In [1]:
```
# import tools
import numpy as np
import scipy as sci
import pandas as pd
import matplotlib
import matplotlib.pyplot as plt
from IPython.display import Markdown, display
import spike

# select a simple display mode
%matplotlib inline

# select simple error messages
%xmode Plain
```

```
    ========================
          SPIKE
    ========================
    Version     : 0.99.21
    Date        : 23-02-2021
    Revision Id : 490
    ========================
*** zoom3D not loaded ***
plugins loaded:
Fitter,  Linear_prediction,  Peaks,  bcorr,  fastclean,  gaussenh,
rem_ridge,  sane,  sg,  test,  urQRd,

spike.plugins.report() for a short description of each plugins
spike.plugins.report('module_name') for complete documentation on
one plugin
Exception reporting mode: Plain
```

Intro 10min

Using SPIKE for advance FTICR processing

- Spike organisation
- noise reduction: urQRD / SANE
- resolution in 2D FTICR
- phase properties in 2D FTICR

- need for theory

Exponential function

French Health Minister : **Olivier Véran** - two months ago...

COVID is not currently in exponential growth - it only grows by 10% every week

It is the very definition of the exponential 😂 *the growth is proportional to the value !*

Moreover if cases grows by 10%,

- speed of growth also growth also grows by 10%
- as well as its accelaration

doubling in 7 weeks (we got it !) ⇒ × 10 in 24 weeks (*would be August* 😢)

```
1 the politician you diserve
```

BoJo

Angela

In [2]:
```
1 1.1**7, 1.1**24
```

Out[2]:
```
(1.9487171000000012, 9.84973267580763)
```

need for / Mathematics

Our *Common Sense* is not always efficient,

the further we are from *Common Life* the less efficient it gets.

Project - 1h22' !

- Intro 10min
  - Exponential funny anecdote
  - need for theory
  - 2D NMR rapid story
- Spike organisation 15 min
  - dataset (NPK) object
  - memory
  - processing pipeline
  - user interface
    - python
    - notebook
    - interactive notebook
- some useful mathematics 10 min
  - complex numbers
  - real exponential
  - complex exponential
  - LP modeling of harmonic signals
  - Toeplitz matrix of the AutoRegressive model / and limitations
  - circulant matrices and FFT
- urQRd, SANE and more 15 min
  - Cadzow historical approach
  - urQRd - speed and robustness compared to Cadzow
  - SANE - choosing a better basis

    - new SVD approach
    - examples in FT-ICR
        - 1D and 2D
- concepts in 2D 5 min
    - basis
        - what drives resolution
        - difference between F1 and F2
    - example with Narrow Band 2D
- some more mathematics 10 min
    - amplitude modulation and phase modulation
    - phase in 2D
    - hypercomplex numbers
- phase sensitive absorption 15 min
    - phase in F2
    - phase in F1
    - results
- conclusion 2 min

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2D NMR

- 1st idea of 2D Fourier Transform in NMR *J.Jeener 1973* $t = 0$
- 1st idea of correlation 2D *R.Ernst ~1976*
  - via a strange quantic effect of spins
- 1st implementation in chemistry lab ~1980 *(I was there)* $\Delta t = 7y$
  - computers were quite uncommun in the lab at that time
- practice of phasing of 2D NMR spectra, *~1985* $\Delta t = 12y$
  - realizing that there are several modulation modalities.
- 1st understanding of what is actually 2D Fourier Transform in NMR *1987-1988* $\Delta t = 15y$!!!
  - allows to actually rephase 2D spectra

for an early history of 2D FT-ICR-MS, check G.Bodenhausen manuscript on preprints.org (https://www.preprints.org/manuscript/202104.0335/v1) .

2D spectroscopy requires a different Mathematics

not directly available to common sense

has an impact on experiment planning *(at least in NMR)*

⇒ has a deep impact on software organisation

Spike organisation 15 min

Spike organisation

I have been working on the Spike documentation lately, you can check it here: github.com/spike-project/spike/#readme (https://github.com/spike-project/spike/#readme) and all the links therein.

In particular, this is covered in Development Guide (https://github.com/spike-project/spike/blob/master/DevelopmentGuide.md)

- dataset (NPK) object
- memory

- processing pipeline
- user interface

Spike is not a program !

It is a python library, that you have to use to process your datasets.

Starting with NMR, It was actually extended to FTICR and even ORBITRAP

user interface

it can used through:

- a python program 😰

- a python notebook, which includes program and graphics 😑

- an interactive notebook, (nearly) no programming, just the mouse 😋

A dataset is a python object

All datasets in Spike are handled through an `NPKData` object, composed of:

- a large n-dimensional real `numpy` nparray object that contains the actual spectroscopic data
  - modified by all the processing methods, called `buffer` and accessed with the `d.get_buffer()` and `d.set_buffer()` methods
- one Axis() object per dimension, which contains all the characteristics along the given axis (calibration, data-type, size, etc…)
  - `d.axis1` for a 1D spectrum
  - `d.axis1` and `d.axis2` for a 2D spectrum - with the `d.axes(i)` convenient method
- some attibutes general to the dataset, in particular the `d.params` which contains a copy of the acquisition parameters, structured as a dictionnary
- a large (and expandable) set of methods that act on the dataset

These several kind of NPK dataset are defined in `spike.NMR` `spike.FTICR` and `spike.Orbitrap` which are typically imported in the beginning of a program.

acting on the object

a typical 1D analysis:

```
from spike.File.Solarix import Import_1D    # load the Impo
rter
d = Import_1D(myfile)   # use the specific importer (for in
stance)
d.hanning()             # apodisation
d.zf(2)                 # zero-filling twice
d.rfft()                # real fast Fourier transform
d.modulus()             # take the modulus
d.set_unit('m/z')       # display in m/z units  (Hz and ind
ex also available)
d.display()             # show the results (assuming calibr
ation was ok)
```

you can do as well

```
# processing as a pipeline
```

Methods act on and modify the object itself ⇒ behaviour in previous slide

Another very typical usage:

- Import the dataset and just test some feature
- no modification it.
- use `.copy()` for this which duplicates the whole objet

```
d = Import_1D(myfile)       # use the specific importer to
load the dataset
d.copy().hamming().rfft().display()     # and use copy() in
the pipeline
                                        # to look at it wit
hout modifying d
```

- minimal amount of memory
- does not clutter your variable space.

The Axis() object

`Axis()` contains all the metadata needed to handle the different unit.

`ML1` `ML2` `ML3` parameters in Bruker imported as `CalibA`, `CalibB`, `CalibC` *(with a caveat, check documentation).*

permits to convert from one unit system to another freely and back, with methods called `.ytox(val)` which computes the value of `val` from unit `y` into unit `x`, and `.xtoy()` which performs the opposite.

For instance in FTICR

```
d.axis1.mztoi(138.85)   # returns the index at which the m/
z 138.85 is located
d.axis2.itos(1234)      # returns the t1 time of the transi
ent at index 1234 along F2 for a 2D
d.axis1.htomz(1000)     # returns the mz value located at 1
000 Hz
```

These are just a few examples.

some useful mathematics 10 min

some useful mathematics

- the exponential function Remember "it only grows by 10% every week" ?

$$C_{n+1} = 1.1C_n$$

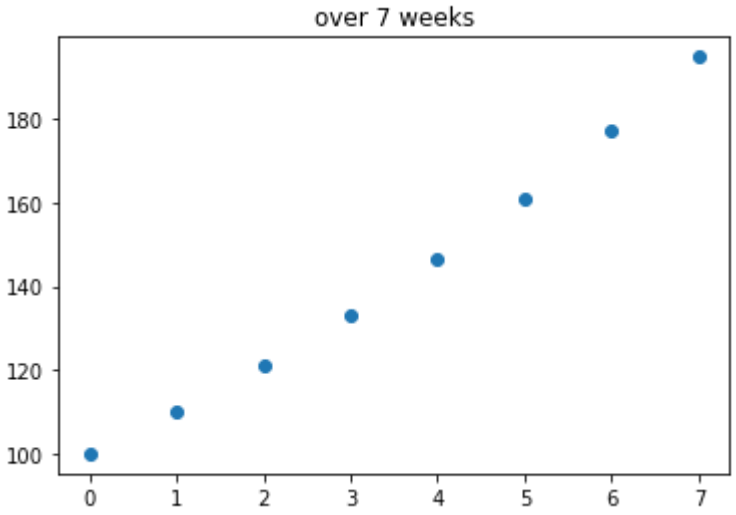
or, with $R = 1.1$

$$C_{n+1} = RC_n$$

and actually, starting at C_o, we have:

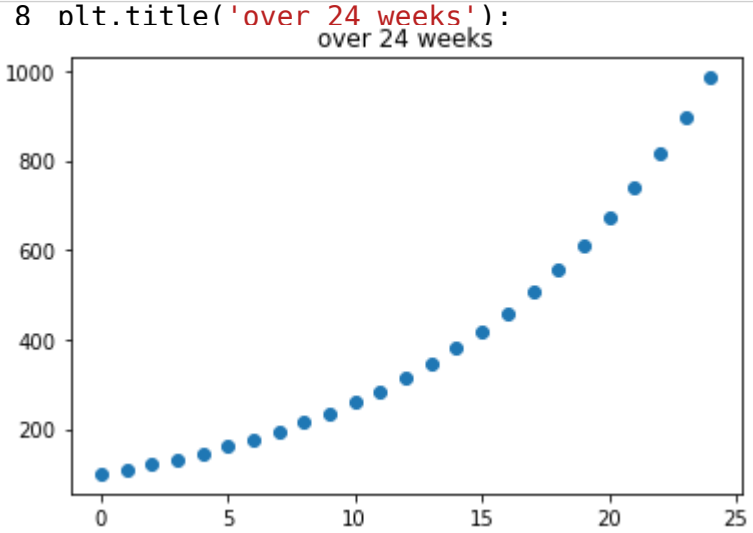
$$C_n = R^n C_o$$

In [3]:
```
# over 7 weeks
weeks = np.arange(8)
Covid = 100*np.ones(8)
plt.figure(figsize=(6,4))
for i in range(1,8):
    Covid[i] = 1.1*Covid[i-1]
plt.scatter(weeks, Covid)
plt.title('over 7 weeks');
```



In [4]:
```
# over 24 weeks
weeks = np.arange(25)
Covid = 100*np.ones(25)
```

```
plt.figure(figsize=(6,4))
for i in range(1,25):
    Covid[i] = 1.1*Covid[i-1]      # 10% per week
plt.scatter(weeks, Covid)
plt.title('over 24 weeks');
```



but if you want to make it continuous, you need a special function $\Rightarrow \exp(t)$

$$C(t) = C_o exp(R't)$$

somehow, $\exp()$ acts like a *continuous* exponent.

That's why it is sometimes noted

$$e^{R't} = \exp(R't)$$

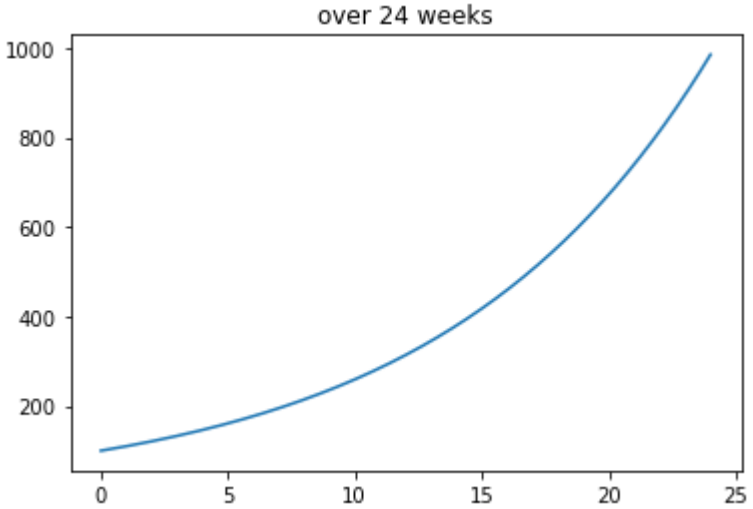
R' is such that $exp(R't)$ when $t = 1$ is 1.1

$$R' = \log(1.1) = 0.0953$$

$\log$ is the *reciprocal* function of $\exp$,

i.e. if $A = \exp(a)$ then $a = \log(A)$

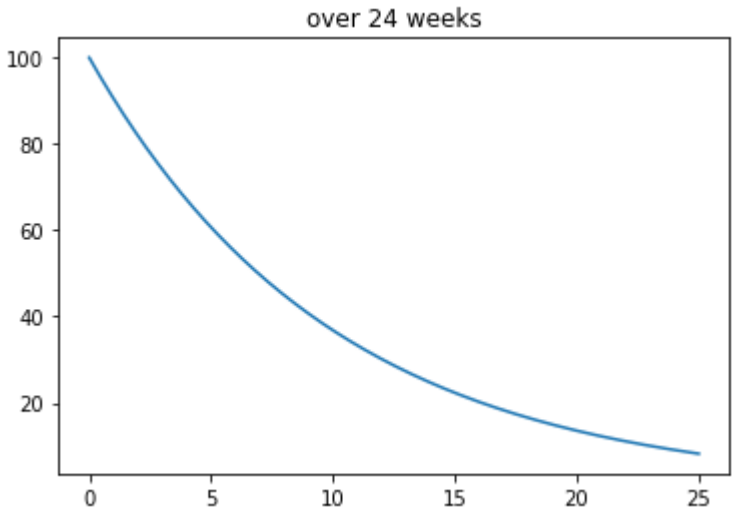
In [5]:
```
# continuous evolution over 24 weeks
time = np.linspace(0,24,1000)      # from 0 to 25 in 1000 point
Rprime = np.log(1.1)
Co = 100
Covid = Co * np.exp(Rprime*time)   # Covid = Co exp(R't)
plt.figure(figsize=(6,4))
plt.plot(time, Covid)
plt.title('over 24 weeks');
```



with a R<0

In [6]:
```
# continuous evolution over 24 weeks with
time = np.linspace(0,25,1000)     # from 0 to 25 in 1000 points
Rprime = -0.1 #np.log(0.9)
print("R' =", Rprime)
Co = 100
Covid = Co * np.exp(Rprime*time)  # Covid = Co exp(R't)
plt.figure(figsize=(6,4))
plt.plot(time, Covid)
plt.title('over 24 weeks');
```

```
R' = -0.1
```



and R = 0 means no evolution

multiplicative rules

the exp() is similar to a continuous exponent and follows the same rules than exponents:

$$\exp(a+b) = \exp(a)\exp(b) \quad (1)$$
$$\exp(2a) = \exp(a)^2$$
$$\exp(na) = \exp(a)^n$$

