



# ENRICHMENT OF Ca AND Ti ISOTOPES FOR THERANOSTIC SC ISOTOPE PRODUCTION

An update

PRISMAP workshop on emerging  
infrastructures and technical development

INFN Legnaro – 21-22 Nov 2022

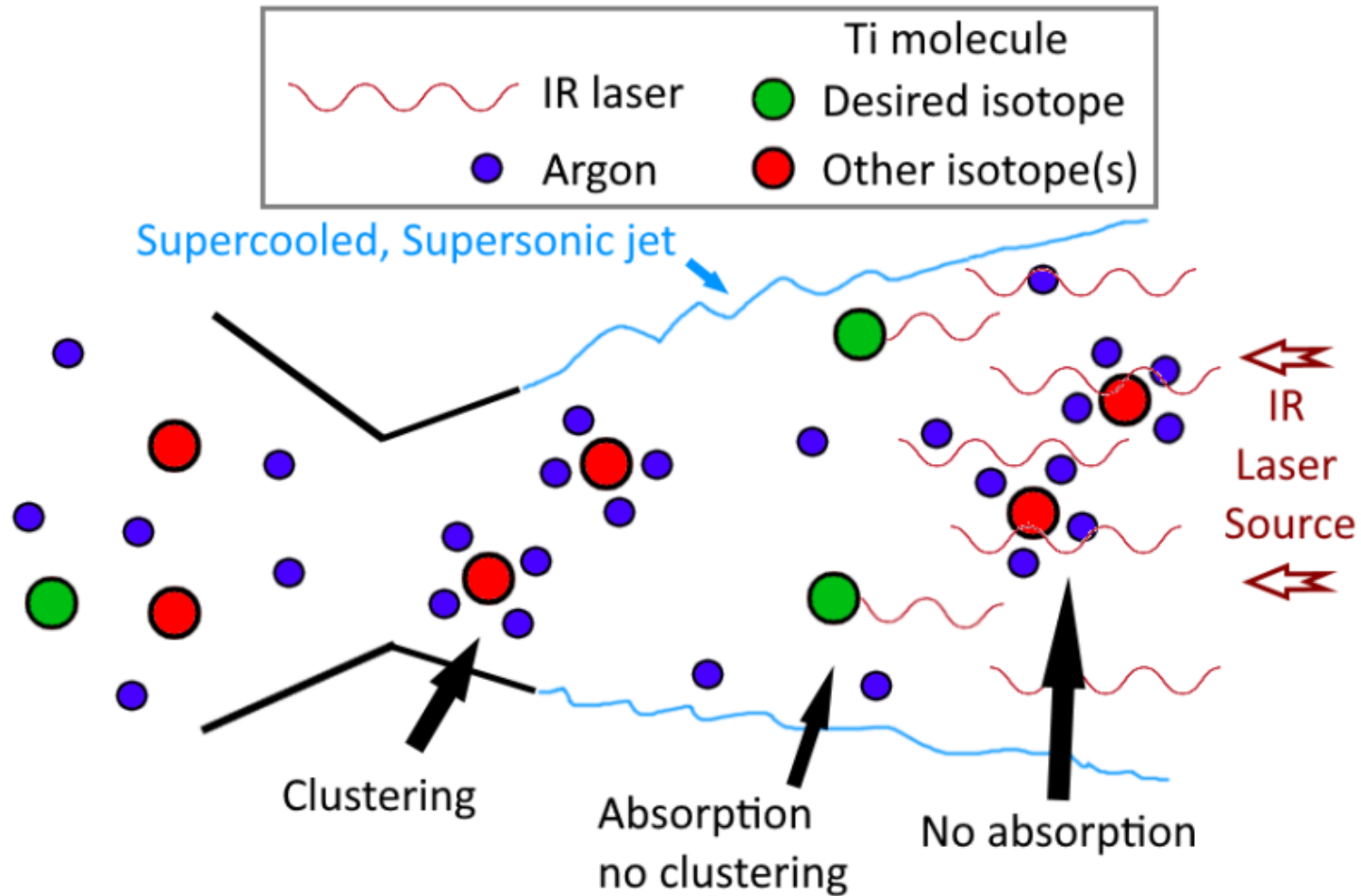
# Sc theranostic set



- $^{43}\text{Sc}$ 
  - $T_{1/2}=3.89\text{h}$
  - $^{40}\text{Ca}(\alpha,p), ^{42}\text{Ca}(d,n), ^{43}\text{Ca}(p,n), ^{\text{nat}}\text{Ca}(\alpha,n)^{43}\text{Ti}$
  - $^{46}\text{Ti}(p,\alpha)$
- $^{44}\text{Sc}/^{44\text{m}}\text{Sc}$ 
  - $T_{1/2}=3.97\text{h}$  and  $T_{1/2}=58.6\text{h}$
  - $^{44}\text{Ca}(p,n), ^{44}\text{Ca}(d,2n), ^{\text{nat}}\text{Ca}(p,xn)$
  - $^{45}\text{Sc}(p,2n)^{44}\text{Ti}$
  - $^{47}\text{Ti}(p,\alpha)$
- $^{47}\text{Sc}$ 
  - $T_{1/2}=3.35\text{d}$
  - $^{46}\text{Ca}(n,\gamma)^{47}\text{Ca}, ^{48}\text{Ca}(p,2n)$
  - $^{47}\text{Ti}(n,p), ^{48}\text{Ti}(\gamma,p), ^{48}\text{Ti}(p,2p), ^{50}\text{Ti}(p,\alpha)$

