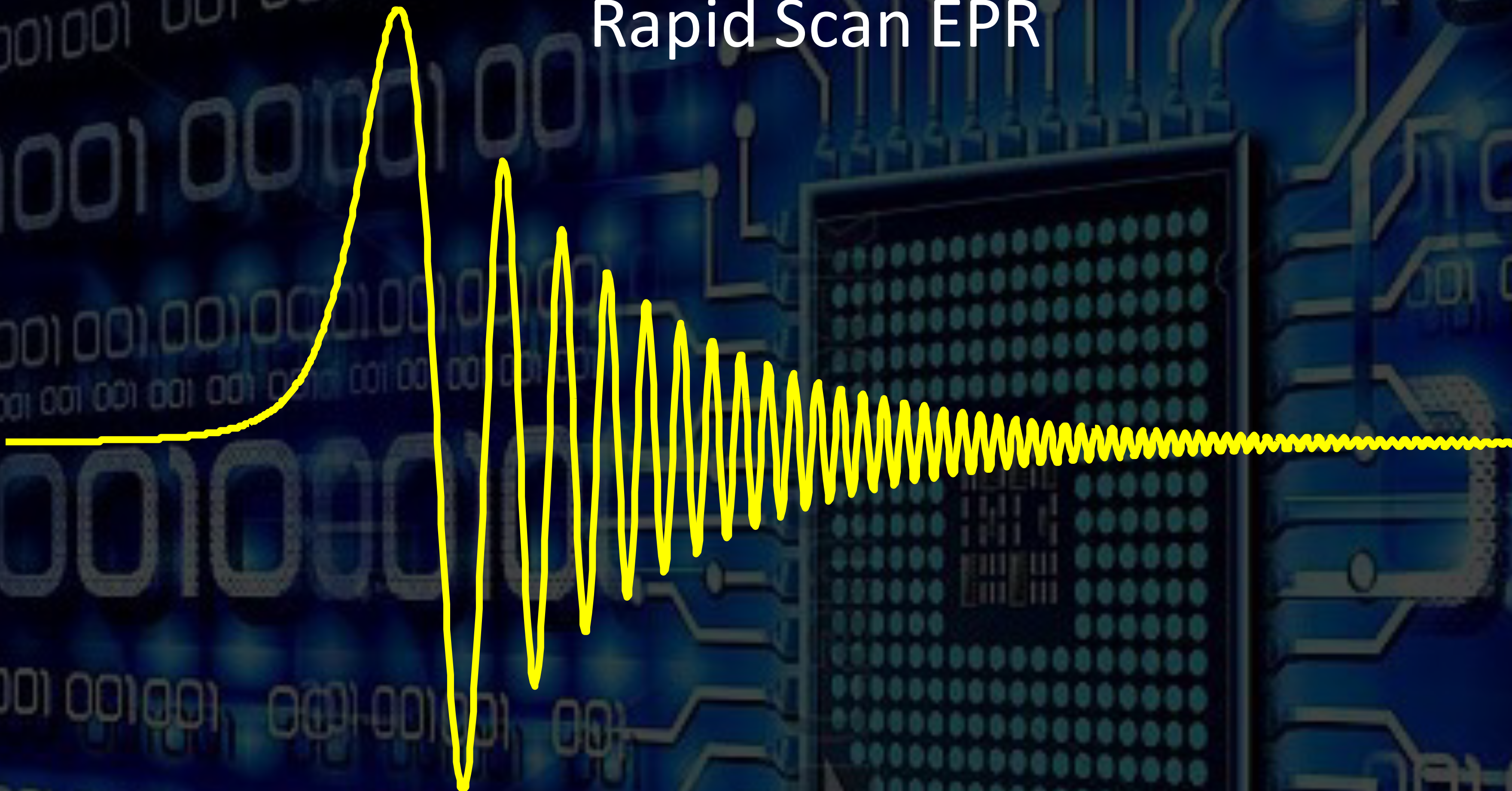
Rapid Scan EPR



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8th BRNO EFEPR SCHOOL

18–25/11/2019

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BRNO, Czech Republic

of the European Federation of EPR groups on Advanced EPR

Outline:

- Rapid Scan (RS) EPR introduction
- RS signal simulations
- RS signal deconvolution algorithms
- Instrumentation
- Applications
- Summary

Rapid Scan (RS) EPR has been many things …

Continuous-wave (**CW**) Magnetic Field Scan EPR:

- Old Bruker RS (50 &200 G) => Fast scan
- Linear scan NARS, including segmented (Hyde lab)
- Triangular RS, including segmented (Eaton lab)
- Sinusoidal scan (Eaton lab)

Frequency rapid-scan
(1970^{th} NMR)
(2010^{th} EPR)
(not for today)

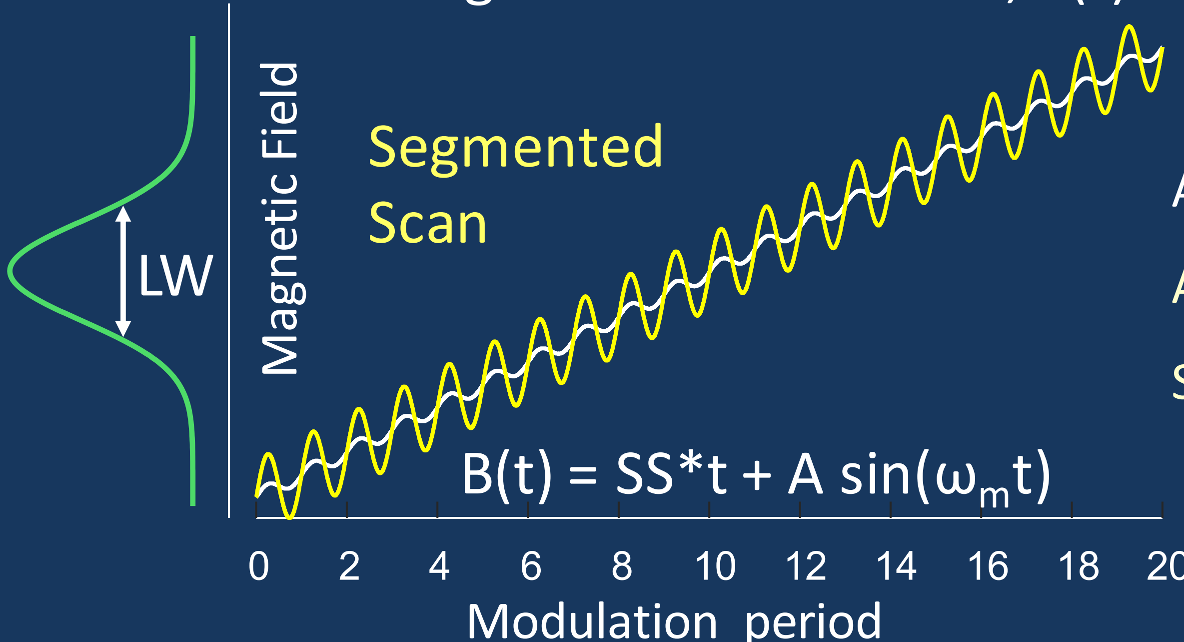
CW method has been evolving to become many. Terminology is confusing.

Two major factors that distinguish 'Rapid Scan' CW methods:

A) Magnetic field function of time , B(t), vs. EPR spectral width, LW.

B) Theoretical model used to transform EPR(t) signals into EPR(B) spectra

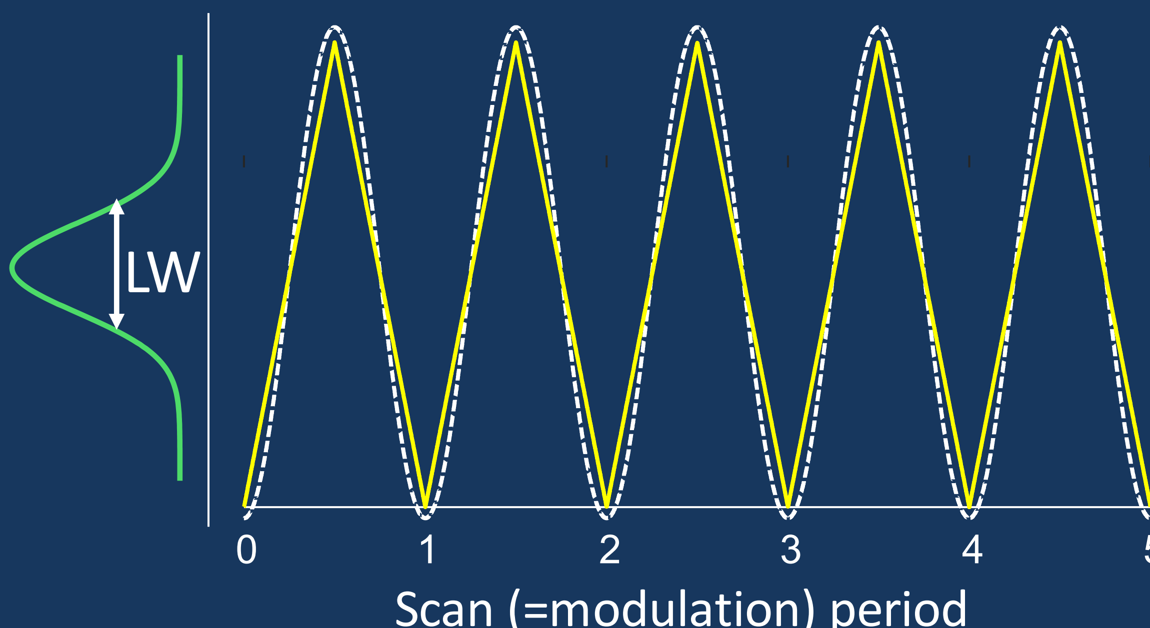
Magnetic Field Function, B(t)



$A < 1/3$ LW: 1st harmonic CW

$A \geq$ LW: N harmonic CW

Segmented linear NARS & RS



Complete Scan

SS=0; A> 10 LW

$B(t) = A \sin(\omega_m t)$

$B(t) = A\,\mathrm{tri}(\omega_m t)$

Theoretical models for spin system response:

1. ‘Slow scan’: Memoryless system: Response R(t)=LineShape[B(t)]

$dB(t)/dt\ T_2^* < LW = (\gamma\ T_2^*)^{-1}$

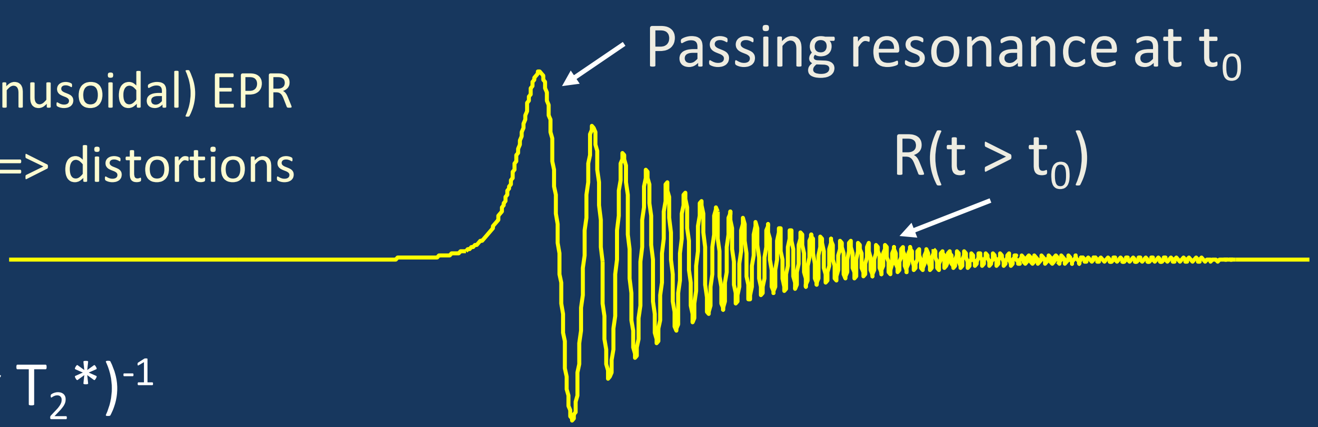
- 1^{st} harmonic CW
- Multi-harmonic CW
- NARS
- ‘Slow’ RS EPR (short relaxation times)

Data processing is rather straightforward: mapping time to field domain.

2. ‘True’ rapid scan: Linear time-invariant (LTI) system (with Memory)

LTI: Output(t) = Input(t) ⊗ impulse_response(t)

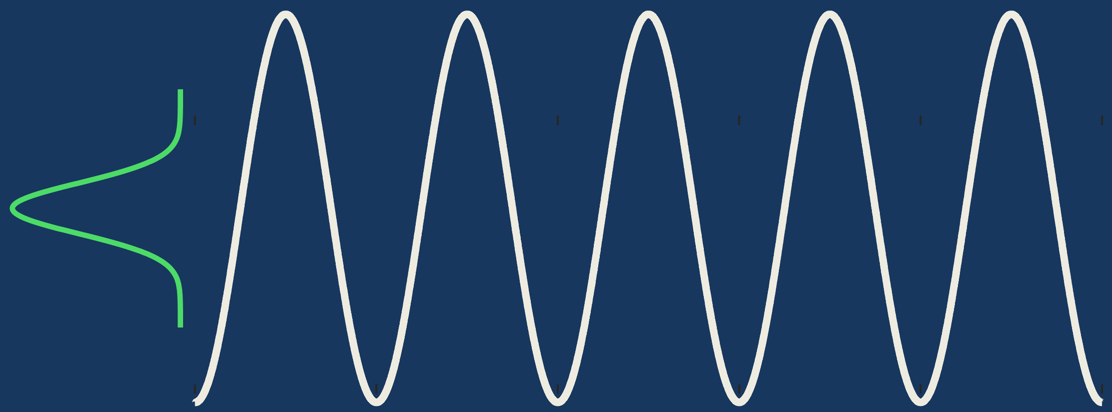
- Full-scan (linear and sinusoidal) EPR
- Standard CW, long T_2 => distortions



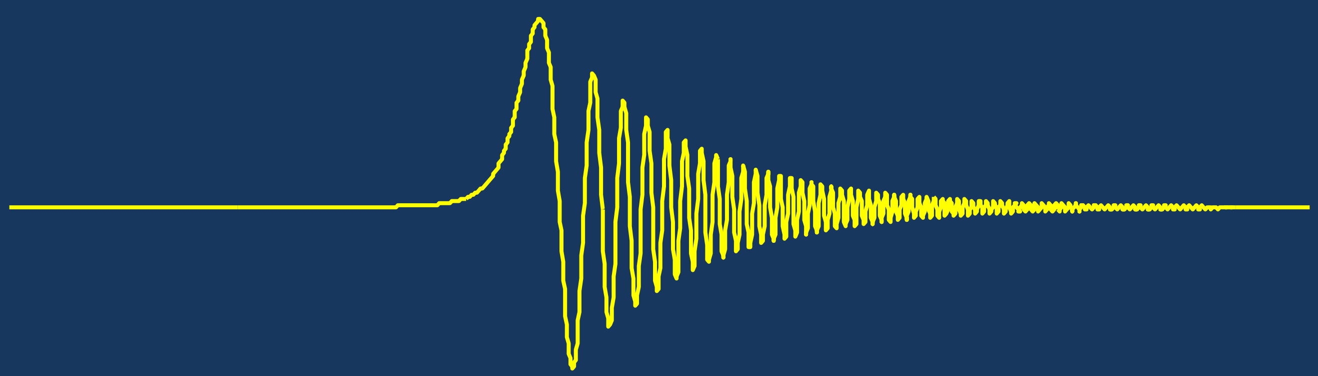
$dB(t)/dt\ T_2^* > LW = (\gamma\ T_2^*)^{-1}$

My today's RS EPR is:

- Sinusoidal scan
- Magnetic field scan covers the entire EPR spectrum



- Spin system approximates as a linear time-independent system (LTI)



What is the advantage of using the LTI rapid scan model?

It is EPR sensitivity enhancement.

Big picture description first, more details later …

For spins, fast transition through the resonance is equivalent to a pulse

Short pulse at high power => larger tipping angles => stronger signal

As in FID EPR, there is no spin saturation at high scan rate (short pulse)

LTI RS EPR vs. FID & echo EPR

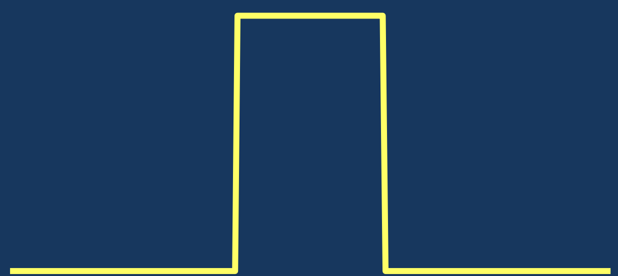
- Both perform better if relaxation times are long
- No dead-time for RS, but LNA protection is problematic (more later)
- RS is bandwidth limited only due to Q-factor (more details later)
- No spin echo for RS (yet)

Again, RS EPR logic:

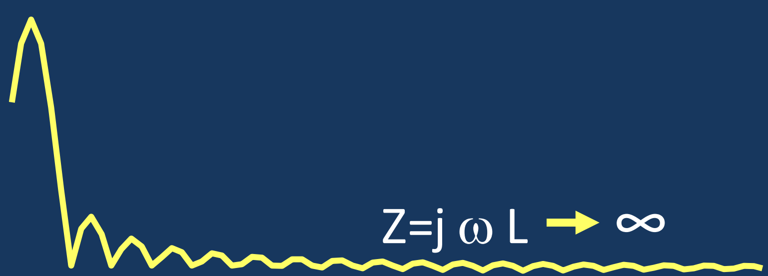
- Faster scan rates => Reduced saturation & Large B_1
- Because linear model and by definition => Signal grows $\propto B_1$

$B(t) = A \sin(\omega_m t)$ vs. $B(t) = A\, \mathrm{tri}(\omega_m t)$

SLOWER



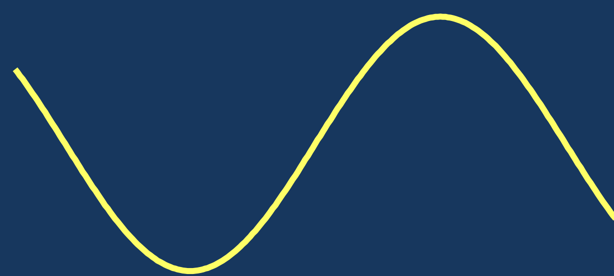
t, Time



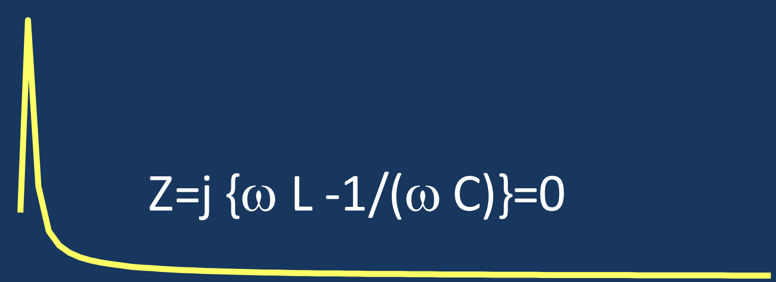
$Z = j\,\omega L \rightarrow \infty$

ω, Frequency

FASTER => SNR ↑



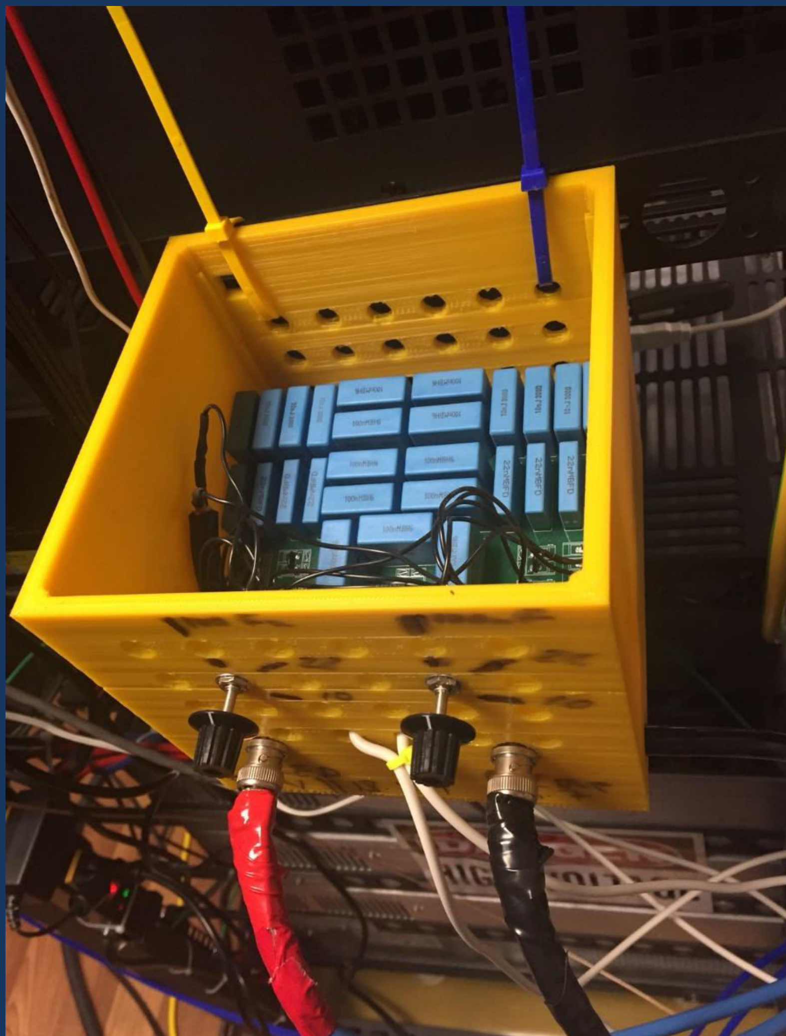
t, Time



$Z = j\{\omega L - 1/(\omega C)\} = 0$

ω, Frequency

A discrete set of resonance frequencies can be achieved by using a switchable capacitors bank

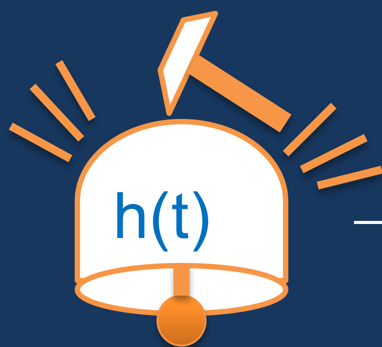


Example:

Our 3D printed box with a PCB inside permits six frequencies from 9 to 27 kHz

LTI RS Theory

Linear system is uniquely described by an impulse response function:

$x(t) \rightarrow$ 

$\rightarrow \; r(t)=x(t) \otimes h(t)$

- $a\, x(t) \rightarrow a\, r(t)$
- $x(t+\tau) \rightarrow r(t+\tau)$
- $R(\omega)=X(\omega)\, H(\omega)$

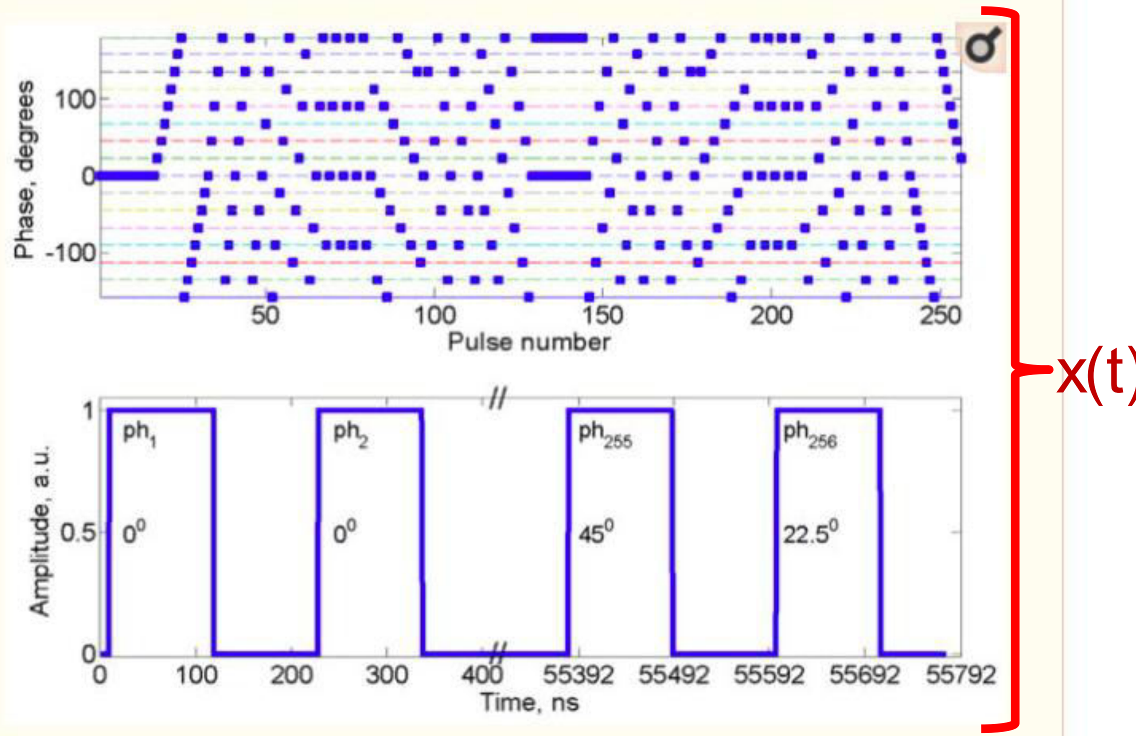
In (small angle) pulsed EPR, $h(t)=FID(t)$ and $x(t)=B_1(t)$.

EPR spectrum: $H(\omega) = R(\omega) / X(\omega)$ < = Deconvolution

Often $X(\omega)\, X^*(\omega) = 1$ => $H(\omega) = R(\omega)\, X^*(\omega)$ not an ill-posed problem

EPR example, Frank Sequence

Paper link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3107679/



Open in a separate window

Figure 1

The pulse sequence that was used to produce the spectra in Figure 2 consisted of 256 pulses of 109 ns with the 16 different phases selected as shown in part a. The time required for the complete sequence was about 56 µs. The detailed timing of the first 2 and last 2 pulses is shown in part b. Data were acquired continuously at 4 ns intervals during the entire pulse sequence, but only the signal corresponding to times between the pulses was analyzed.

$r(t) = x(t) \otimes h(t)$

r : EPR signal

h : FID

$R(\omega) = X(\omega)\, EPR(\omega)$

Before looking into RS EPR data processing

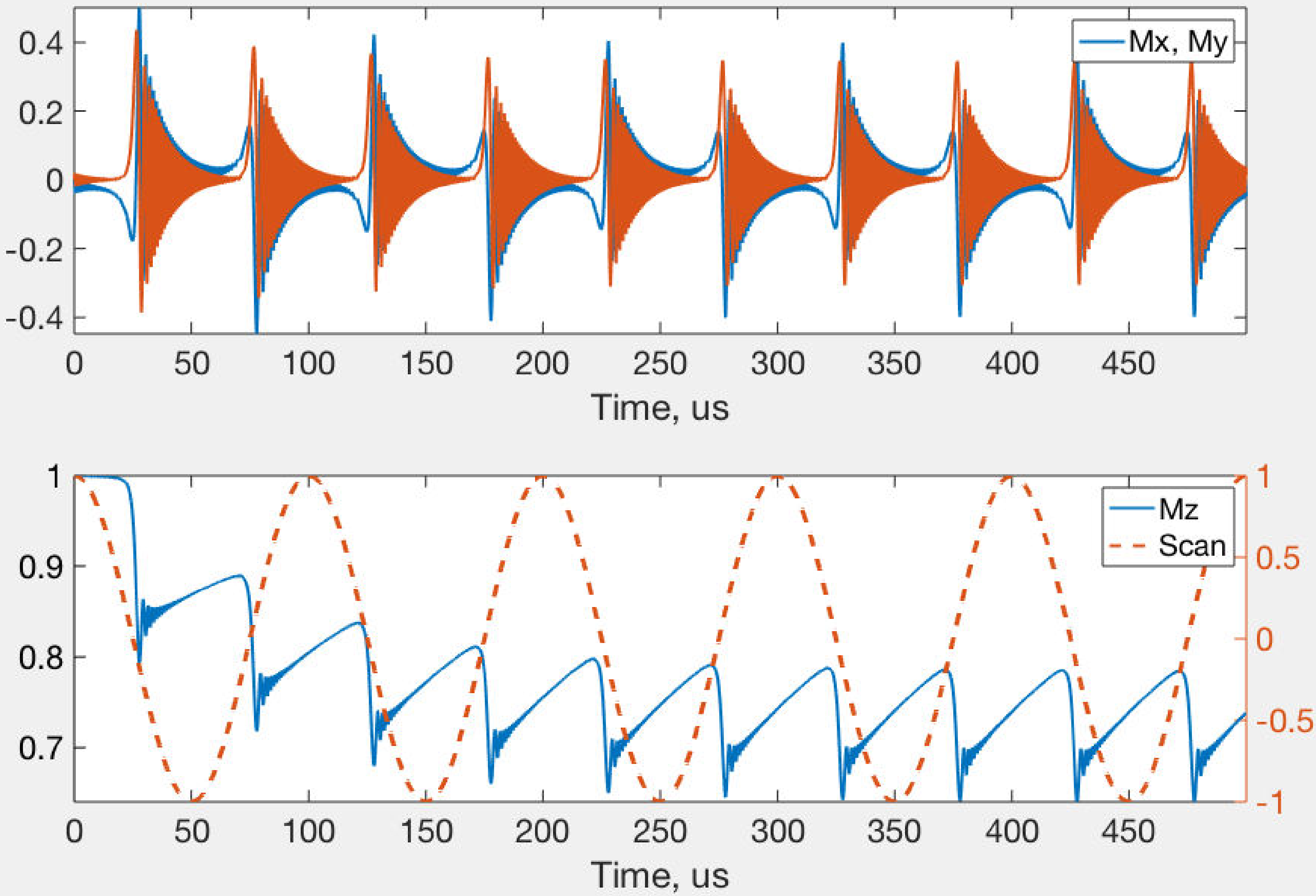
let's see how to compute RS EPR signal for spin 1/2 system?

