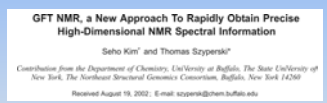
Quadrature detection, reduced dimensionality and GFT-NMR


GFT NMR, a New Approach To Rapidly Obtain Precise High-Dimensional NMR Spectral Information

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Measuring time in NMR

1D: 32 scans: 42 seconds

2D: 512 FIDs, 16 scans: 10650 sec, 3 hours

3D: 128 x 128 FIDs, 8 scans: 170394 sec, 48 hours

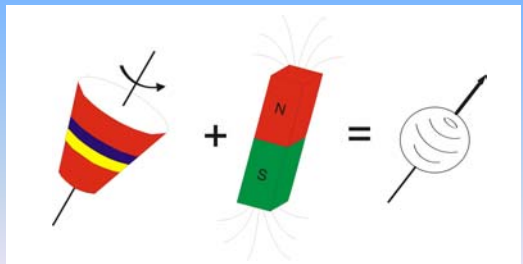
4D: 32 x 32 x 64 FIDs, 4 scans: 340787 sec, 96 hours

oder 512 x 128 x 128 FIDs, 1 scan: 10905190 sec, 3030 hours, 126 days

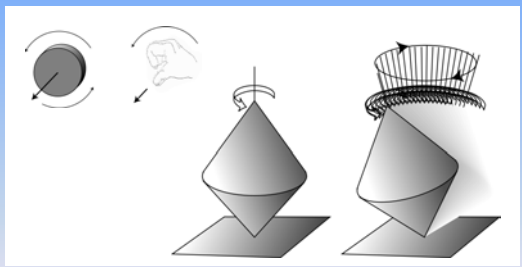
We are at the sampling limit rather than at the sensitivity limit

1. NMR basics (4 - 16)
2. Fourier transformation (17 – 21)
3. Quadrature detection (22 – 34)
4. Reduced dimensionality (35 - 37)
5. GFT-NMR (38 – 49)

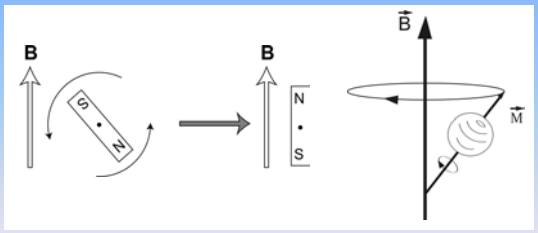
Basis for NMR spectroscopy is the nuclear spin that can be viewed as a combination of magnet and spinning top

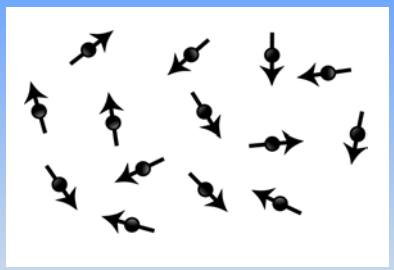


A spinning top has an angular momentum the axis of the angular momentum constant in space



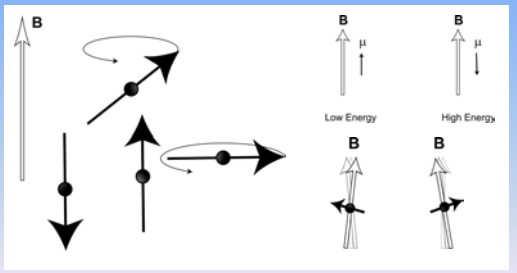
A magnet orients in the direction of the magnetic field, this is prevented by the fact that its a spinning top
A precession begins

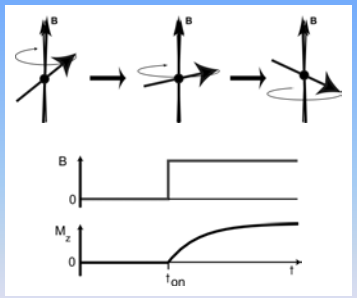




Without an external magnetic field
spins are oriented randomly in all possible directions