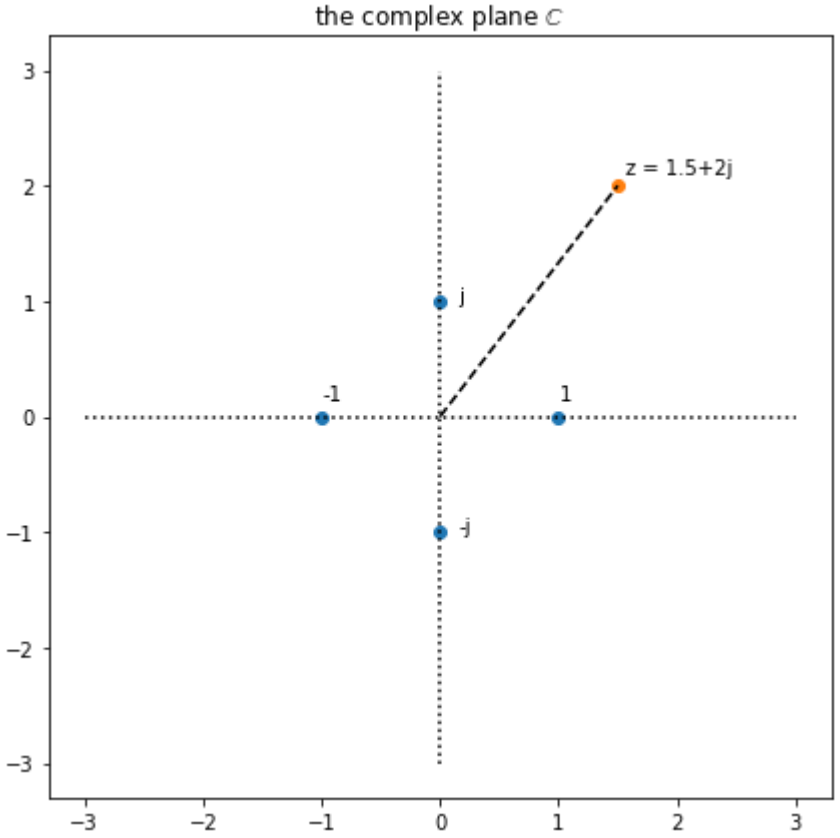
In [7]:
```
def drawaxes():
    plt.plot([-3,3],[0,0],':k') # the real axis
    plt.plot([0,0],[-3,3],':k') # the imaginary axis
    plt.scatter([1,0,-1,0],[0,1,0,-1])
    plt.text(1,0.15,'1')
    plt.text(-1,0.15,'-1')
    plt.text(0.15,1,'j')
    plt.text(0.15,-1,'-j')
    plt.title('the complex plane $\mathbb{C}$')
def drawcpx(z, name='z'):
    plt.scatter(z.real, z.imag)
    plt.plot([0,z.real],[0,z.imag],'--k')
    plt.text(1.05*z.real, 1.05*z.imag,'%s = %s'%(name,str(z)[1:
```

complex numbers

A very smart method to handle 2D values. *Check github.com/delsuc/Fourier_Transform/complex_reminder.ipynb (https://github.com/delsuc/Fourier_Transform/blob/master/complex_reminder.ipynb) .*

- ⇒ two values (x & y) to store, noted along two axes 1 *(real part)* and j *(imaginary part)*
- space called $\mathbb{C}$
- a position in the plane determines a point, but also a **length** and an **angle**

In [8]:
```
# let's draw this using 2 little utilities defined in backgroun
plt.figure(figsize=(7,7))
drawaxes()
z = 1.5 + 2j
drawcpx(z)
```

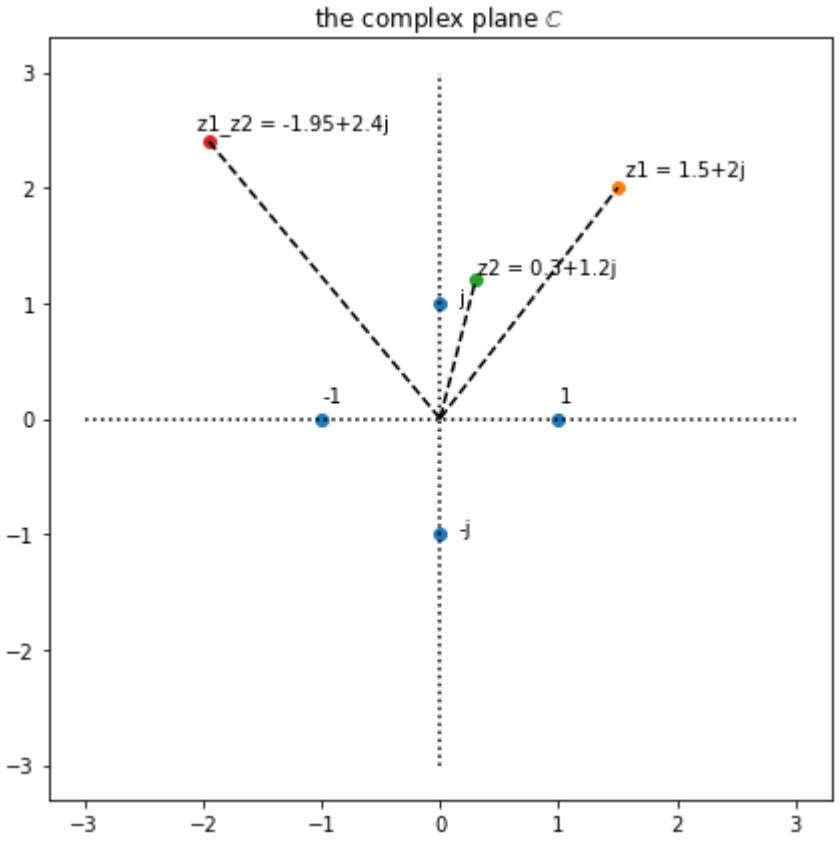


you can do addition, and multiplication

- addition of complexes is adding both real and imaginary part. ≡ to adding vectors.
  - No big deal
- multiplication of complexes is multiplying **lengths** (people say "modulus") and adding **angles**

In [9]:
```
# let's draw this
plt.figure(figsize=(7,7))
drawaxes()
z1 = 1.5 +2j
```

```
z2 = 0.3 + 1.2j
z1_z2 = z1*z2
for nz in ('z1','z2','z1_z2'):
    drawcpx(eval(nz), name=nz)
```



- so multiplication by complexes of modulus 1 *(on the unity circle)* is like a pure rotation by the angle of this complex number

Quiz

- what is the angle of the rotation when
  - multiplying by -1
  - multiplying by j
  - multiplying by $-j$
  - multiplying by $\frac{1+j}{\sqrt{2}}$

Quiz - solution

- what is the angle of the rotation when
  - multiplying by -1 180°
  - multiplying by j 90°
  - multiplying by $-j$ -90°
  - multiplying by $\frac{1+j}{\sqrt{2}}$ 45°
  - etc.

complex exponential

Those multiplicative and additive rules fit perfectly the exponential we described earlier.

⇒ let's define the exponential of a complex number:

$\exp(z) = exp(R)exp(j\theta) = R' \exp(j\theta) = R' e^{j\theta}$ (modulus R' and angle θ)

So if we have: $z_1 = R'_1 e^{j\theta_1}$ and $z_2 = R'_2 e^{j\theta_2}$ then

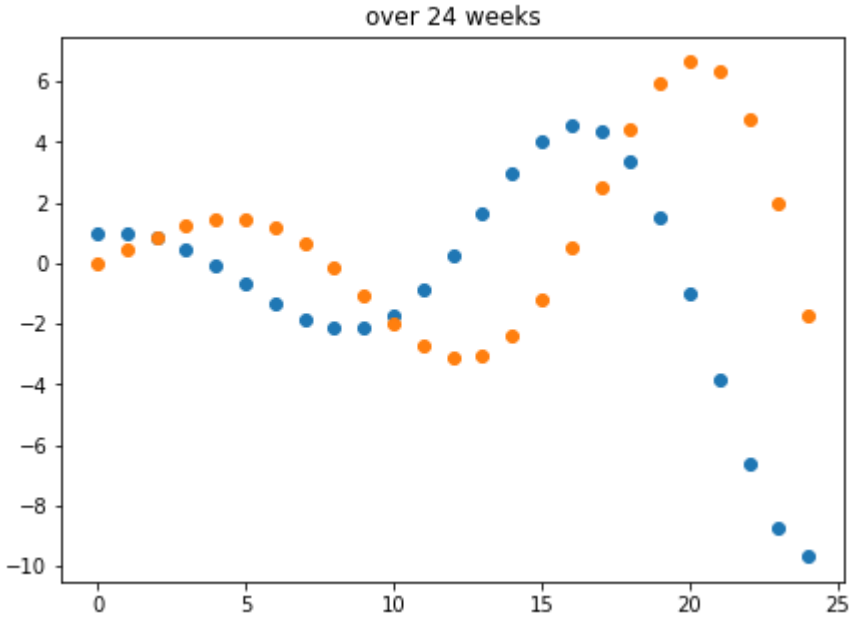
$$z_1 \times z_2 = R'_1 R'_2 e^{j(\theta_1+\theta_2)} \quad (2)$$

just following the rules for the exponential:

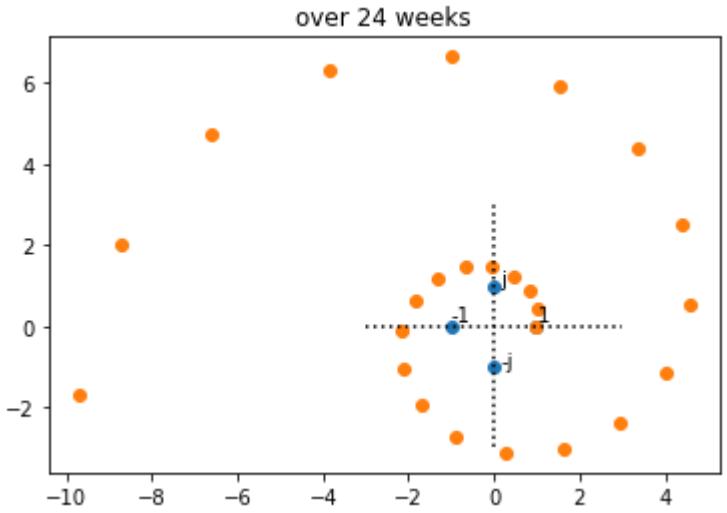
⇒ multiplying **lengths** and adding **angles**

In [ ]:
```
1
```

In [10]:
```
# let's draw this over 24 weeks
weeks = np.arange(25)
Covid = 1*np.ones(25) +0j
for i in range(1,25):
    Z = 1.1*np.exp(0.4j)        # angle of 0.7 radian, modulus o
    Covid[i] = Z*Covid[i-1]     # Z % per week
plt.figure(figsize=(7,5))
plt.scatter(weeks, Covid.real)
plt.scatter(weeks, Covid.imag)
plt.title('over 24 weeks');
```

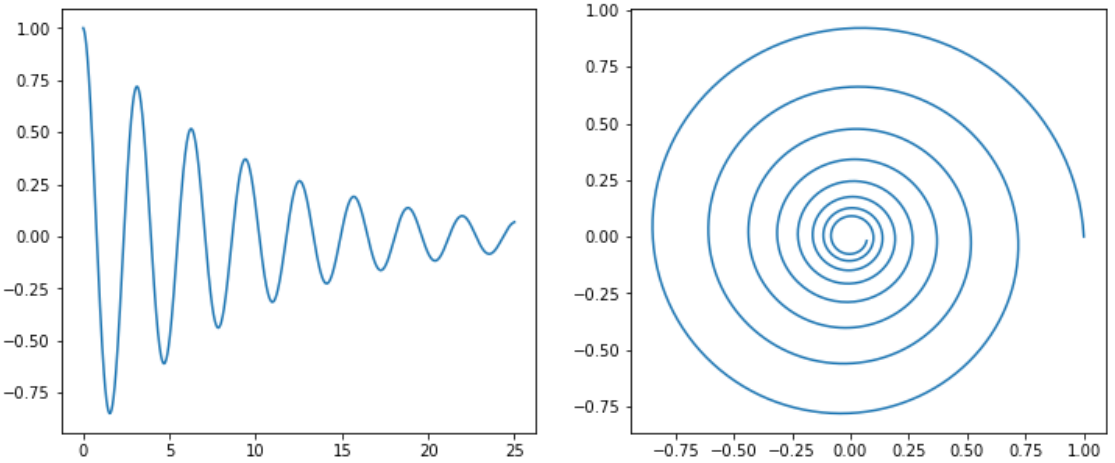


In [11]:
```
# let's draw this over 24 weeks
weeks = np.arange(25)
Covid = 1*np.ones(25) +0j
drawaxes()
for i in range(1,25):
    Z = 1.1*np.exp(0.4j)        # angle of 0.7 radian, modulus o
    Covid[i] = Z*Covid[i-1]     # Z % per week
plt.scatter(Covid.real, Covid.imag)
plt.title('over 24 weeks');
```



with R<0

In [12]:
```
# continuous evolution over 24 weeks
time = np.linspace(0,25,1000)  # from 0 to 25 in 1000 points
Rprime = np.log(0.9)+2j        # angle of 2 radian, modulus of (
Co = 1
Covid = Co * np.exp(Rprime*time)
fig, (axis1, axis2) = plt.subplots(ncols=2, figsize=(12,5))
axis1.plot(time, Covid.real)
axis2.plot(Covid.real, Covid.imag);
```



a damped sinusoid ! ⇒ not so different from a FTICR signal !!!