- The scandium isotopes have long been identified as relevant for theranostics applications thanks to the combination of  $^{47}\text{Sc}$  for beta therapy with imaging with either  $^{43}\text{Sc}$ ,  $^{44}\text{Sc}$ , or  $^{44\text{m}}\text{Sc}$ .
- The production of either member of this set requires the use of enriched Ca or Ti target material.
- In particular, the imaging isotopes are best produced with stable isotopes from the middle of the natural distribution, which are the most difficult to obtain from centrifuge separation.
- The only existing supply is based on electromagnetic separation, currently only operated in Russia. The lack of sustainability of this supply had been identified during the preparation of PRISMAP, and our initial worries have unfortunately been confirmed, as the supply has now dried out, given the current geopolitical situation.

# SILARC

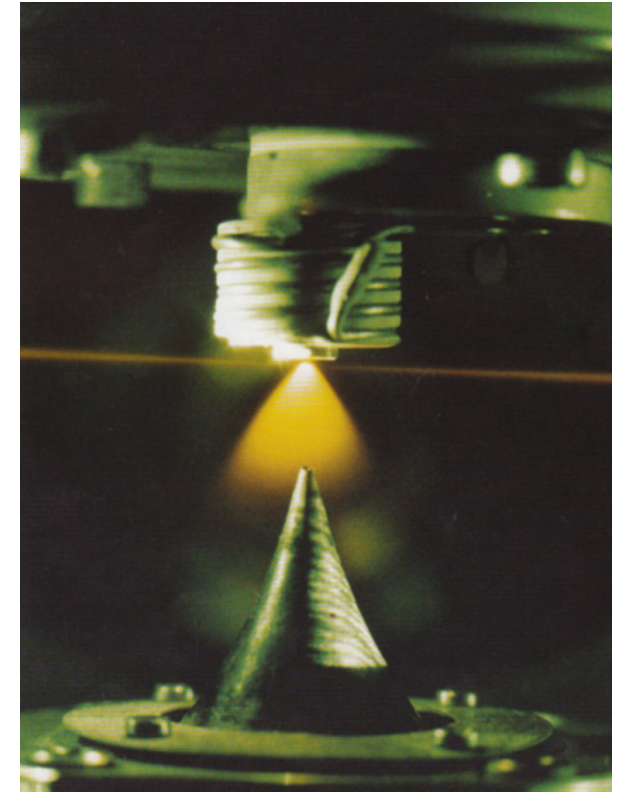


- The alternative proposed within PRISMAP is the Separation of Isotopes by Laser-Assisted Retardation of Condensation (SILARC)
- A molecule containing the element of interest is introduced in a buffer gas cell.
- The mixture is released through an aperture and the expanding gas jet becomes supersonic, resulting in sudden cooling (to  $\sim 15\text{K}$ ).
- The buffer gas condensates on the molecules and forms clusters.
- Isotope-selective infrared (IR) excitations of the molecules heats up an isotopomer (molecule containing a specific isotope), preventing clusterization.
- The heavy clusters and clean isotopomer experience different drag forces and can be separated by a skimmer.
- Recycling of the material allows for multiple passages for improved enrichment of the isotope of interest.

*J-M Zellweger, J-M Philippoz, P Menilon, R Monot, H van den Bergh. PRL 52 (1984) 522-525*

# Identifying the needs

- Earlier proof of concept:
  - SILARC has been demonstrated in the past for Sulfur enrichment with SF<sub>6</sub> – as illustrated here.
- Key elements for this developments are:
  - A volatile molecule featuring a single atom of the element of interest
  - Infrared transitions that are sensitive to the isotope shift and that are accessible
  - A setup to perform the separation (gas cell, skimmer, laser)



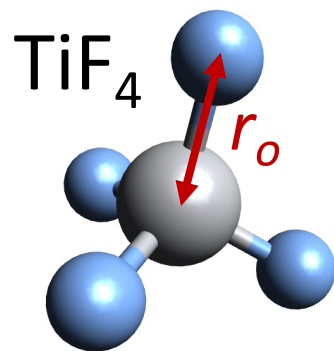
*J-M Zellweger, J-M Philippoz, P Menilon, R Monot, H van den Bergh. PRL 52 (1984) 522-525*