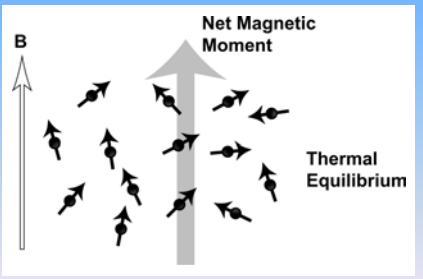
When a magnetic field is switched on, this does not change immediately, but thermal motion drives spins to orient predominantly along the field



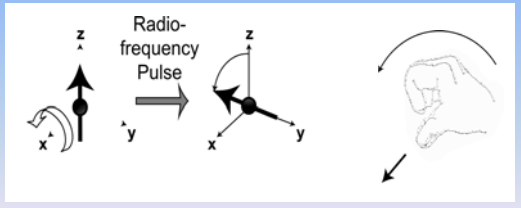


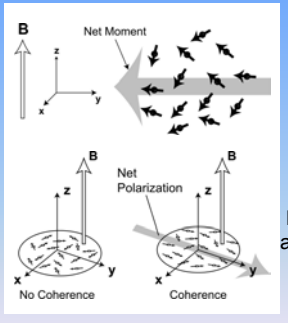
That builds up
a net magnetization...

...along the main field,
resulting in a Bolzman distribution



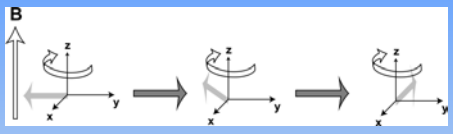
A radio frequncy pulse turns the spins….

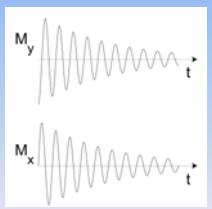




And with them the net magnetization

Note the difference between an orientation in the x,y plane and a coherence





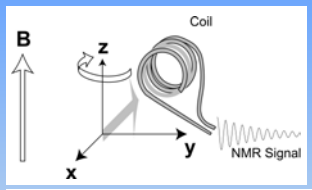
The net magnetization performs a precession

$M_y = \cos \omega t \exp(-t/T_2)$

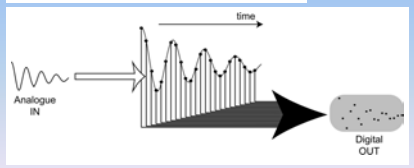
$M_x = \sin \omega t \exp(-t/T_2)$

$M = M_y + i M_x$

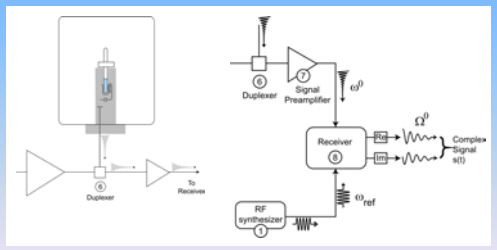
$M = \exp(i\omega t) \exp(-t/T_2)$



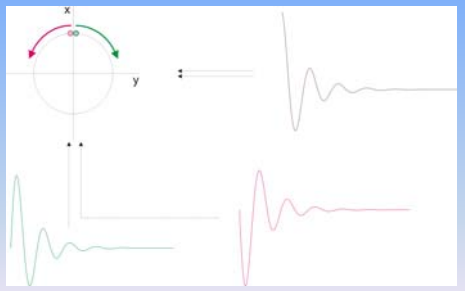
The signal is detected via a coil and then digitized using an ADC (analog-digital-converter)



To make digitization possible, we subtract the original signal from the one returned from the sample



The reference signal is normally the center of the spectrum



A complex NMR signal has the following form

$$s(t) = \exp(i\phi) \exp(-t/T_2) \exp(i\Omega_0 t)$$

phase of the signal (time independent !)

decay of the signal (relaxation)

oscillation of the signal (the frequency)