Approach 1.

Straightforward but time consuming way is to solve the Bloch Equations.

```
function dM = RSS(t,M,par)
gamma=1.7608e7; % rad s-1 G-1
%%  ---------------------- %
B1=par.B1; Vm=par.Vm; hm=par.hm; dH=par.dH; T2=par.T2; T1=par.T1;
%%
wy=0;
wx=gamma*B1;
WF=-cos(2*pi*Vm*t);
A=gamma*(dH+0.5*hm*WF);
% -------------------%
dM = zeros(3,1);    % (x,y,z) a column vector
M0=1;
%           M1          M2          M3          M0
dM(1) = -M(1)/T2     -A*M(2)    +wy*M(3)     +0;
dM(2) = +A*M(1)     -M(2)/T2   -wx*M(3)     +0;
dM(3) = -wy*M(1)     +wx*M(2)    -M(3)/T1     +M0/T1;
```

It may take several cycles to get a steady-state solution

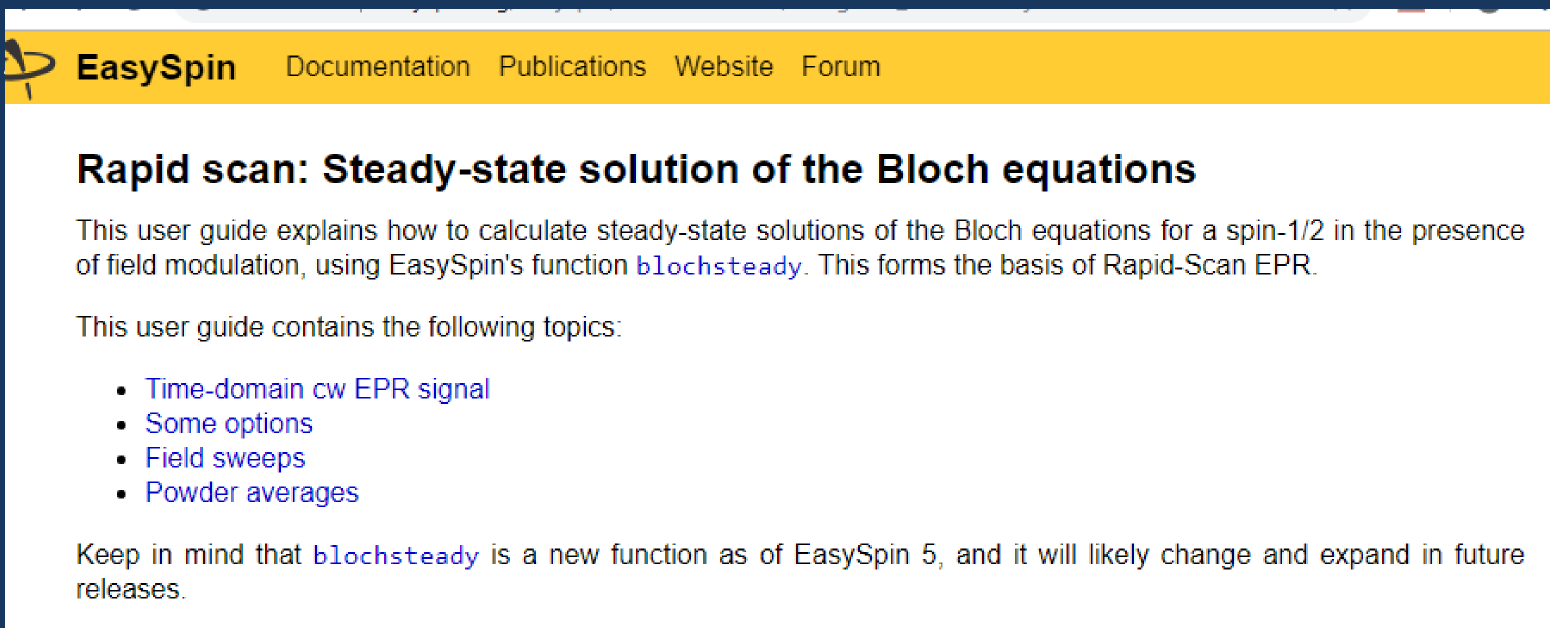


Approach 2.

Solve directly for steady state solution

Differential become algebraic equations

Much faster computation based on inversion of five-diagonal matrix.



EasySpin Documentation Publications Website Forum

Rapid scan: Steady-state solution of the Bloch equations

This user guide explains how to calculate steady-state solutions of the Bloch equations for a spin-1/2 in the presence of field modulation, using EasySpin's function `blochsteady`. This forms the basis of Rapid-Scan EPR.

This user guide contains the following topics:

- Time-domain cw EPR signal
- Some options
- Field sweeps
- Powder averages

Keep in mind that `blochsteady` is a new function as of EasySpin 5, and it will likely change and expand in future releases.

Our MATLAB version with examples from www.TseytlinLab.com

Link to MATLAB RS EPR demonstrations, including GUI app

https://www.tseytlinlab.com/we-share

tseytlinlab.com

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Downloadables:

- Interactive graphical user interface MATLAB Rapid-scan app.

Contains:
Single RS_EPR_Demonstration_Ver1_Nov2019.mlapp file
The app generates rapid-scan signal and shows two deconvolution steps.
It was made for teaching purposes and may not be used to process experimental data due to a
Created/Tested using MATLAB 2019b, may not properly work with earlier versions.
Feedback and bug-catching will be appreciated: mark.tseytlin[at]hsc.wvu.edu

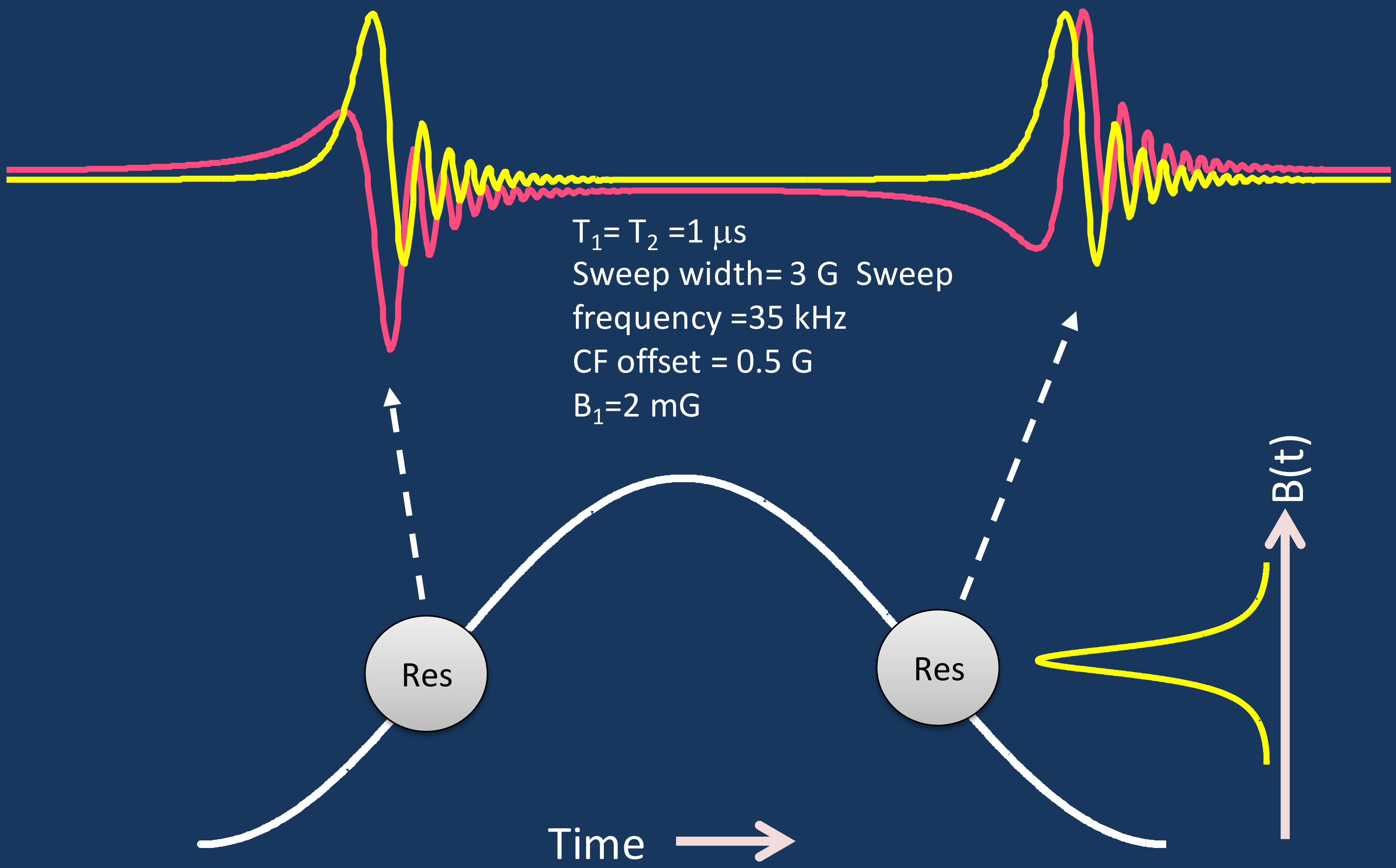
- MATLAB (scripts)files for Rapid Scan EPR signal simulations

Contains:
RSS.m : Bloch Equations
blochSin.m: solver
pentsolveM.m: matrix inversion
DemoWithComparison.m: major program to run

Download to play with RS

When run simulations, you should notice some important details:

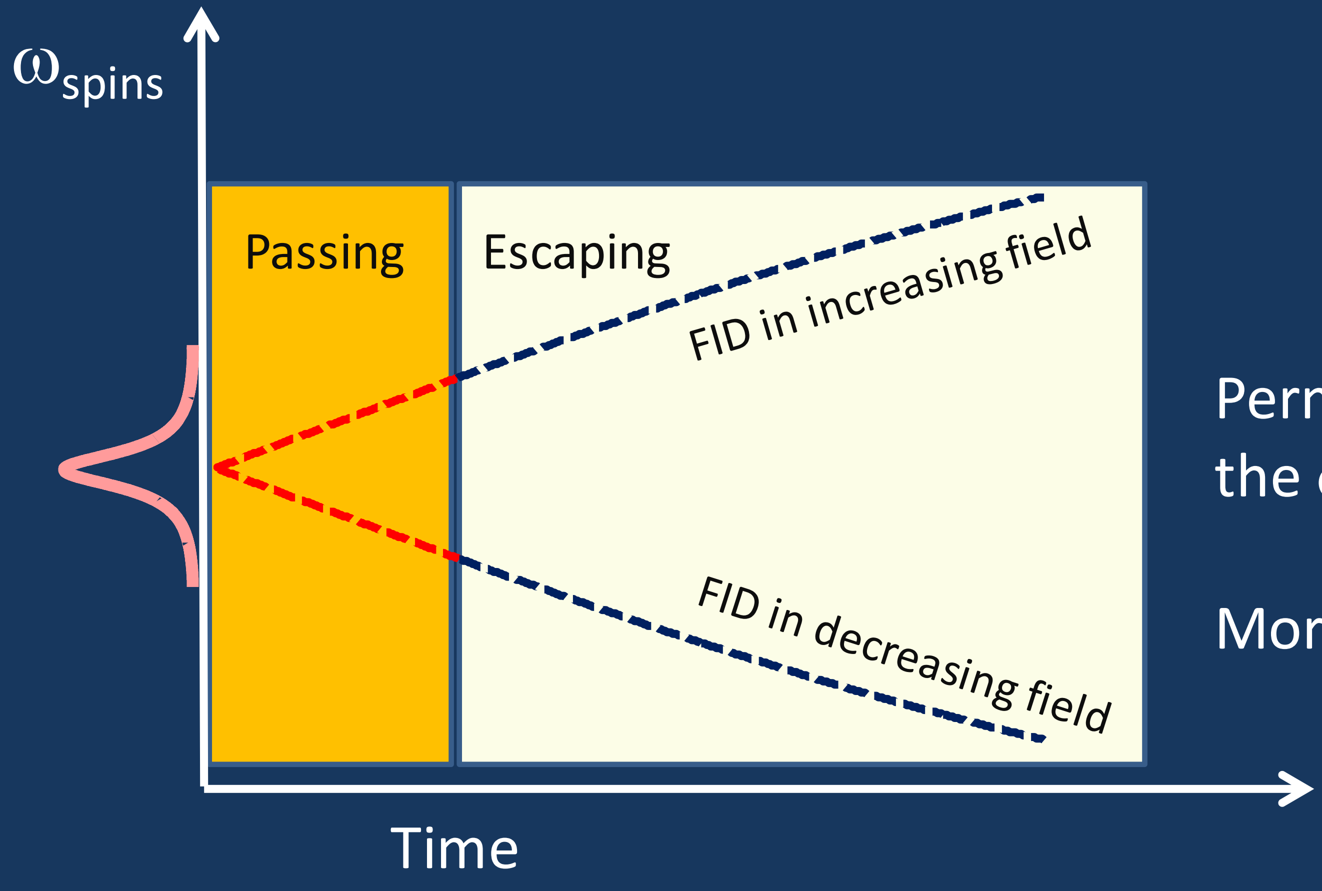
Two RS signals per period.



During scan, two time periods can be very roughly distinguished:

Passing through resonance (strong interaction with B_1)

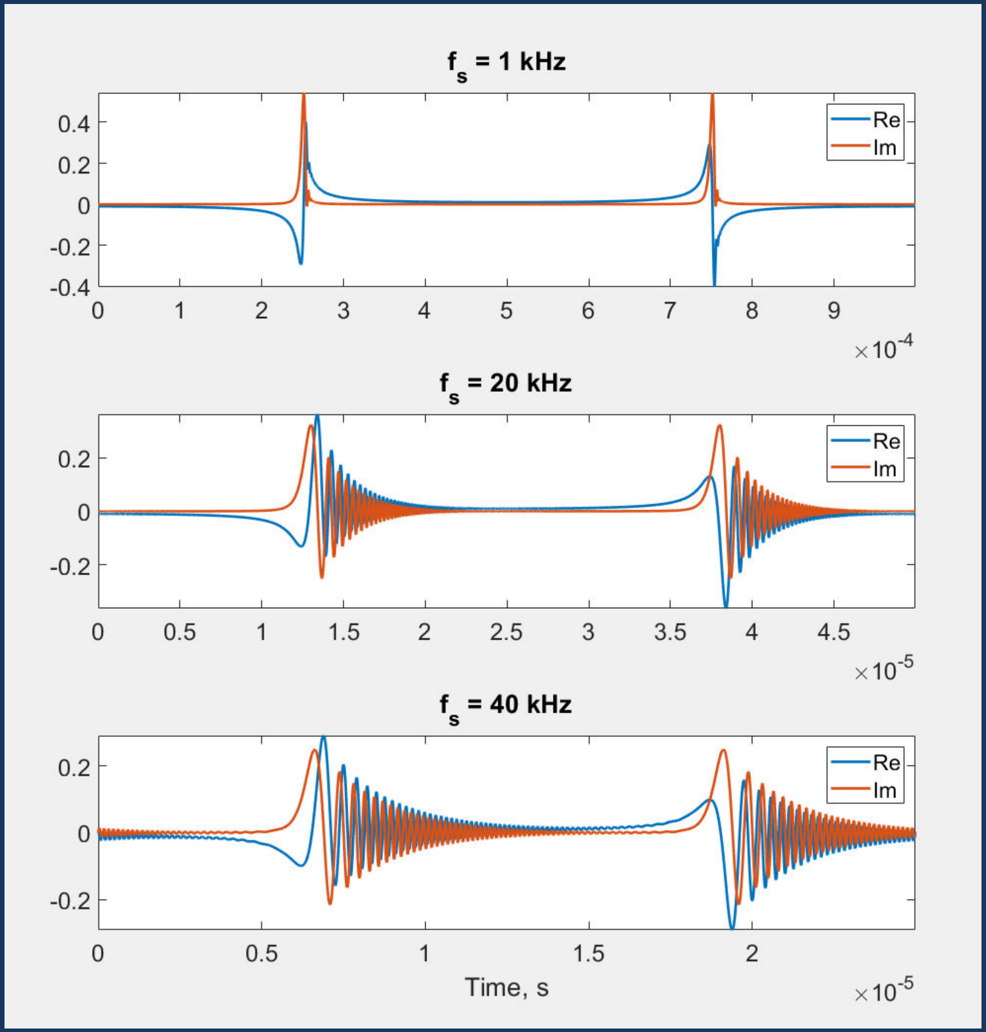
Escaping from the resonance (very weak interaction with B_1)



Permits separation in the ω-domain !!!

More later ...

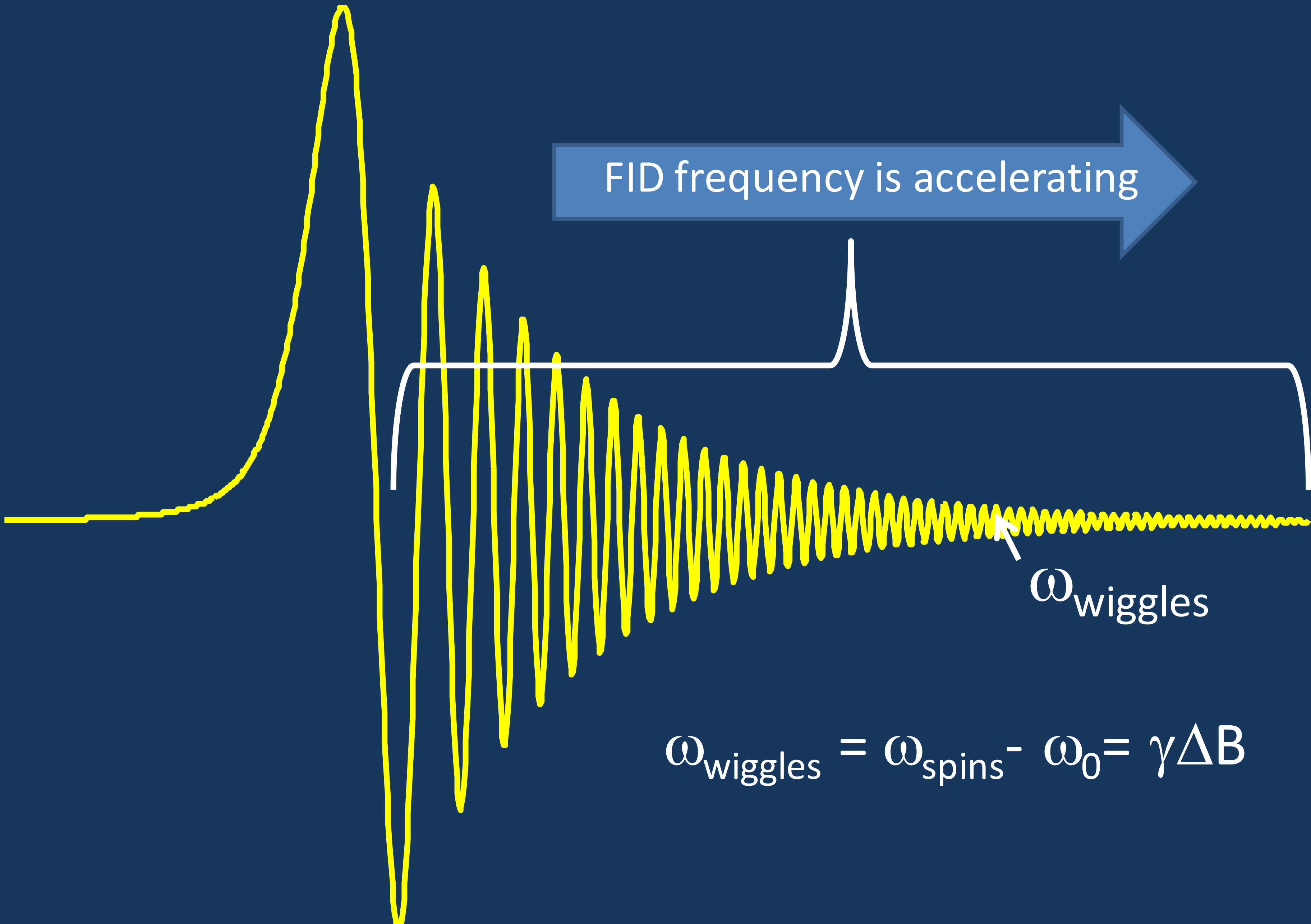
Scan rate increase: Absorption/Dispersion --> FID - like signal



RS is in-between CW and pulse!

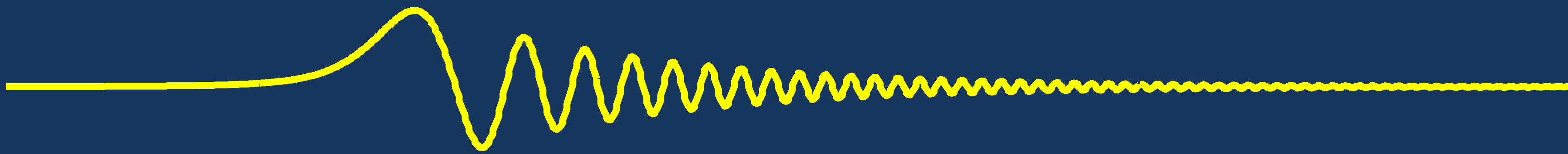
```
par.hm=5;        % Bpp modulation amplitude [G]
par.dH=0;        % Offset from central field position [G]
par.T1=2e-6;     % T1 [s]
par.T2=2e-6;     % T2 [s]
par.B1=0.01;     % B1 field [G]
```

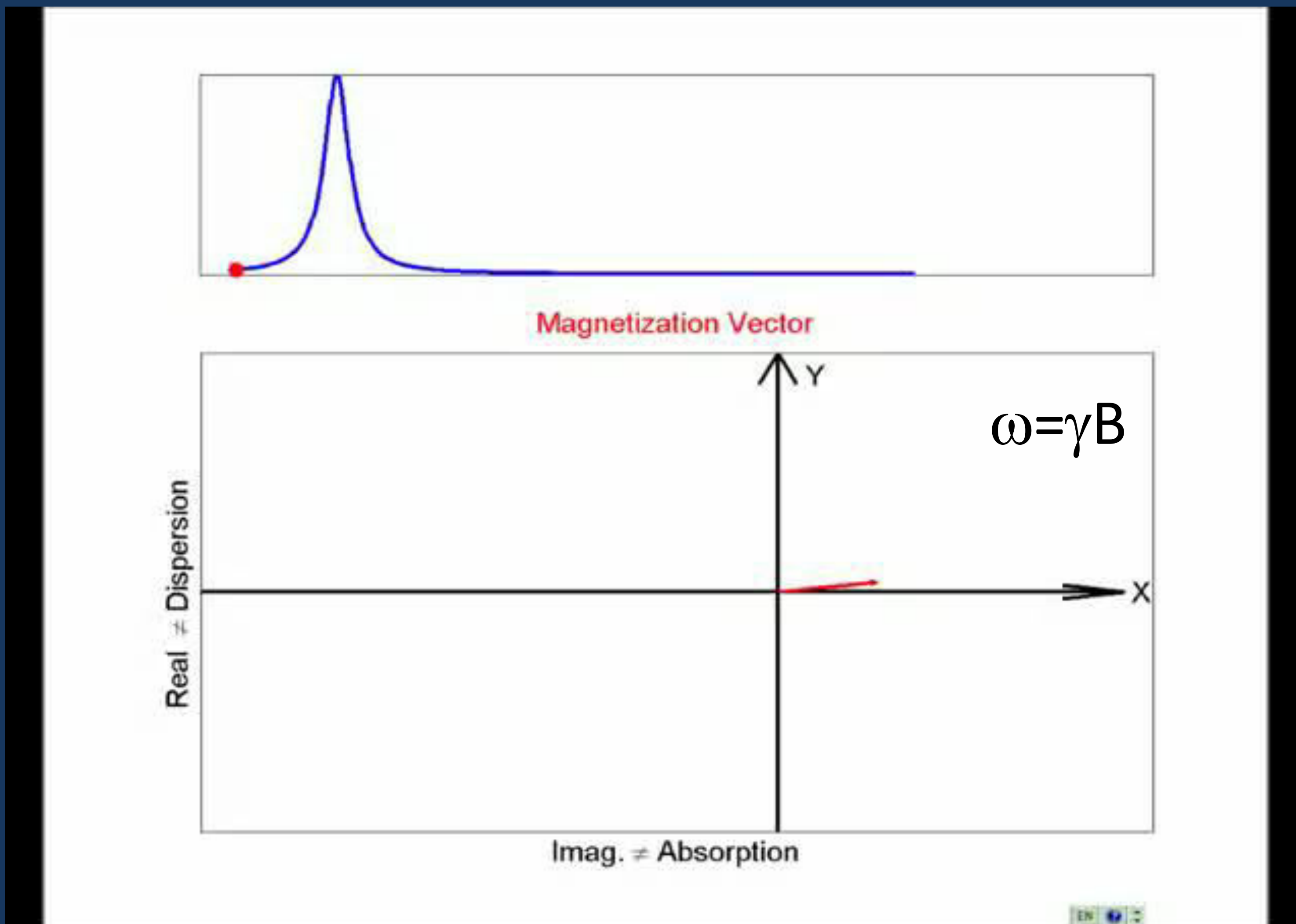
More nuances: accelerating oscillations ?



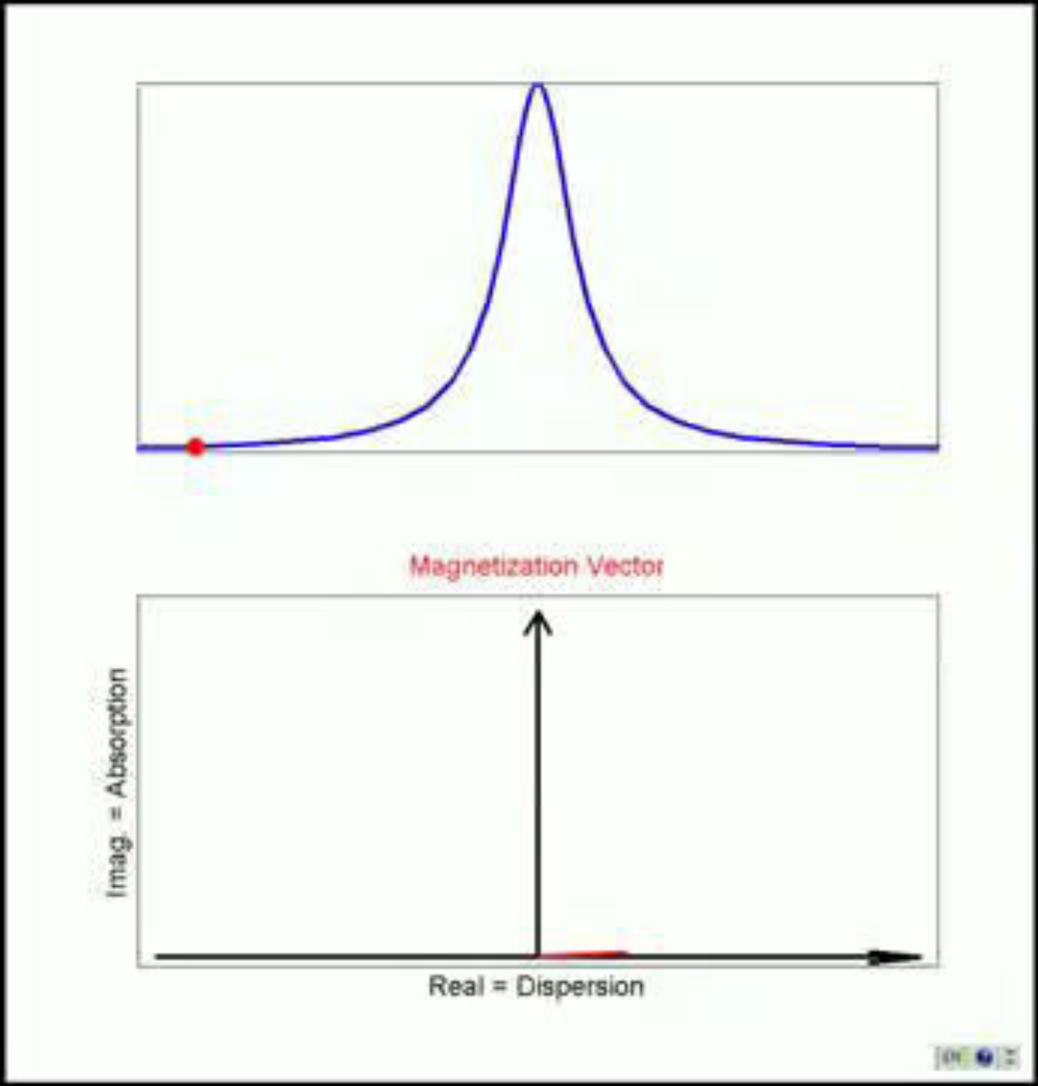
$$\omega_{wiggles} = \omega_{spins} - \omega_0 = \gamma \Delta B$$

RS EPR signal is measured in the constantly changing magnetic field B(t)





For comparison Slow Scan EPR...