modeling of a "harmonic" signal

- one line, decay at rate R (negative) and rotation at speed θ:

$$S(t) = A\exp(Rt)\exp(j\theta t) \tag{3}$$

- if regularly sampled at time $t_n = n\Delta t$, it becomes

$$S_n = A\exp(nR\Delta t)\exp(nj\theta\Delta t) = A\exp(R\Delta t + j\theta\Delta t)^n = AZ^n$$

with $Z = \exp(R\Delta t + j\theta\Delta t)$

- in other words, we have a regression form:

$$S_n = ZS_{n-1} \tag{4}$$
$$S_o = A$$

A is the amplitude of the signal *(can be complex ⇒ phase)*
Z is the characteristic pole of this "harmonic" signal

extended to more than one line:

for K different lines, with intensities A_k and "poles" Z_k we have:

$$S_n = W_1S_{n-1} + W_2S_{n-2} + W_3S_{n-3}\cdots W_KS_{n-K} \tag{5}$$

where the W_k uniquely depend on the Z_k *(in a complicated way)*
and $[S_1 \cdots S_K]$ depend on the A_k

Here eq(5) represents the **Autoregressive model (AR)** of this harmonic signal
*(aka **Linear Prediction** model)*

Hankel matrix and the AutoRegressive model

eq(4) can be written for any points of the sampled signal (except the K first points)

we write the following $M \times (N-M)$ matrix $\mathbf{H}$ $\quad H_{i,j} = S_{i+j-1}$:

$$\mathbf{H} = \begin{vmatrix} S_1 & S_2 & S_3 & \cdots & S_{N-M} \\ S_2 & S_3 & S_4 & \cdots & S_{N-M+1} \\ S_3 & S_4 & S_5 & \cdots & S_{N-M+2} \\ \vdots & & & \ddots & \\ S_M & S_{M+1} & S_{M+2} & \cdots & S_N \end{vmatrix} \tag{6}$$

$\mathbf{H}$ is a **Hankel** matrix. *(Toeplitz matrices tell a miror image story)*
Because of AR, the rank of $\mathbf{H}$ is K *(in a noise free system)*

Note how S_n with $n : [1 \cdots N]$: runs on the edge of $\mathbf{H}$

circulant matrices

$\mathbf{H}$ is a circulant matrix (*circulating* a single vector)

Multiplication with such a matrix ≡ Convolution with the generating vector.

Convolution can be performed efficiently with Fast Fourier Transform (FFT)

Computation time $O(N^2) \rightarrow O(N \log N)$

if 1k takes 1 msec for both, 1M will take 10sec instead of 16min

In [13]:
```
1E6/1000/60. 10*1000
```

Out[13]:
```
(16.666666666666668, 10000)
```

and limitations

urQRd, SANE and more 15 min

Noise reduction - Cadzow's method (1988)

From a signal S we can build a $M \times (N - M)$ matrix $\mathbf{H}$ If *noise-free* $\text{rank}(\mathbf{H}) = K$

but usually there is noise, so rank is not limited anymore

Cadzow approach[1] is

- from S compute $\mathbf{H}$
- extract the **SVD** of $\mathbf{H}$ *(slow - memory hungry)*
- truncate **SVD** to K *(if K signals are expected)*
- from truncation, rebuild $\mathbf{H}$ then S
- iterate

Very efficient (used in many techniques)
BUT this is *slooow* and unrealistic for large S $(N > 10.000)$

1. Cadzow JA *IEEE Trans. ASSP* **36** p49-62 (1988)

Noise reduction - urQRd[1] (2014)

Same as Cadzow, *but...*

- Truncate $\mathbf{H}$ first, thanks to *random projection* theorem
- use **QR** to estimate **SVD** from truncated $\mathbf{H}$ *(fast)*
- from **QR** decomposition, rebuild $\mathbf{H}$ then S
- iterate

plus...

- use FFT trick to compute all matrix products *(reduces the memory burden)*

1.Chiron L., van Agthoven M. A., Kieffer B., Rolando C., Delsuc M-A. *Proc Natl Acad Sci USA*,

Noise reduction - urQRd[1] (2014)

Same as Cadzow, *but*...

- Truncate $\mathbf{H}$ first, thanks to *random projection* theorem urQRd
- use **QR** to estimate **SVD** from truncated $\mathbf{H}$ urQRd
- from **QR** decomposition, rebuild $\mathbf{H}$ then S urQRd
- iterate

plus...

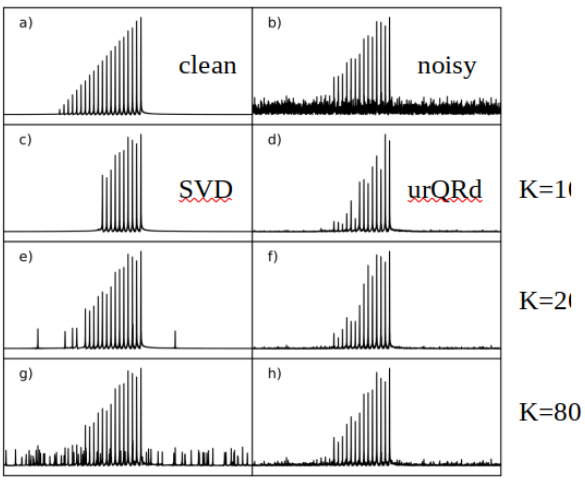
- use FFT trick to compute all matrix products. urQRd

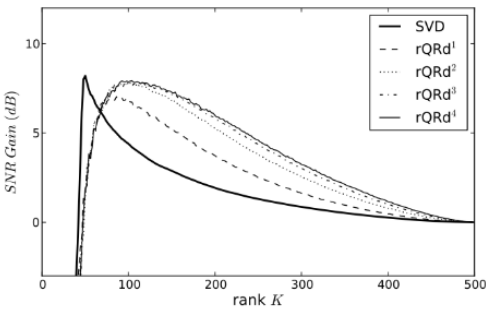
1.Chiron L., van Agthoven M. A., Kieffer B., Rolando C., Delsuc M-A. *Proc Natl Acad Sci USA*, **111** (4) :1385–1390, (2014)

H (M x N_M) O (N-M K) = H' (M x K) tH' = Q (K K) R (K M) Q Q* H = H"

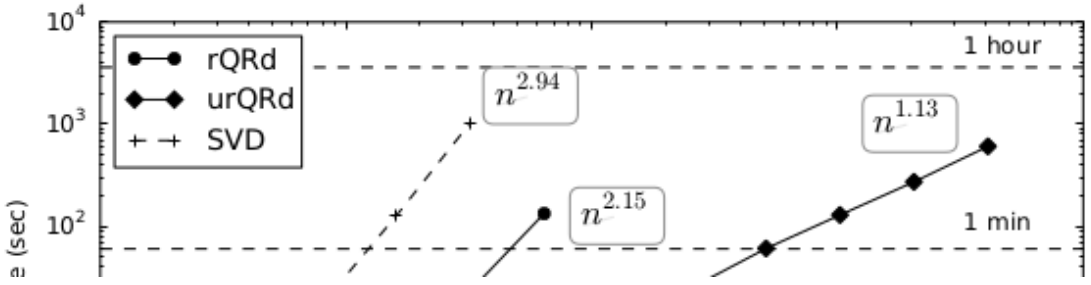
urQRd - speed and robustness compared to Cadzow

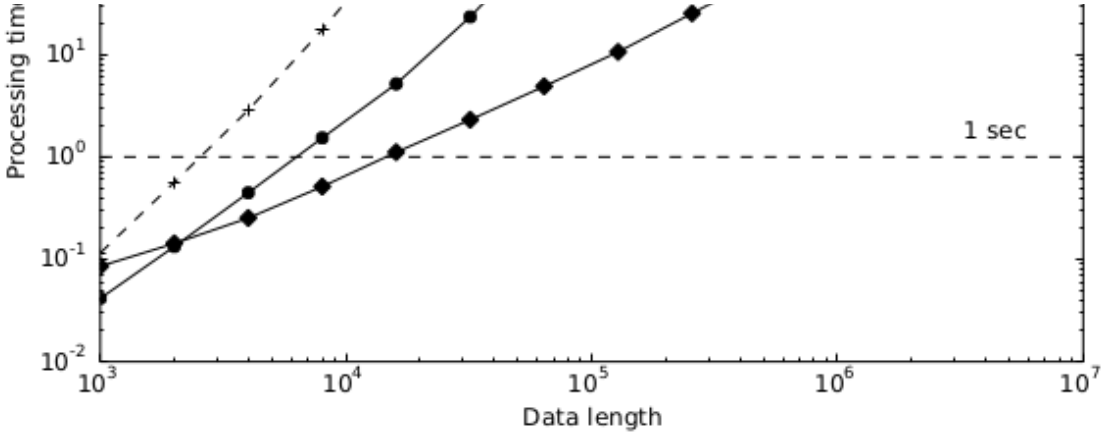
on a synthetic dataset





urQRd - speed and robustness compared to Cadzow





- less memory burden
- theoretical processing time in $KN \log N$ with $K \ll M < N$

SANE - choosing a better basis

Quiz! *find the differences*

(u)rQRd

Algorithm S1 rQRd

given a time series X, rank K and order M, returns $\tilde{X}$ a denoised approximation of X
Require: $X, K, M \quad K \leq M \leq length(X)/2$
Require: Function RANDOM : $n, p \mapsto \Omega$ ▷ Ω a $\mathcal{N}(0,1)$ $n \times p$ matrix
Require: Function QR : $A \mapsto Q, R$ ▷ the QR decomposition of A
$L \leftarrow$ LENGTH(X)
$N \leftarrow L - M + 1$
$X^1 \leftarrow X$ ▷ initialize vector to process
for $k \leftarrow 1, ITER$ **do** ▷ main iteration loop
  for $i \leftarrow 1, M \quad j \leftarrow 1, N$ **do**
    $H_{ij} \leftarrow X^k_{i+j-1}$ ▷ H is a $M \times N$ matrix
  end for
  $\Omega \leftarrow$ RANDOM(N, K)
  $Y \leftarrow H\Omega$
  $(Q, R) \leftarrow$ QR(Y)
  $\tilde{H} \leftarrow QQ^*H$
  for $l \leftarrow 1, L$ **do**
    $X^{k+1}_l \leftarrow \langle \tilde{H}_{ij} \rangle_{i+j=l+1}$
  end for
end for
return X^{ITER}

SANE

Algorithm S2 SANE

given a time series X, rank K and order M, returns $\tilde{X}$ a denoised approximation of X
Require: $X, K, M \quad K \leq M \leq length(X)/2$
Require: Function RANDOM : $n, p \mapsto \Omega$ ▷ Ω a $\mathcal{N}(0,1)$ $n \times p$ matrix
Require: Function QR : $A \mapsto Q, R$ ▷ the QR decomposition of A
$L \leftarrow$ LENGTH(X)
$N \leftarrow L - M + 1$
$X^1 \leftarrow X$ ▷ initialize vector to process
for $k \leftarrow 1, ITER$ **do** ▷ main iteration loop
  for $i \leftarrow 1, M \quad j \leftarrow 1, N$ **do**
    $H^k_{ij} \leftarrow X^k_{i+j-1}$ ▷ H is a $M \times N$ matrix
  end for
  $\Omega \leftarrow$ RANDOM(N, K)
  $Y \leftarrow H^k\Omega$
  $(Q, R) \leftarrow$ QR(Y)
  $\tilde{H} \leftarrow QQ^*H^1$ ▷ **difference is here, keeping original data**
  for $l \leftarrow 1, L$ **do**
    $X^{k+1}_l \leftarrow \langle \tilde{H}_{ij} \rangle_{i+j=l+1}$
  end for
end for
return X^{ITER}

SANE - choosing a better basis

urQRd

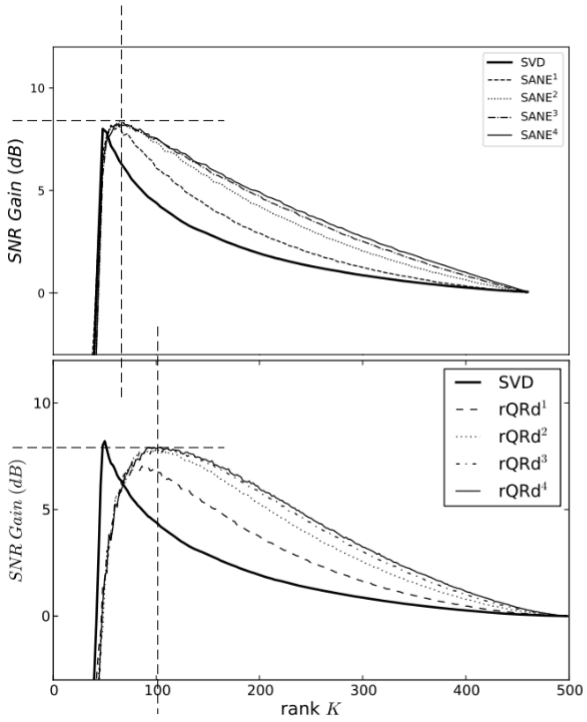
for $k \leftarrow 1, ITER$ **do**
  for $i \leftarrow 1, M \quad j \leftarrow 1, N$ **do**
    $H_{ij} \leftarrow X^k_{i+j-1}$
  end for
  $\Omega \leftarrow$ RANDOM(N, K)
  $Y \leftarrow H\Omega$
  $(Q, R) \leftarrow$ QR(Y)
  $\tilde{H} \leftarrow QQ^*H$
  for $l \leftarrow 1, L$ **do**
    $X^{k+1}_l \leftarrow \langle \tilde{H}_{ij} \rangle_{i+j=l+1}$
  end for
end for