We ignore the phase factor for the time being and apply a Fourier transformation

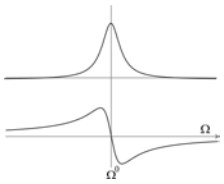
$$s(\Omega) = \int_0^\infty s(t) \exp(-i\Omega t) dt$$

$$s(\Omega) = \frac{1}{(1/T_2) - i(\Omega - \Omega_0)}$$

We obtain a complex „Lorentian“ line shape,
it consist of an absorbtive and a dispersive part

$$A(\Omega) = \frac{(1/T_2)}{(1/T_2)^2 + (\Omega - \Omega_0)^2}$$

$$D(\Omega) = \frac{(\Omega - \Omega_0)^2}{(1/T_2)^2 + (\Omega - \Omega_0)^2}$$



Now we reintroduce the phase factor

$$S(\Omega) = [A(\Omega) + i\,D(\Omega)\,]\exp(i\phi)$$

$$S(\Omega) = R(\Omega) + i\,I(\Omega)$$

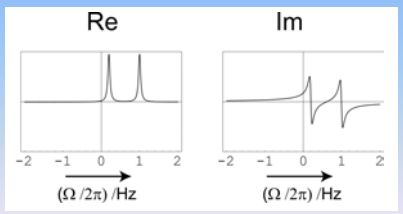
Real and imaginary part are mixtures of
absorptive and dispersive line shapes

$$R(\Omega) = A(\Omega)\cos\phi - D(\Omega)\sin\phi$$

$$I(\Omega) = D(\Omega)\cos\phi + A(\Omega)\sin\phi$$

We apply a zero-order „phase correction“

$$A(\Omega) = R(\Omega)\cos\phi + I(\Omega)\sin\phi$$
$$D(\Omega) = I(\Omega)\cos\phi - R(\Omega)\sin\phi$$



What if we have only one of the components
either cosine or sine

$$\exp(i\alpha) = \cos\alpha + i\sin\alpha$$

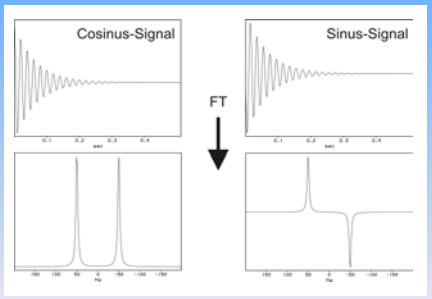
$$\exp(-i\alpha) = \cos\alpha - i\sin\alpha$$

$$\cos\alpha = \exp(i\alpha) + \exp(-i\alpha)$$

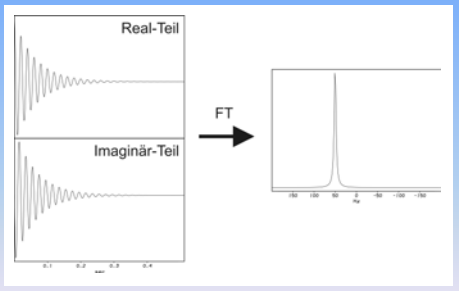
$$\sin\alpha = \exp(i\alpha) - \exp(-i\alpha)$$

(the „famous“ Euler formulas)

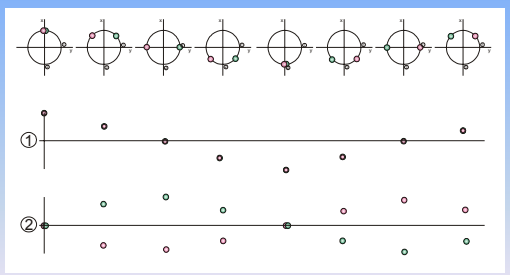
We get two signals each



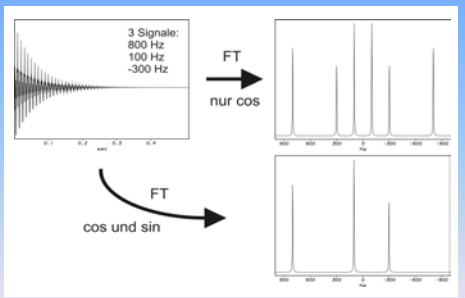
So we have to do a „quadrature detection“



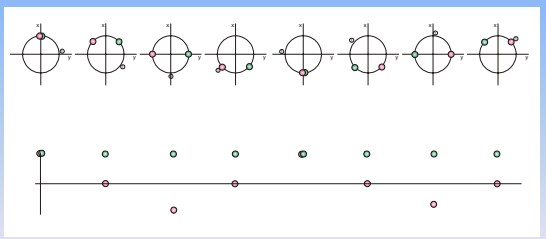
The first way to do it is „States“ (or Ruben-States-Haberkorn)