RS signal bandwidth & its estimation

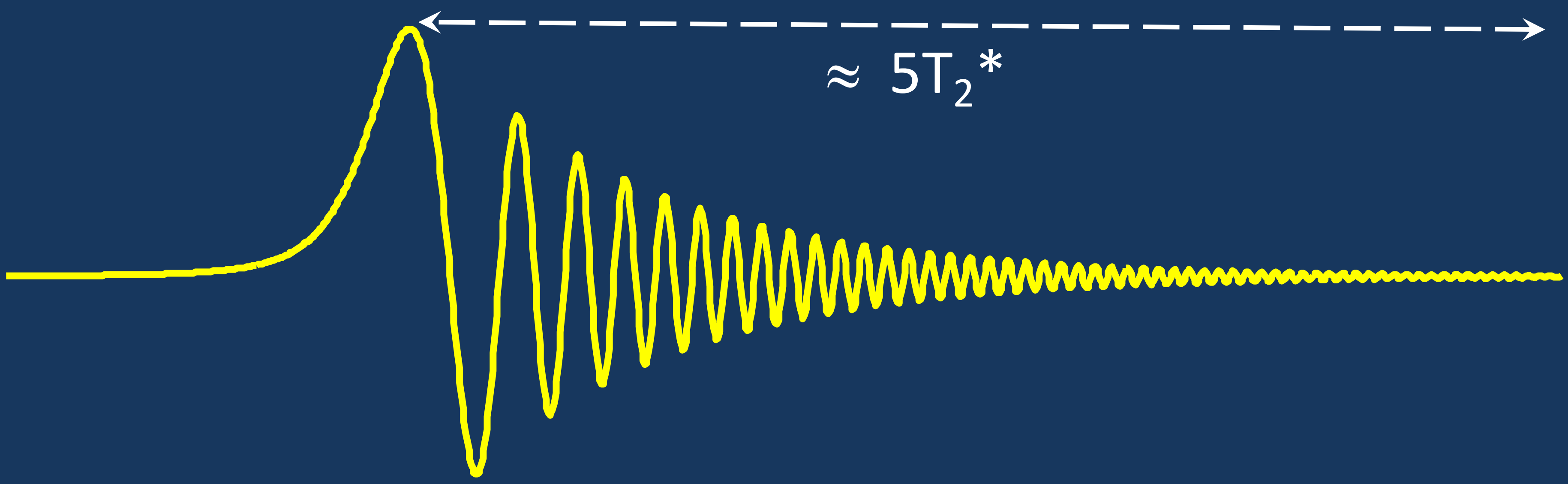
$B(t) = 0.5\, B_{pp} \sin(2\pi\, f_s\, t)$, where f_s is scan frequency

Highest rate is at $t = 0$, and equal to $rate_{max} = \pi\, B_{pp}\, f_s$

During $5T_2^*$ ring-down time, the Larmor frequency will change by:

$$\Delta\omega_L = \gamma \Delta B \approx \gamma\, rate_{max}\, 5T_2^* = \gamma\, 5\pi\, B_{pp}\, f_s\, T_2^*$$

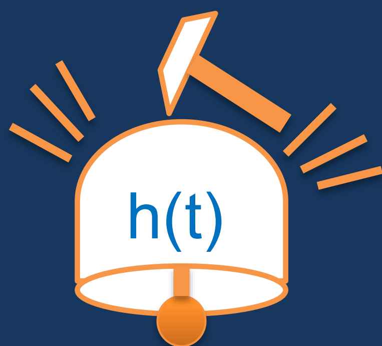
Bandwidth estimates as $2\,\Delta f_L = \Delta\omega_L / \pi = \gamma\, 5\, B_{pp}\, f_s\, T_2^*$ must be $< f_0/Q$



Back to LTI RS Theory: Data Processing

Any linear system is uniquely characterized by an impulse response function:

$x(t) \rightarrow$



$\rightarrow \quad r(t) = x(t) \otimes h(t)$

$a\,x(t) \rightarrow a\,r(t)$

$x(t+\tau) \rightarrow r(t+\tau)$

$R(\omega) = X(\omega)\,H(\omega)$

$\text{Detected\_signal}(t) = B_1(t) \otimes \text{FID}(t)$

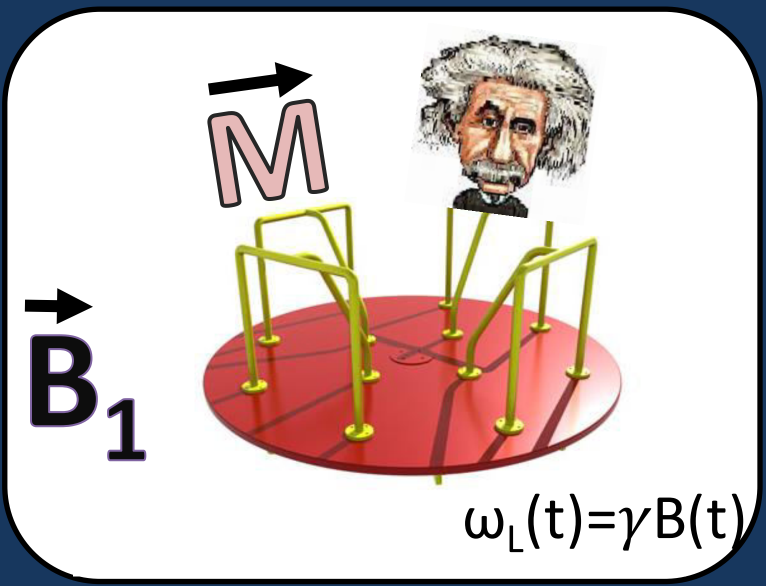
- CW RS EPR (B_1 = const) => deconvolution as-is does not work
- FT(const) =const * $\delta(\omega)$

In principle, RS signals can be fitted as is. However, not very practical

(Absorption) EPR spectra can be obtained in two major steps:

Step 1. Transformation into the frame reference of the Larmor frequency

$$\left\{ \begin{array}{l} x(t)= B_1 \\ B_0=B_0(t) \\ r(t) \end{array} \right\} \xrightarrow[\varphi(t)= \gamma\int B_0(t)dt]{f(t) = \exp\{-j\,\varphi(t)\}} \left\{ \begin{array}{l} x(t)= B_1 f(t) \\ B_0=\mathrm{const} \\ r'(t)=r(t)\, f(t) \end{array} \right\}$$



In the new accelerating frame:

- Larmor frequency does not accelerate
- $\mathbf{B_1}(t)$ vector becomes time-dependent

Field sweep mathematically transforms into frequency sweep!

Step 2. Deconvolution

$R'(\omega)=X(\omega)\, H(\omega)$

$EPR\,(\omega)= H(\omega) = R'(\omega)/X(\omega)$

$R'(\omega) = FT\,(r')$, r' – RS signal after transformation

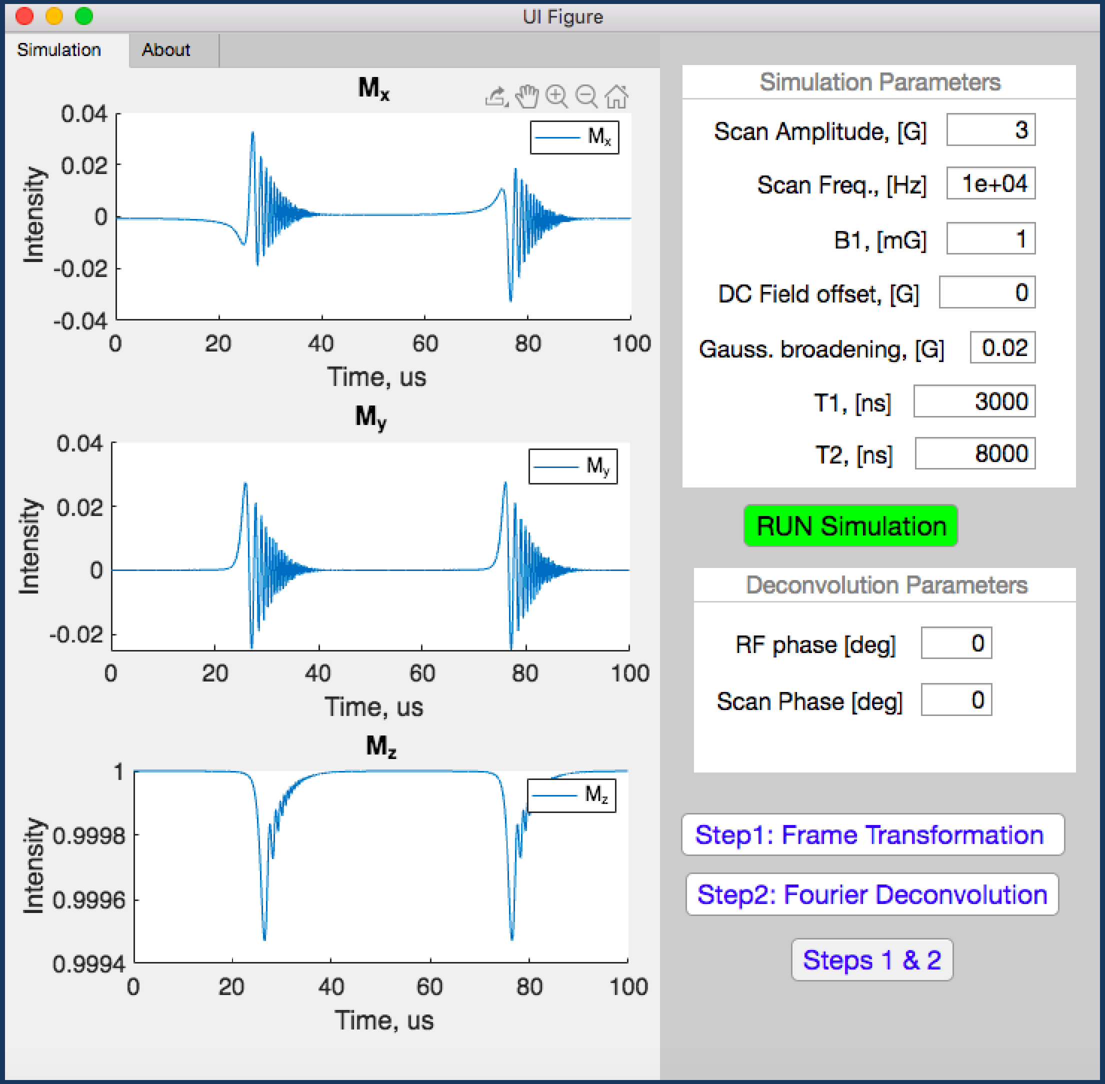
$X(\omega) = FT\,(x)$, x - $B_1(t)$ in the new frame

$H(\omega) = FT\,(h)$, h - FID

MATLAB real-time demonstrations ….

MATLAB GUI app can be downloaded from

https://www.tseytlinlab.com/we-share



Suggested exercises:

https://www.tseytlinlab.com/we-share

1. RUN Simulation, Step1, Step2 using default parameters
2. Increase Scan Amplitude to 10, again Run & Step 1 & Step 2
3. Increase T_2 to 8000, Run, Step1, Step2
4. Scan Frequency to 1000, Scan Amp to 3, …

Observe transitions: Absorption/Dispersion <-> FID-like signals

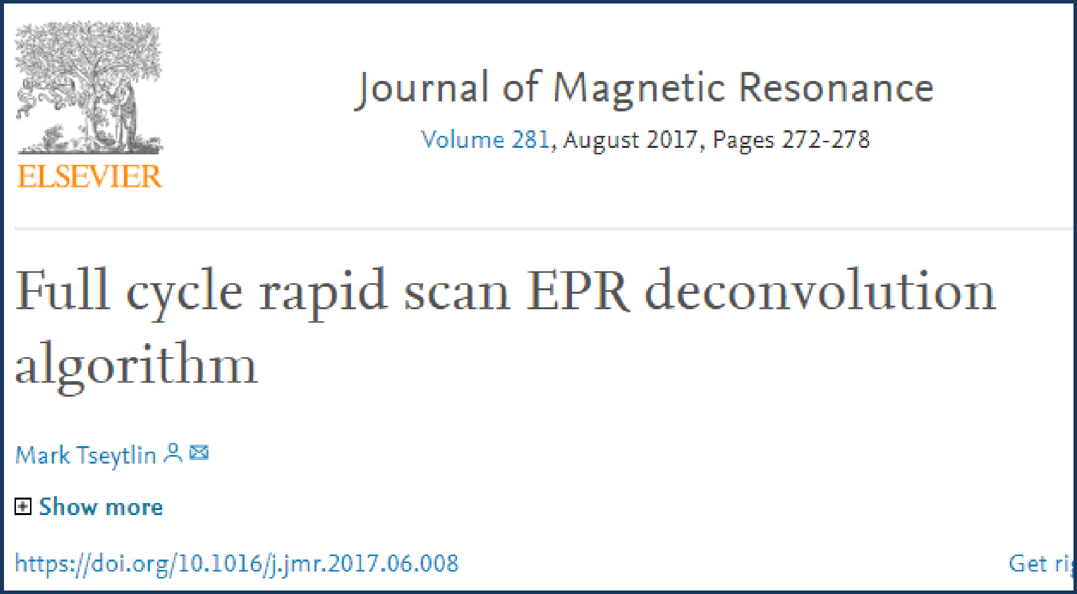
1. Increase B1 to 40 mG. Observe broadening
2. Increase Scan Frequency to 15000. Observe EPR line narrowing

Do your own simulations,

Observe RS physics & limitations of this algorithm

The most recent version of the LTI algorithm (2017)

https://www.sciencedirect.com/science/article/pii/S1090780717301635?via%3Dihub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Journal of Magnetic Resonance

Volume 281, August 2017, Pages 272-278

Full cycle rapid scan EPR deconvolution algorithm

Mark Tseytlin

Show more

https://doi.org/10.1016/j.jmr.2017.06.008

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Some limitations still remain:

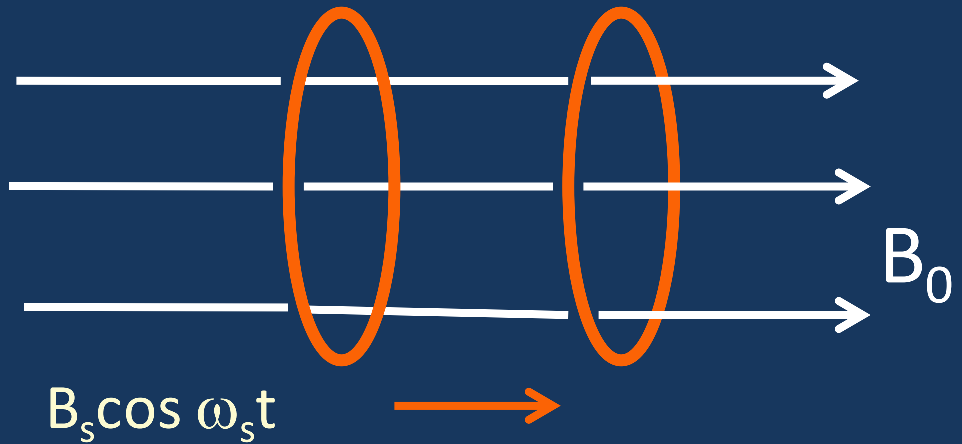
- Spin system is linear (obvious)
- Periodicity constraint: longest FID duration equal to the scan period
- Reliably removes 1st and 2nd background harmonics, higher problematic

  Why/what is background?

Scan magnetic field coils in the external magnetic field are essentially single frequency speakers. Vibrations modulate power reflection/transmission to produce EPR-like periodic signals. The highest is the fundamental harmonic.

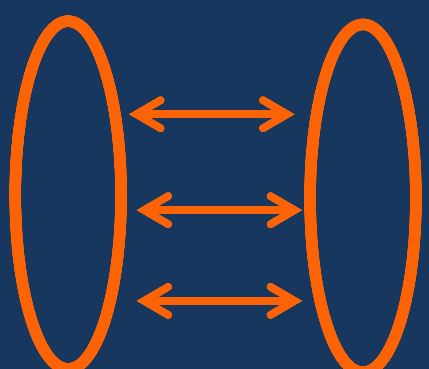
MATLAB code has a number of 'cleaning' features, such as background removal due to the Microphonic Effect

1st harmonic microphonic, speakers

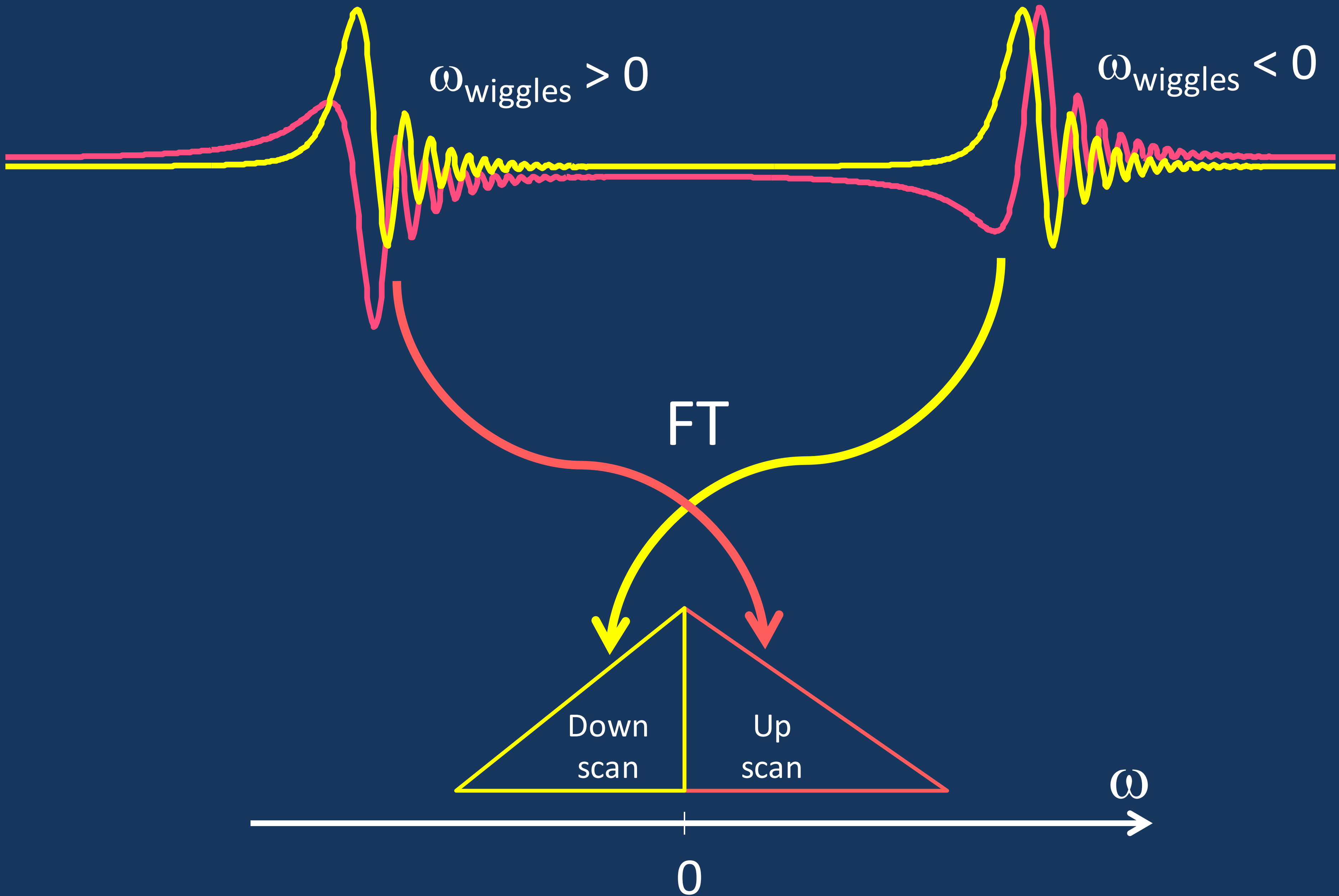


$$\text{Force} \propto B_0 B_s \cos \omega_s t$$

2nd harmonic microphonic



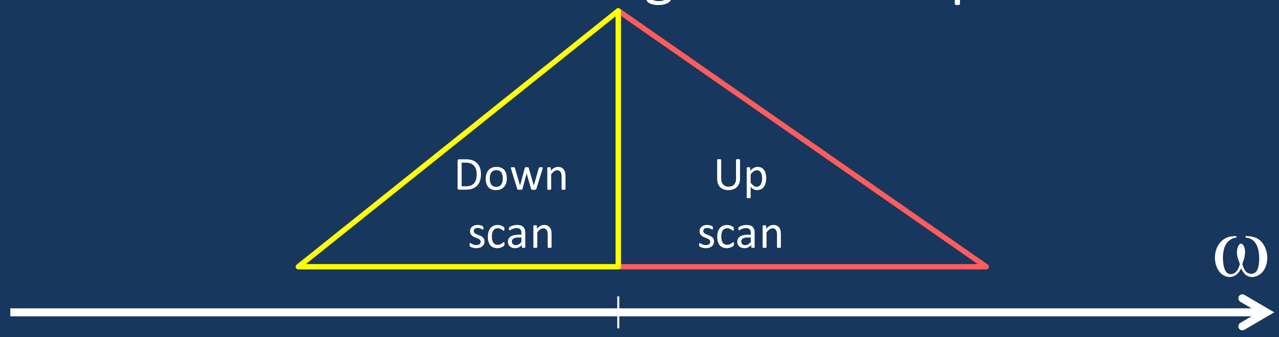
$$\text{Force} \propto (B_s \cos\omega_s t)^2 \propto \cos 2\omega_s t$$



Up-field and down-field scans are separated in the ω-domain!

As a result:

Up-field and down-field RS signals are separated in the ω-domain



Background removal algorithm

Step 1. Fourier transformation of rapid scan signal plus background

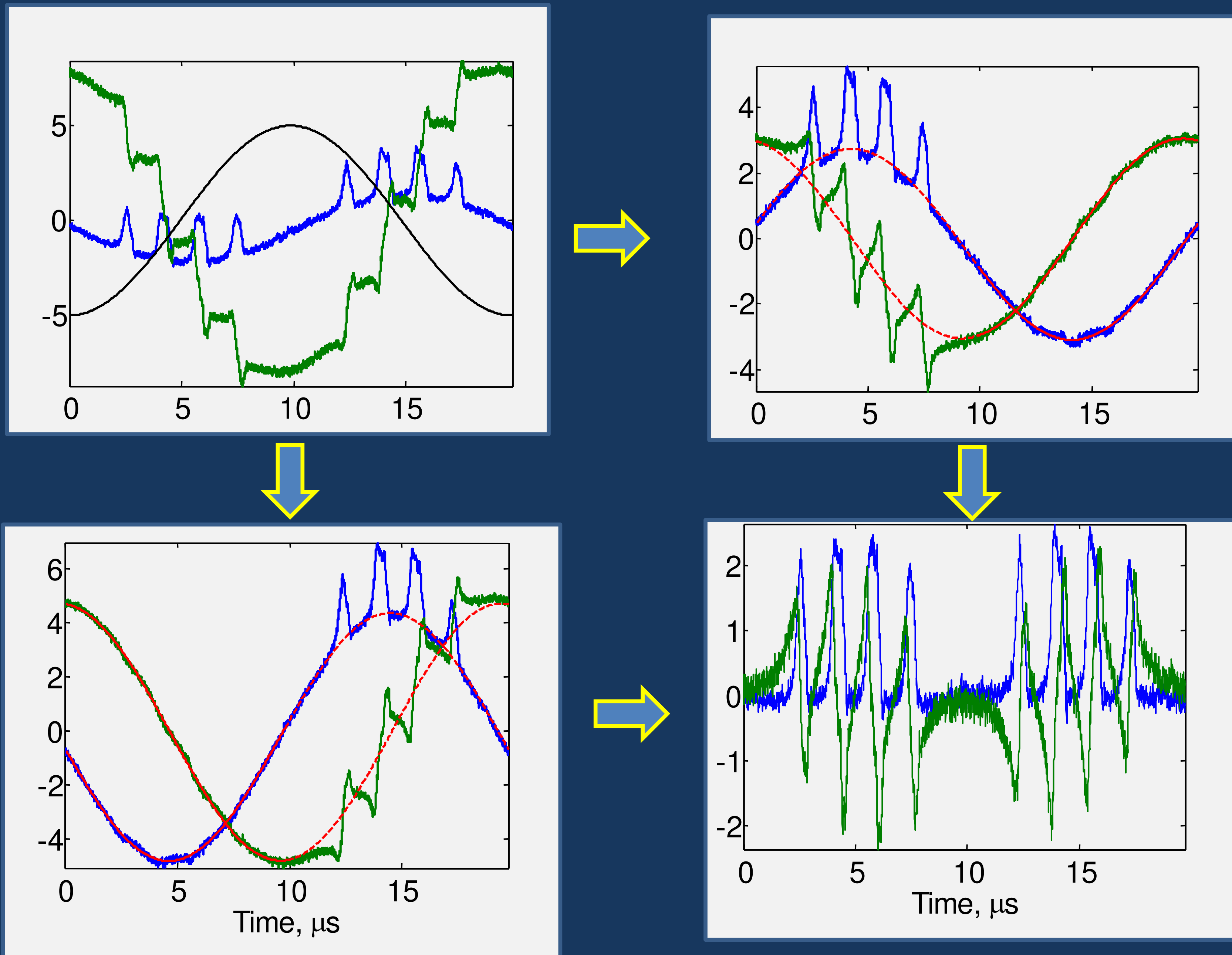
Step 2. Separation of up-field and down-field components.

The result is two frequency domain signals.

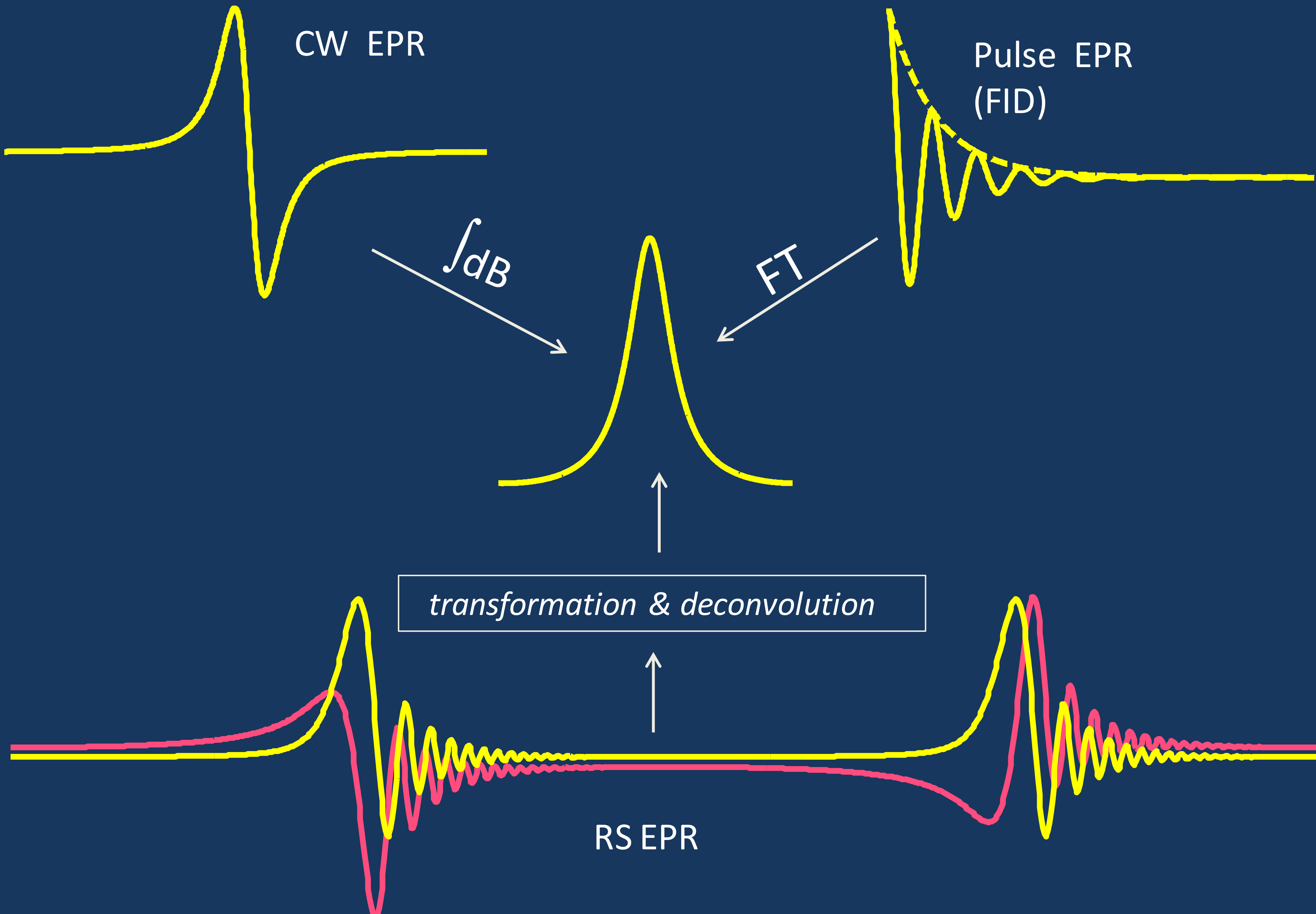
Step 3. These two signals are Inverse Fourier transformed into the time-domain

Step 4. Background signals are fitted in the areas with no EPR , extrapolated into EPR containing areas and subtracted.

Example: background subtraction procedure to spectra of BMPO-OOH at X-band.



