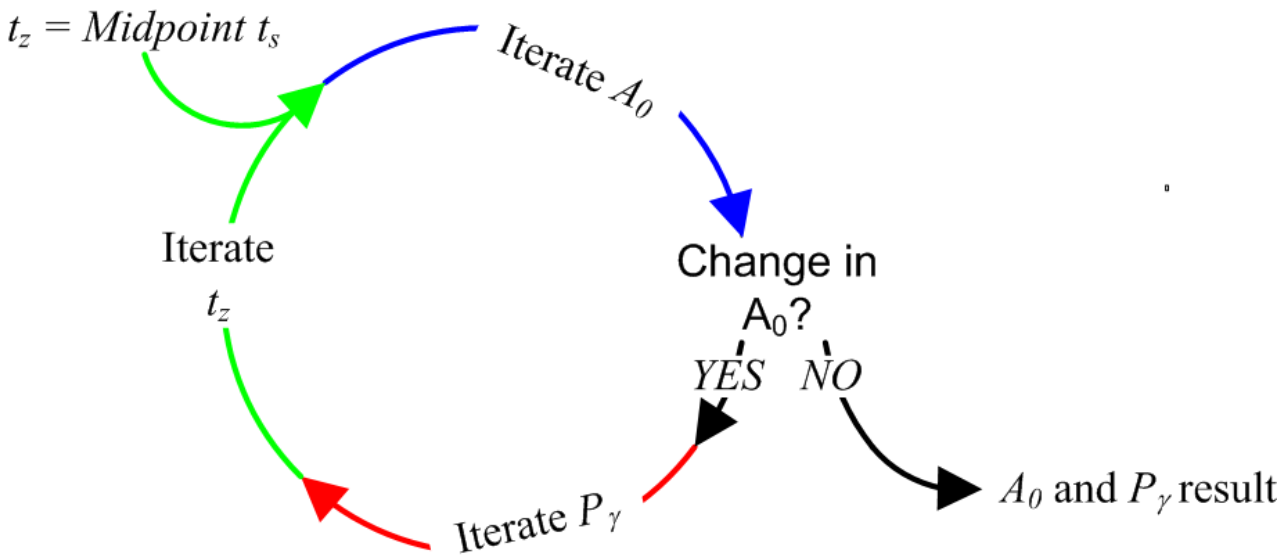


08:23 ± 44 min

- Bias for each doublet
- Combining both reduces the observed bias…is this correct though?
- Errors in the γ-ray emission intensities may be the problem.

Iterative approach to improve accuracy

- Ideally we would like smaller uncertainties for the zero time
- We could use an iterative approach



What was the effect of using the iterative approach

- **Zero time of 08:29 ± 16 min**
  - Much improved uncertainty
  - We can now suggest that the chemical separation not 100 % effective
- **Zero time resulted in a 0.18 % relative change in the absolute activity**
  - Size of change within relative uncertainty of absolute activity
  - Still an important consideration for improving the accuracy
  - Important that the zero time measured to confirm efficacy of separation

Preliminary emission intensities – from absolute standard

Source	Normalisation factor
ENSDF	0.129 (11)
NPL	0.12578 (64)

- Relative difference in values of 2.5 %

- Massive difference in precision (~ x 16)

Energy /keV	ENSDF	NPL	Relative Difference /%
49.8 + 50.1	8.81 (85) %	9.013 (50) %	2.3
234.8 + 236.0	13.4 (11) %	13.052 (56) %	2.6

Chemical separation method (2013)

- ^{227}Th as anionic complex $[Th(NO_3)_6]^{2-}$ in 8 M HNO_3
- Separated from decay progeny using Bio-Rad AG1-X9 anion exchange resin
- Decay progeny and Ac are not absorbed onto resin
- Separation started at 09:00 and completed at 09:38
- Assumed zero time at 09:19 ± 11 min
- Uncertainty of the zero time from these times considered a rectangular distribution

Investigation of resins for ^{227}Th separation

- Original chemical separation in 2013
  - Used ion exchange resin (AG1)
- Extraction chromatographic resins have been investigated
  - TEVA and UTEVA
- Two areas of the investigation
  - Th recovery
  - Separation efficiency

Summary of test conditions

National Physical Laboratory

	AG1-X8	TEVA	UTEVA
Conditioning	20 mL 8 M HNO_3	20 mL 3 M HNO_3	20 mL 8 M HNO_3
Loading	5 mL 8 M HNO_3	5 mL 3 M HNO_3	5 mL 8M HNO_3
Rinse	10 mL 8 M HNO_3	10 mL 3 M HNO_3	10 mL 8 M HNO_3
Elution 1	10 mL 1 M HNO_3 +0.5 M HNO_3 + 0.1 HNO_3	10 mL 1 M HNO_3 +0.5 M HNO_3 + 0.1 HNO_3	10 mL 1 M HNO_3 +0.5 M HNO_3 + 0.1 HNO_3
Elution 2	10 mL 1 M HCl	10 mL 1 M HCl	10 mL 1 M HCl