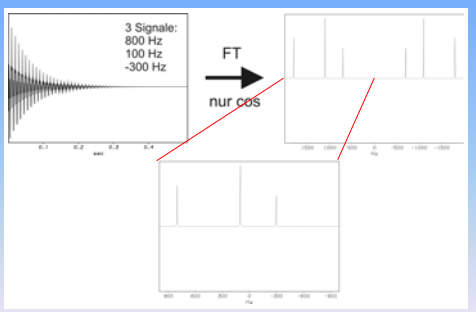
Cosine and sine signal are then combined



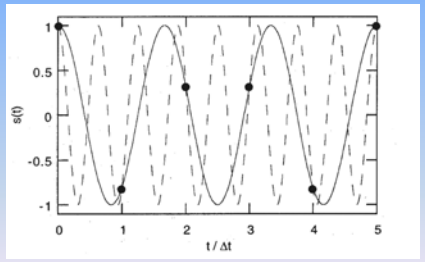
A second way to do it is TPPI (time proportional phase increment)



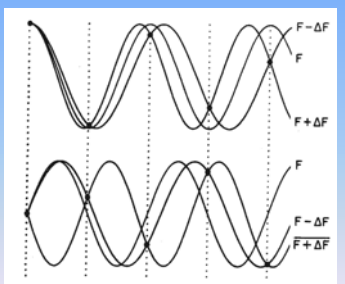
One half of the spectrum is then discarded



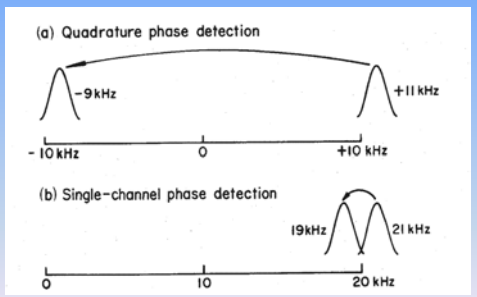
When a continous signal *s(t)* is sampled at evenly spaced intervals as *s(kΔ t),* the highest detectable frequency is the Nyquist frequency: $f_n = 1(2\Delta t)$



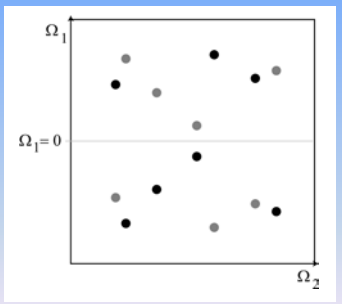
That has consequences depending on the type of quadrature detection



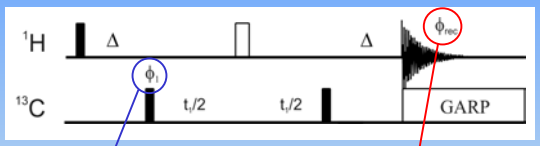
Aliasing and folding



The same problem exists for indirect dimensions



Quadrature detection in F1



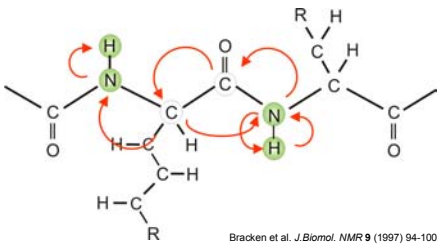
1.FID: ϕ_1 = x, -x
2.FID: ϕ_1 = y, -y

1.FID: ϕ_{rec} = +, -
2.FID: ϕ_{rec} = +, -

Methods for quadrature detection

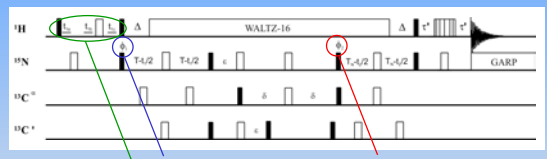
Methode	Phase des Präparations pulses	Empfänger-phase	Art der Fouriertrans-formation	Position der Axialpeaks
Redfield	x (t_1 + 0*Δ)	x	reell	Zentrum
	y (t_1 + 1*Δ)	x		
	x (t_1 + 2*Δ)	-x		
	y (t_1 + 3*Δ)	-x		
TPPI	x (t_1 + 0*Δ)	x	reell	Rand
	y (t_1 + 1*Δ)	x		
	-x (t_1 + 2*Δ)	x		
	-y (t_1 + 3*Δ)	x		
SHR	x (t_1 + 0*Δ)	x	komplex	Zentrum
	y (t_1 + 0*Δ)	x		
	x (t_1 + 2*Δ)	x		
	y (t_1 + 2*Δ)	x		
TPPI-States	x (t_1 + 0*Δ)	x	komplex	Rand
	y (t_1 + 0*Δ)	x		
	-x (t_1 + 2*Δ)	-x		
	-y (t_1 + 2*Δ)	-x		