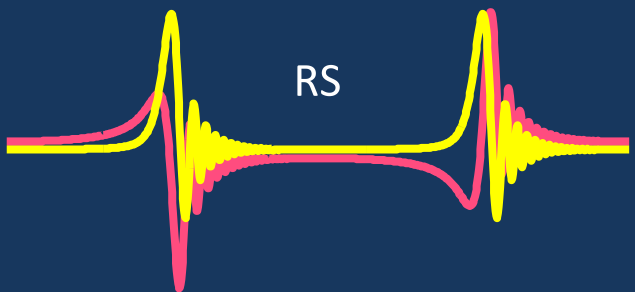
FID vs. RS vs. 1st harmonic CW (CW^{1h}) comparison:



CW^{1h} vs. RS vs. FID

1st harmonic CW = CW^{1h}

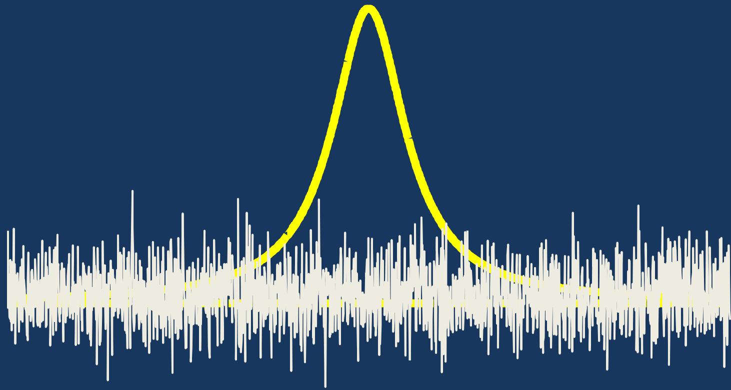
No dead time, no bandwidth (BW) limit, lower SNR



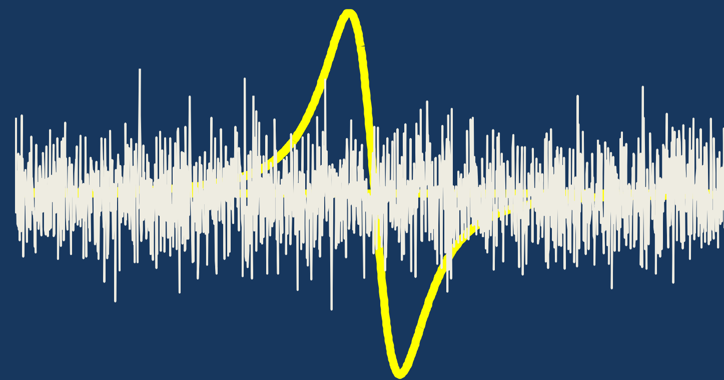
No dead time, Q-limited BW detection, higher SNR with higher CW power, however LNA saturation.

Dead time, Q-limited BW detection & excitation
Pulse length limited excitation
Signal detected in ‘silence’ after dead-time

How to compare RS and CW^{1h} EPR?

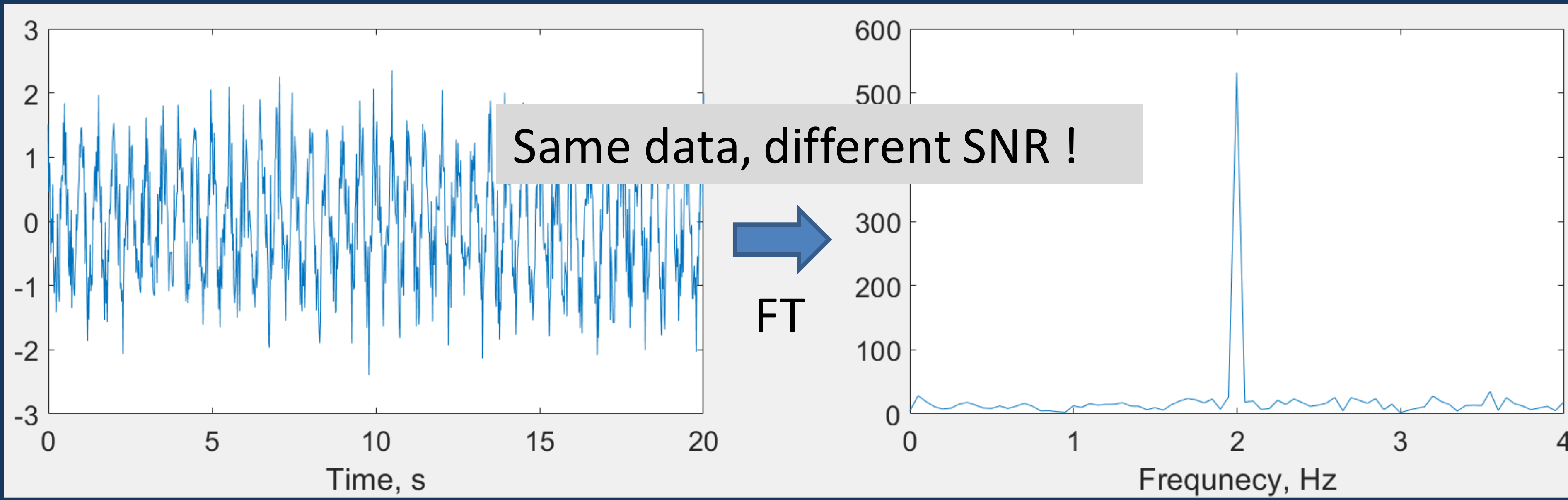


vs.



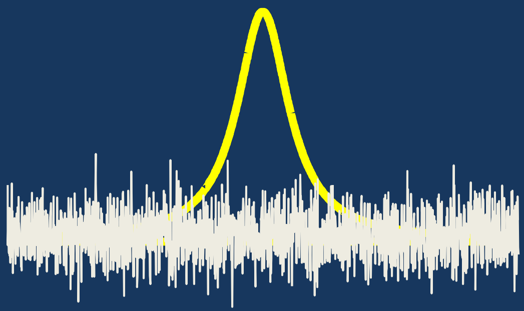
Most straightforward approach: directly compare signal-to-noise (SNR) ratios

However, not very informative: you cannot compare SNR of different shapes



A meaningful quantitative approach is to focus on the information

An example: a single Lorentzian line + noise is measured

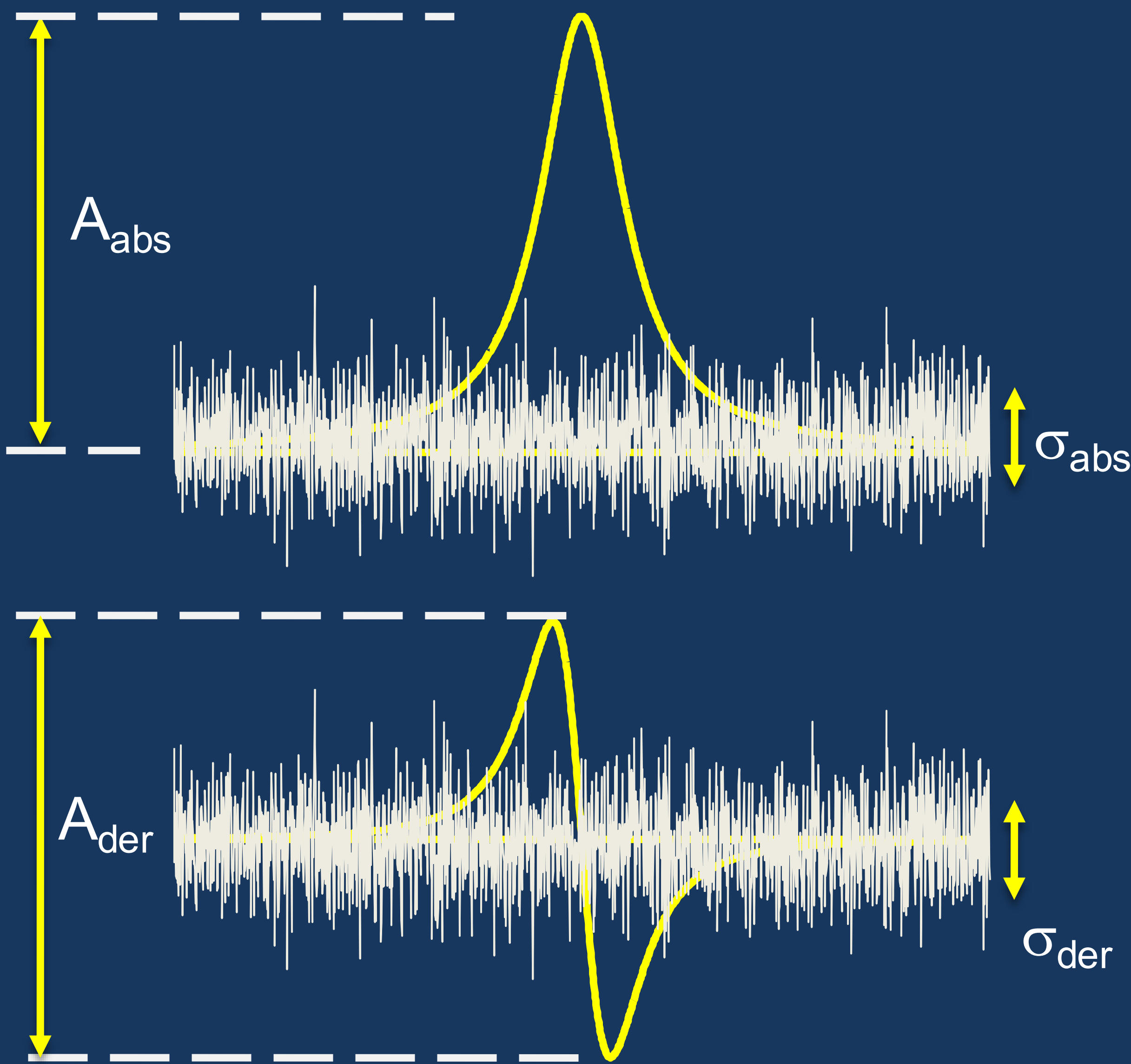


This line is uniquely defined by two parameters:

1. Amplitude , A
2. Line Width, Lw
3. We will not consider phase

- A meaningful question (vs. SNR): what is the uncertainty to measure A and Lw?
- Same questions can be asked about the derivative line
- Comparison can be made base on the uncertainties in A and Lw.
- Interestingly, a relation between SNR and uncertainties can be found
  - Analytically for some cases
  - Numerically

SNR definition, example for a single EPR line



SNR definition

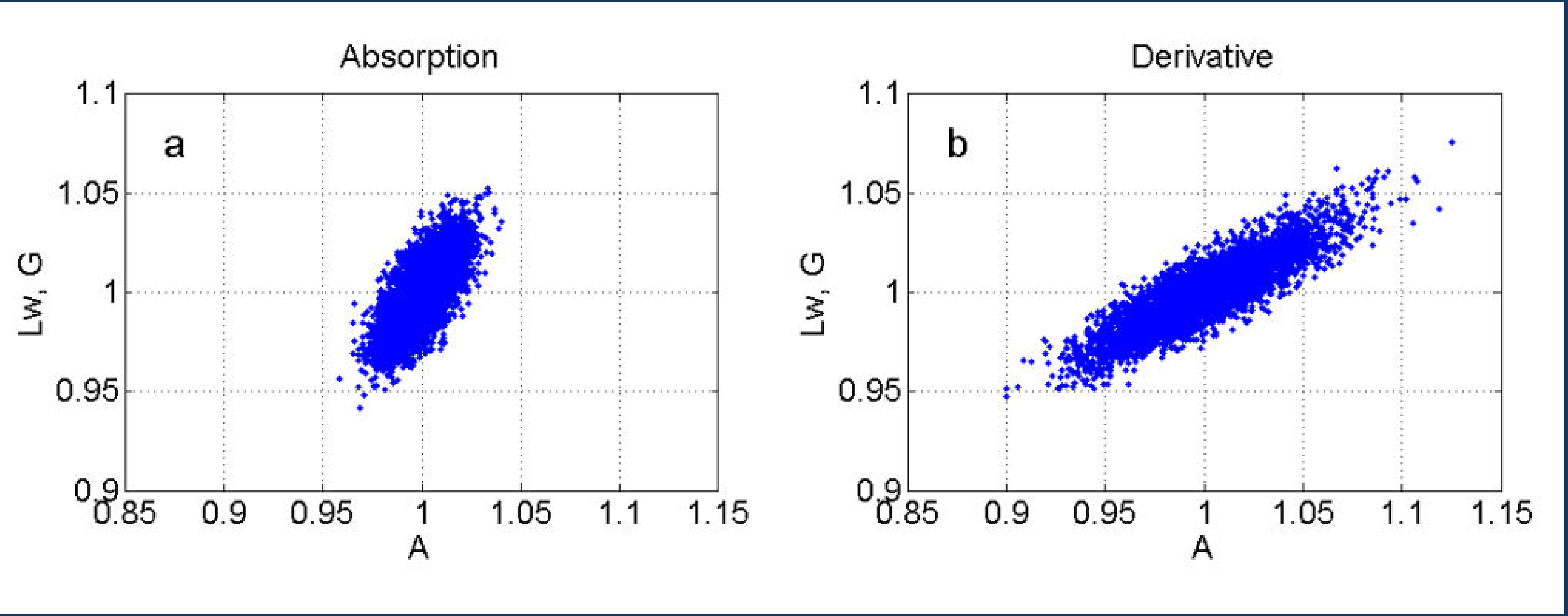
$$SNR_{abs} = A_{abs} / \sigma_{abs}$$

$$SNR_{der} = A_{der} / \sigma_{der}$$

Uncertainty analysis

Equal SNR = 5 absorption and derivative spectra

Results of line fitting:

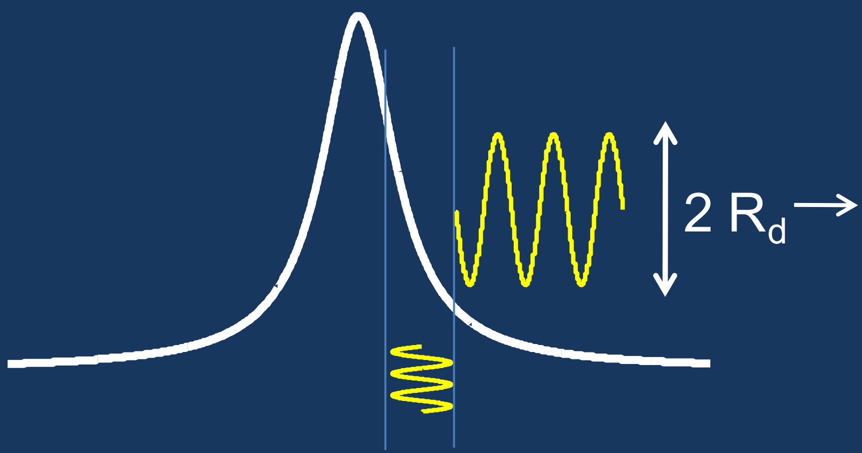


- Uncertainty (SD) in linewidth measurements are similar
- Uncertainty for integral intensities is > twice as large for derivative.

SNR has to be redefined in terms of the accuracy of measurements!

Tseitlin, et al, Concepts in Magnetic Resonance Part A, V40A, Issue 6, 295-305 (2012)

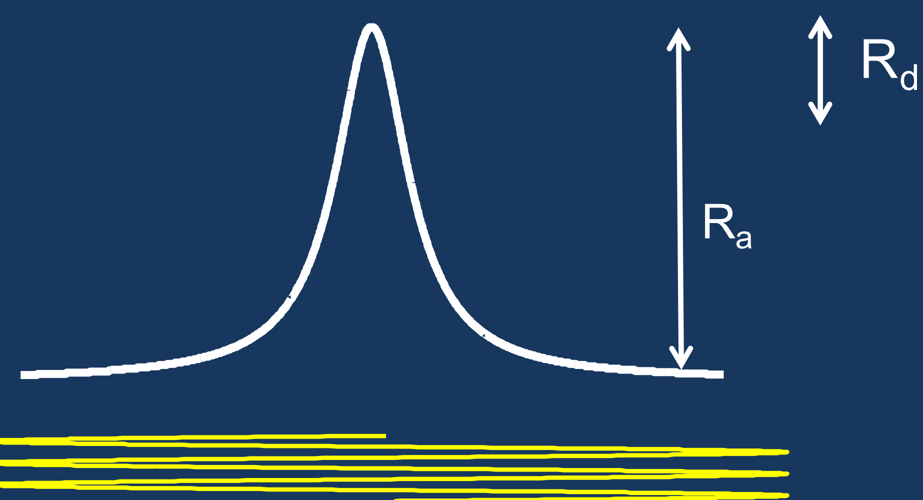
Signal comparison



Phase sensitive detection

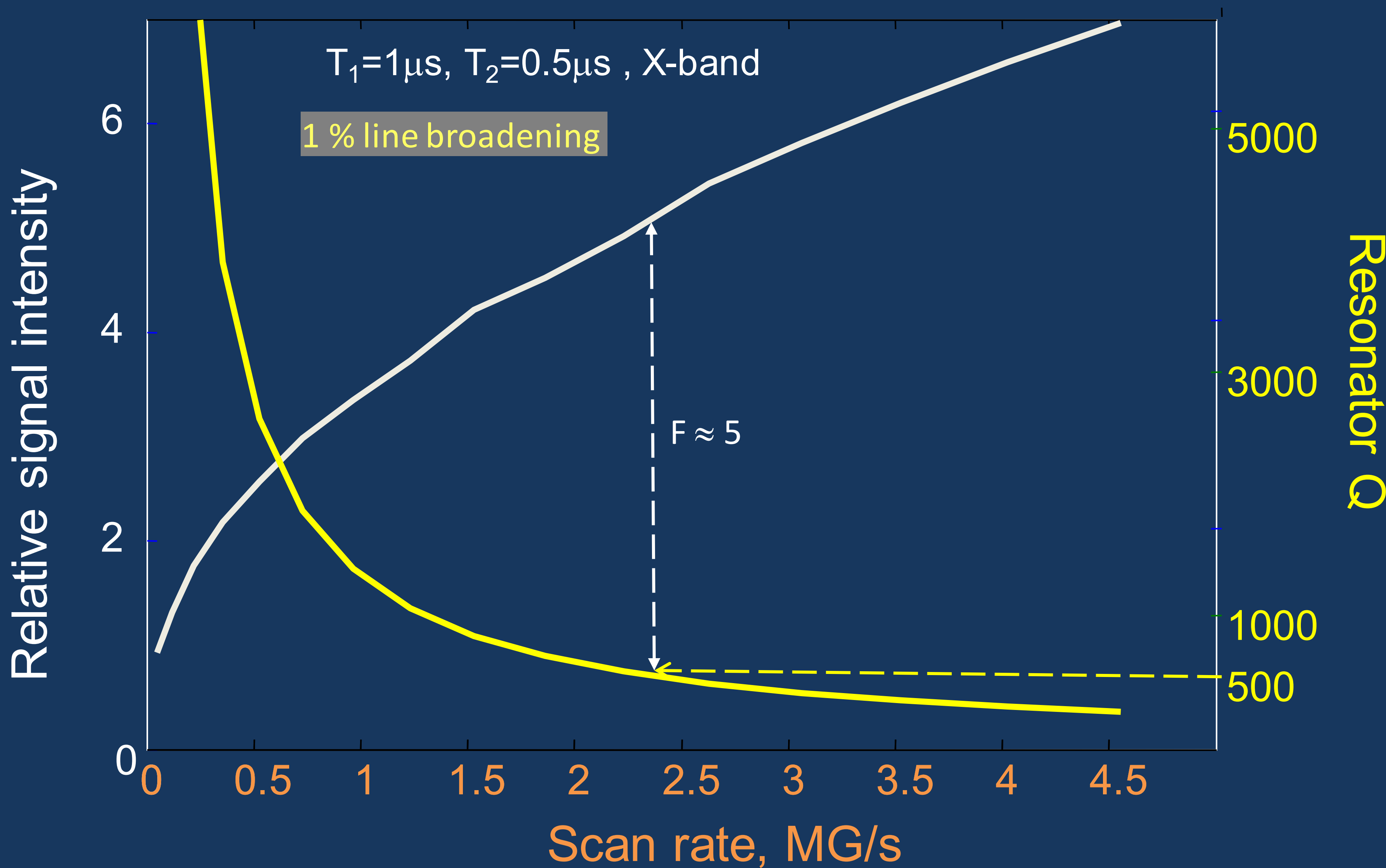
$R_d \cos^2\omega t = R_d/2 (\cos 2\omega t + 1) = R_d/2$

x2 in SNR definition => R_d



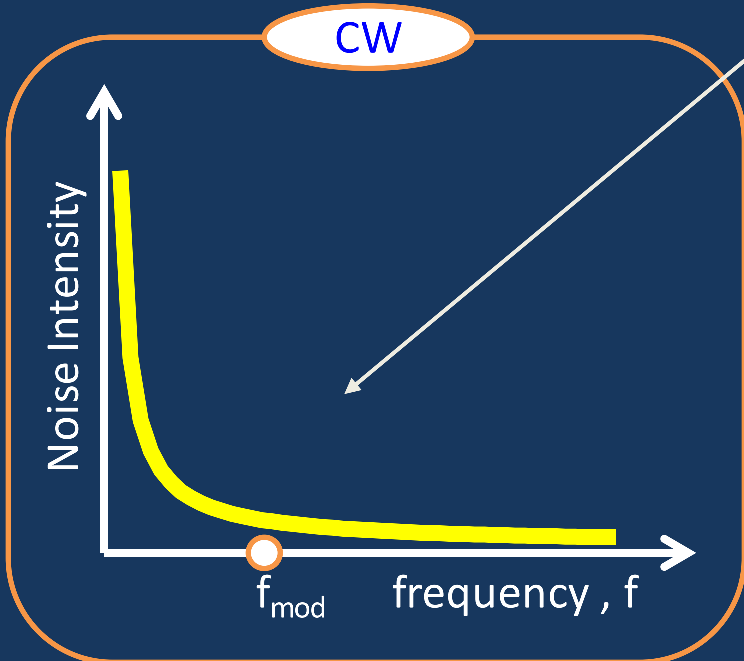
$R_a/R_d \approx$ 3-5, depending on the modulation amplitude.

RS signal optimization ($B_1 \neq$ const)



F = increase in the signal amplitude due to rapid scan

Experimental noise (is not white)



e.g.: 20 kHz => Period = 50 us.

EPR spectrum each 25 us.

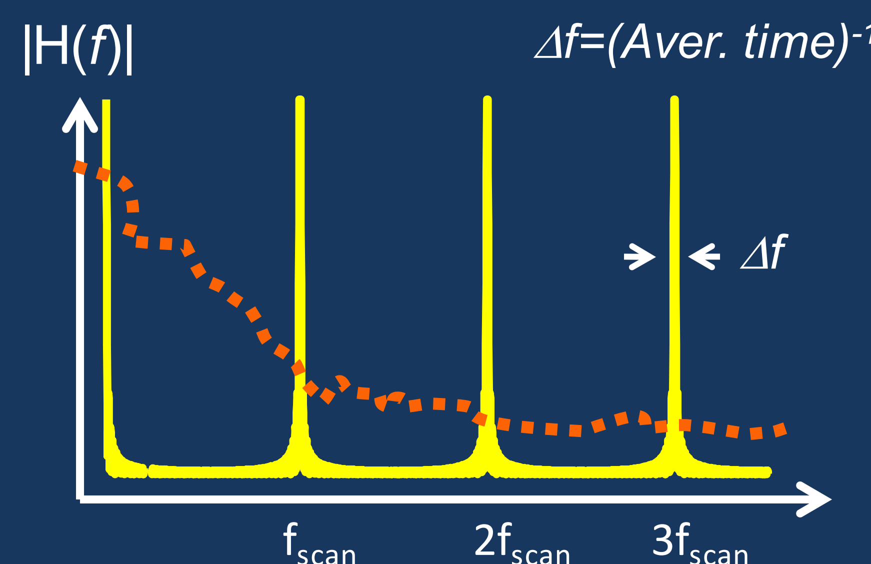
We average 10 – 10'00'000 of RS signals. Averaging of a periodic signal in the time is equivalent to applying a comb filter in the frequency domain

Concept: Averaging of periodic signal.

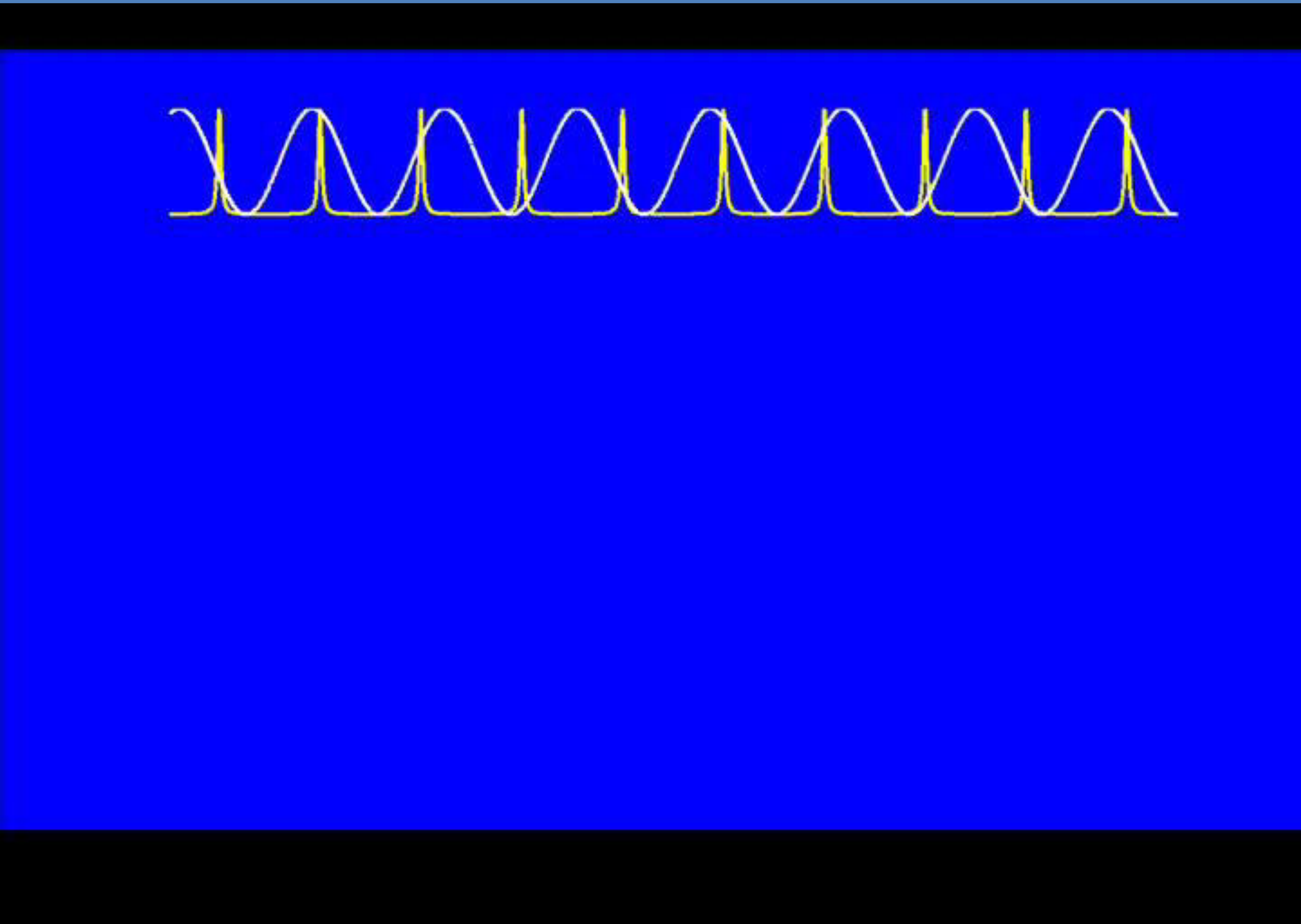
Time domain: $\sigma \propto 1/(N_{aver})^{1/2}$

Frequency domain comb filter

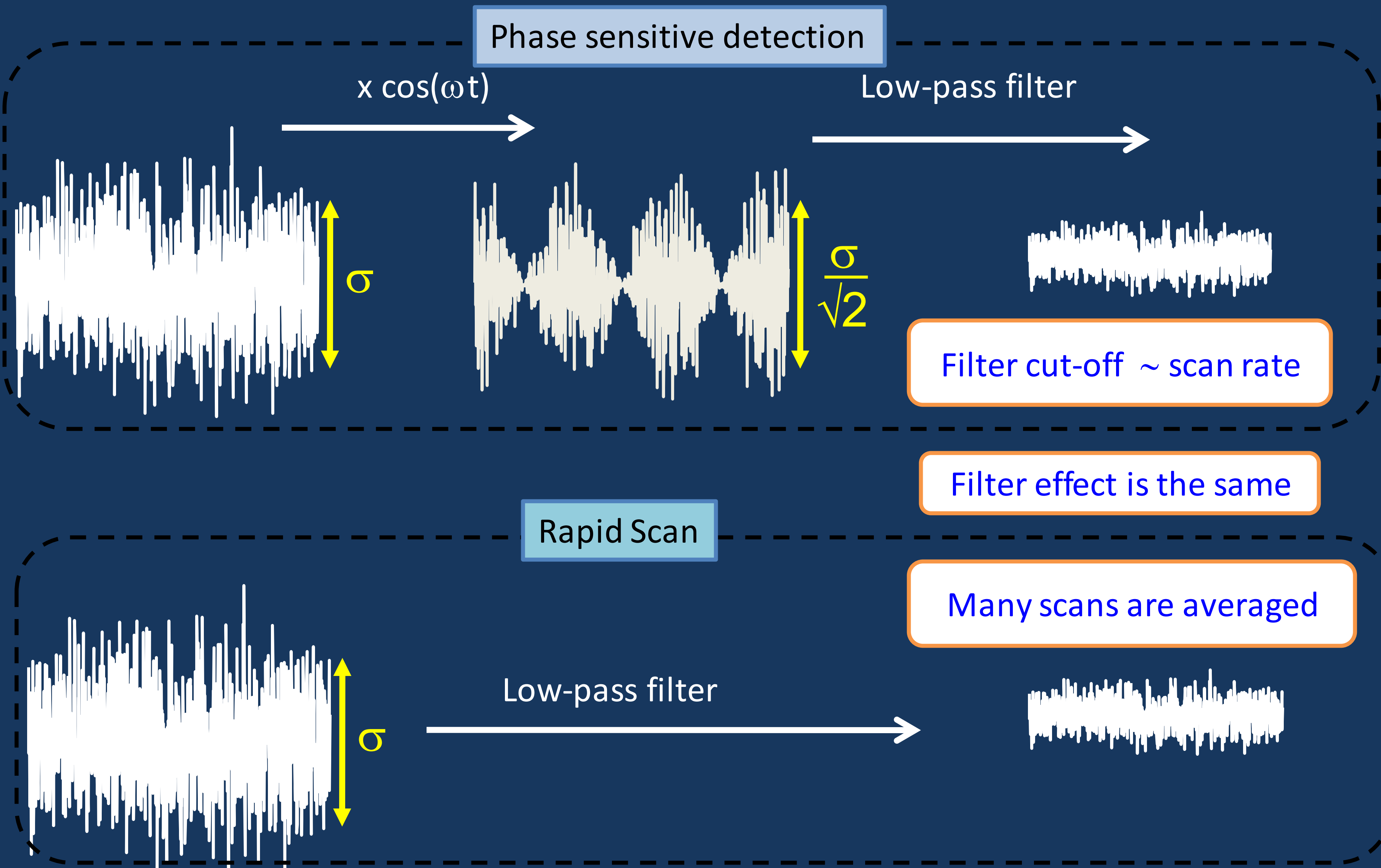
$$|H(f)| = \frac{\sin\,(N_{aver}\,\pi\, f\,/\,f_{scan})}{\sin\,(\pi\, f\,/\,f_{scan})}$$



Example: 50 kHz scan frequency & 38 kHz noise component



If noise is white, phase-sensitive detection is $\sqrt{2}$ noise-less vs. direct detection



Fact: Increasing scan frequency does NOT improve SNR

Example:

A. One CW spectrum with SW = 10 G, sweep time 10 s

B. Two CW same spectra w/sweep time 5 mins. each, spectra are averaged.

For A and B optimized noise filtering is used

SNR (A) = SNR(B)

It is because:

Faster x 2 means noise x $\sqrt{2}$ but averaging x $1/\sqrt{2}$

Conclusion 1 Faster scan doesn't reduce noise if experimental time is const.