SANE

for $k \leftarrow 1, ITER$ **do**
  for $i \leftarrow 1, M \quad j \leftarrow 1, N$ **do**
    $H^k_{ij} \leftarrow X^k_{i+j-1}$
  end for
  $\Omega \leftarrow$ RANDOM(N, K)
  $Y \leftarrow H^k\Omega$
  $(Q, R) \leftarrow$ QR(Y)
  $\tilde{H} \leftarrow QQ^*H^1$
  for $l \leftarrow 1, L$ **do**
    $X^{k+1}_l \leftarrow \langle \tilde{H}_{ij} \rangle_{i+j=l+1}$
  end for
end for

SANE vs urQRd

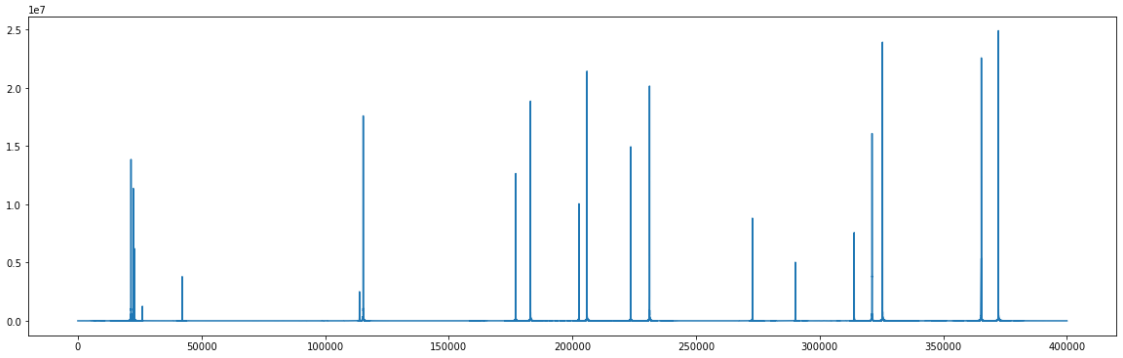
same test on 50 lines.



- Lower rank (+20% instead of x2)
- slightly better noise rejection
- 2 iterations are enough
- Faster !
  - *lower rank*
  - *improved code*

In [14]:
```
1 import figure_sup2 as s2
2 from urQRd import urQRd
3 from sane import sane
4 from figure_sup2 import mfft, gene, SNR
5 data,data0 = gene(lendata=100000, noise=300, noisetype='additiv
6 fig, ax = plt.subplots(figsize=(20,6))
7 plt.plot( mfft(data0) );
8 display(Markdown('## Synthetic dataset with 20 lines'))
```

Synthetic dataset with 20 lines



SANE vs urQRd

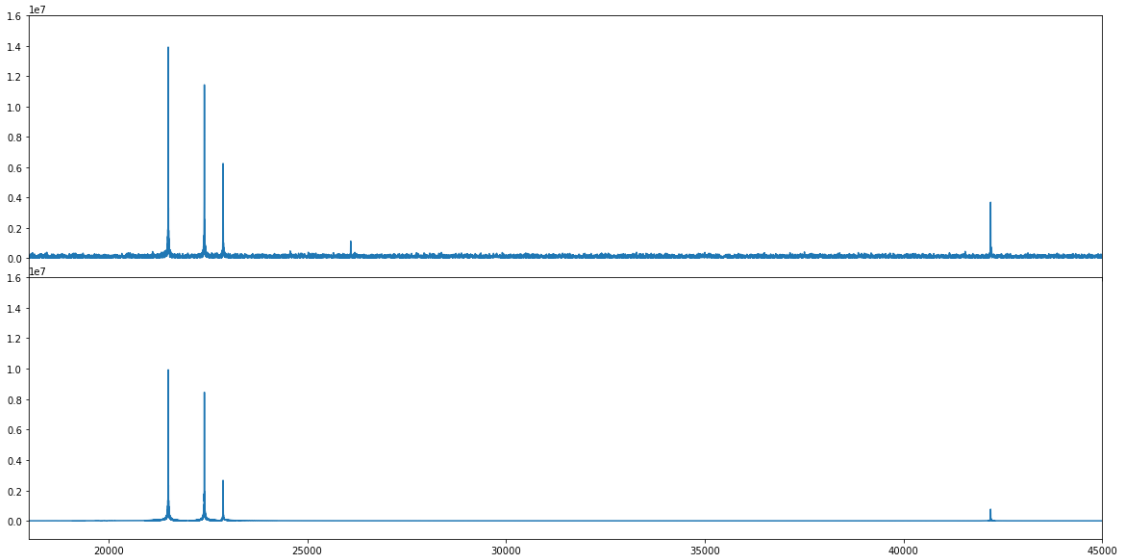
ADDITIVE noise (typically in 1D and along F2 in 2D)

In [15]:
```
1 def compare(noisy, clean):
2     fig, ax = plt.subplots(nrows=2, sharex=True, figsize=(20,10
```

```
    fig.subplots_adjust(hspace=0)
    ax[0].plot( mfft(noisy) )
    ax[1].plot( mfft(clean) )
    ax[0].set_xbound((18000,45000))
    for i in (0,1):
        ax[i].set_ylim(ymax=1.6E7)
```

In [17]:
```
data_urqrd = urQRd(data, k=40, orda=15000, iterations=2) # deno
compare(data, data_urqrd) # defines in the background
display(Markdown('<big>**urQRd** Gain %.1f dB</big>'%SNR(data_u
```

urQRd Gain 14.0 dB

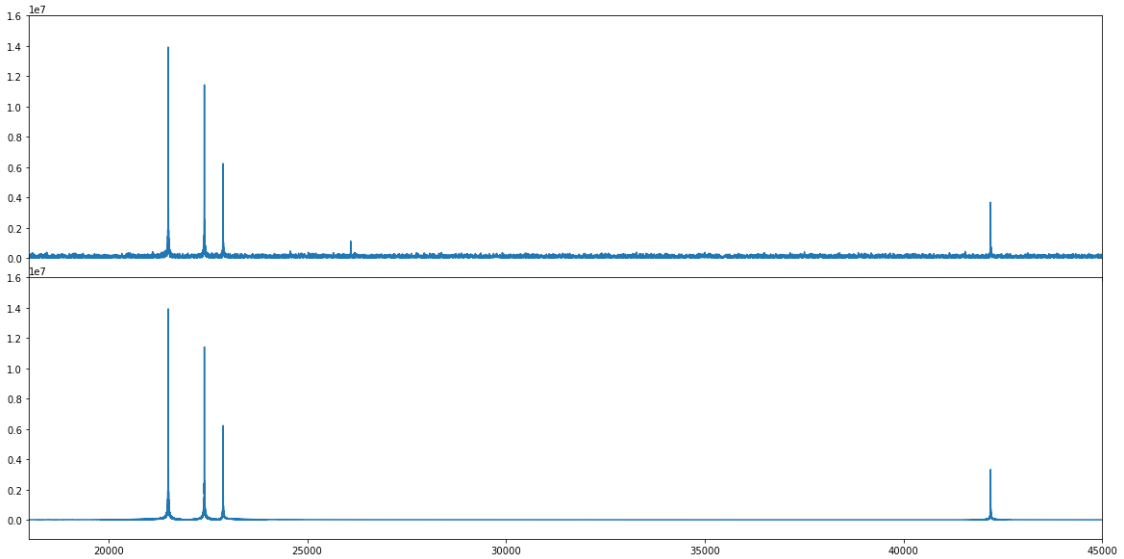


SANE vs *urQRd*

ADDITIVE noise (typically in 1D and along F2 in 2D)

In [18]:
```
data_sane = sane(data, k=24, orda=15000, iterations=2) # denois
compare(data, data_sane)
display(Markdown('<big>**SANE** Gain %.1f dB</big>'%SNR(data_sa
```

SANE Gain 30.1 dB

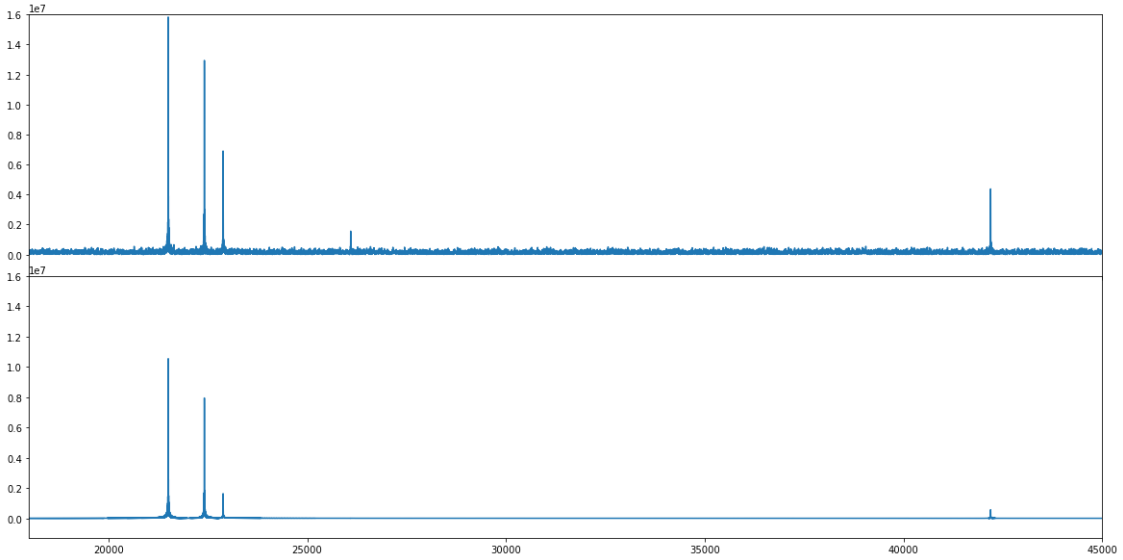


SANE vs urQRd

MULTIPLICATIVE noise (typically along F1 in 2D)

In [19]:
```
data,data0 = gene(lendata=100000, noise=200, noisetype='scintil
data_urqrd = urQRd(data, k=40, orda=15000, iterations=2) # deno
compare(data, data_urqrd)
display(Markdown('<big>**urQRd** Gain %.1f dB</big>'%SNR(data_u
```

urQRd Gain 12.7 dB

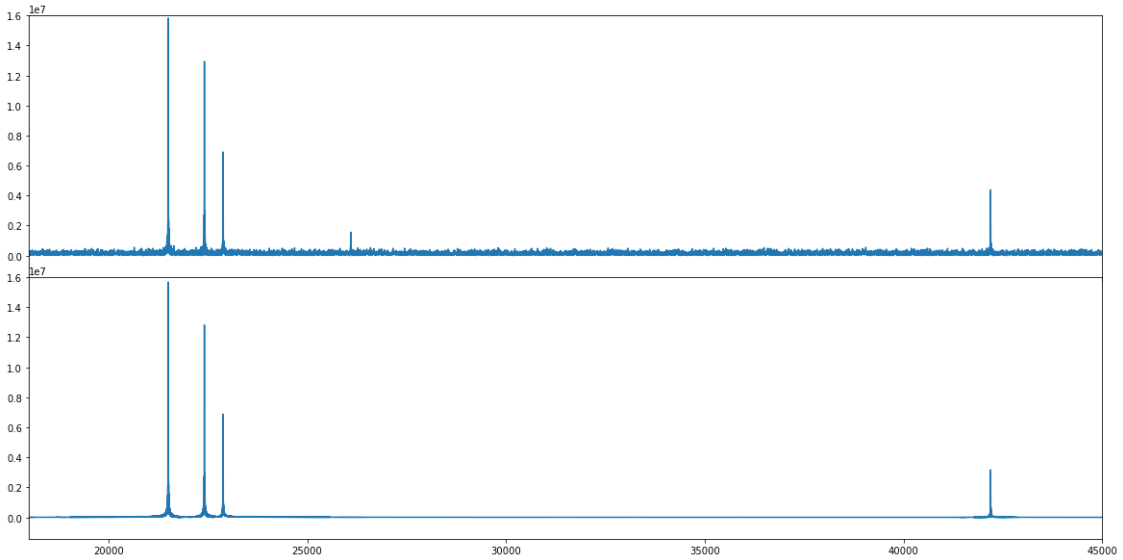


SANE vs *urQRd*

MULTIPLICATIVE noise (typically along F1 in 2D)

In [21]:
```
data_sane = sane(data, k=24, orda=15000, iterations=2) # denois
compare(data, data_sane)
display(Markdown('<big>**SANE** Gain %.1f dB</big>'%SNR(data_sa
```