(H)N(COCA)NH and HN(COCA)NH



Bracken et al. *J.Biomol. NMR* **9** (1997) 94-100

(H)N(COCA)NH and HN(COCA)NH

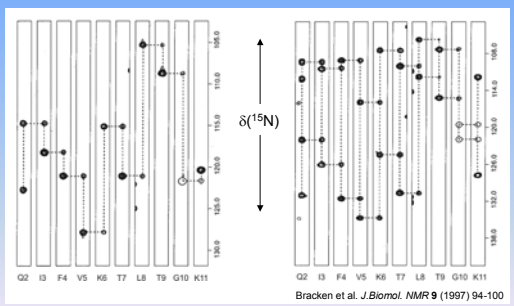


quadrature detection in t_1

quadrature detection in t_2

reduced dimensionality:
evolution on H^N is recorded concomitantly with the evolution on N but without any scheme for quadrature detection

(H)N(COCA)NH HN(COCA)NH



Bracken et al. *J.Biomol. NMR* **9** (1997) 94-100

reduced dimensionality:

nD information in an (n-1)D spectrum

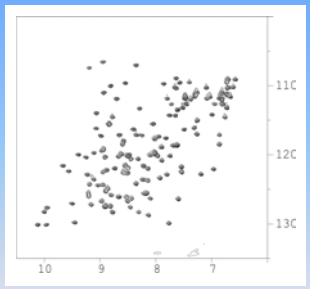
GFT-NMR:

Generalization of the this principle

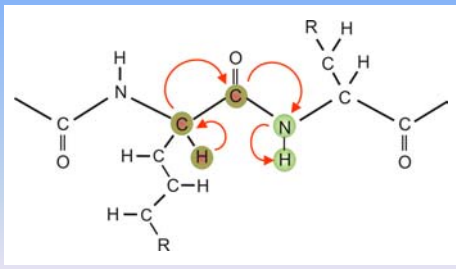
nD information in an (n-k)D spectrum

First the "target dimensionality" is selected

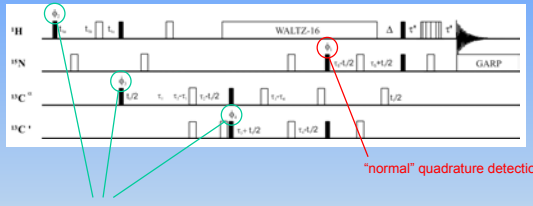
If there is barely Overlap in the ^{15}N-HSQC the target dimensionality is 2D



5D-HACACONHN and (5,2)D-HACACONHN



(5,2)D HACACONHN



Three additional dimensions require 8 "basic spectra"

$S1 \propto \cos(\Omega_0\, t)\, \cos(\Omega_1\, t)\, \cos(\Omega_2\, t)\, \cos(\Omega_3\, t)$

$S2 \propto \cos(\Omega_0\, t)\, \sin(\Omega_1\, t)\, \cos(\Omega_2\, t)\, \cos(\Omega_3\, t)$

$S3 \propto \cos(\Omega_0\, t)\, \cos(\Omega_1\, t)\, \sin(\Omega_2\, t)\, \cos(\Omega_3\, t)$

$S4 \propto \cos(\Omega_0\, t)\, \sin(\Omega_1\, t)\, \sin(\Omega_2\, t)\, \cos(\Omega_3\, t)$

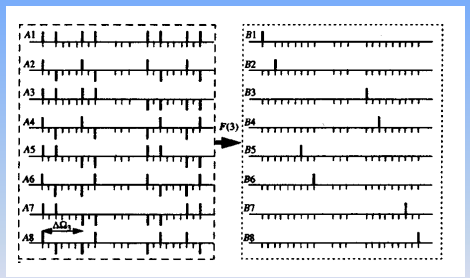
$S5 \propto \cos(\Omega_0\, t)\, \cos(\Omega_1\, t)\, \cos(\Omega_2\, t)\, \sin(\Omega_3\, t)$