Conclusion 2: Phase sensitive detection reduces noise $\cong \sqrt{2}$

In practice, a lot will depend on prior amplification stages

SNR gain for RS vs. CW[1h]

Assuming white noise. SNR gain is estimated as $\sqrt{2}\ F\ R_a/R_d$

This or a single EPR line this translates into reductions of uncertainties

For amplitude: $\sqrt{2}\ F\ R_a/R_d$

For line width: $2\sqrt{2}\ F\ R_a/R_d$

- Up to x100 SNR gain for samples having long relaxation times.
- Spin system saturates at lower powers but the detection system is not.
- More about this issue later …

Instrumentation: RF/MW units

But before, brief summary of facts we learned and related conclusions:

- RS algorithm requires quadrature signal, both M_x and M_y components.
- Slow scan regime: M_x and M_y are dispersion and absorption, respectively.
- Rapid passage: not any more when FID-like signal
- RS bridge is similar to pulse bridge. In fact, a pulse bridge can be used.
- A limiter may be needed to protect the detection system, depending on power
- Power is CW. However, detection is broadband and limited by the resonator Q.
- Signal is periodic with no gaps in data acquisition (compare to pulsed EPR)
- RS signals have to be real-time averaged, ideally using an FPGA digitizer.
- RS sensitivity comes from increased power without spin system saturation
- However, LNA saturation and source noise (related to power) is a major problem

LNA: low noise amplifier; Q : resonator quality factor
FPGA: field programmable gate array ; RF: radiofrequency; MW microwave

Let's start with a simplistic RF/MW power diagram

RF/MW power
Phase noise

Two Resonator types:
R. Reflection type
T. Transmission type

R

T

I/Q
Down-conversion

A/D conversion
with real-time
averaging

Design aspects that we will address:

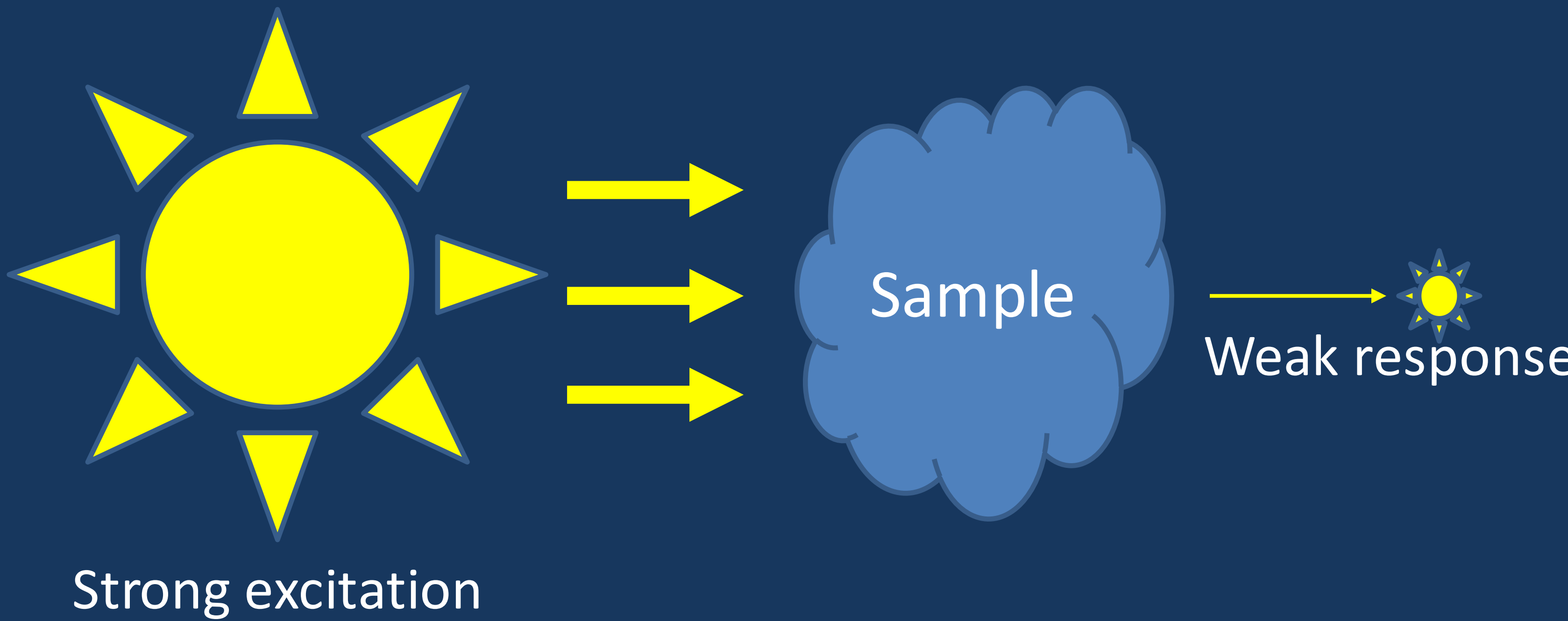
- Non-EPR reflection (R) and transmission (T) needs to be minimized to avoid LNA saturation and noise

- Noise transformation

Before looking into LNA saturation, a general for spectroscopy problem:

Excitation/detection decoupling

Optics, EPR, NMR, sound, …



Everyday life example:

We do not see stars (except for the sun) at day time

Approaches to excitation/detection decoupling:

Approach 1. Time-domain decoupling

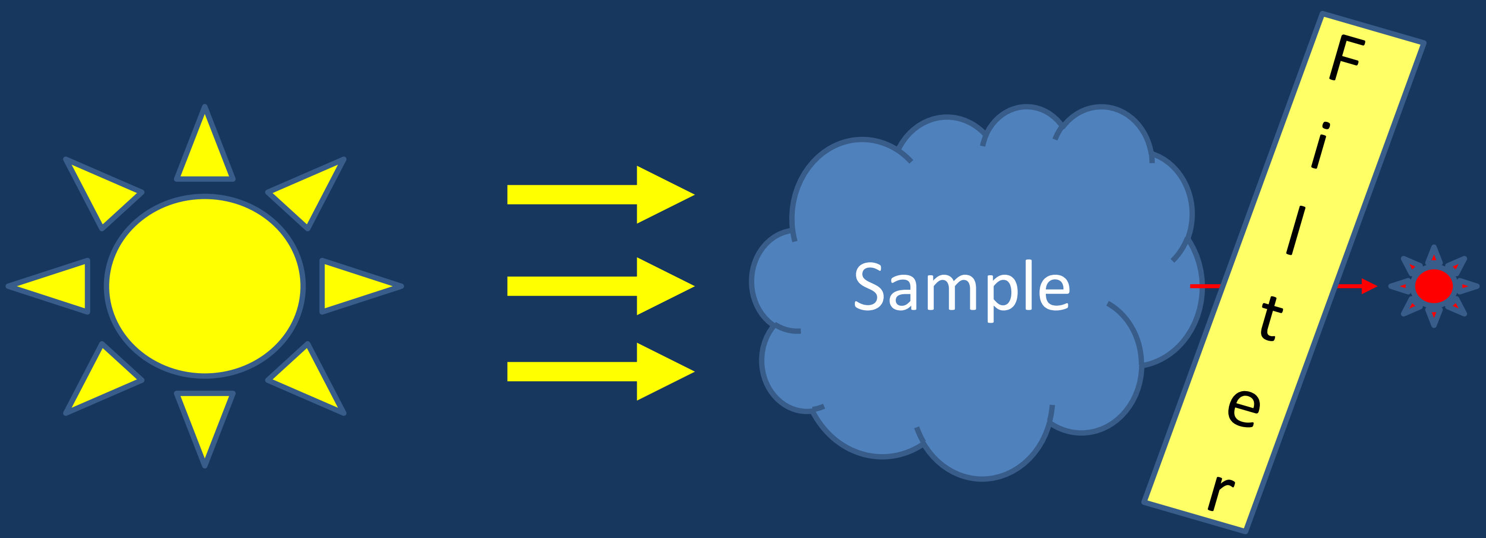
Examples:

Most of the echo-based methods such as radar, pulsed EPR & NMR

Requires blocking detection during excitation pulse => dead-time

Approach 2. Frequency-domain decoupling

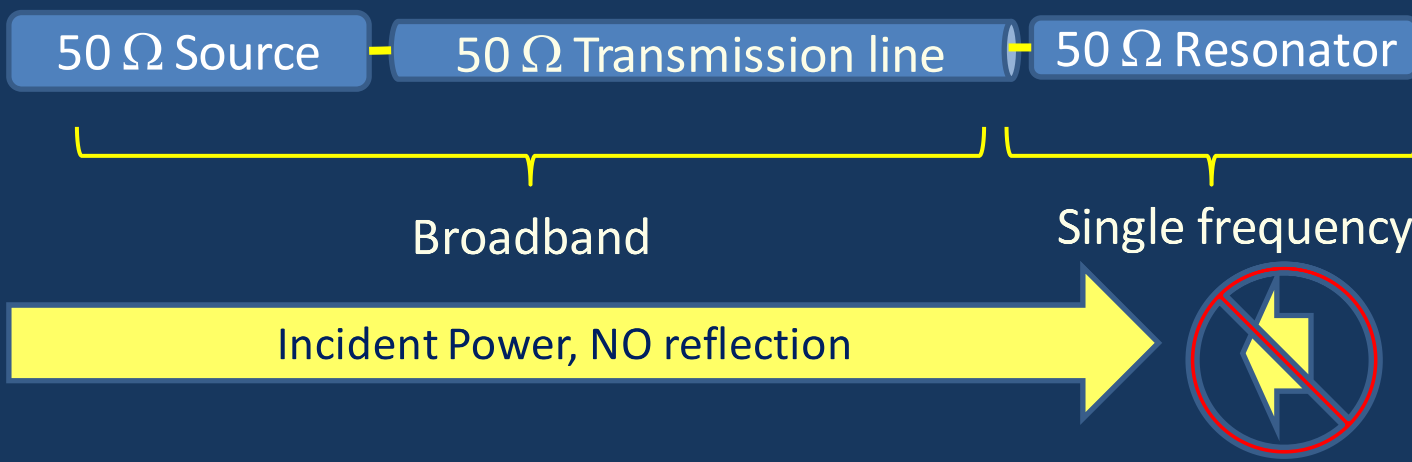
Example: Fluorescence , later RS EPR example



There is a 3rd approach used in magnetic resonance:

’Critical’ coupling (CC) of the resonator to the transmission line.

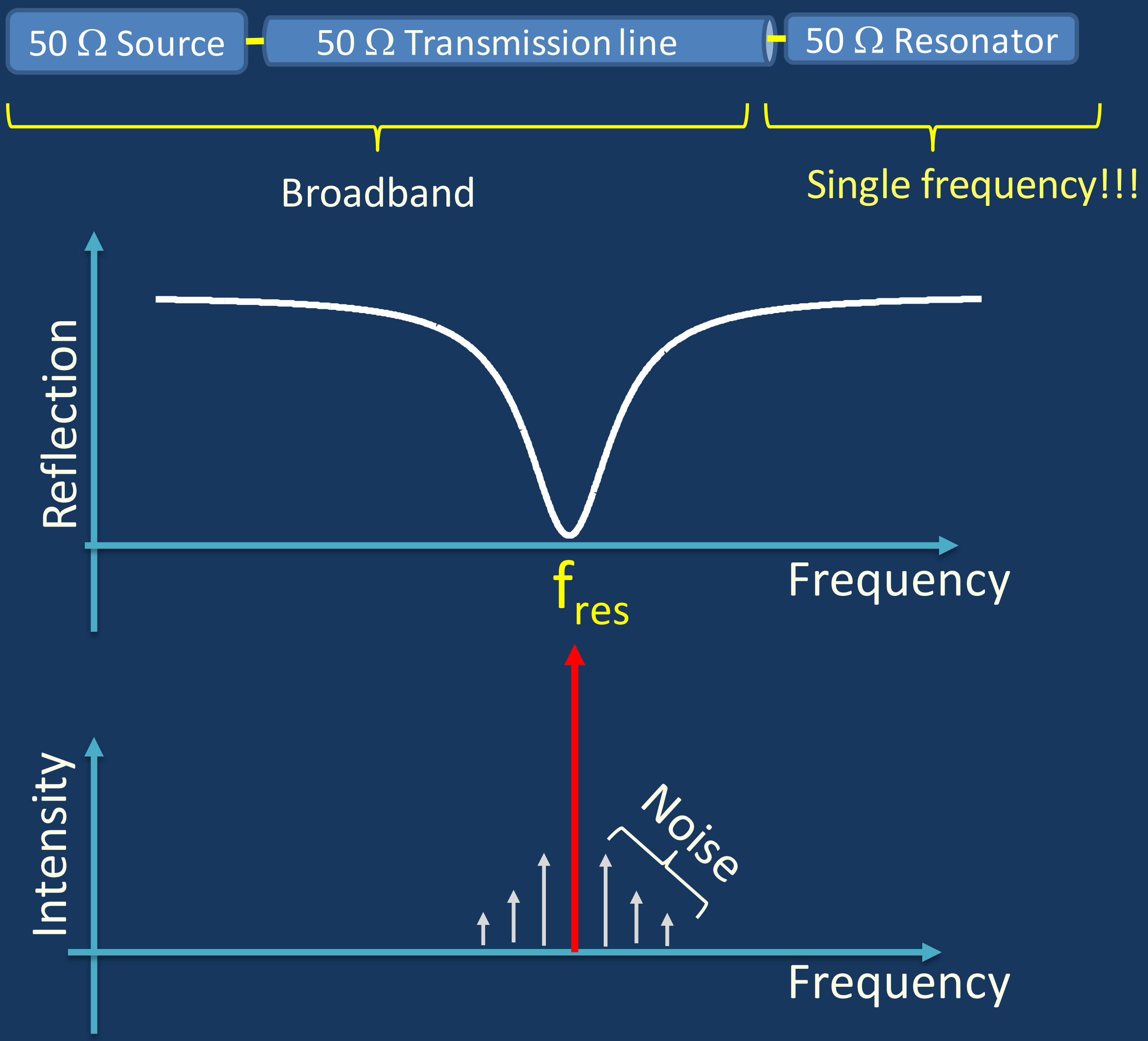
CC is essential for reflection types of resonators

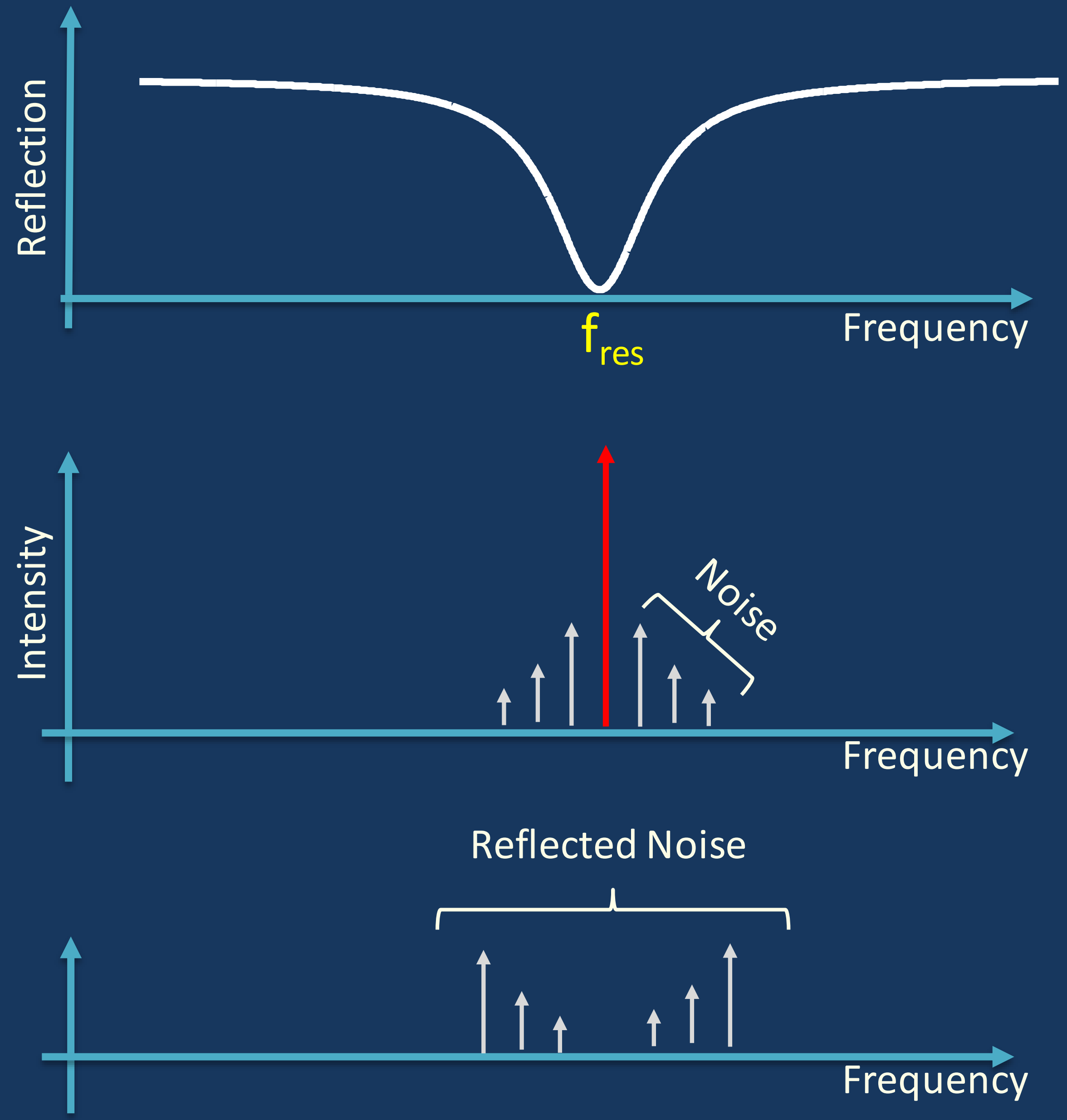


This approach is a narrow-banded (single frequency) decoupling:

- A small deviation from critical coupling leads to RF/MW reflection
- Reflection may saturate LNA and increase noise
- So we back to the problem of invisible at the day time stars

Noise & Reflection resonators



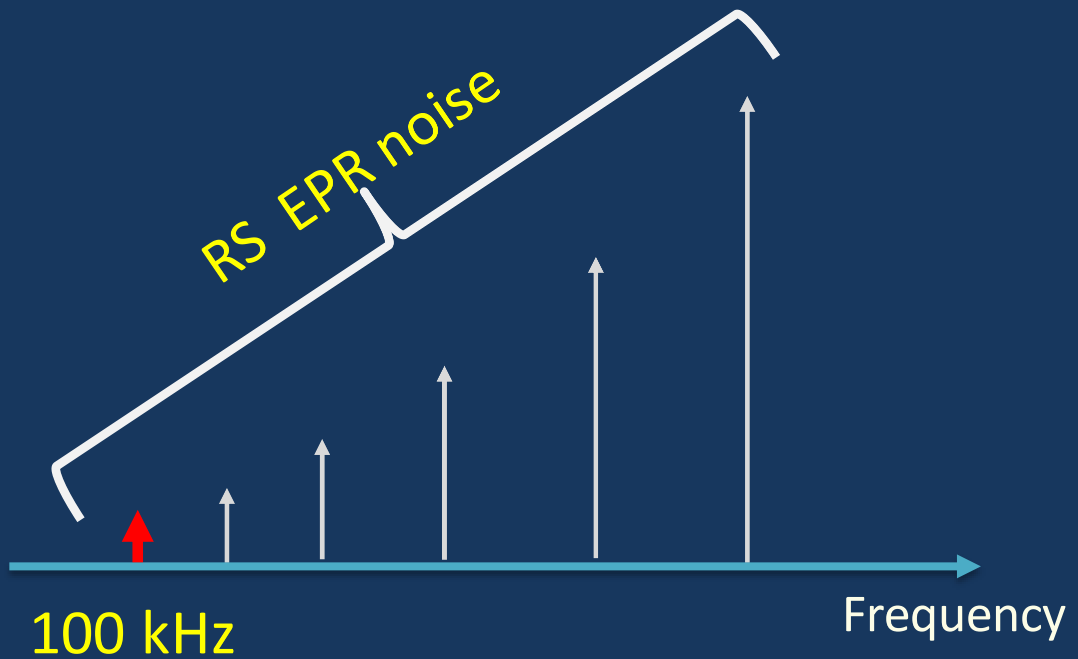


Higher Q => Sharper curve => More reflected noise

Single frequency CW 1h vs. broadband RS

CW 1h bandwidth often 100 kHz or less

RS EPR bandwidth matches that of the resonator > 10 MHz



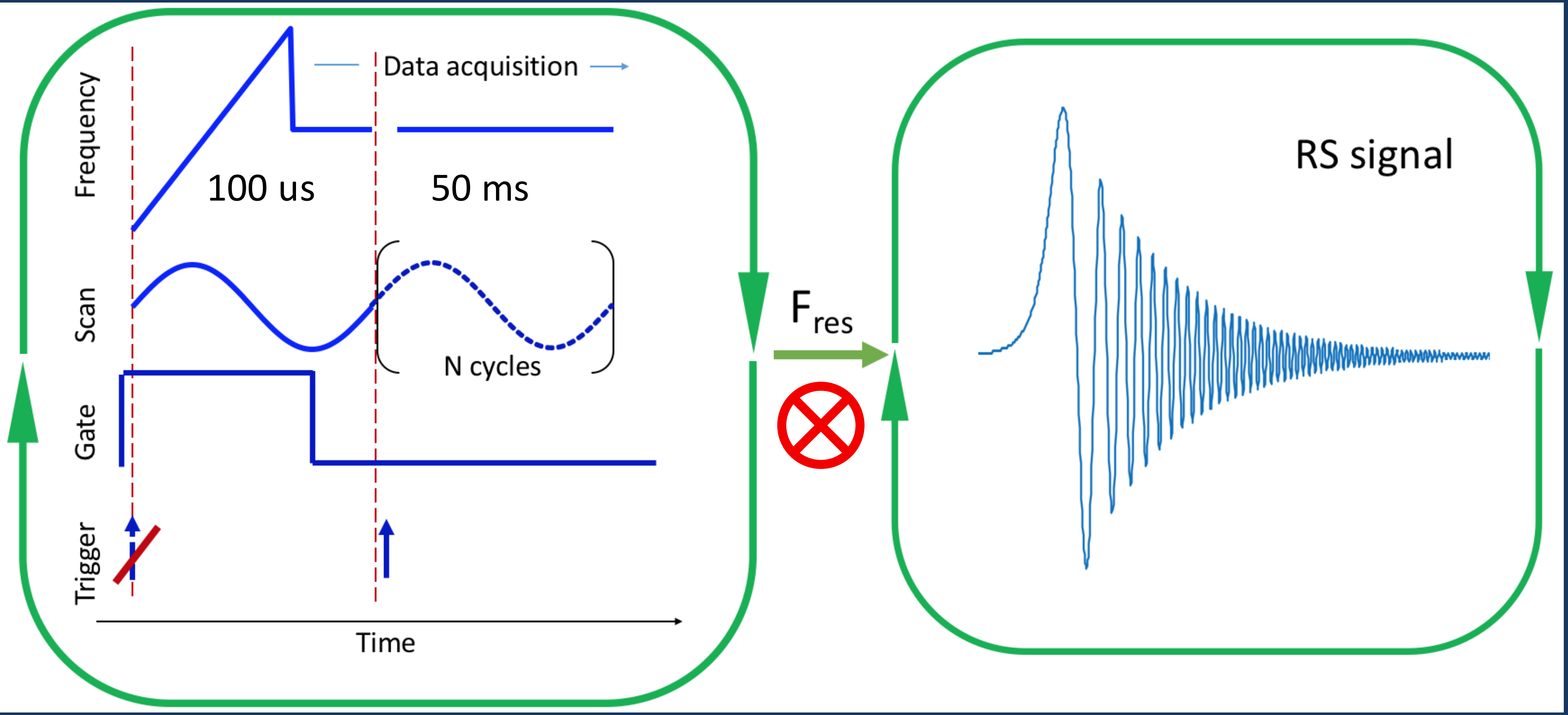
If Q is low and/or EPR frequency is high, signal gain outperforms noise

Reflection resonators deliver sub-optimum RS EPR performance

Problem of resonator detuning is more severe for RS EPR (high power)

Digital auto-frequency control for reflection resonators

Tuning mode (100us) – CW mode (50 ms) – Tuning – CW - ....

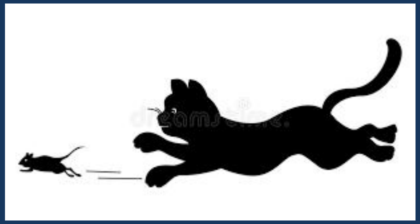


Wide tuning BW, 2-30 MHz (trade-off)
Do not interfere with RS data acquisition

Discrete AFC (DAFC) vs. Standard AC AFC & DC AFC

Global one-step target search

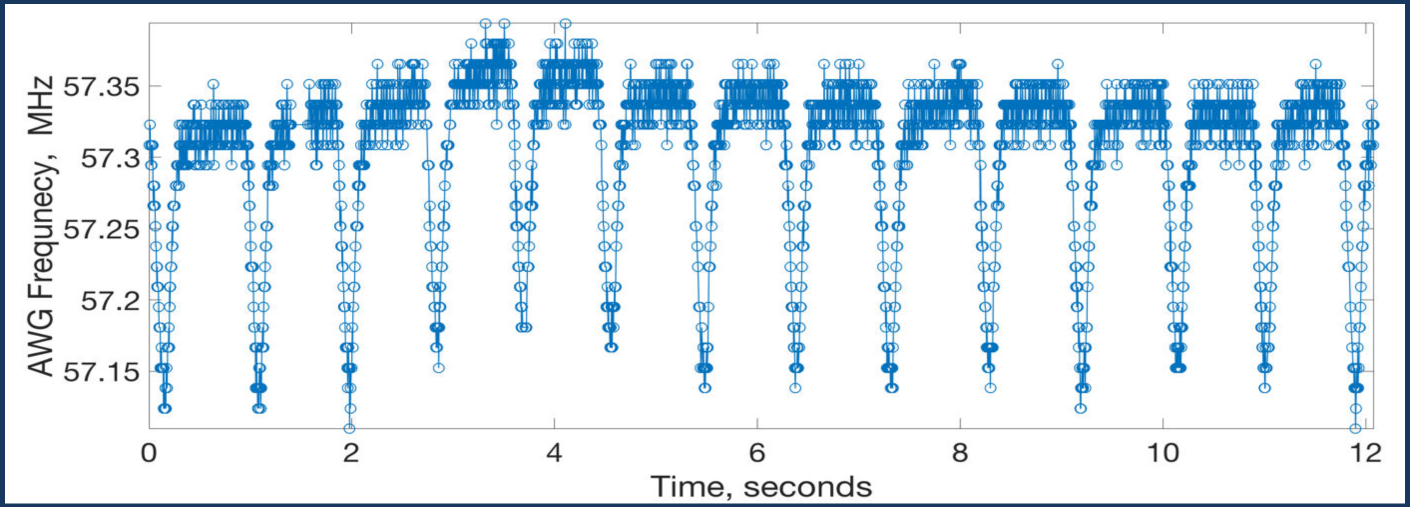
Local iterative convergence



What happens when the cat loses sight of the mouse?