# Identification of a suitable molecule

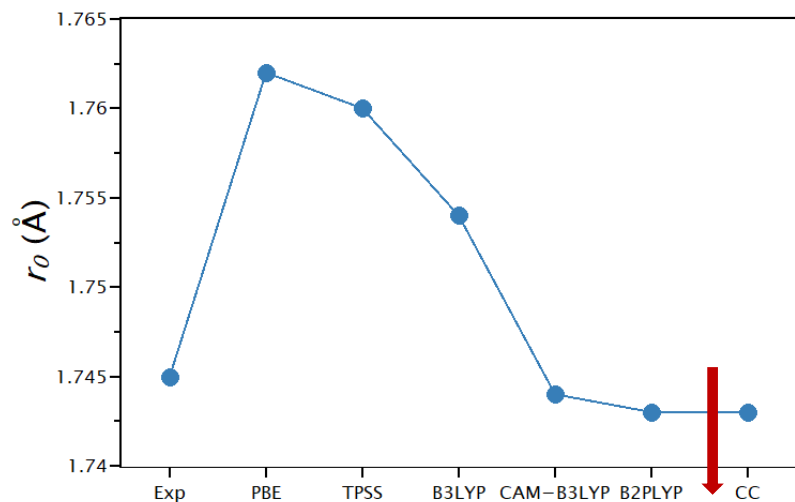
- We proceeded with a calculation-based approach where we defined different possible Ti-containing molecules and explored their different vibration modes, and the dependence on the Ti isotope.
- ✓ Phase 0: check global feasibility of performing the DFT calculations and choose the appropriate functional.
- ✓ Phase 1: perform extended systematic calculations with  $\text{TiF}_x$  ( $x=1-4$ ) to determine the optimal conditions for the enrichment of natural Ti.
- ✓ Phase 2: explore more complex Ti-based molecules.
  - Reported in deliverable D10.5: Check on the member section or Zenodo: <https://zenodo.org/record/6607408#.Y3q5X-SZOHv>
- ✓ Phase 3: explore volatile Ca-based complexes.

*Work performed by Dr Piero Ferrari and two Bachelor students: Lucas Dooms & Oliver Payne*

# Phase 0: Benchmark analysis

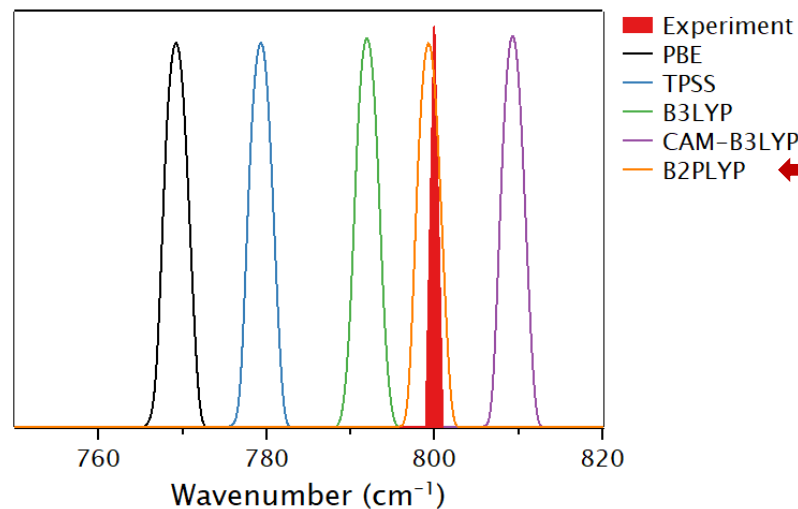


## Bond length



*J. Chem. Phys.*, **102** (1995) 20.