$S6 \propto \cos(\Omega_0\, t)\, \sin(\Omega_1\, t)\, \cos(\Omega_2\, t)\, \sin(\Omega_3\, t)$

$S7 \propto \cos(\Omega_0\, t)\, \cos(\Omega_1\, t)\, \sin(\Omega_2\, t)\, \sin(\Omega_3\, t)$

$S8 \propto \cos(\Omega_0\, t)\, \sin(\Omega_1\, t)\, \sin(\Omega_2\, t)\, \sin(\Omega_3\, t)$

Proper combination results in spectra with only one peak

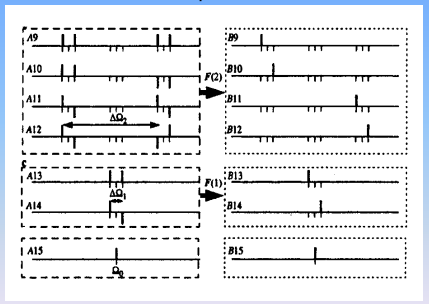


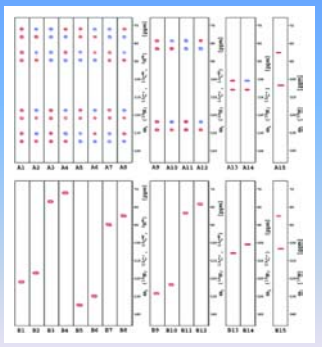
FT of S1-S8

That corresponds to a matrix operation

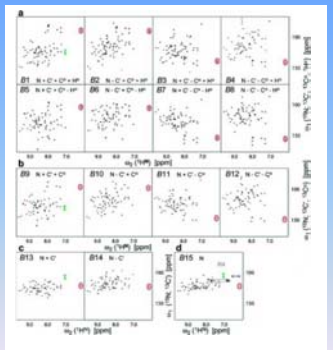
$$\begin{bmatrix} B1 \\ B2 \\ B3 \\ B4 \\ B5 \\ B6 \\ B7 \\ B8 \end{bmatrix} = \begin{bmatrix} 1 & 1 & 1 & 1 & 1 & 1 & 1 & 1 \\ 1 & -1 & 1 & -1 & 1 & -1 & 1 & -1 \\ 1 & 1 & -1 & -1 & 1 & 1 & -1 & -1 \\ 1 & -1 & -1 & 1 & 1 & -1 & -1 & 1 \\ 1 & 1 & 1 & 1 & -1 & -1 & -1 & -1 \\ 1 & -1 & 1 & -1 & -1 & 1 & -1 & 1 \\ 1 & 1 & -1 & -1 & -1 & -1 & 1 & 1 \\ 1 & -1 & -1 & 1 & -1 & 1 & 1 & -1 \end{bmatrix} \begin{bmatrix} A1 \\ A2 \\ A3 \\ A4 \\ A5 \\ A6 \\ A7 \\ A8 \end{bmatrix}$$

It is difficult to decide which peak is which, therefore “central peaks” are recorded

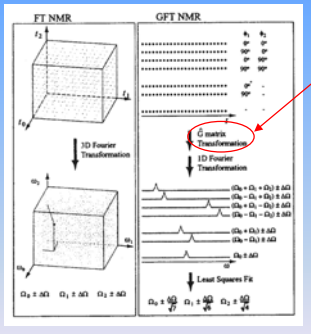




Thats how it looks



The result are 15 2Ds



The G-matrix does it all in the time domain

Comparison of numbers:

(5,2)D HACACONHN

15 spectra can be recorded in 34 min and yields a set of two-dimensional spectra

5D HACACONHN

$10*(t_1) \times 11*(t_2) \times 22*(t_3) \times 13* (t_4) \times 512*(t_5)$

1scan per FID, 1 second per scan	5.83 days
Processed to the same resolution	618 GB

The acquisition of multidimensional NMR spectra within a single scan

Lucio Frydman[†‡], Tali Scherf[§], and Adonis Lupulescu

Proc. Natl. Acad. Sci. USA **99**, 15858-15862 (2002)

4D spectrum in 194 msec.....