DAFC in use: Resonator loop is placed on a mouse breast tumor.

AWG frequency time variation during *in vivo* measurements using DACF.
DACF tracks mouse breathing that modulates the resonator frequency.

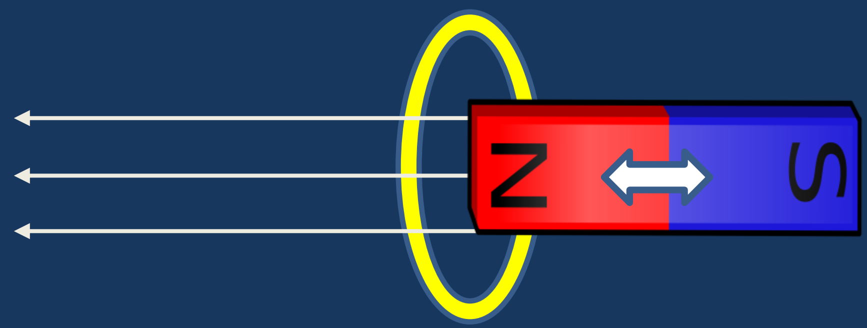


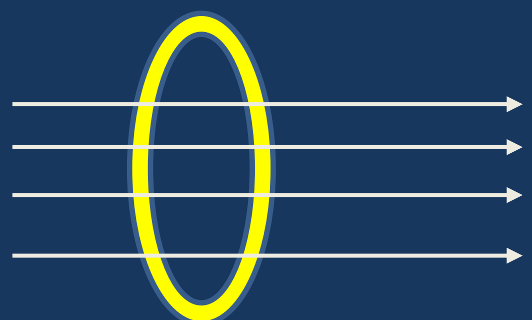
Does not work with the standard first-derivative CW EPR
Standard AFC => background, and blurring

Transmission mode and 4th decoupling approach

it is based on the Faraday's law.

Electromotive force ∝ rate of change of magnetic flux through the loop

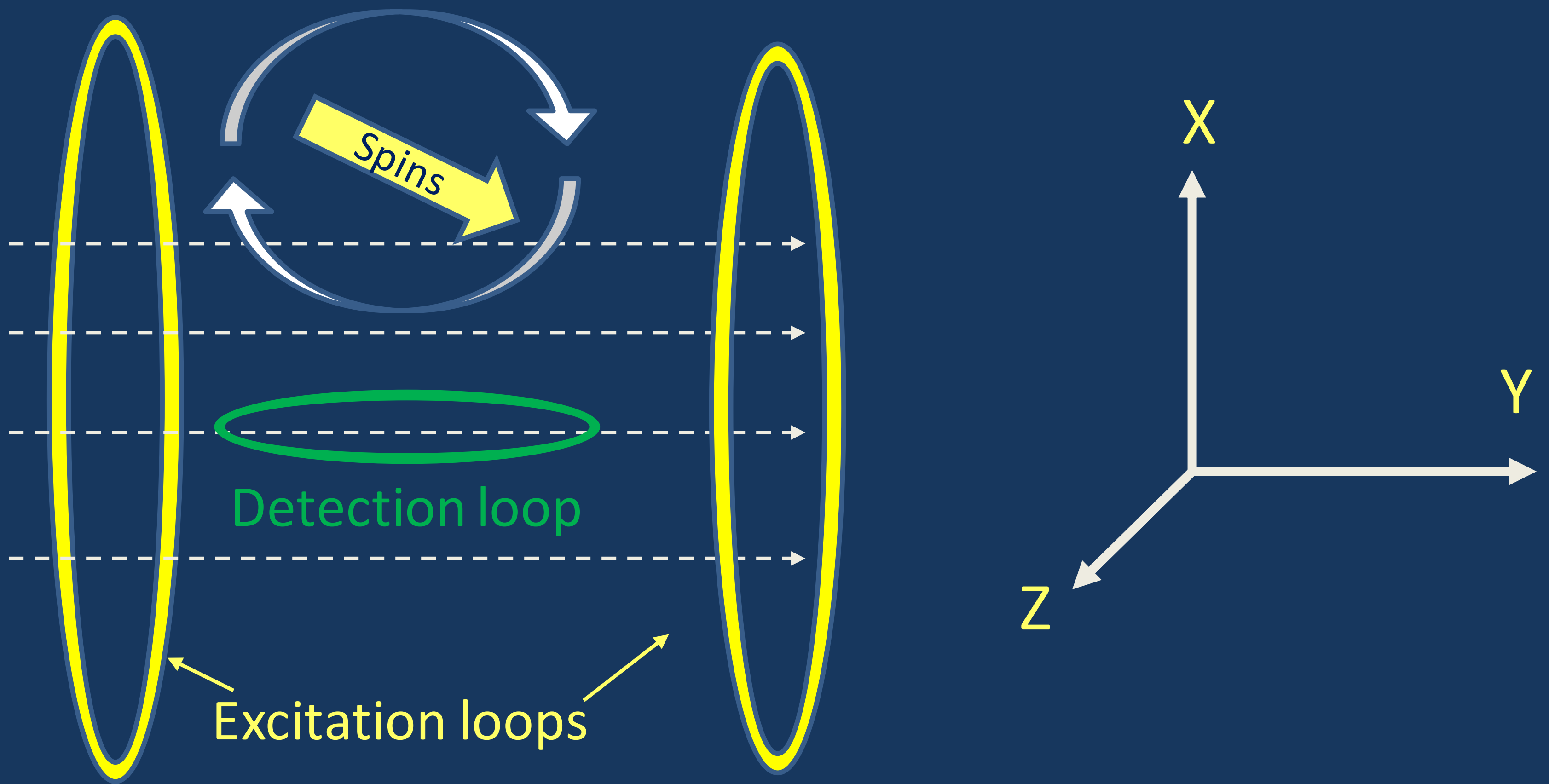




Maximum EMF

Zero EMF

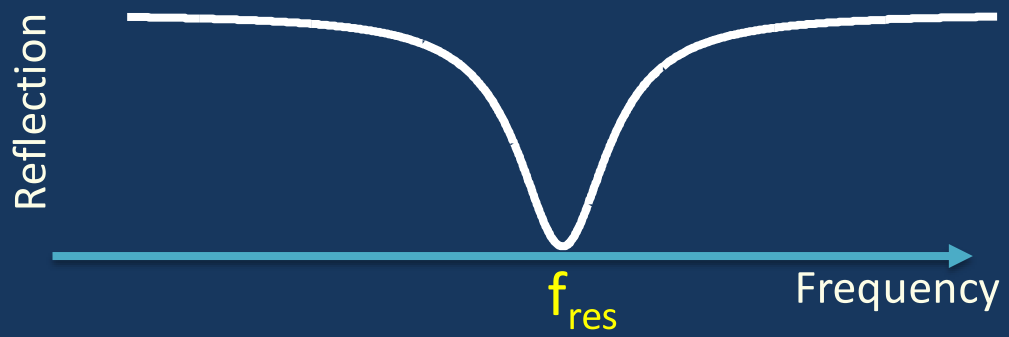
Bi-modal design (quadrature coils)

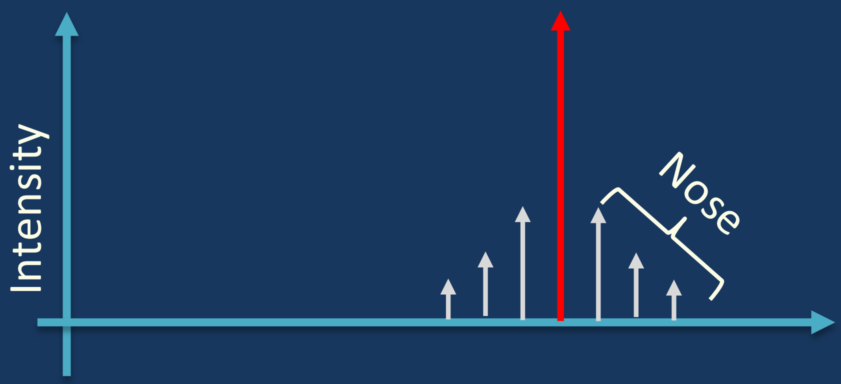


Excitation resonator (ER) creates RF/WM magnetic field along y-axis

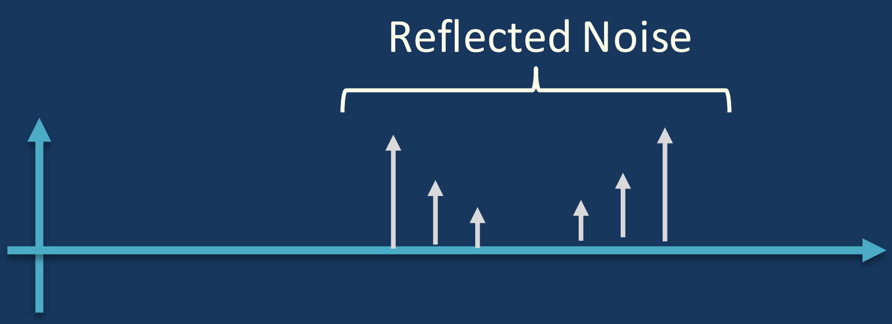
Detection resonator (DR) tuned to the same frequency is isolated from ER excitation

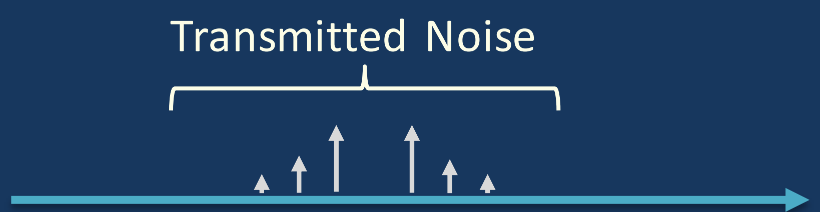
Spin magnetization rotates in the xy-plane to induce EPR signal in DR





Excitation resonator acts as a bandpass filter. High frequency noise is suppressed, which is beneficial for RS EPR.





SignalCore source: SC5510A

Sideband phase noise [3] (dBc/Hz)

	RF Frequency							
Offset	1 GHz		5 GHz		10 GHz		20 GHz	
	typ	*max*	typ	*max*	typ	*max*	typ	*max*
100 Hz	-80	*-74*	-66	*-60*	-60	*-54*	-54	*-48*
1 kHz	-122	*-116*	-108	*-104*	-102	*-96*	-96	*-90*
10 kHz	-134	*-128*	-121	*-115*	-115	*-110*	-110	*-105*
100	-135	*-129*	-121	*-115*	-115	*-110*	-110	*-105*
1 MHz	-135	*-129*	-121	*-115*	-115	*-110*	-110	*-105*
10 MHz	-150	*-145*	-139	*-136*	-133	*-130*	-131	*-130*
FLoor	-152	*-145*	-150	*-144*	-147	*-145*	-145	*-145*

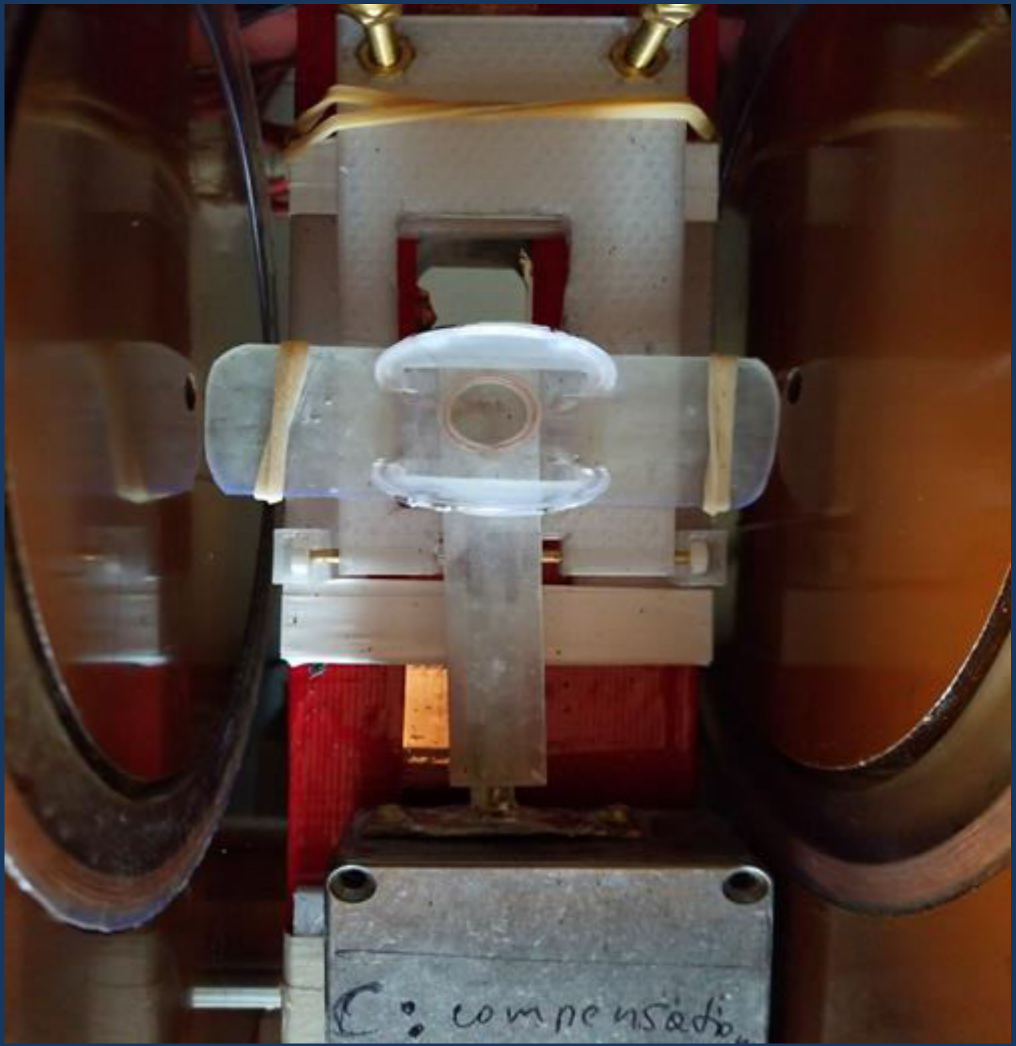
Additional advantage of the bimodal design:

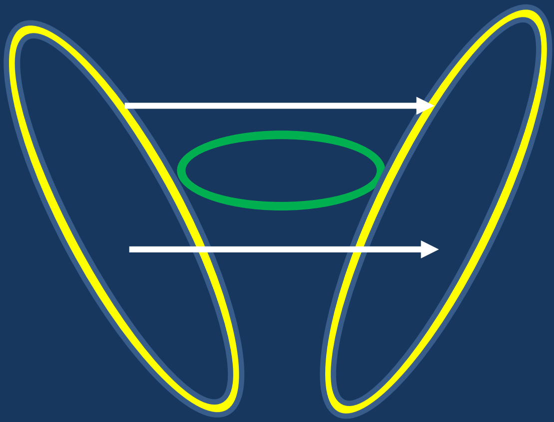
Stability w/respect to detection resonator de-tuning.

Major challenge:

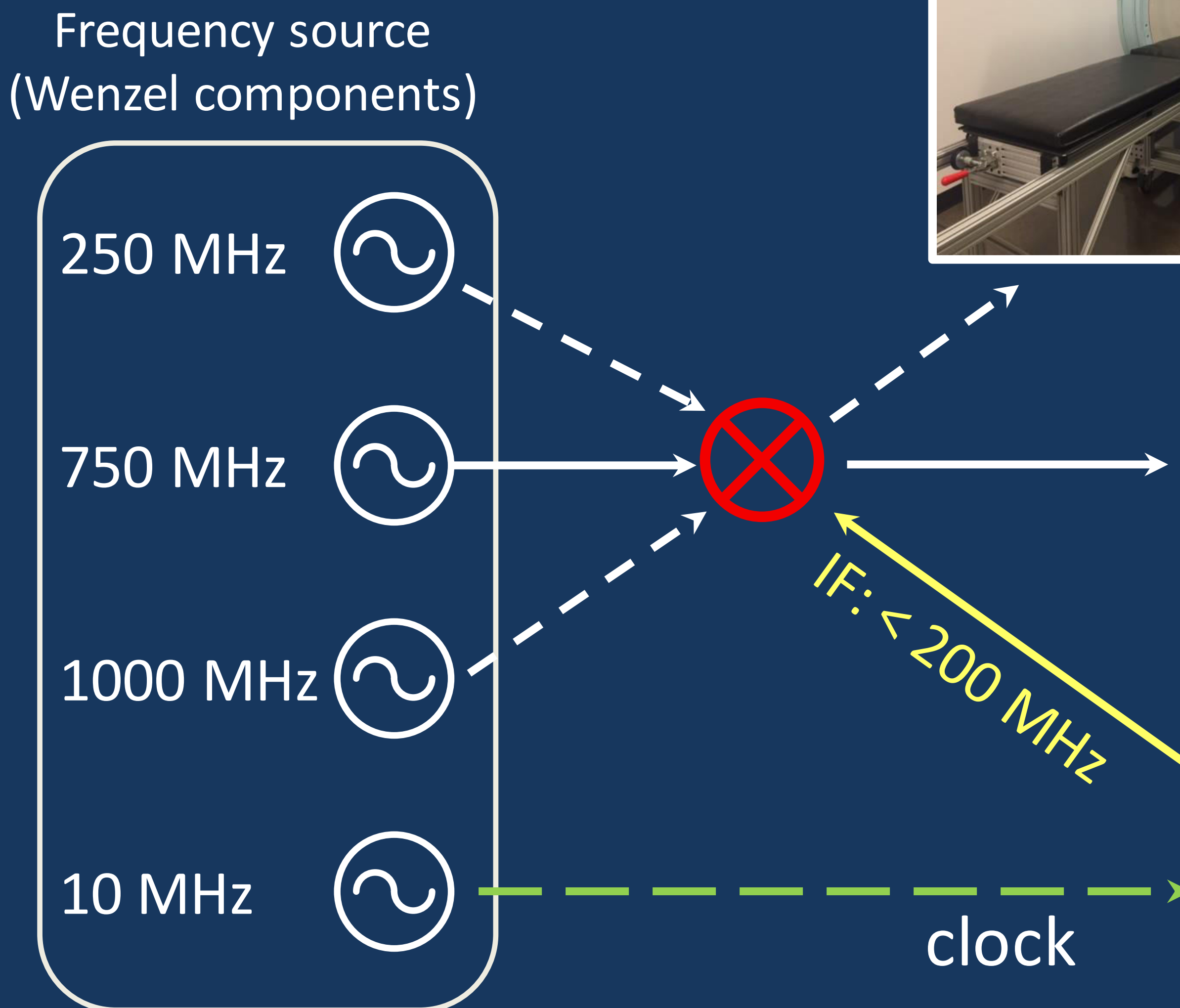
is to keep insolation high enough

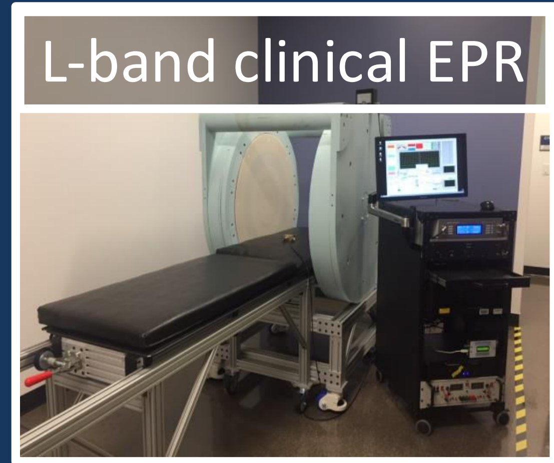
Locket type resonator developed in our laboratory for RS EPR imaging of mouse breast tumor models:

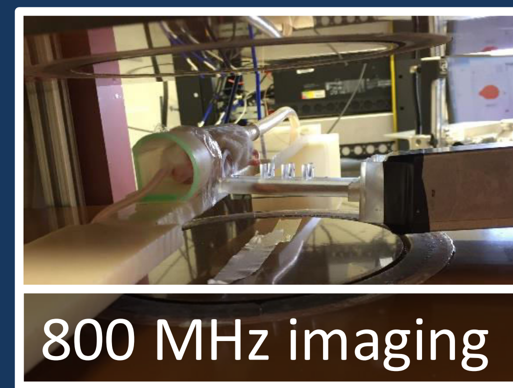




Semi-digital multi-frequency System in our laboratory



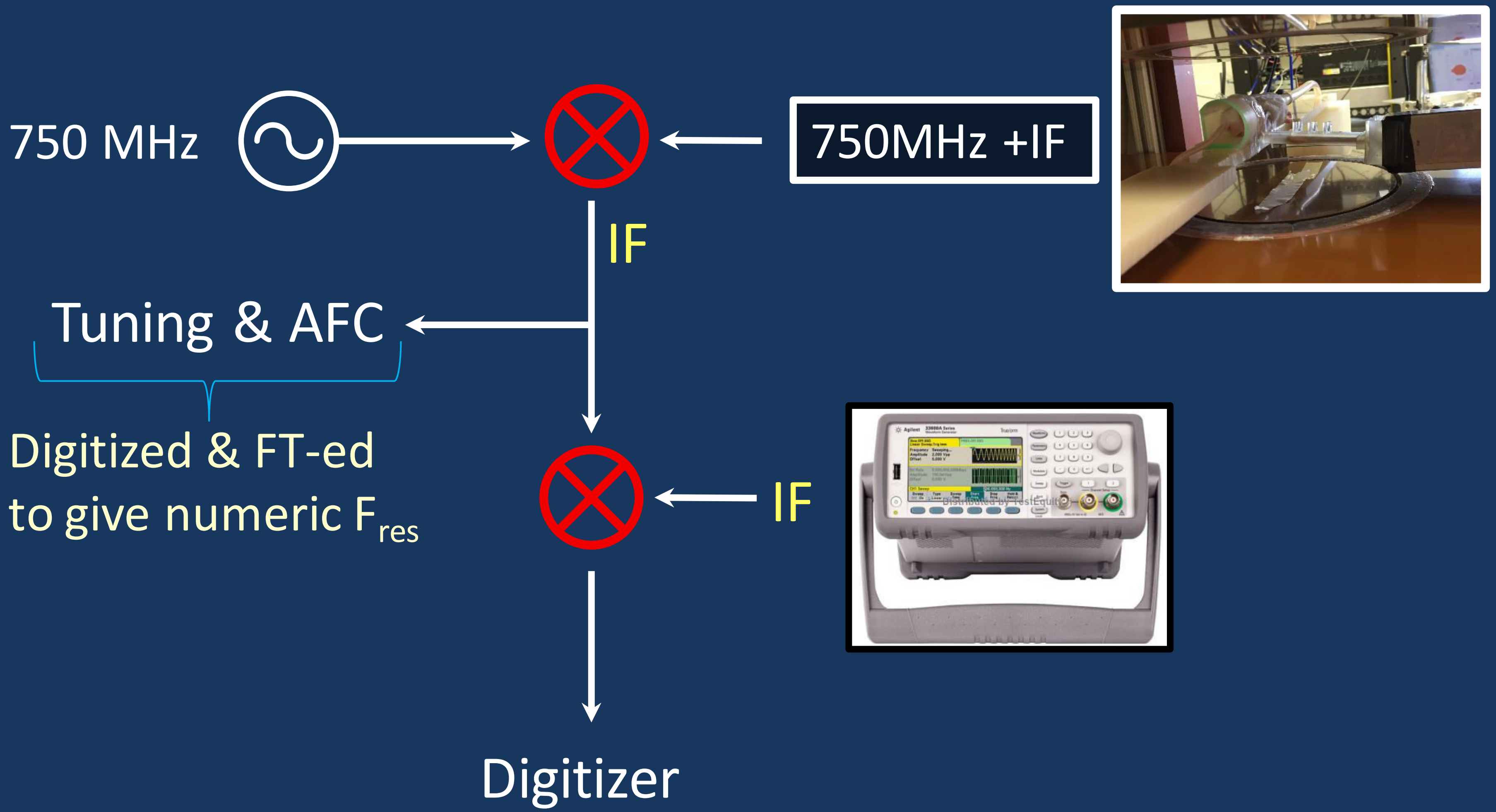




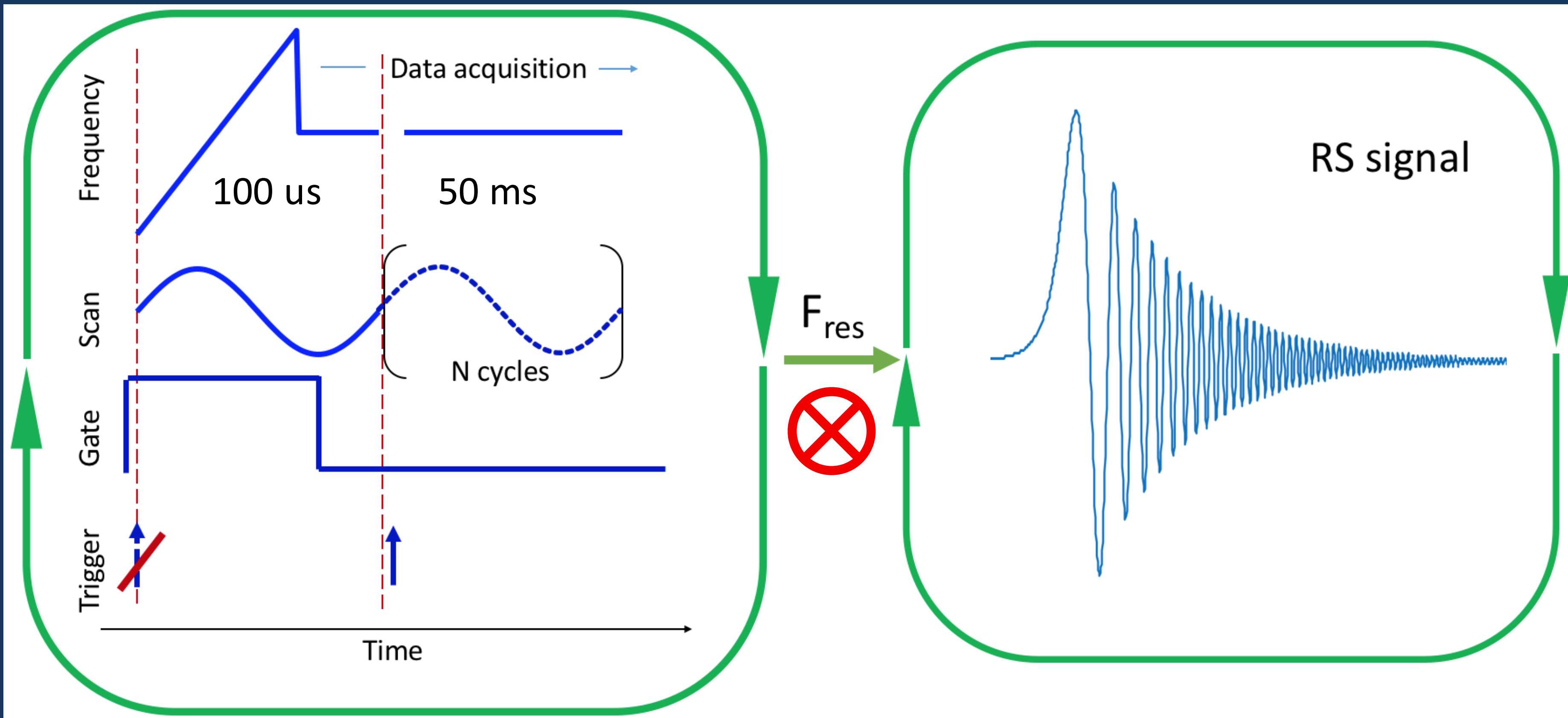
Arbitrary Waveform Generator
BW=120 MHz (up to 200 MHz)
Is more than needed

Flexibility, can be used for CW, RS, pulse.

On the detection side: two-step down-conversion



This design enables digital AFC (introduced above) at IF frequency



Wide tuning BW, 2-30 MHz (trade-off)
Do not interfere with RS data acquisition

Instrumentation: Scan coil/driver

- Implementation RS EPR requires generation of stable sinusoidal scans

  $B(t) = 0.5\ B_{pp} \sin(2\pi\ f_s\ t + \text{phase})$

- To achieve large B_{pp}, coil inductance is resonated with capacitors
- B_{pp} has to be accurately measured and very stable
- Small phase change => time shift (dt) => field shift = dt*scan_rate=> broadening
- One full scan produces two EPR spectra, used for fine phase tuning
- The use of digital feedback control is reliable, also inexpensive

More details in next slides….