## Vibrational frequency

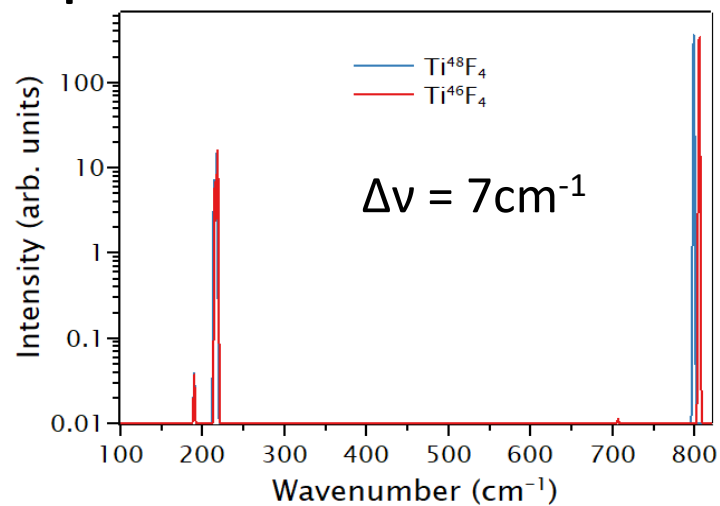


KU LEUVEN

QUANTUM SOLID STATE PHYSICS

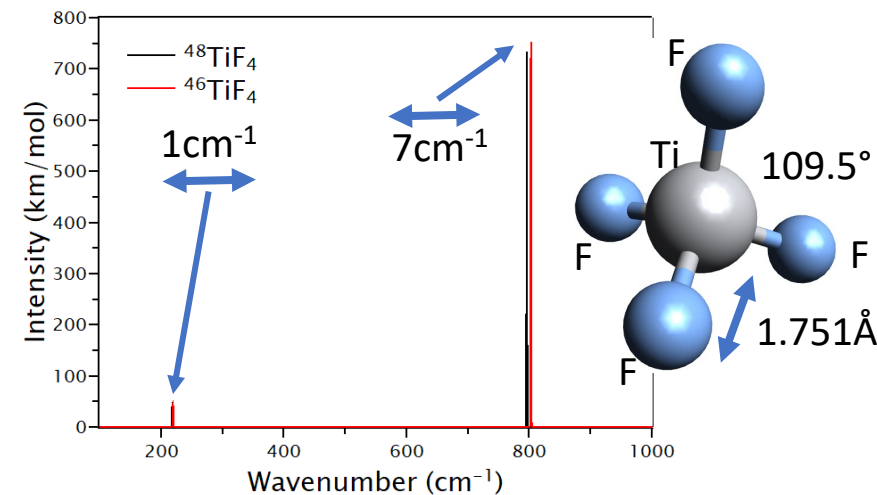
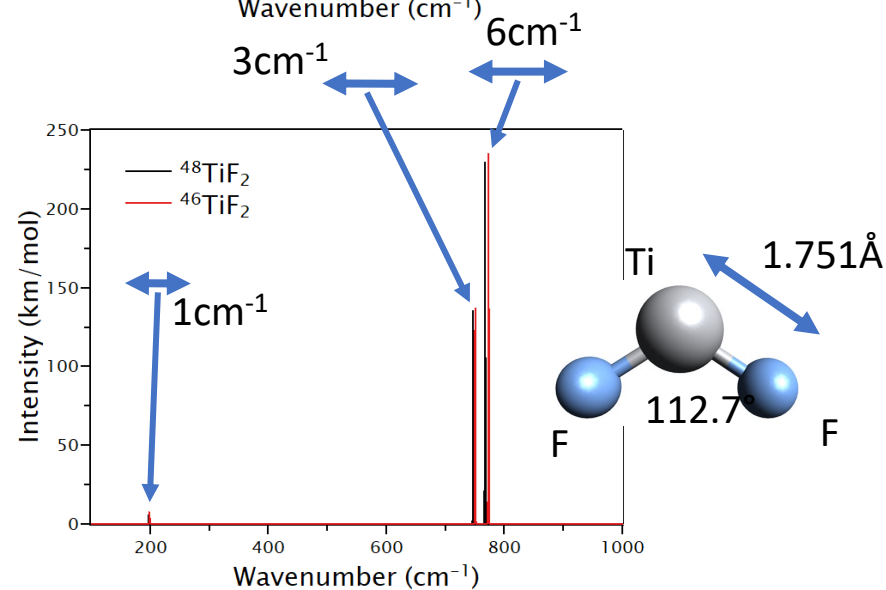
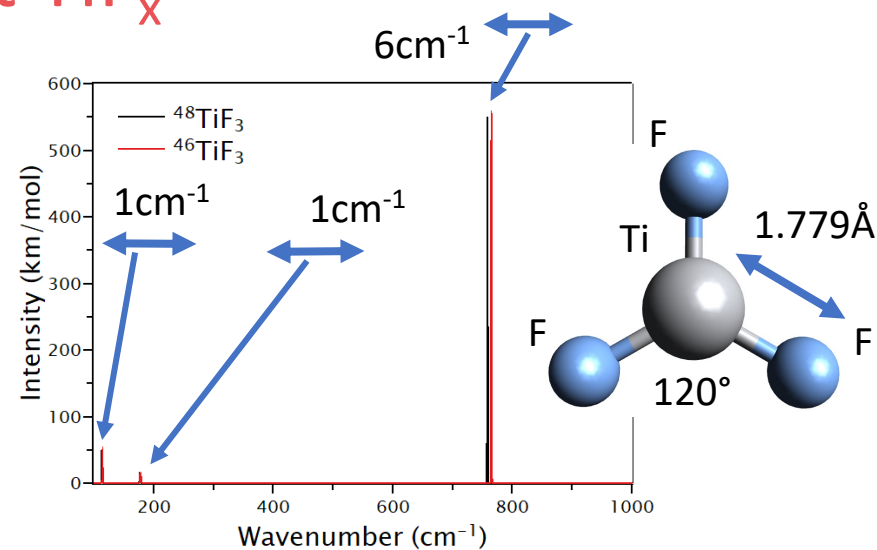
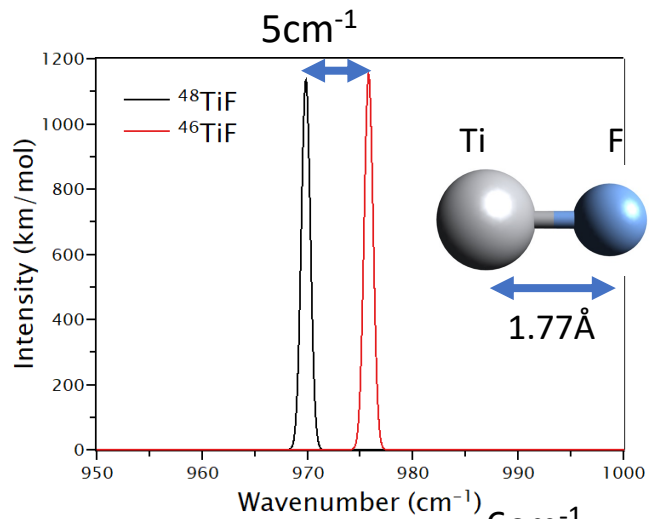
*J. Chem. Phys.*, **92** (1990) 6.