SANE Gain 14.8 dB

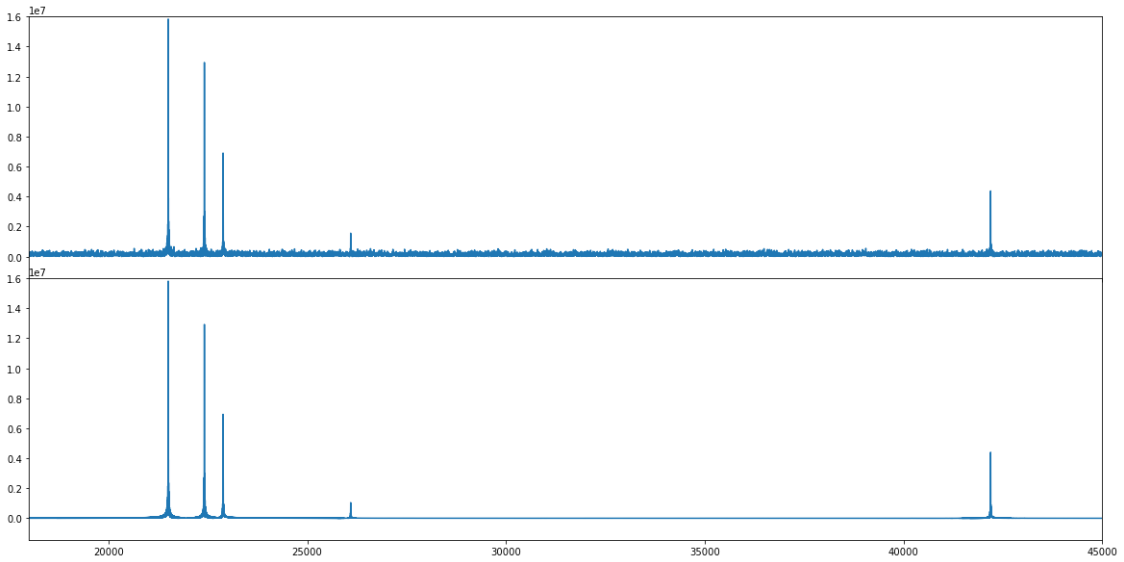


SANE vs *urQRd*

using a larger K on a proposition from Peter:

In [20]:
```
data_sane = sane(data, k=100, orda=15000, iterations=2) # denoi
compare(data, data_sane)
display(Markdown('<big>**SANE** Gain %.1f dB</big>'%SNR(data_sa
```

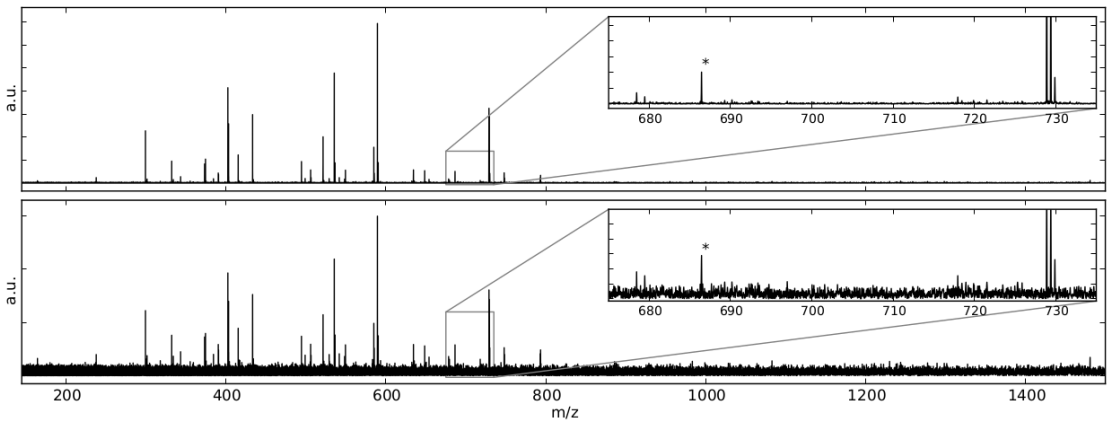
SANE Gain 14.6 dB



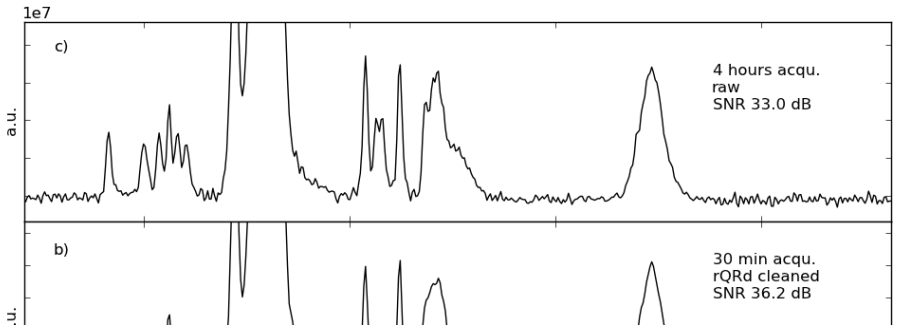
notice how the noise rejection is *officially* not as good (lower gain in dB), the small peaks is beter recovered

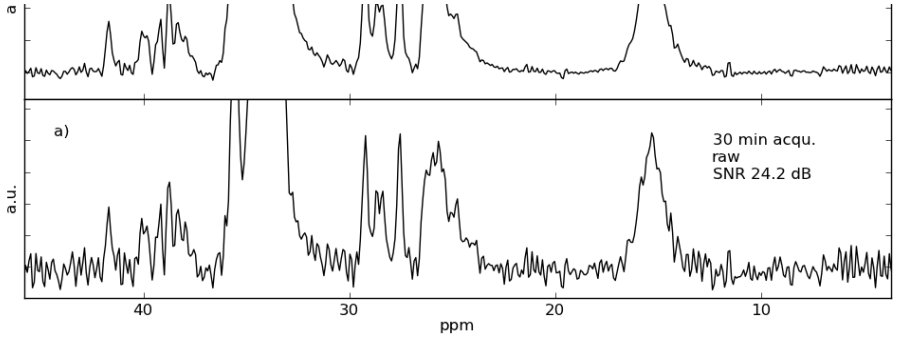
also, it is 100/24 times slower

example in FT-ICR

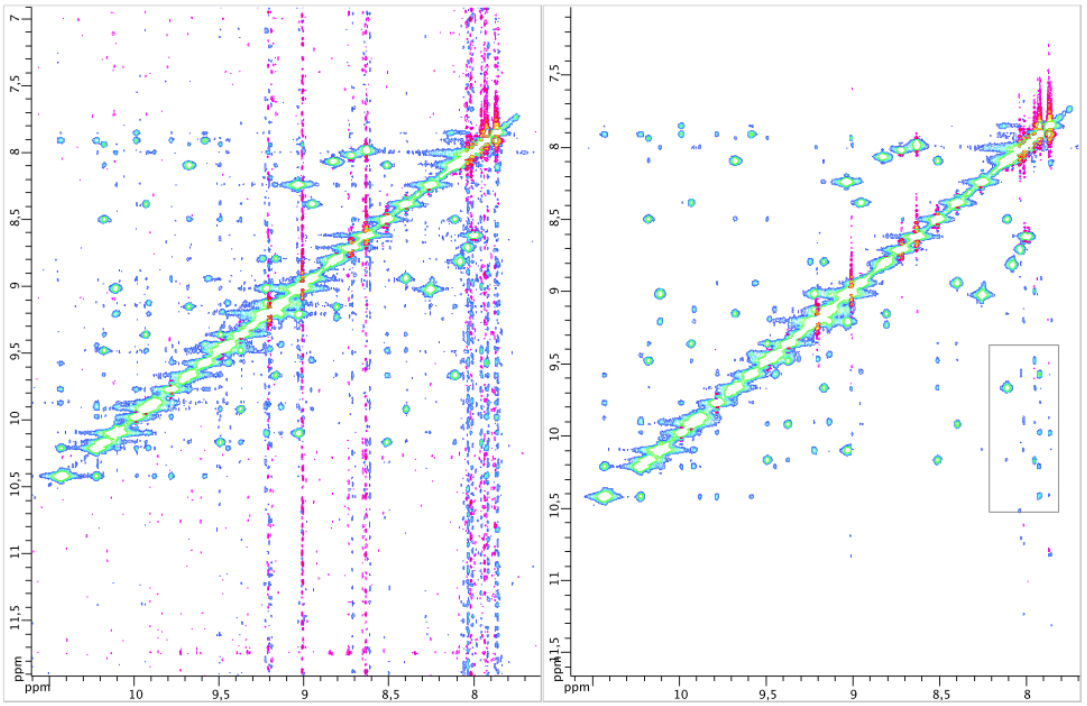


example in 1D ss-NMR





in 2D ^{1}H NMR

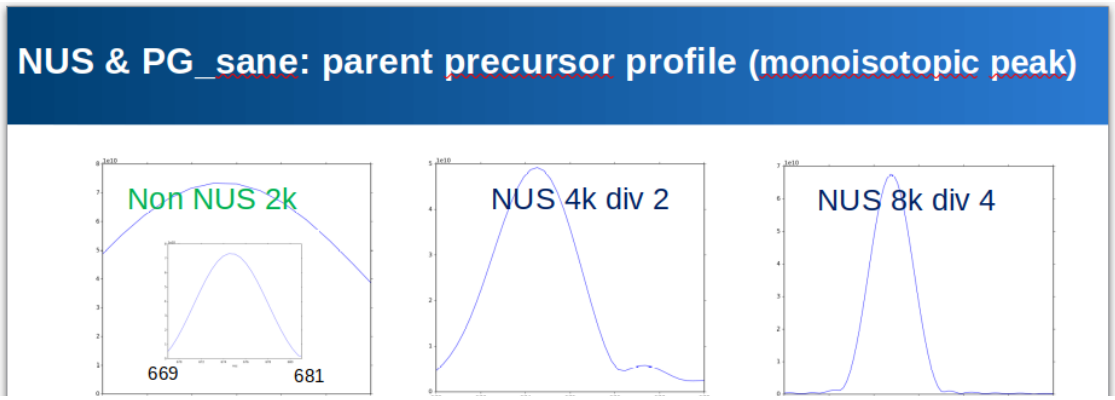


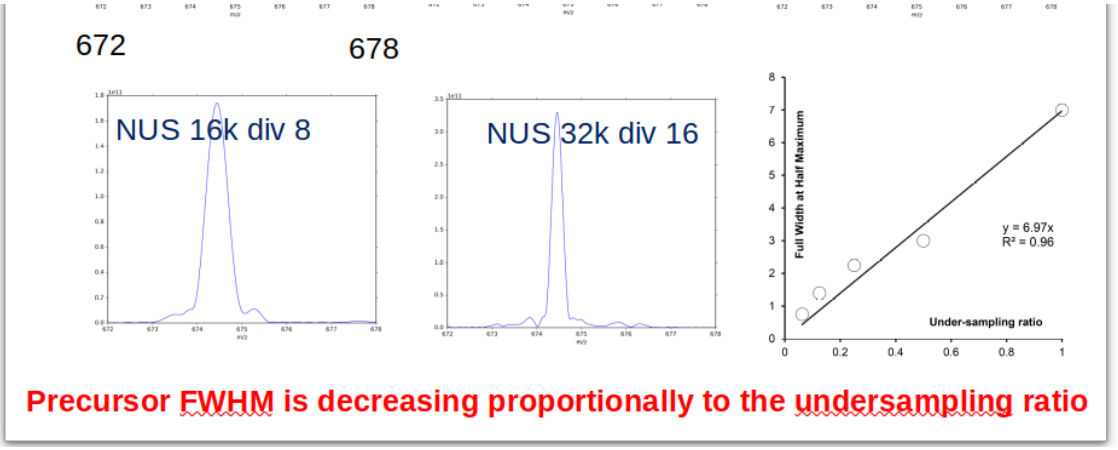
thanks to the symmetry, the weak peaks recovered under the t_1-noise are validated

in Non Uniform Sampling...

it is another story

from C.Rolando presentation





Nonuniform Sampling Acquisition of Two-Dimensional Fourier Transform Ion Cyclotron Resonance Mass Spectrometry for Increased Mass Resolution of Tandem Mass Spectrometry Precursor Ions. Bray F., Bouclon J., Chiron L., Witt M., Delsuc M-A., Rolando C. (2017) *Anal Chem* 10.1021/acs.analchem.7b01850

concepts in 2D 5 min

Narrow Band 2D

what drives resolution in FTICR ?

$$R = \frac{m/z}{\Delta m/z} = \frac{\Delta f}{f} \qquad m/z \propto \frac{B_o}{f}$$

so $R \nearrow$ whenever $\Delta f \nearrow$ and $\Delta f = \frac{1}{2} T_{max}$ does not depends on sampling nor on f.