Digital feedback to control scan amplitude and phase (Coil driver)

CV-1800 1.8 kW audio amplifier
BW up to 100 kHz, $399

Function generator

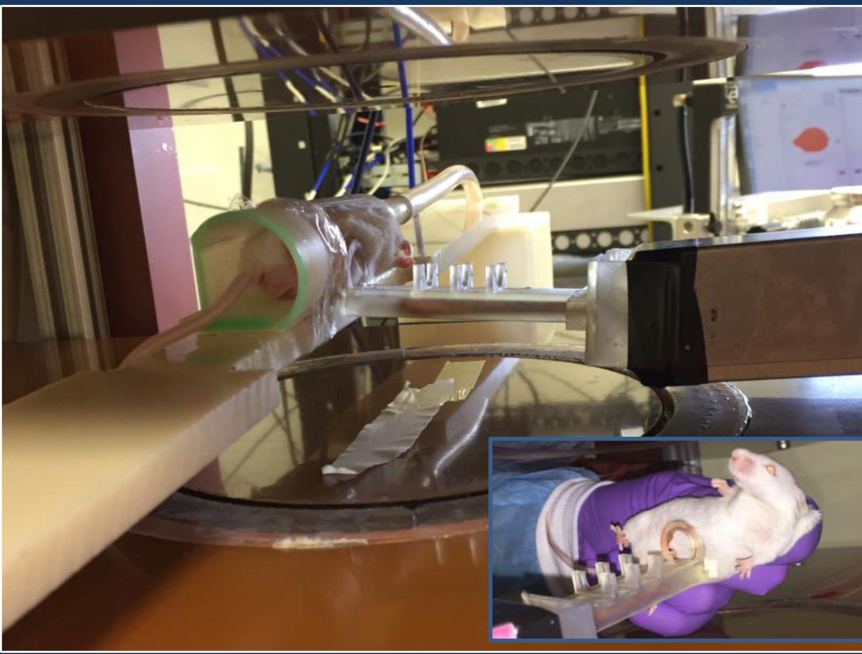
Digitizer card

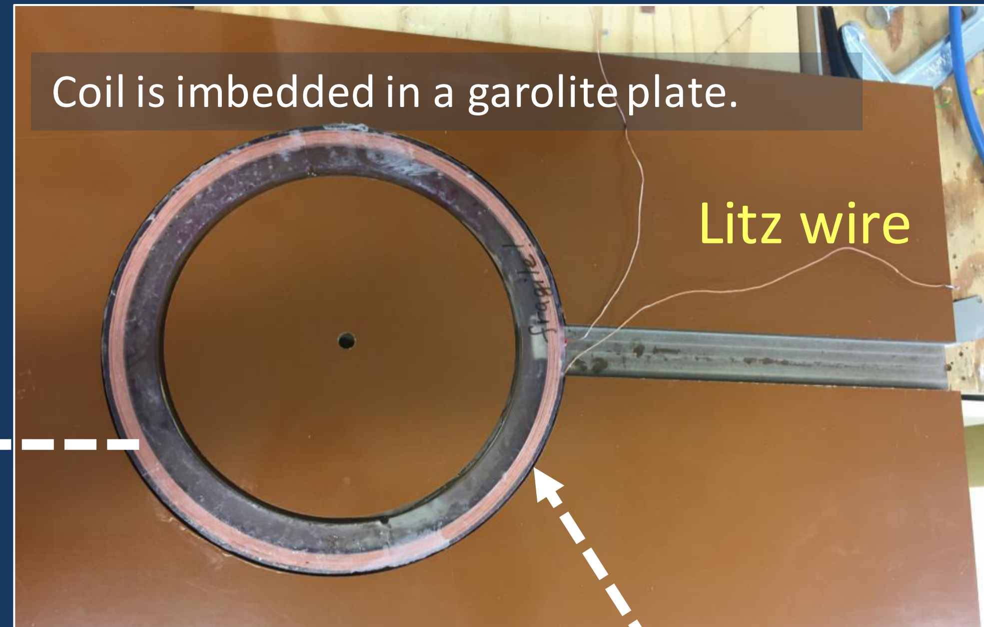
MATLAB

Controls A & ϕ of the input

C vs. R (higher SNR &Q)
Phase stability sufficient to measure 24 mG_{pp} lines

‘Large’ RS coils, 10 cm gap, used for conscience mouse measurements

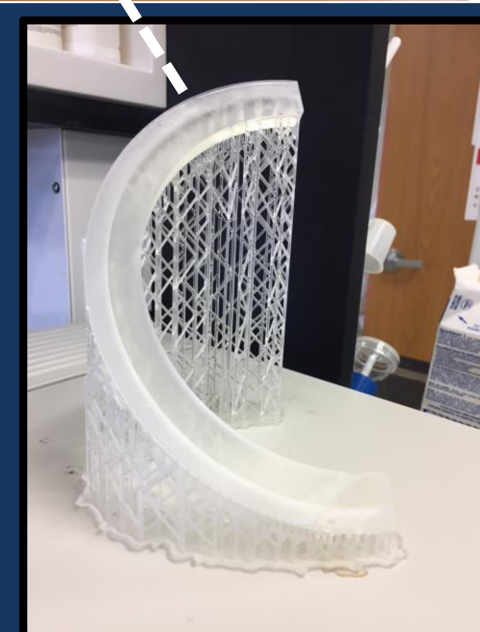


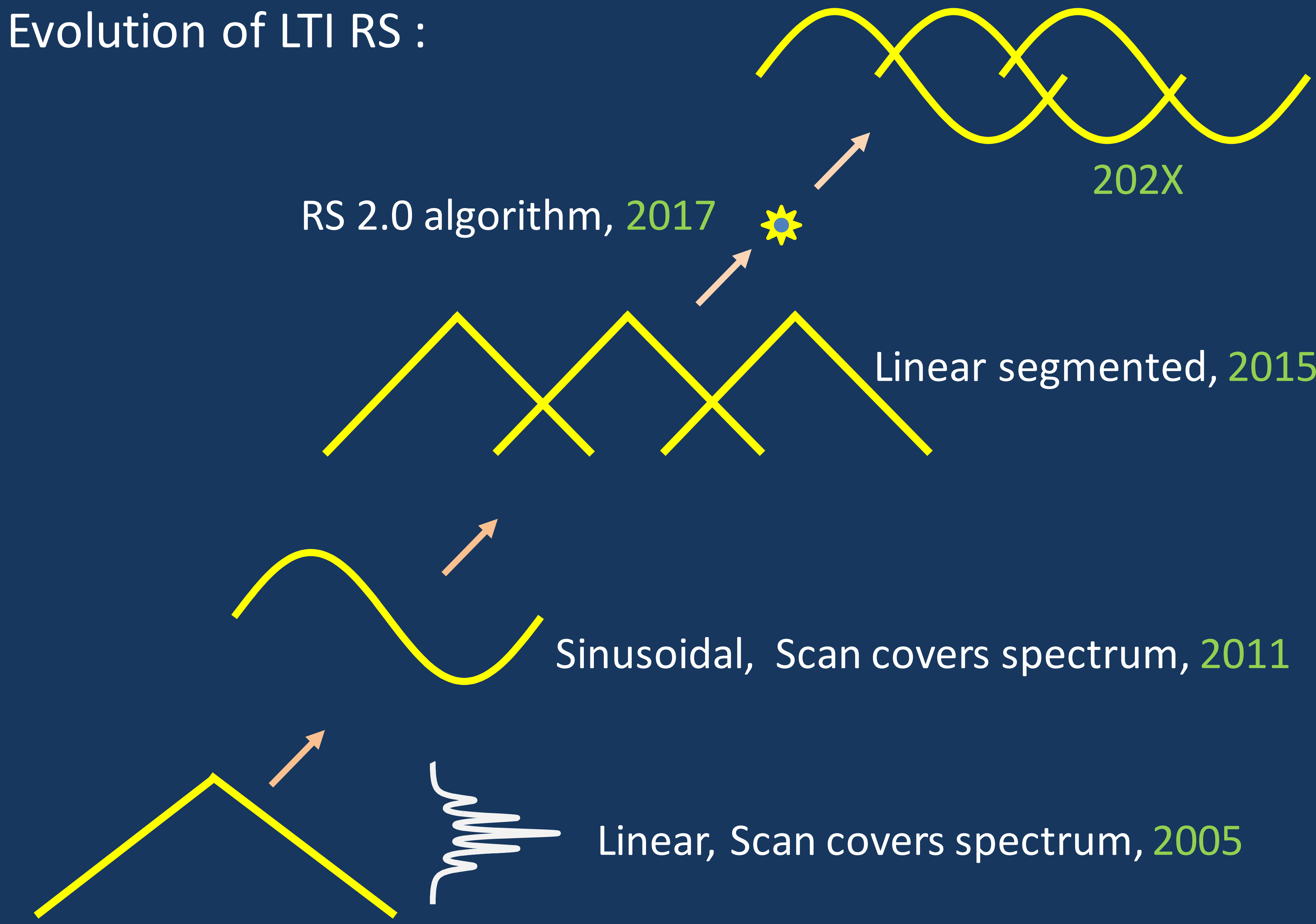


Tested at to 100 kHz & 12 Gpp

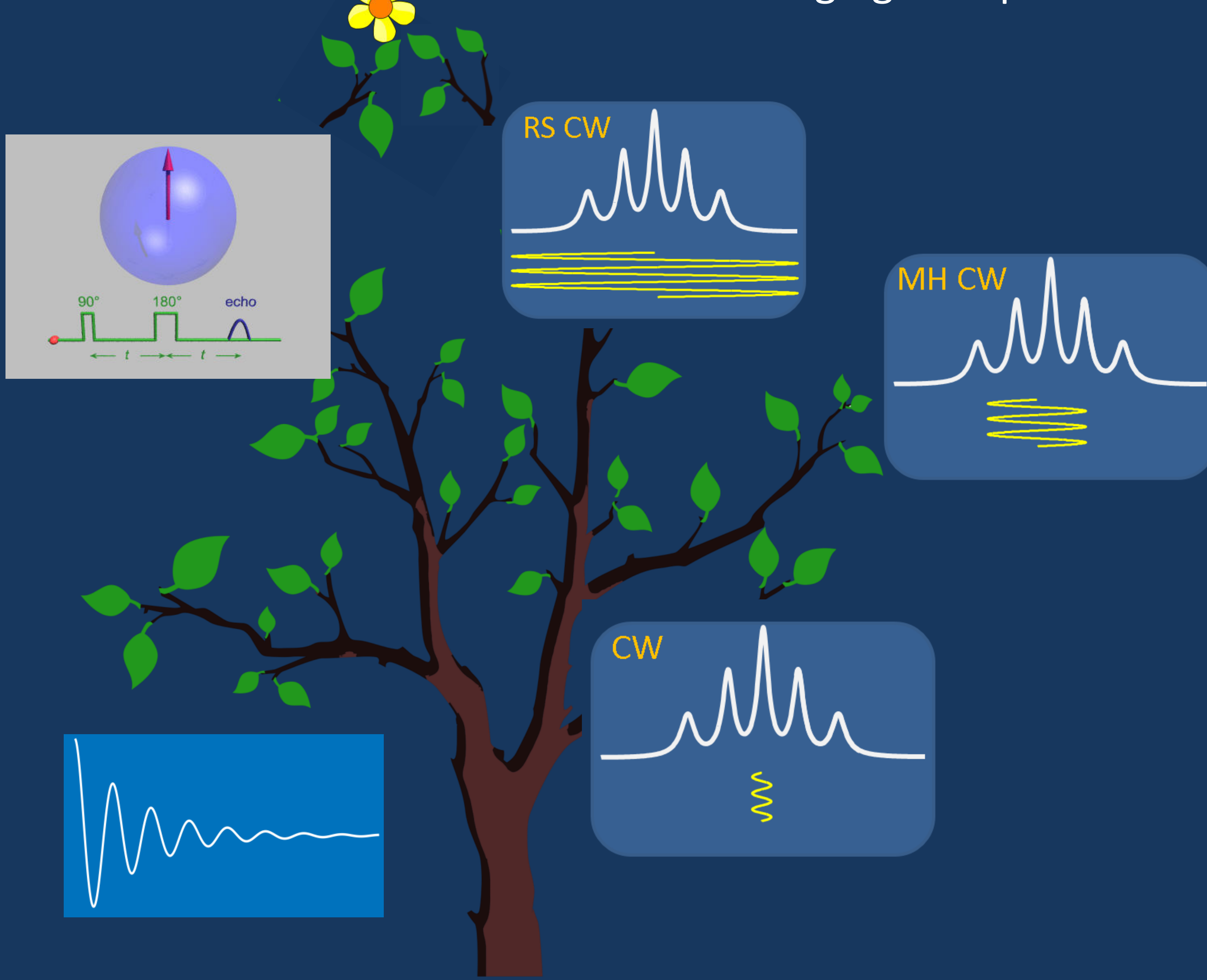
3D printed

halve-coil



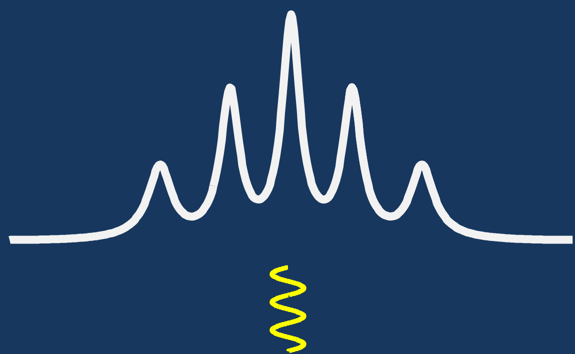

Evolution of LTI RS :
202X
RS 2.0 algorithm, 2017
Linear segmented, 2015
Sinusoidal, Scan covers spectrum, 2011
Linear, Scan covers spectrum, 2005

Future: RS merging with pulsed EPR



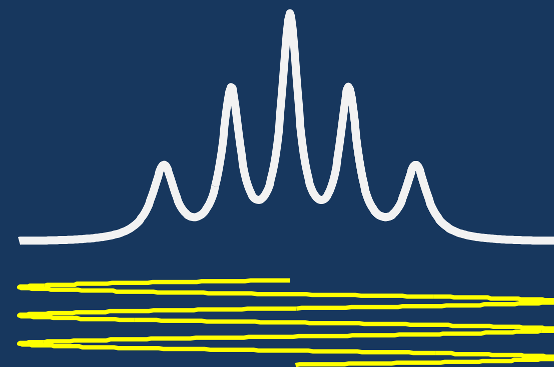
Rapid Scan (RS) CW EPR: What's Next?

CW



vs.

RS CW

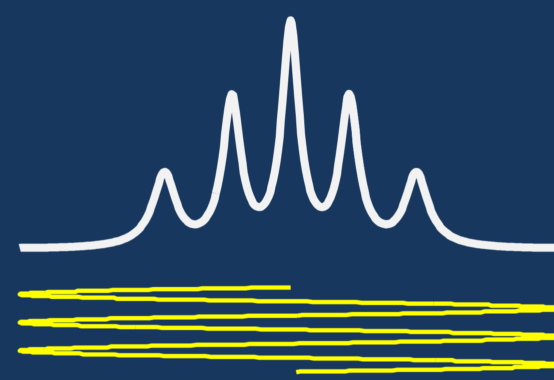


More spins & Less saturations same info

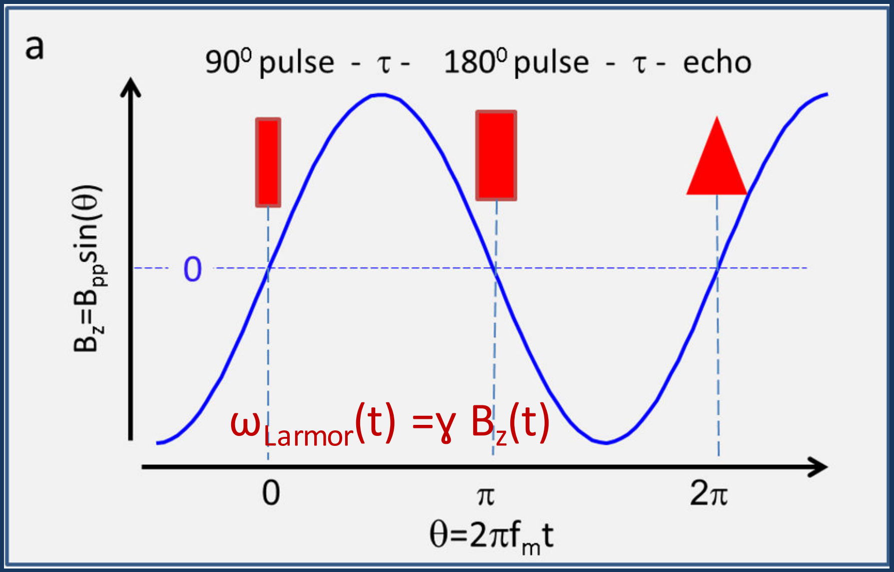
Next step in RS evolution

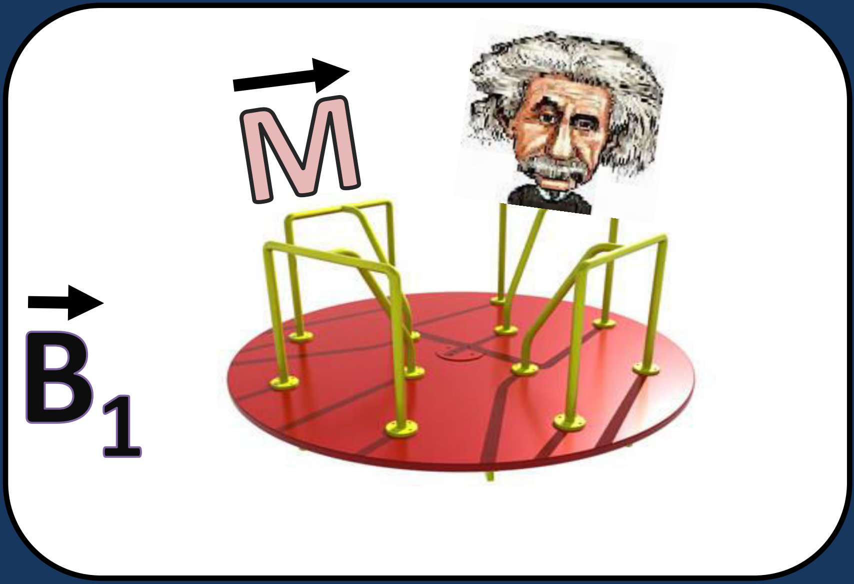
Pulsed

RS EPR



Rapid scan spin echo/ phase cycling





In the new accelerating frame

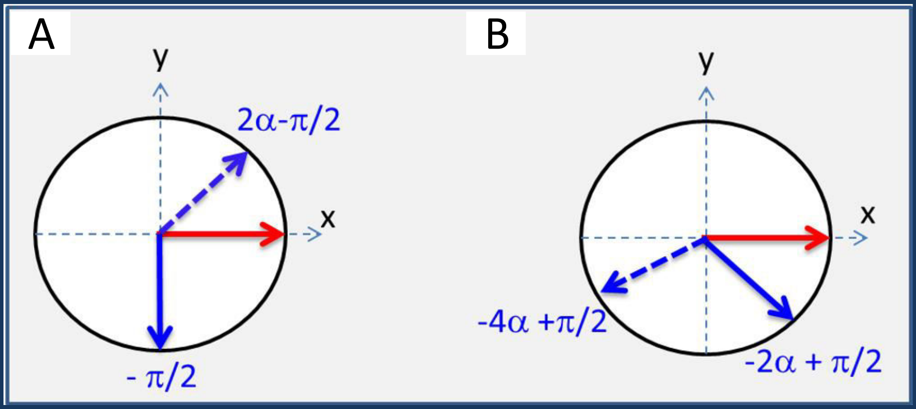
- Magnetization phase does not rotate
- Instead, B_1 phase changes with time

$M(t) \to B_1(t)$

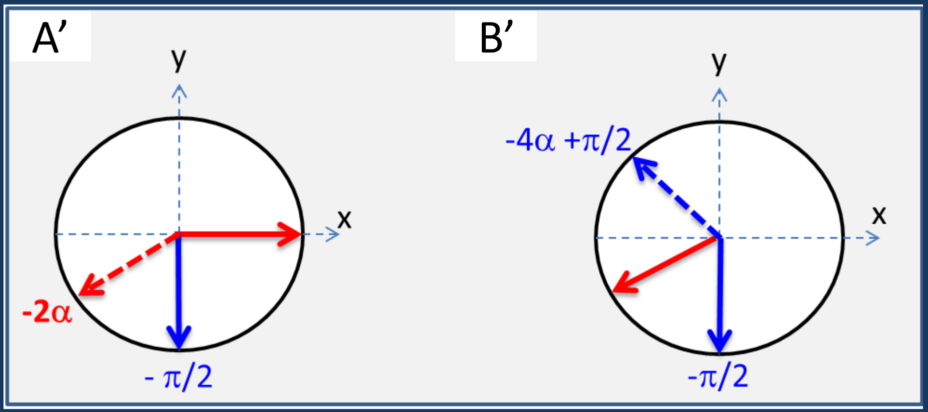
Pulse phases is controlled with magnetic field modulation !

Tseytlin M. Z Phys Chem (N F). 2017 Mar;231(3):68

Reference Frame Transformation Enables Phase Cycling



After transformation: A→ A' , B→ B'



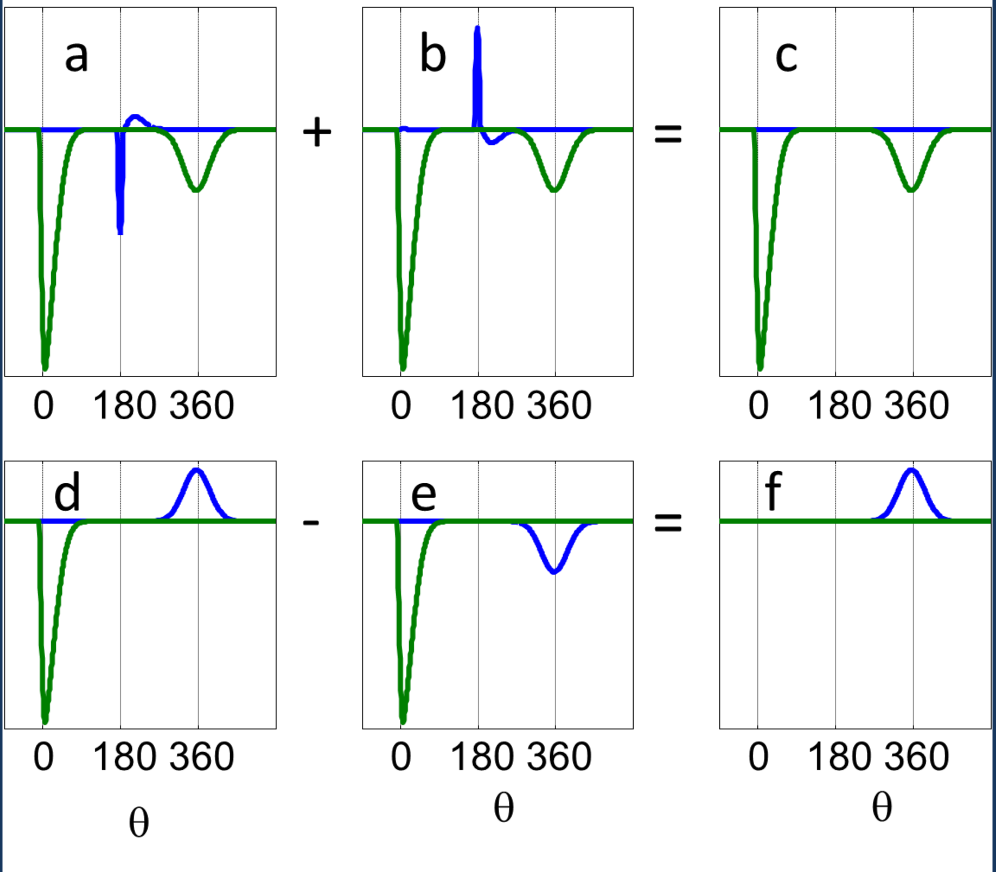
$$\Phi=\begin{pmatrix} phase\ FID_1 \\ phase\ FID_2 \\ phase\ Echo \end{pmatrix}=\begin{pmatrix} -\pi/2 \\ -2\alpha-\pi/2 \\ -4\alpha+\pi/2 \end{pmatrix}, \quad \alpha=\frac{\gamma B_{pp}}{4\pi f m}$$

Tseytlin M. Z Phys Chem (N F). 2017 Mar;231(3):68

FM Phase Cycling

Phase cycling requires two measurements with different $\alpha = \frac{\gamma B_{pp}}{4\pi f m}$

Relative phases for the measurement in the accelerating frame: $\Delta\Phi = \begin{pmatrix} 0 \\ 2 \\ 4 \end{pmatrix} \Delta\alpha$



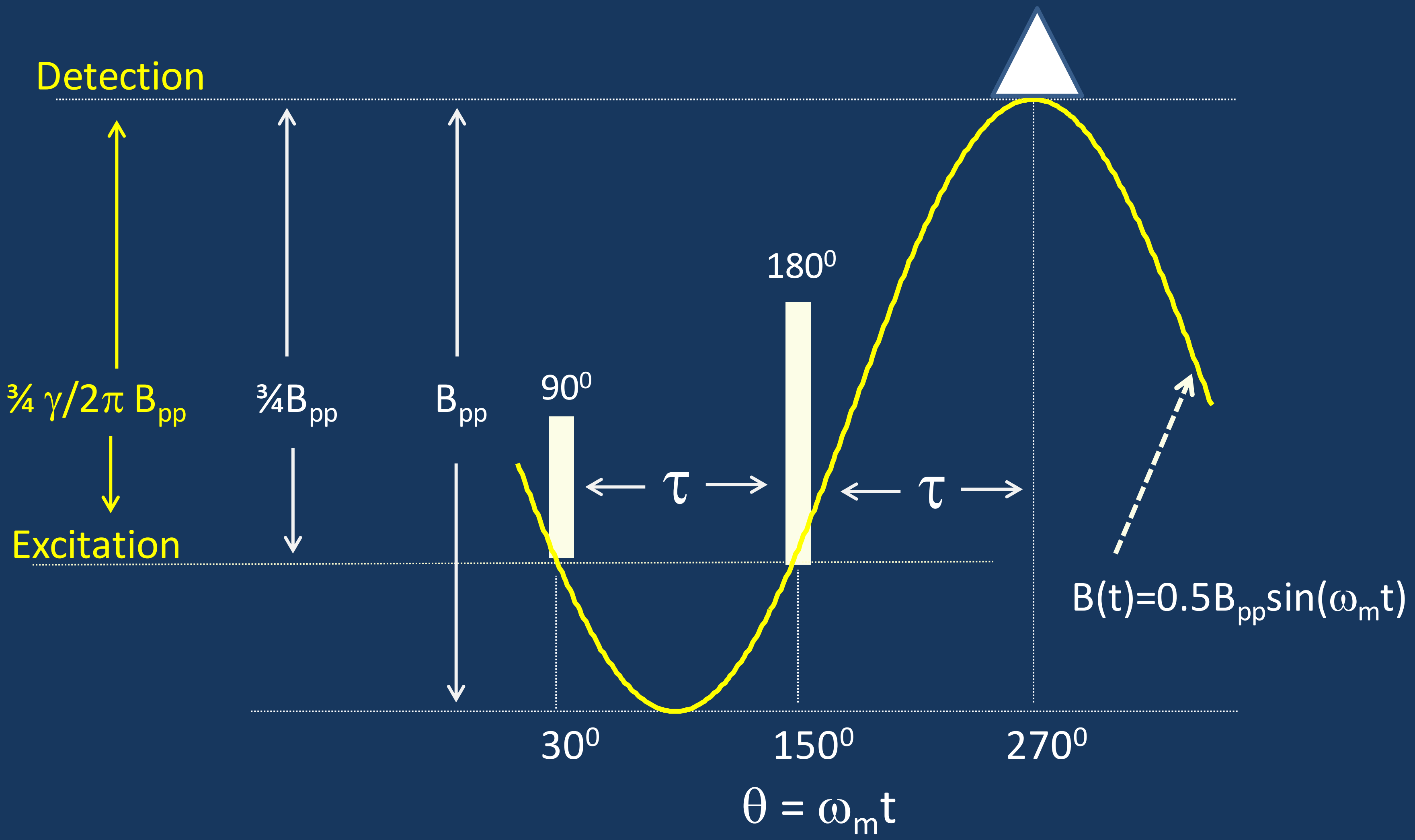
$\Delta\alpha = \pi/2\ ;\ \Delta\Phi = \begin{pmatrix} 0 \\ \pi \\ 2\pi \end{pmatrix} = \begin{pmatrix} 0 \\ \pi \\ 0 \end{pmatrix}$