## Isotope shift



The analysis suggests the use of B2PLYP/Def2-QZVPP as the final theory level

# Phase 1: Compare different $TiF_x$

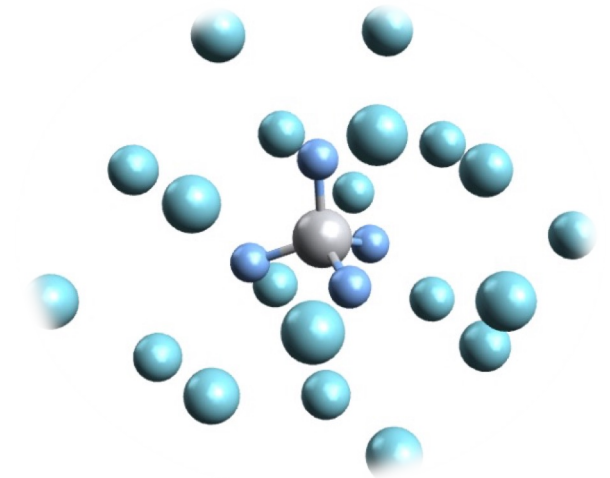


- An intense line is available close to 800  $cm^{-1}$ .
- There is also the dimer line at 970  $cm^{-1}$ .
- All lines seem to show substantial isotopomer shift.
- Exploring more complex molecules may provide other transitions



## Phase 1 bonus: clustering of Ar atoms

- The basis of the SILARC methods relies on the temperature dependence of the clusterization of the buffer gas to the molecules.
- Within the framework established here, simulations with an increasing number of Ar atoms were performed to estimated the binding of Ar to  $\text{TiF}_4$  at 15K and 300K.
- Ar is not bound to this molecule at room temperature, however even with Ar atoms, the system is still bound. This shows that controlling the temperature of the molecule through vibrational excitation may indeed provide the selection of interest.