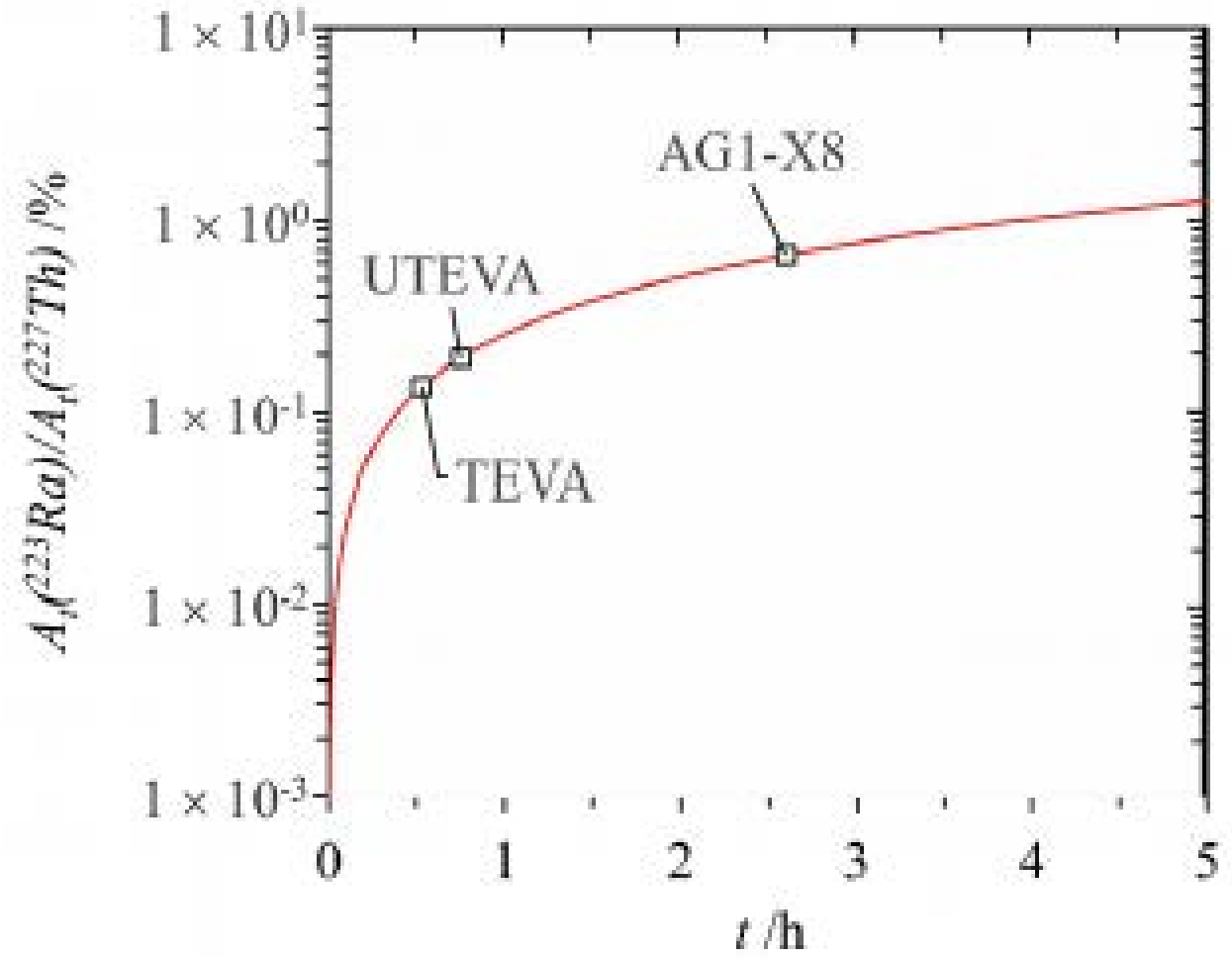
Th recovery

- Recoveries determined using mass spectrometry
- Elution of Th from resin using 1 M HCl or 0.5 M HNO_3
- Recoveries varied for each resin
  - AG1 = 53 %
  - TEVA/UTEVA = 82.9-88.9 %
- TEVA and UTEVA resins showed greater potential for Th recovery under tested conditions

Separation efficacy

- Efficacy of separation assessed using zero time measurements
- Closer the zero time to separation mid-point the better the separation
  - More decay progeny removed
  - Assumes that all decay progeny removed in the same ratio
- We used the γ-ray emission intensities determined from absolute standard

Activity ratio of $^{223}Ra/^{227}Th$ after separation



SUMMARY

- NPL has worked closely with: BIPM, via CCRI(II), NIST and PTB to harmonise international efforts in provision of international standard for ^{223}Ra.

  All in agreement now.

  Demonstrates the importance of international harmonisation, via comparisons, and the Mutual recognition Arrangement etc …
- NPL has also worked closely with Bayer to release data and publications in a manner that would not jeopardize the efficacy of ongoing clinical trials.
- Results used to determine calibration factors/dial settings for clinical dose calibrators
- NPL calibration service in place
- New nuclear data published : VAST improvement on existing data.
- Continuation of project with Bayer to include similar studies for ^{227}Th (parent of ^{223}Ra) currently undergoing clinical trials.

  (Much more complicated !!!!)

Time dependent Dial Factors for Th-227

- I have completed a scheme to make the instrument yield the CORRECT Th-227 activity at the time of measurement
- Leading to a lookup table of correction factors …
- TIME DEPENDENT DIAL FACTORS

Thank you for your attention

and to all of my colleagues from NPL's Radioactivity Group.

Department for Business, Energy & Industrial Strategy

FUNDED BY BEIS