But large T_{max} requires

- many data-points at constant Spectral BandWidth

or

- reduced BandWidth at constant number of data-points

or

- Non Uniform Sampling → *another story*

difference between F1 and F2

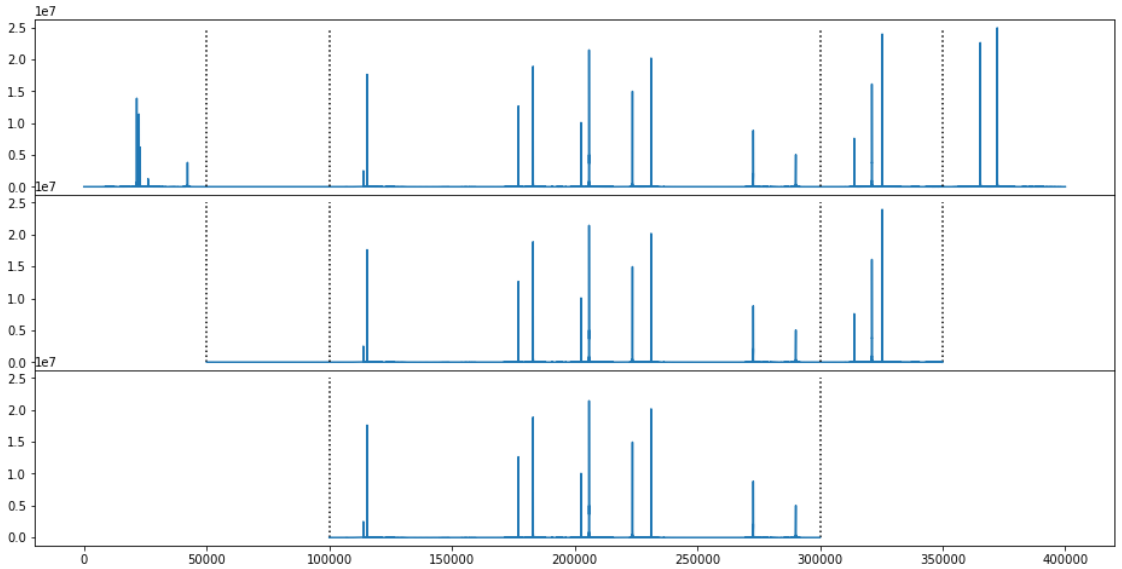
in F2 *(classical axis)*

reducing Bandwidth "zooms" into the spectrum - because of filters

In [24]:
```
1 def F2_BW():
```

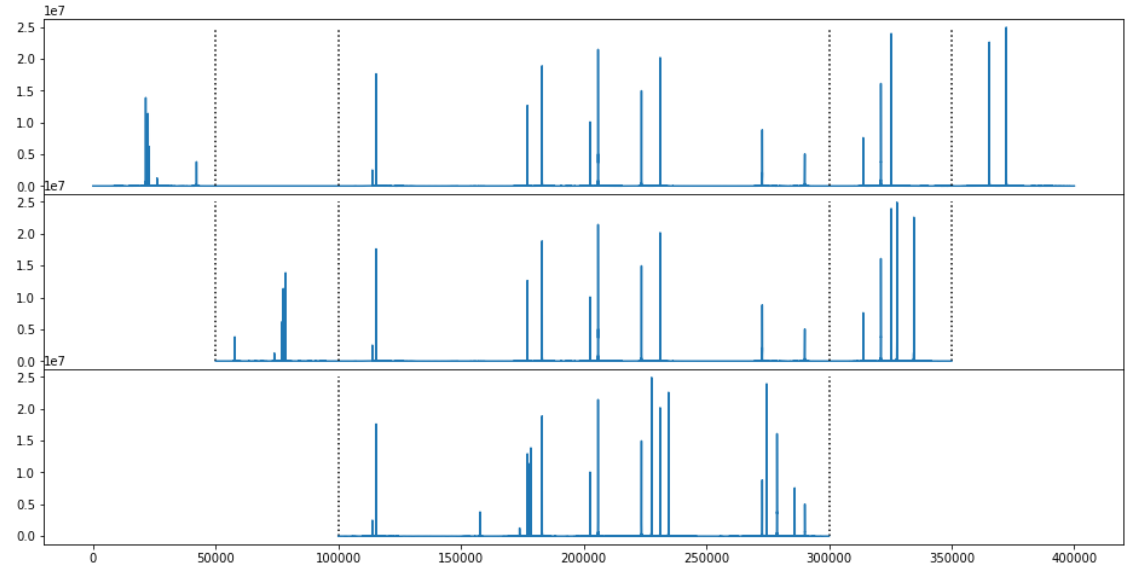
```
    "show the effect of reduced BandWidth on a classical axis"
    D = mfft(data0)
    fig, ax = plt.subplots(nrows=3, sharex=True, figsize=(16,8)
    fig.subplots_adjust(hspace=0)
    ax[0].plot(D)
    for i in range(1,3):
        xm = 50000*i
        xM = len(D)-xm
        for j in range(i+1):
            ax[j].plot([xm,xm],[0,2.5E7],'k:')
            ax[j].plot([xM,xM],[0,2.5E7],'k:')
        D[0:xm] = np.nan
        D[xM:] = np.nan
        ax[i].plot(D)
```

In [23]:
```
F2_BW()
```

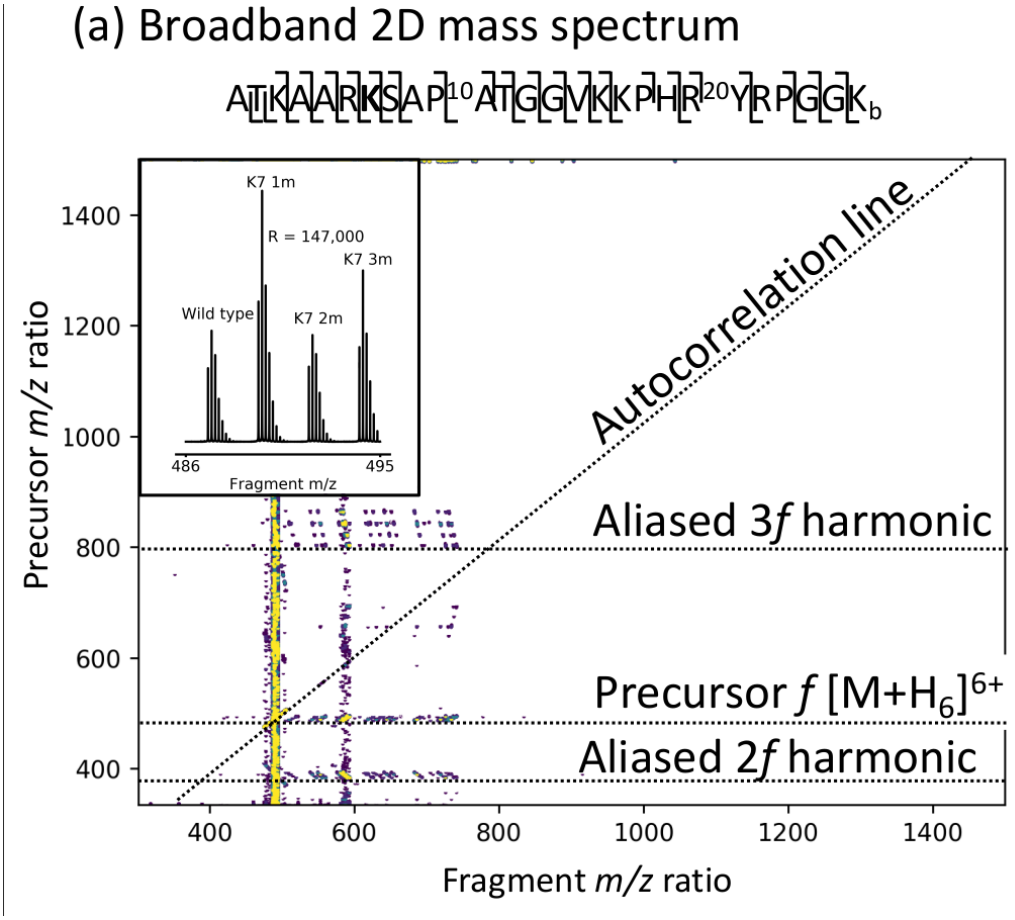


In [44]:
```
def F1_BW():
    "show the effect of reduced BandWidth on a non-classical ax
    D = mfft(data0)
    N = len(D)
    fig, ax = plt.subplots(nrows=3, sharex=True, figsize=(16,8)
    fig.subplots_adjust(hspace=0)
    ax[0].plot(D)
    for i in range(1,3):
        DBW = np.zeros_like(D)
        xm = 50000*i
        xM = len(D)-xm
        for j in range(i+1):
            ax[j].plot([xm,xm],[0,2.5E7],'k:')
            ax[j].plot([xM,xM],[0,2.5E7],'k:')
        DBW[xm:xM] = D[xm:xM]
        DBW[xm:2*xm] += D[xm:0:-1]
        DBW[-2*xm:-xm] += D[-1:-xm-1:-1]
        DBW[0:xm] = np.nan
        DBW[xM:] = np.nan
        ax[i].plot(DBW)
```

In [45]:
```
1 F1.BW()
```

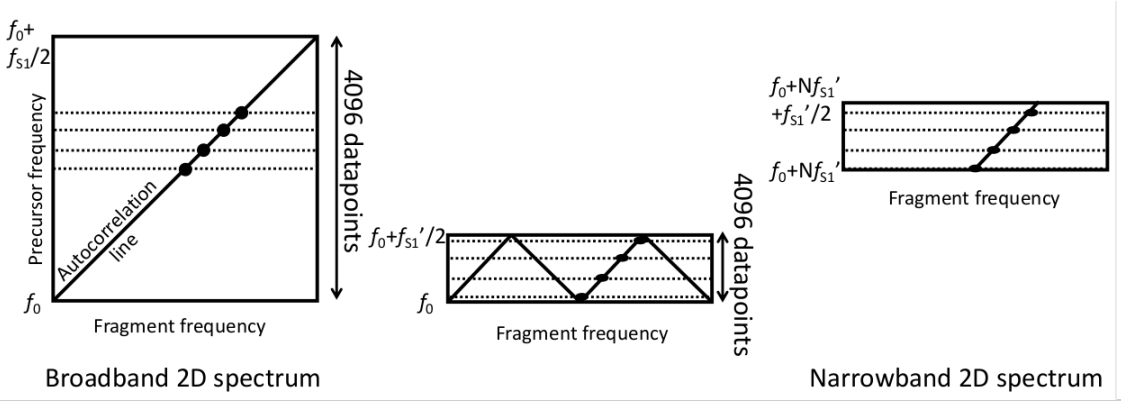


example on histones peptides[1]



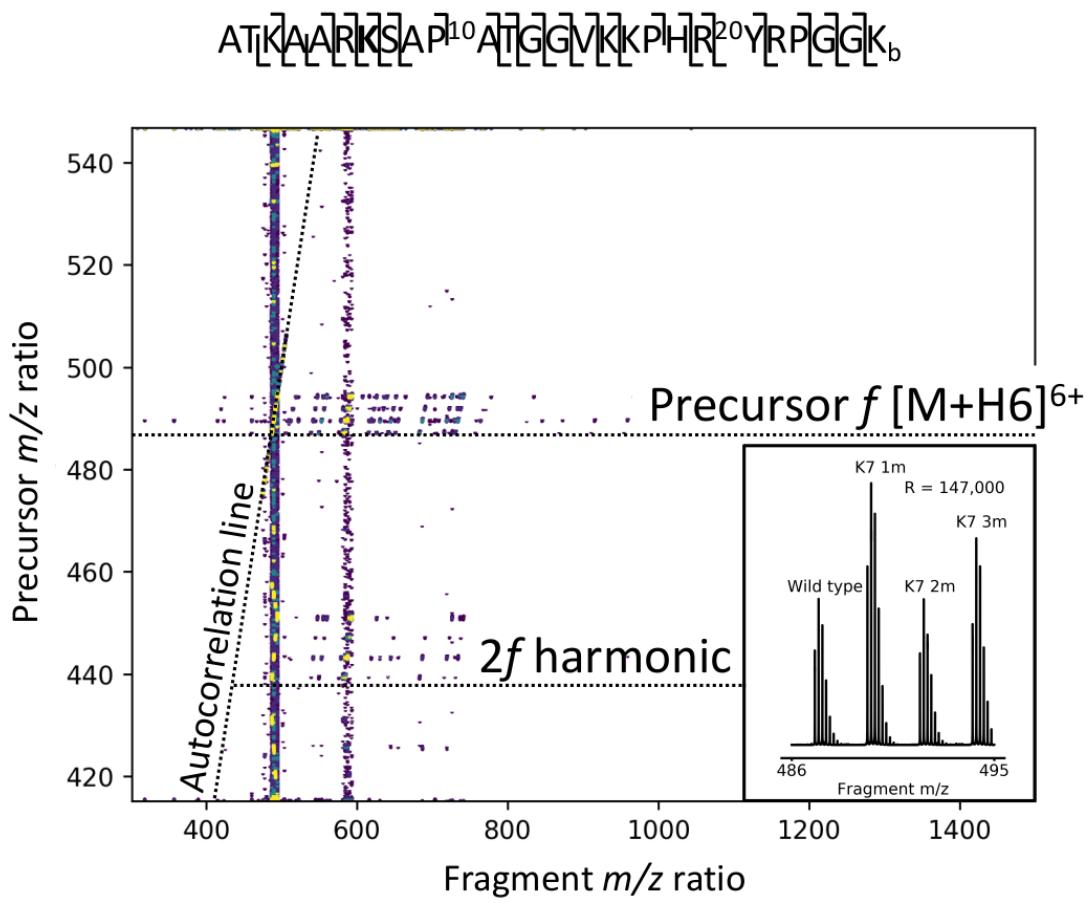
1.Narrowband modulation two-dimensional mass spectrometry and label-free relative quantification of histone peptides
Halper M., Delsuc M-A., Breuker K., van Agthoven M. A. (2020) *Anal Chem*
10.1021/acs.analchem.0c02843