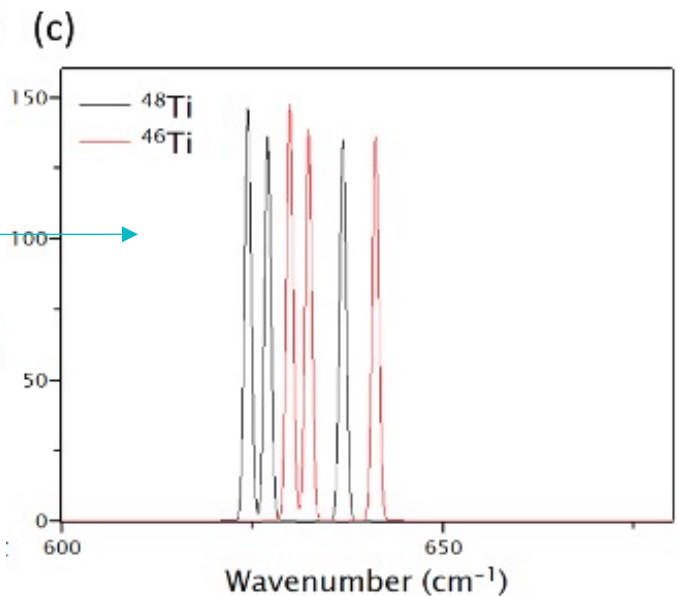
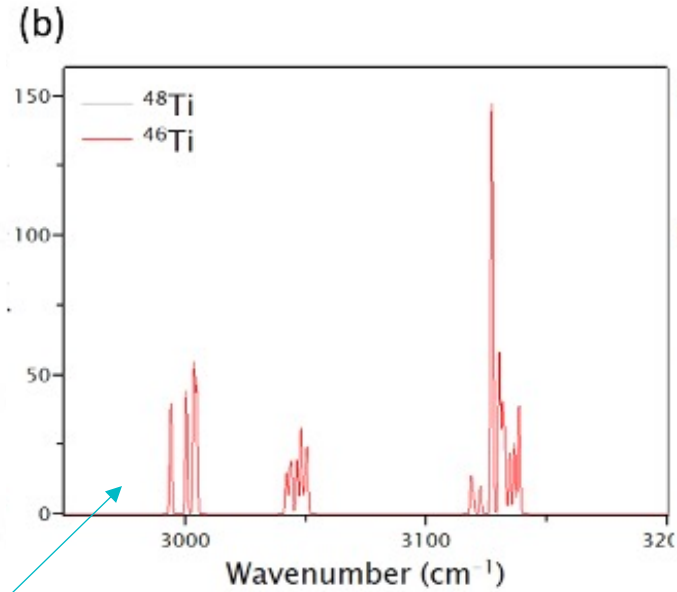
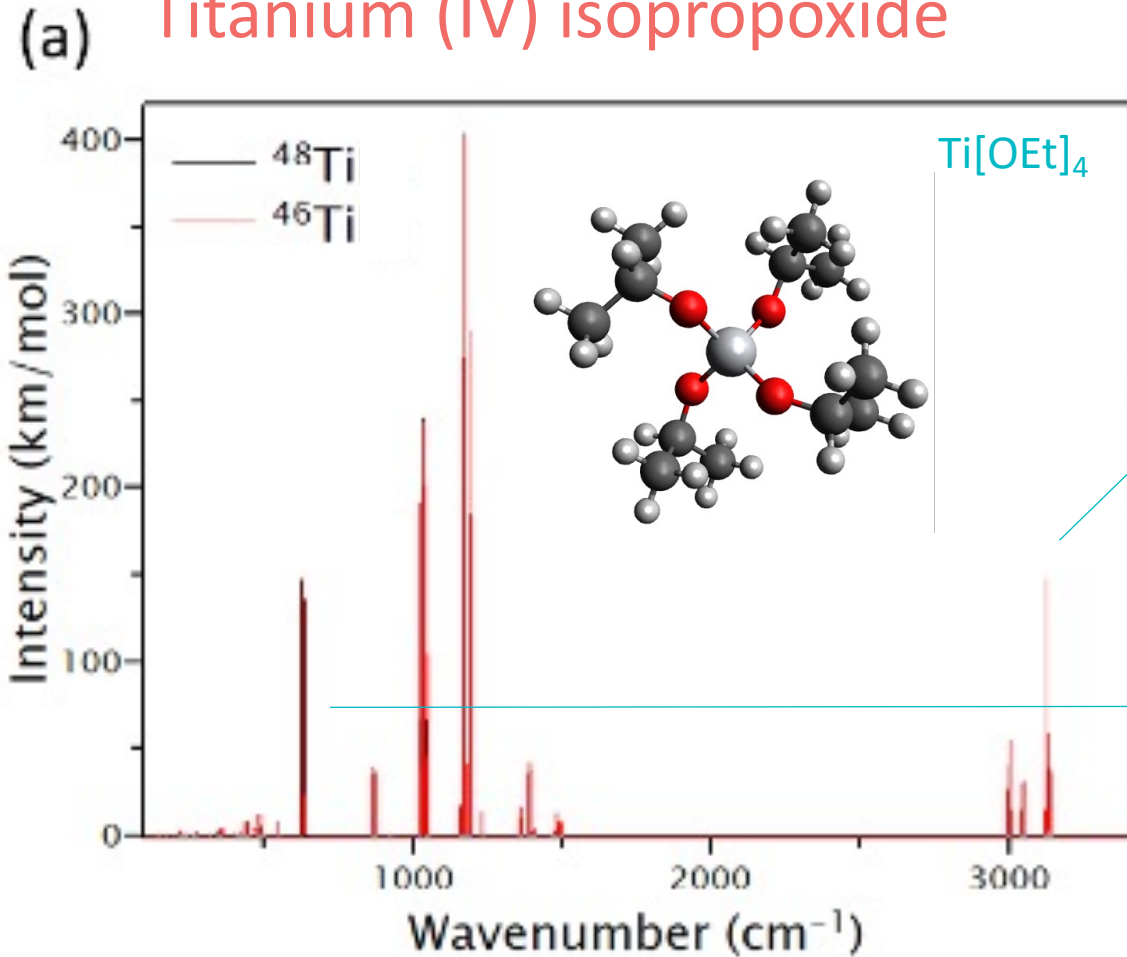
$\text{TiF}_4\text{Ar}_{20}$  at 15K



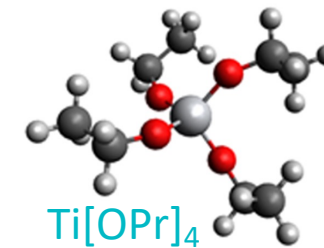


# Phase 2: More complex molecules

## Titanium (IV) ethoxide and Titanium (IV) isopropoxide



- Two complex molecules with known infrared spectrum ranging to useable frequencies were calculated: Ti[OEt]<sub>4</sub> and Ti[OPr]<sub>4</sub>.
- The experimental spectra were reproduced, however they concluded that the reachable transitions were not sensitive to the Ti isotope but were rather vibrations of the outer complexes.
- The Ti-sensitive transitions were again in the same frequency range as the simpler molecules.