effect of folding in F1



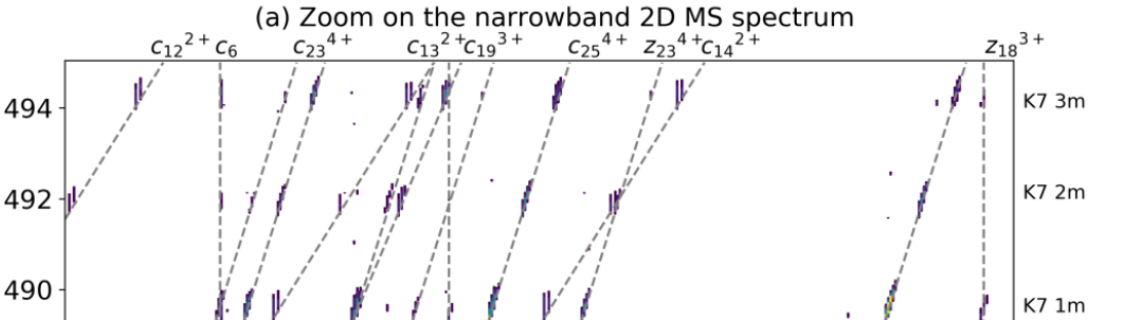
effect of folding in F1

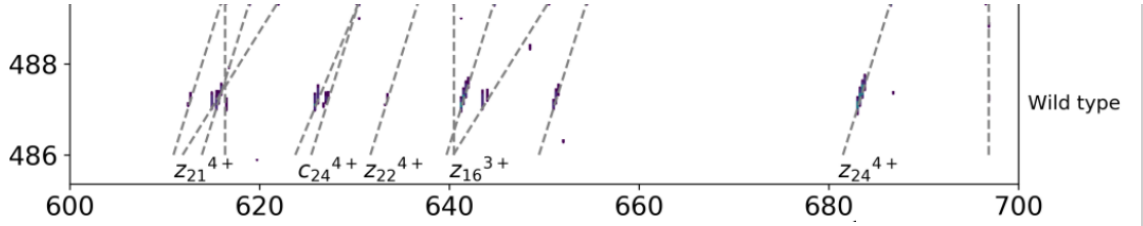
(b) Narrowband 2D mass spectrum



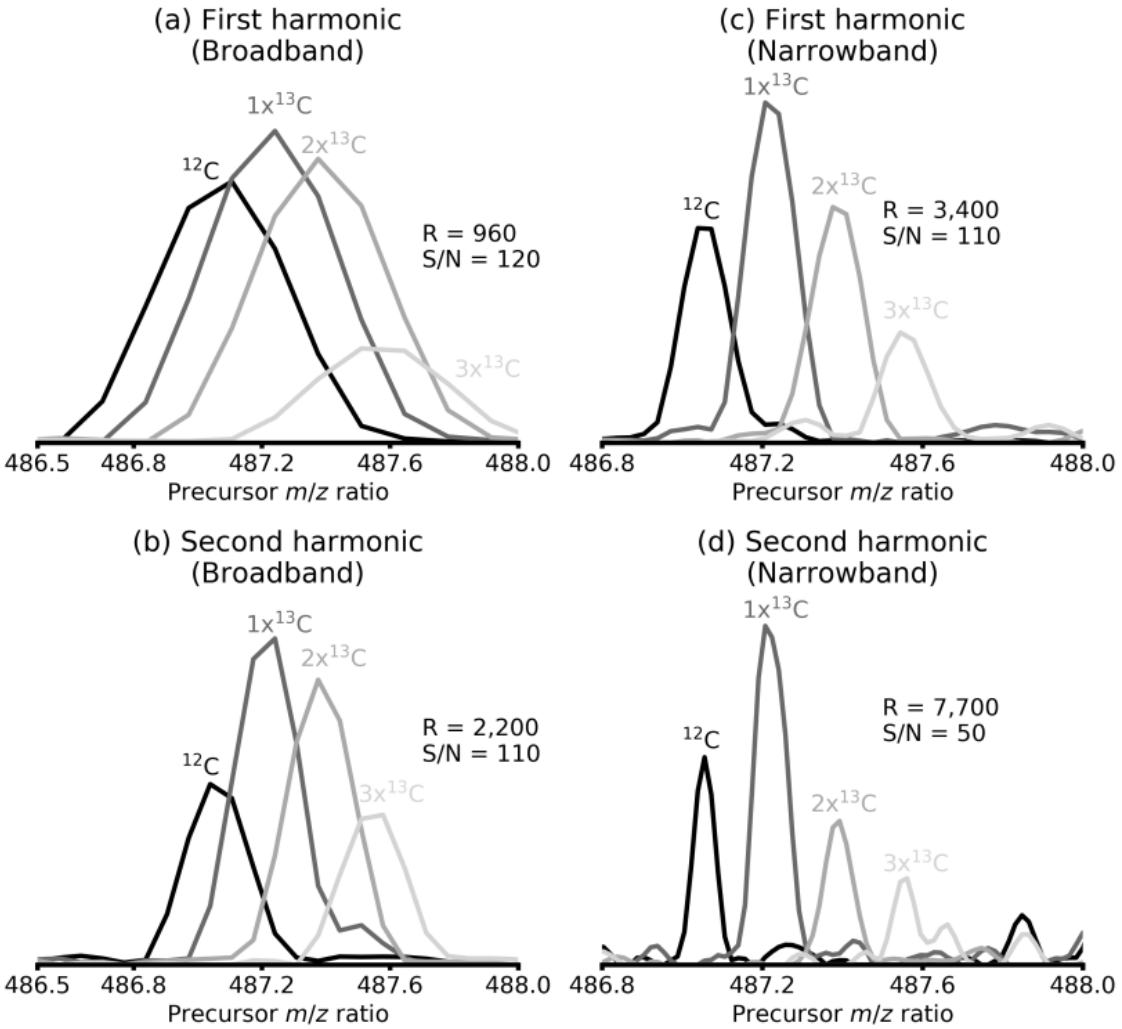
effect of folding in F1

(a) Zoom on the narrowband 2D MS spectrum





effect of folding in F1



some more mathematics 10 min

- amplitude modulation and phase modulation
- phase in 2D
- hypercomplex numbers

phase sensitive absorption 15 min

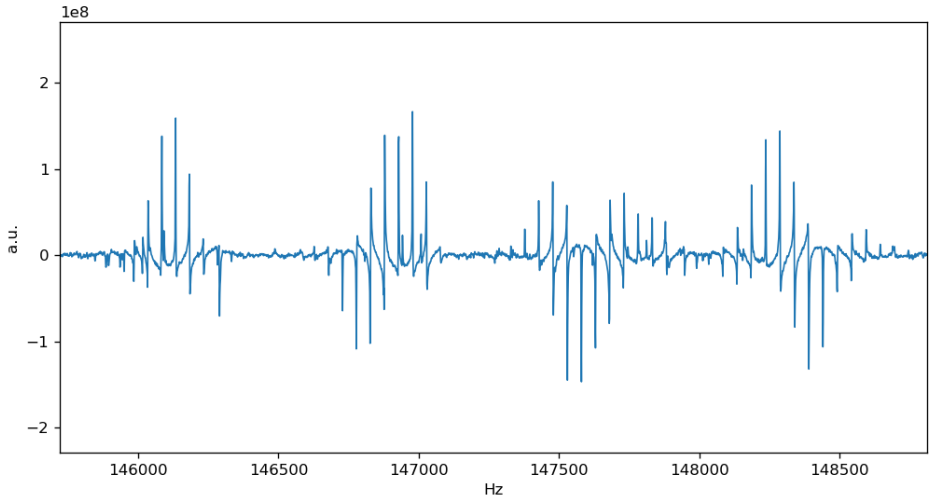
(results from this preprint: https://www.preprints.org/manuscript/202104.0445/v1 (https://www.preprints.org/manuscript/202104.0445/v1))

- phase in F2
- phase in F1
- results

Phase sensitive FTICR-MS

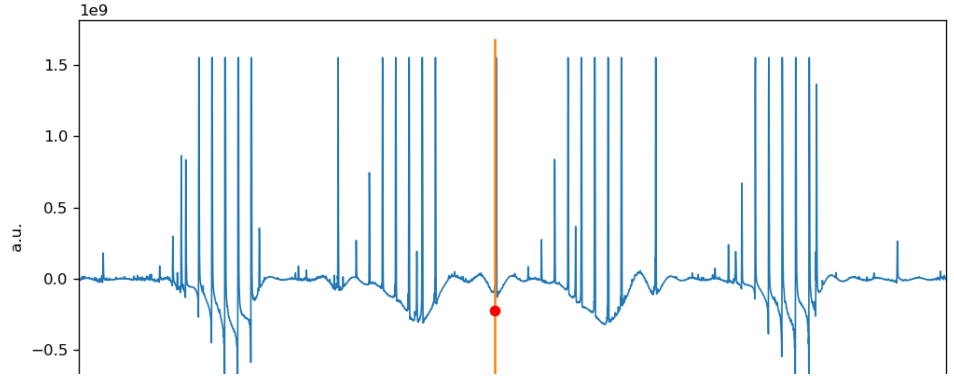
- in all the spectra we saw so-far, spectra were in modulus.
- however the Fourier Transform of the transien is complex *(a series of complex numbers)*
- "*phasing*" a spectrum consists in rotating this numbers by a complex number of length 1.0: $e^{j\theta}$
  - θ can be constant over the spectrum: 0^{th} order phase
  - θ can be linearly varying over the spectrum: 1^{st} order phase
  - θ can be quadratically varying over the spectrum: 2^{nd} order phase

Phase sensitive FTICR-MS



- The phase mix the absorption and dispersion linesphapes
- We see a strong linear dependence of phase (here a small spectral window)

Phase sensitive FTICR-MS

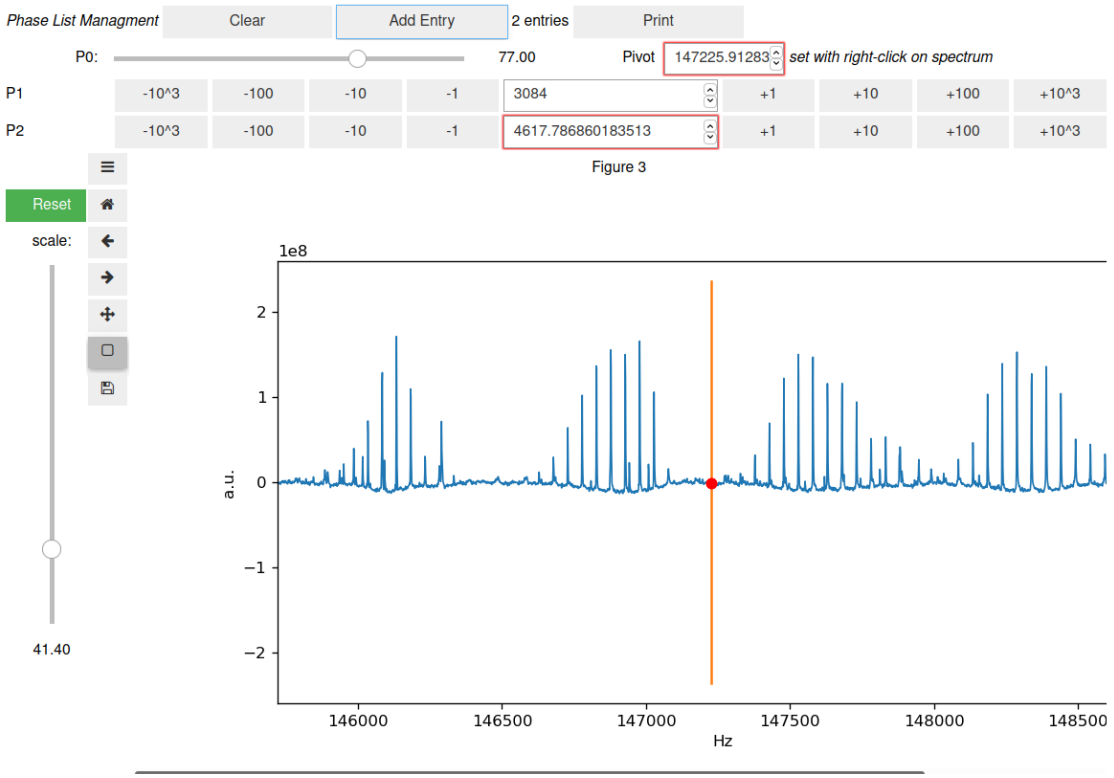


linear phase correction in not enough

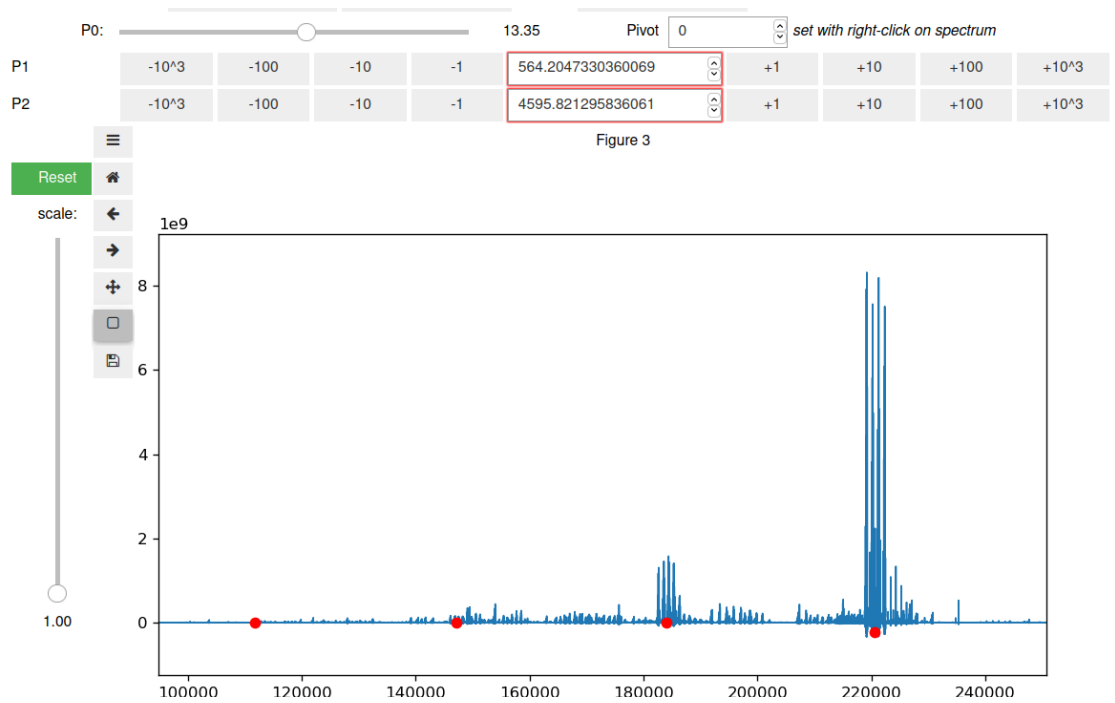
⇒ quadratic phase correction

Phase sensitive FTICR-MS

interactive/automatic module for FTICR phasing in Spike (not finished yet, but soon)