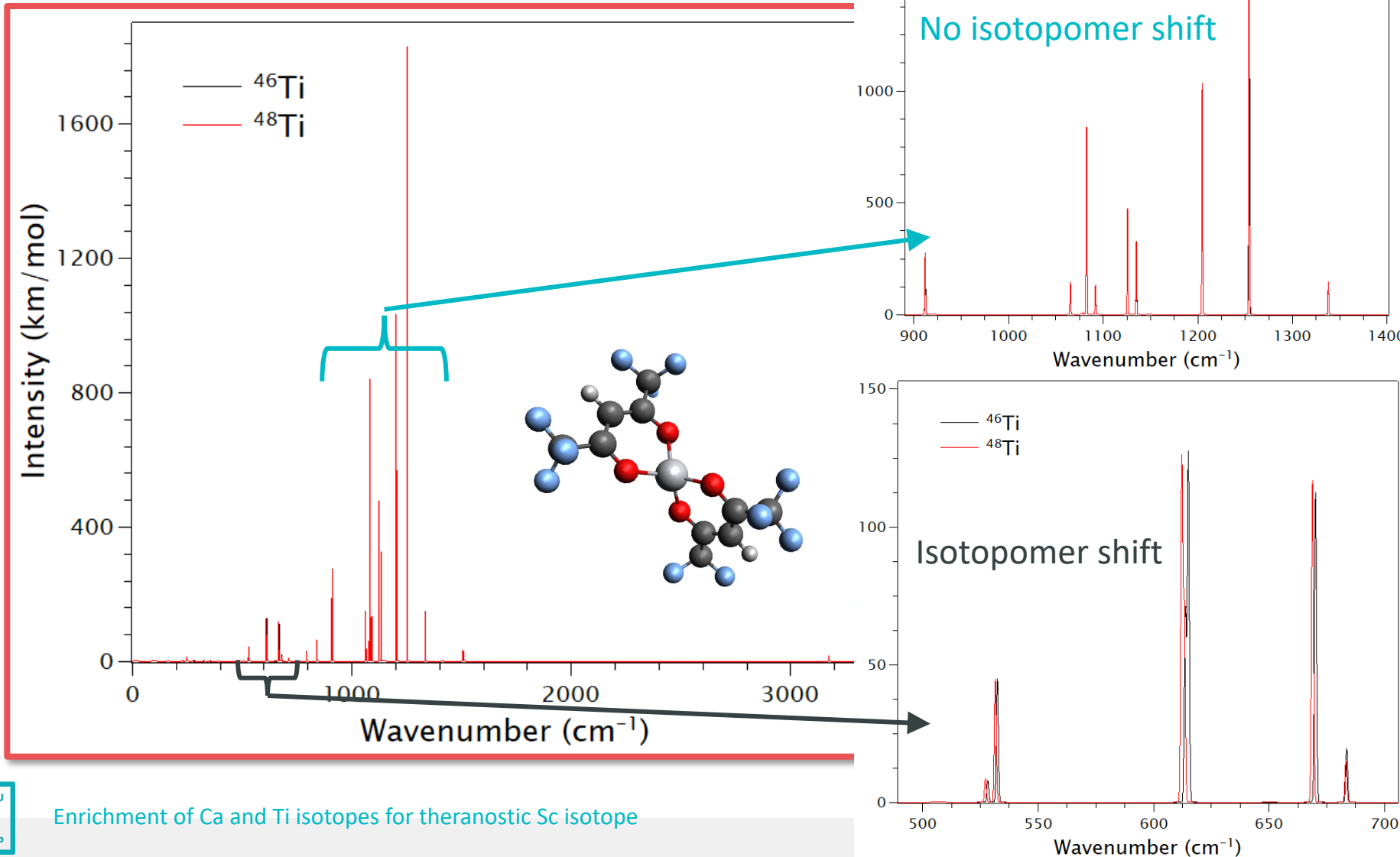
# Phase 3: Choosing a volatile molecule

## Titanium hexafluoroacetyl acetonate

Presented at the EMIS2022 conference in Daejeon (South Korea). To be published in the proceedings.

KU LEUVEN

QUANTUM SOLID STATE PHYSICS

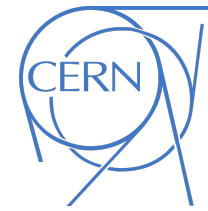


- A molecule which synthesis is already under control at EPFL was then chosen as the working molecule:  $C_{10}H_2TiF_{12}O_4$
- The expected response is seen with Ti-sensitive transitions between 500  $cm^{-1}$  and 700  $cm^{-1}$ , with a shift of 1.5  $cm^{-1}$  between the two isotopes.



# Next phase

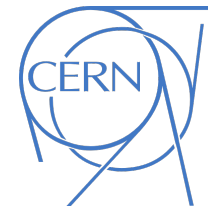
## Molecule synthesis



- The team of Paul Dyson at EPFL (as third-party subsidiary to CERN) will work on the synthesis of Titanium hexafluoroacetyl acetonate and Calcium hexafluoroacetyl acetonate
- The volatility of those molecules could make them suitable for separation in centrifuge as well as with SILARC
  - Centrifuge separation would be useful for  $^{48}\text{Ca}$  only, as  $^{44}\text{Ca}$  and  $^{48}\text{Ti}$  are in the middle of the natural distribution, thus not efficiently separated in centrifuges.
  - GANIL's contacts with the enrichment industry should be exploited to explore this possibility.
  - Synergies with the radioactive beam community's need for  $^{48}\text{Ca}$  makes this a very timely and relevant opportunity.

# Next phase

## Laser development



- The calculations have concluded that for the molecule of interest, infrared light with a wavelength around 12-15  $\mu\text{m}$  is required. This frequency is not available from any commercial laser and developments are required.
- A possible alternative is difference frequency generation, a form of frequency mixing where the light from two lasers are brought together in a crystal so that the output is the difference of their frequencies: e.g., mixing lasers at 1200 nm and 1312 nm from a Cr:fosterite laser yields light at 14,057 nm, as  $1/1200 - 1/1312 = 1/14057$ .
- Recent investigations into non-linear crystals have identified BGSe ( $\text{BaGa}_4\text{Se}_7$ ) as an appropriate medium for this effect. However, its damage threshold seems to be quite low, so that the power of the generated light might be limited.
- Such a DFG setup is being developed at CERN to test the concept and possibly validate the calculations.