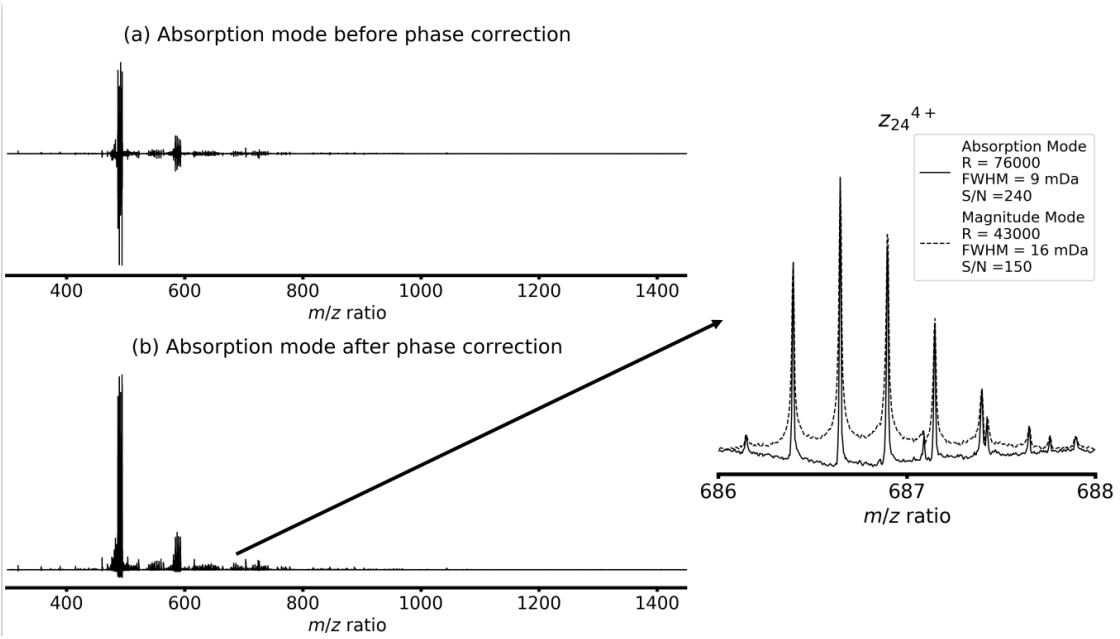


Phase sensitive FTICR-MS



Hz

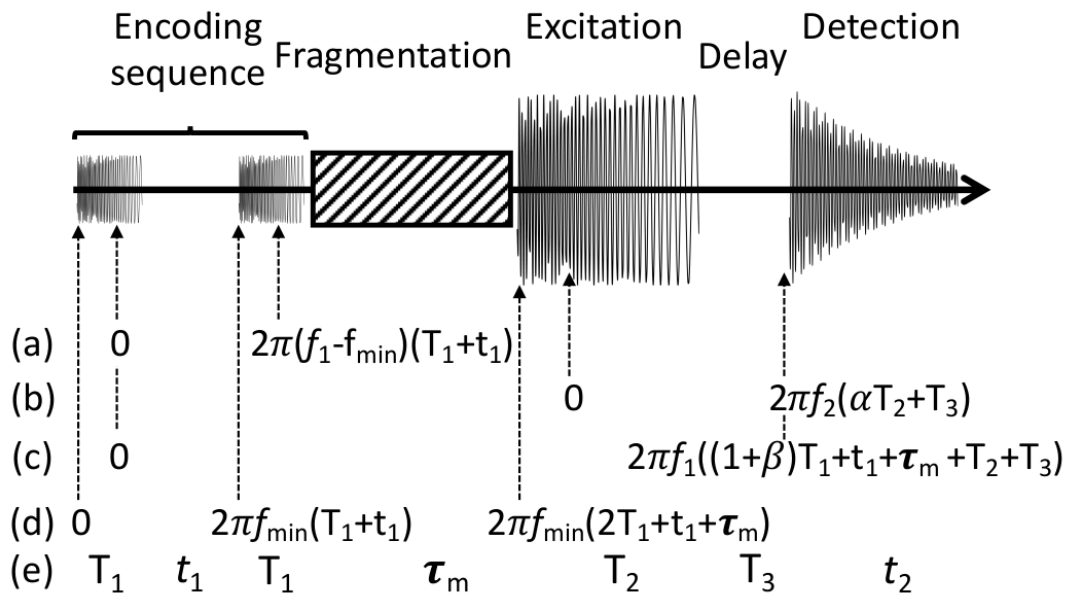
Phase sensitive FTICR-MS



notice the baseline distortion

Phase sensitive 2D FTICR-MS

(results from this preprint: https://www.preprints.org/manuscript/202104.0445/v1 (https://www.preprints.org/manuscript/202104.0445/v1))



- F2 ⇒ quadratic phase correction
- F1 ⇒ linear phase correction

Phasing rule of thumb

- global phase (O^{th} order) is due to
  - electronic delays
  - computation
  - ⇒ easy
- frequency linearly dependent phase (1^{st} order) is due to
  - delay between pulse and acquisition
  - error on the position of $t = 0$ origin of time
  - ⇒ doable
- frequency quadratically dependent phase (2^{nd} order) is due to
  - frequency dependent delay between pulse and acquisition
  - frequency swept pulses
  - ⇒ a pain

but there is more... *it took 15 years to NMR guys to realize that...*

phases in F1 and in F2 are independent

you cannot do that in $\mathbb{C}$, we have "only" one phase, one j

⇒ have to go to hypercomplex algebra $\mathbb{H}$, a 4 dimensionnal, commutative, non-invertible algebra.

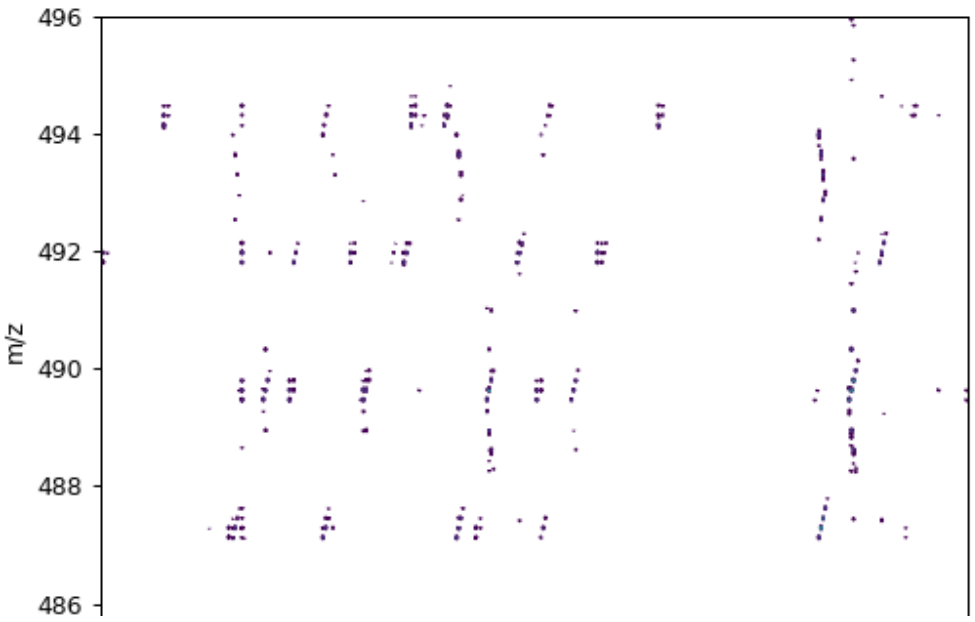
$$z = a + ib + jc + kd \tag{7}$$
$$i^2 = -1 \quad j^2 = -1 \quad k^2 = 1$$
$$ij = ji = k \quad ik = ki = -j \quad jk = kj = -i$$

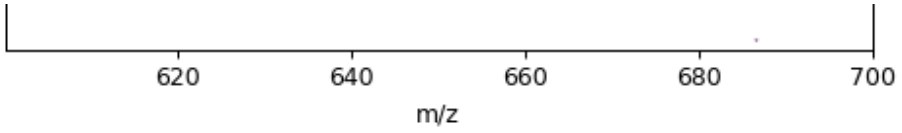
in $\mathbb{H}$ you can define independent phases: $e^{i\theta}$ and $e^{j\phi}$

and you can write (for a sub class of the element of $\mathbb{H}$) :

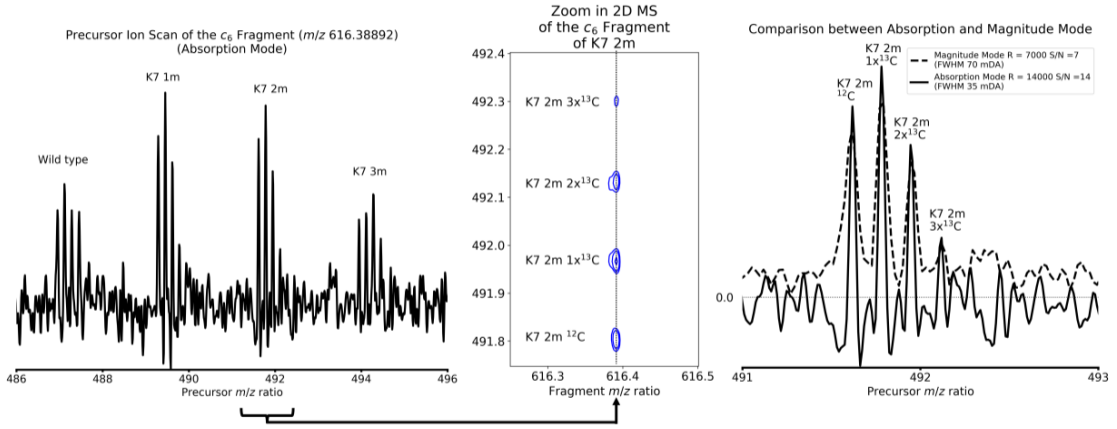
$$z = Ae^{i\theta}e^{j\phi} \tag{8}$$

Phase sensitive 2D FTICR-MS

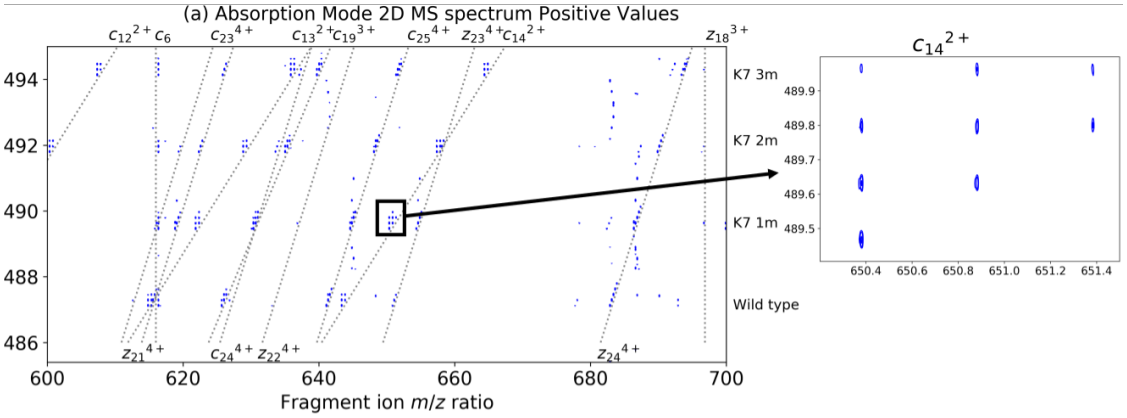




Phase sensitive 2D FTICR-MS

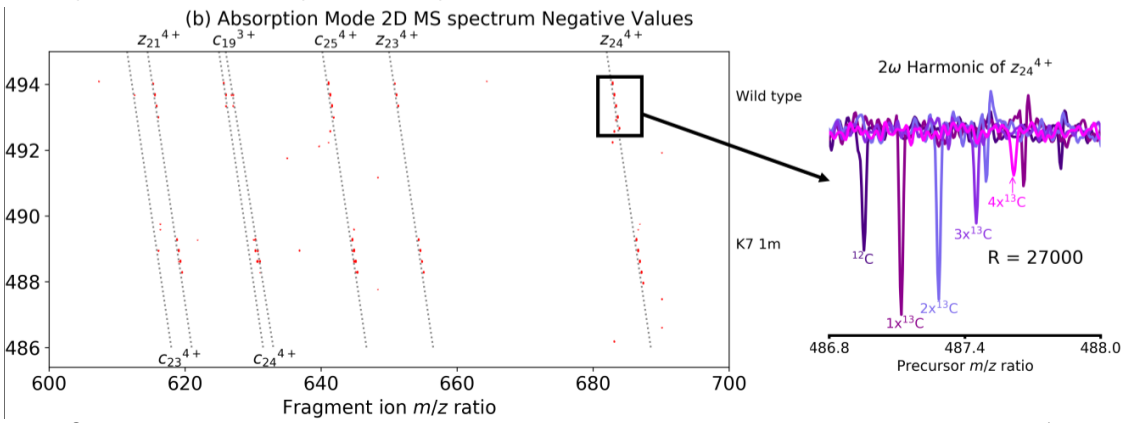


Phase sensitive 2D FTICR-MS



Phase sensitive 2D FTICR-MS

folding also invert the sign of the signal.



here 2ω harmonics are folded an odd number of times ⇒ separates them from the 1ω signal

double the resolution

conclusion

- resolution is paramount in MS
  - Narrow Band is a nice and simple trick to enhance it
  - harmonics is another (Bruker played it already)
  - Phasing is a nicer but not so simple trick to still enhance it
- we (you guys) still have to explore what to do with all this room !

- finally
  - know your exponentials 😊
  - and the rest
  - it's always more complex that you thought

- though it's doable !

- I love python (did you notice ?)

Thank you !