*E. Boursier et al., Optics Letters 41 (2016) 2731.*

# Next phase

## Validate the calculations



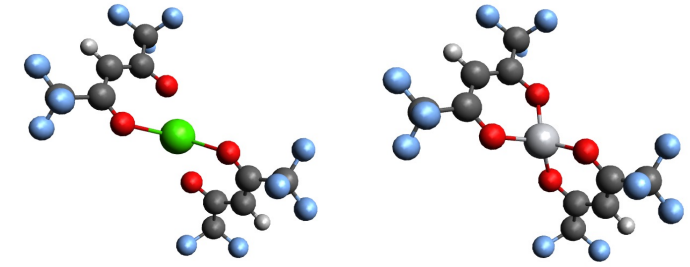
- Another approach to generate the necessary frequencies to test the transitions in those molecules is the use of a free electron laser, e.g., FELIX in Radboud Universiteit (NL), where Piero Ferrari now works.
- We are considering submitting a request via Laserlab Europe, a H2020 Infrastructure on lasers and laser applications to perform this test.  
<https://www.laserlab-europe.eu/>
- While this would give us the necessary information, it is also not an appropriate solution for the SILARC application, where a dedicated laser system still has to be developed.

# Final phase

## Experimental demonstration

- Our final goal is to demonstrate the enrichment in a single-pass system.
- This requires a gas cell with a pin-hole nozzle and a skimmer to separate the hot molecules from the cold clusters and the laser light.
  - The KULeuven In-Gas (jet) Laser Ion Source (IGLIS) laboratory will host the test as it covers the necessary infrastructure (gas cell front end + laser laboratory).  
<https://fys.kuleuven.be/iks/ns/experimental-facilities/experimental-facilities>
  - A new nozzle will be produced and characterized for this application (simple pin-hole design).
  - A skimmer needs to be designed or procured.
  - The new DFG laser system from CERN is proposed for this proof of principle.
- The outcome of the separation will be characterized by performing trace analysis on the central and outer samples.
  - E.g., by laser spectroscopy or mass spectrometry.

# Where we stand on Ca and Ti enrichment



- A calculation framework has been developed to explore possible molecules of interest.
- All Ti- and Ca-sensitive resonances are located in the mid-infrared (12-15  $\mu\text{m}$ ) which is rather challenging to access.
- Calcium and Titanium hexafluoroacetyl acetonate have been identified as the molecules of choice for further investigation.
- Synthesis and experimental validation are next on the books.
  - New laser developments needed at CERN
  - Possible study with a free electron laser in the meantime
- Final demonstration to be planned at KULeuven in the later phase of the project.
- Possible synergies with the RIB community and test in centrifuge is being considered.

<b>42Ti</b> 208.65 ms $\epsilon = 100.00\%$	<b>43Ti</b> 509 ms $\epsilon = 100.00\%$	<b>44Ti</b> 60.0 y $\epsilon = 100.00\%$	<b>45Ti</b> 184.8 m $\epsilon = 100.00\%$	<b>46Ti</b> <b>STABLE</b> 8.25%	<b>47Ti</b> <b>STABLE</b> 7.44%	<b>48Ti</b> <b>STABLE</b> 73.72%	<b>49Ti</b> <b>STABLE</b> 5.41%	<b>50Ti</b> <b>STABLE</b> 5.18%
<b>41Sc</b> 596.3 ms $\epsilon = 100.00\%$	<b>42Sc</b> 680.70 ms $\epsilon = 100.00\%$	<b>43Sc</b> 3.891 h $\epsilon = 100.00\%$	<b>44Sc</b> 3.97 h $\epsilon = 100.00\%$	<b>45Sc</b> <b>STABLE</b> 100%	<b>46Sc</b> 83.79 d $\beta^- = 100.00\%$	<b>47Sc</b> 3.3492 d $\beta^- = 100.00\%$	<b>48Sc</b> 43.67 h $\beta^- = 100.00\%$	<b>49Sc</b> 57.18 m $\beta^- = 100.00\%$
<b>40Ca</b> $> 3.0E+21$ y 96.94% $2\epsilon$	<b>41Ca</b> 9.94E4 y $\epsilon = 100.00\%$	<b>42Ca</b> <b>STABLE</b> 0.647%	<b>43Ca</b> <b>STABLE</b> 0.135%	<b>44Ca</b> <b>STABLE</b> 2.09%	<b>45Ca</b> 162.61 d $\beta^- = 100.00\%$	<b>46Ca</b> $> 0.28E+16$ y 0.004% $2\beta^-$	<b>47Ca</b> 4.536 d $\beta^- = 100.00\%$	<b>48Ca</b> $> 5.8E22$ y 0.187% $2\beta^- = 75.00\%$

Natural abundances