In combination with B_1 cycling

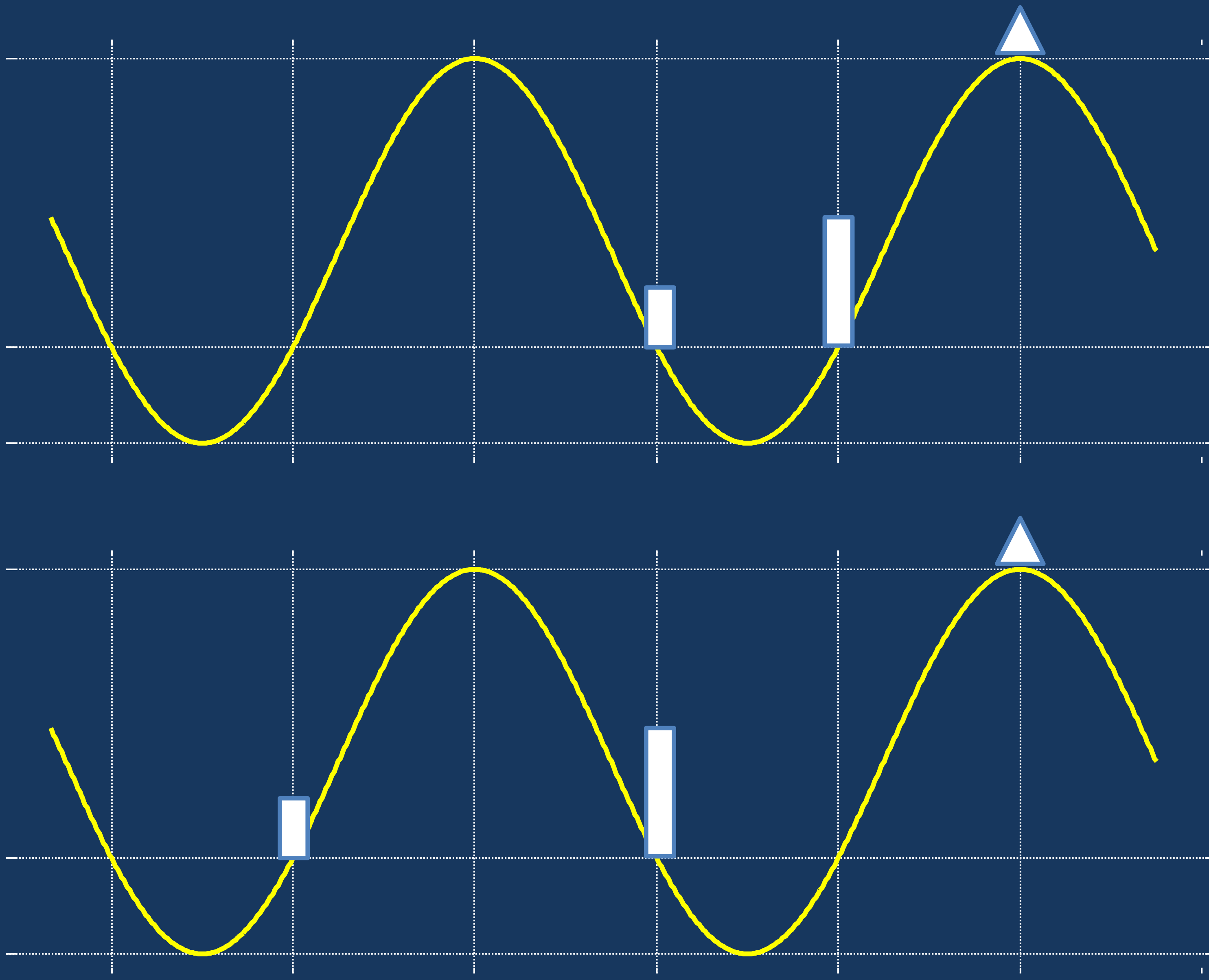
$\Delta\alpha = \pi/4\ ;\ \Delta\Phi = \begin{pmatrix} 0 \\ \pi/2 \\ \pi \end{pmatrix}$

Second example FM pulsed EPR:

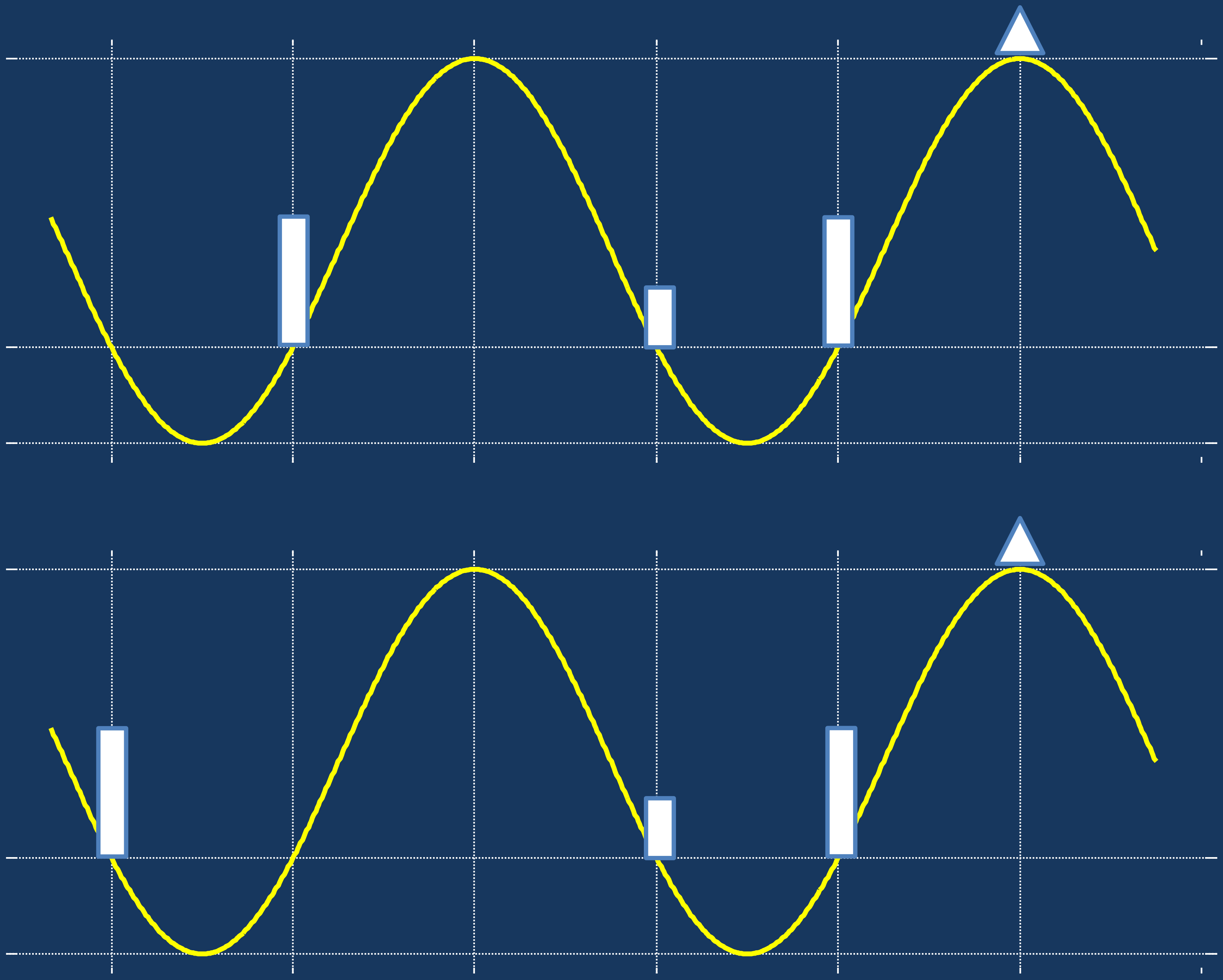
Isolation of the excitation from detection in a bi-modal resonator



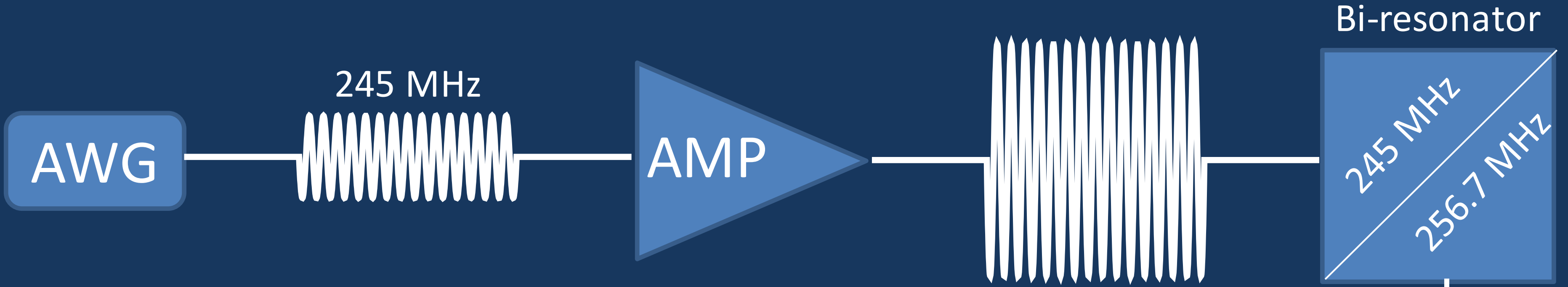
T_2 measurement

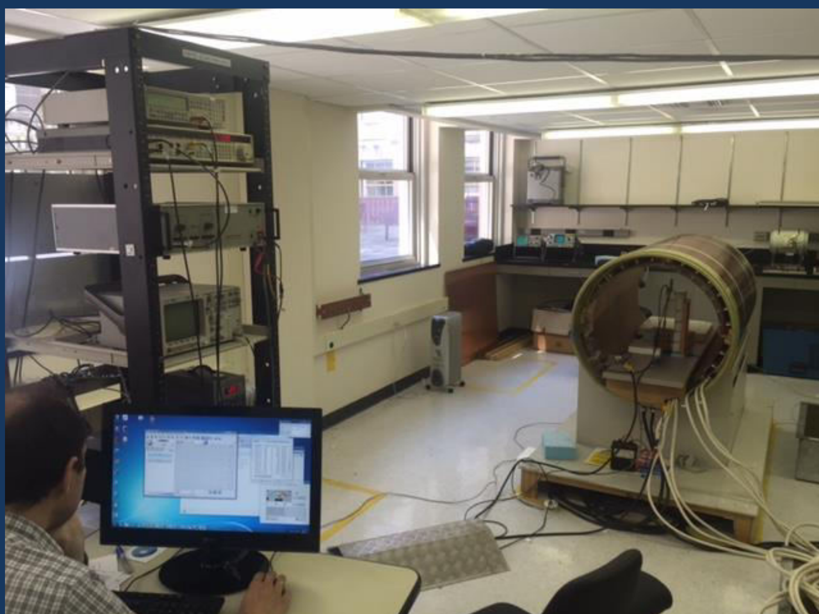


T_1 measurement

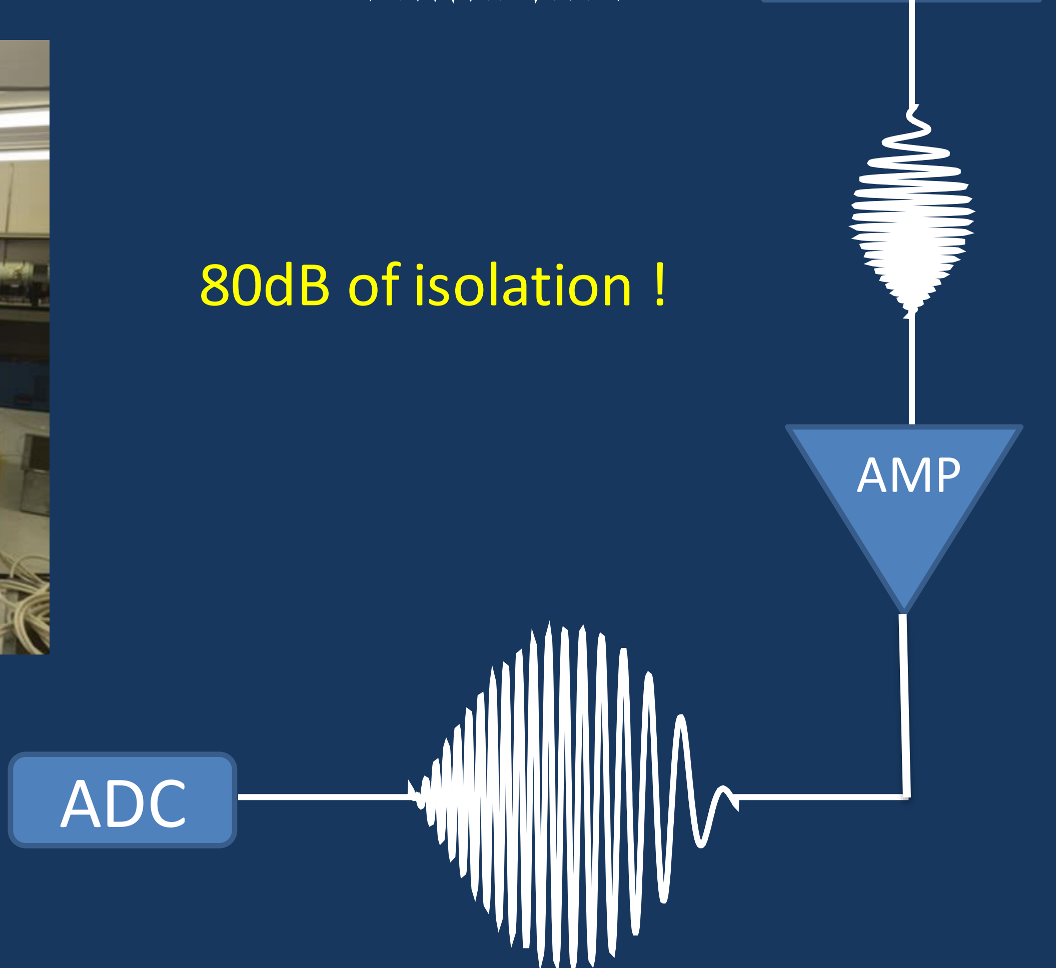


Block diagram of 'digital' pulsed spectrometer

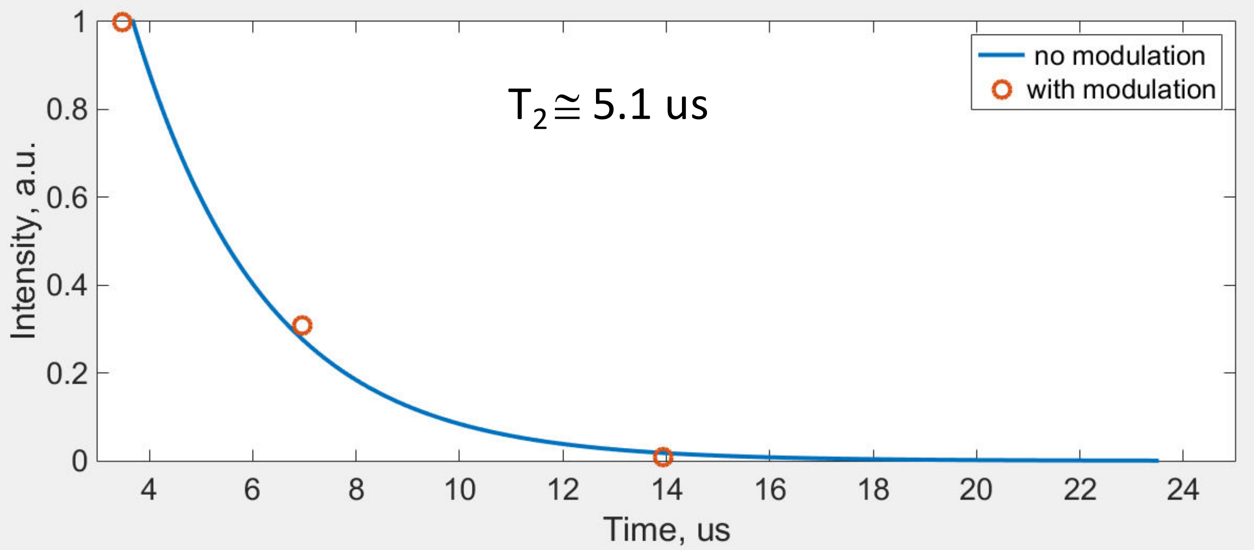


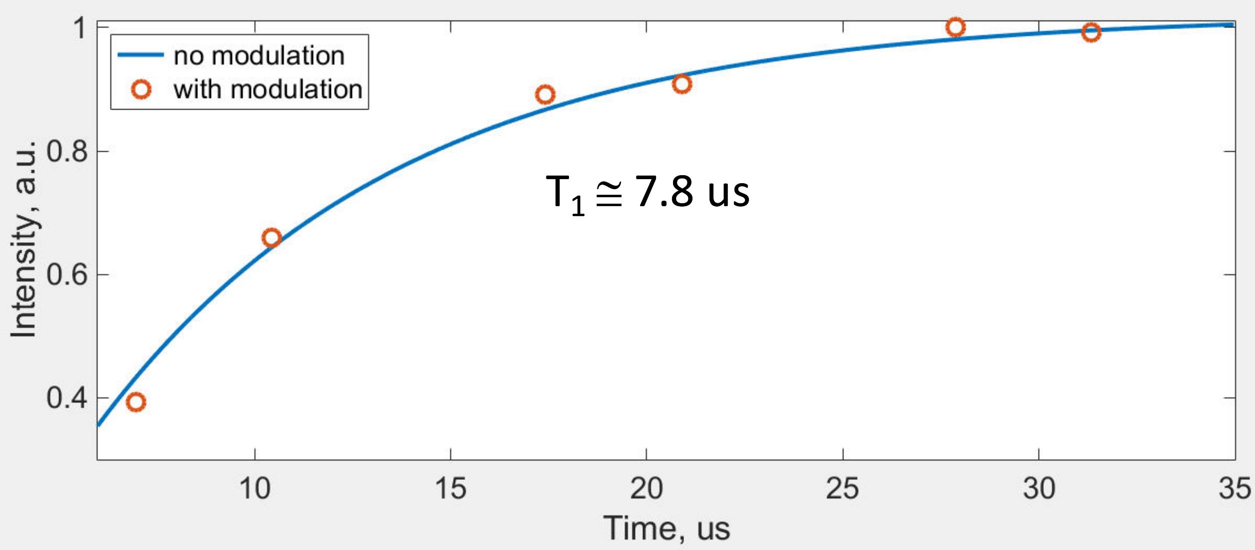


80dB of isolation !

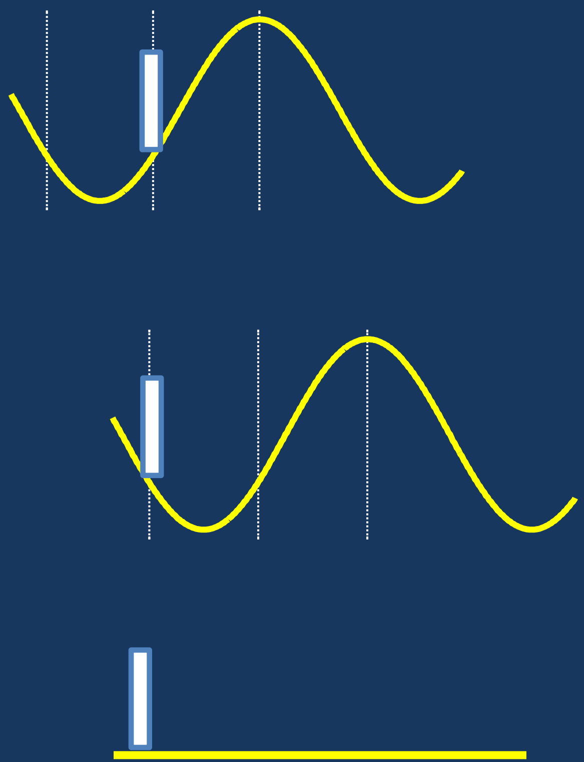


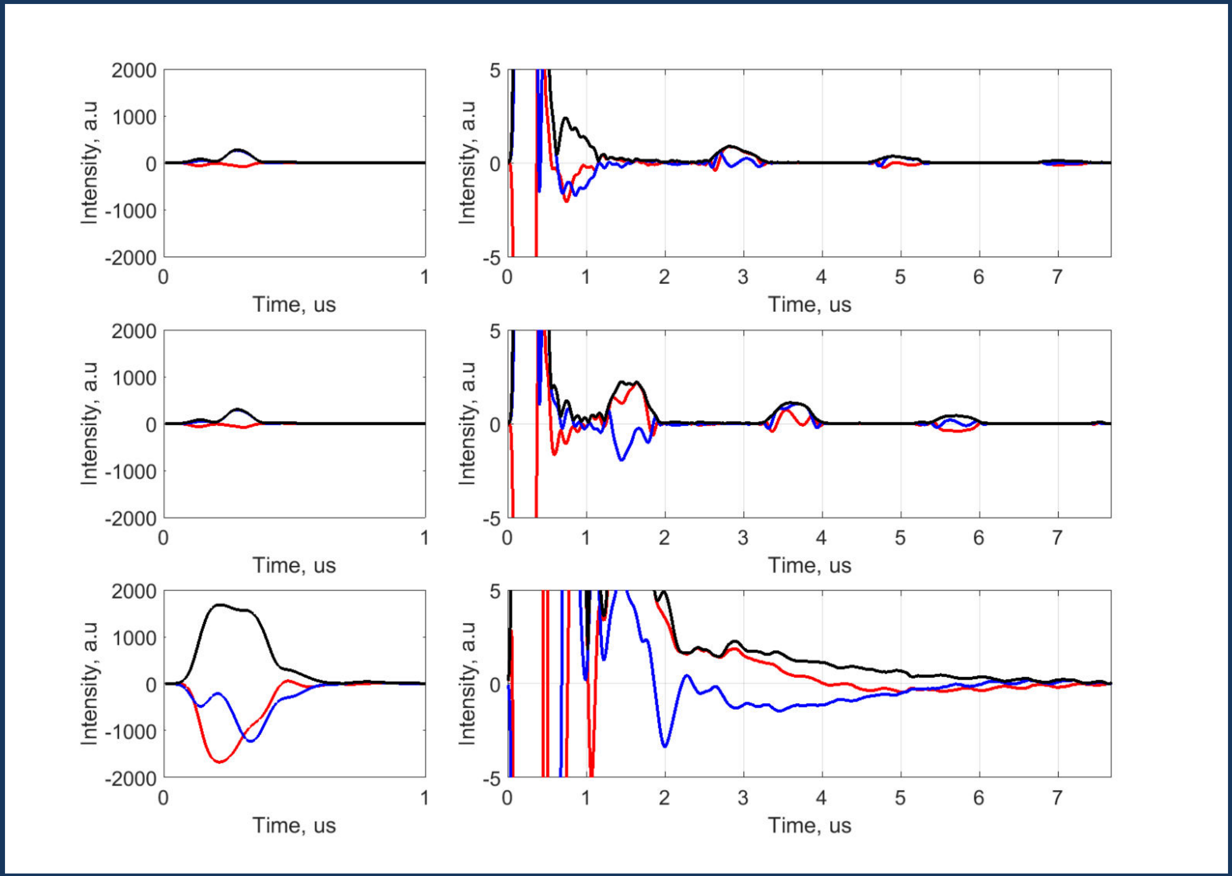
Relaxation times measurement of trityl radical using RS resonator
B_{pp} = 6G, f_m=96 kHz not sufficient to demonstrate dead-time reduction





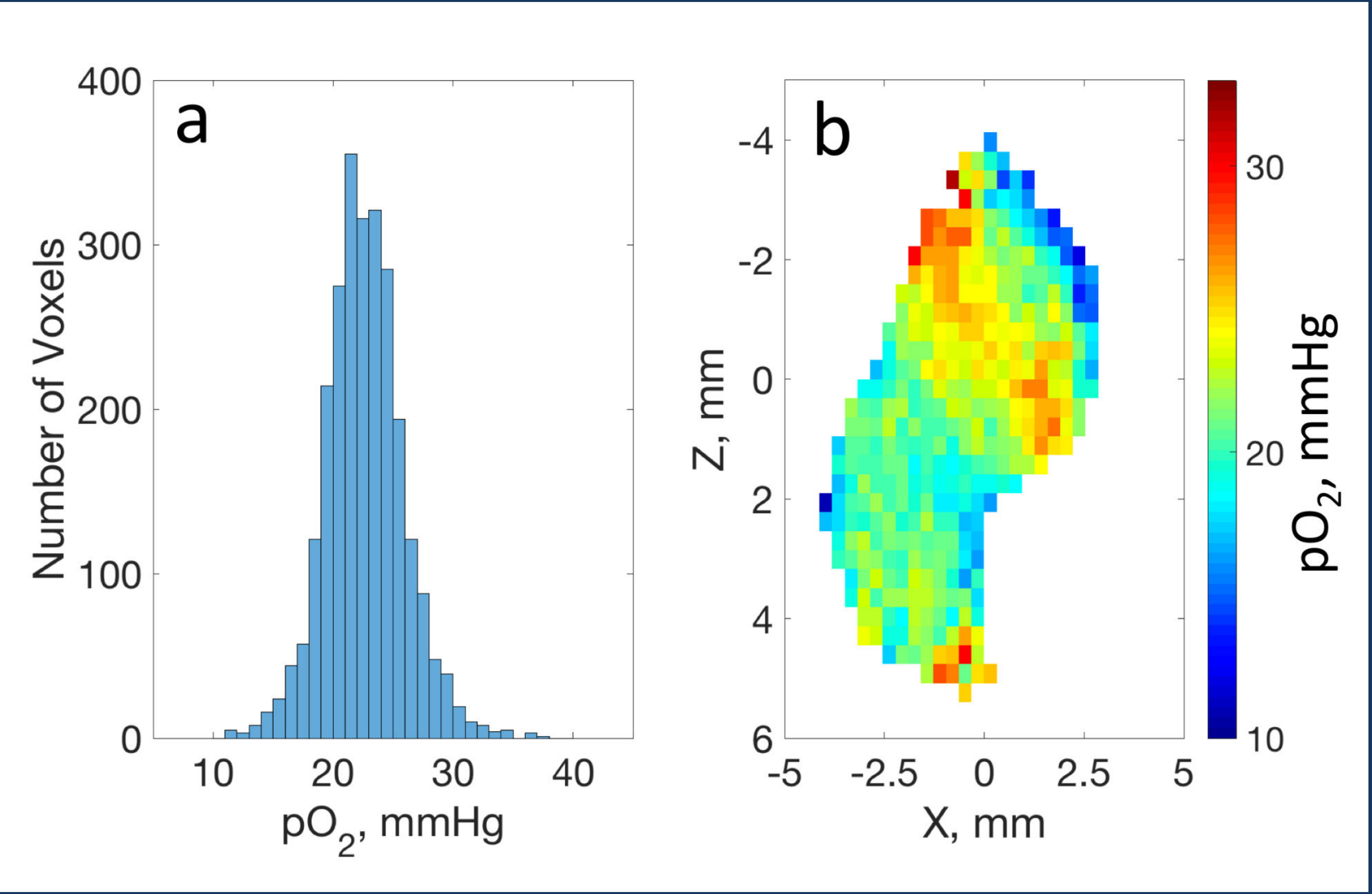
L-band , Modulation 480 kHz; FID with 100 ns pulse, 26 MHz de-tuning, Q=100





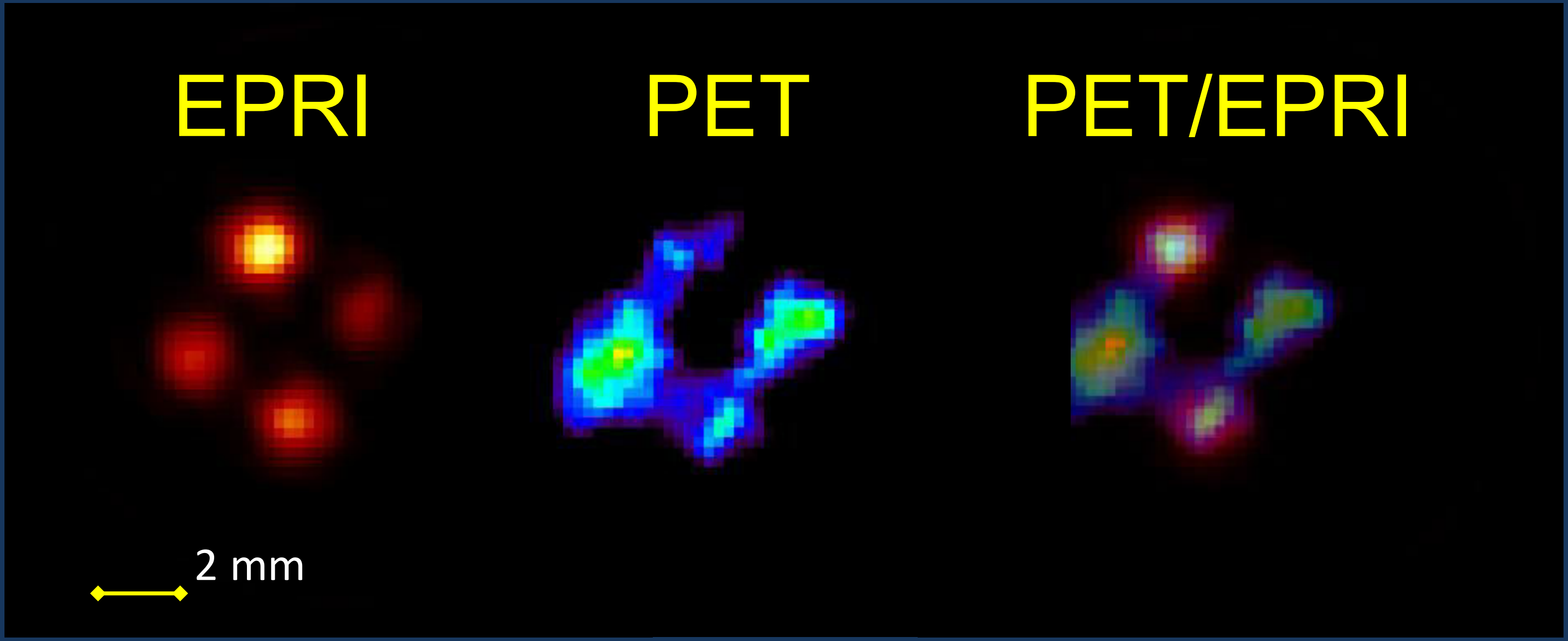
1. Isolation
2. More importantly, ring-down is 26 MHz away from EPR

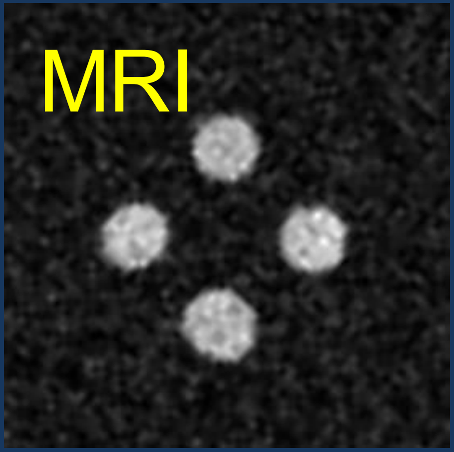
Applications in our lab. Functional imaging



EPR oximetric imaging of a mouse breast tumor. (a) Histrogramm of pO_2 distribution. (b) 2D slice of pO_2 image.

First ever /to our knowledge/ real-time PET/EPR co-imaging





https://www.ncbi.nlm.nih.gov/pubmed/29676283

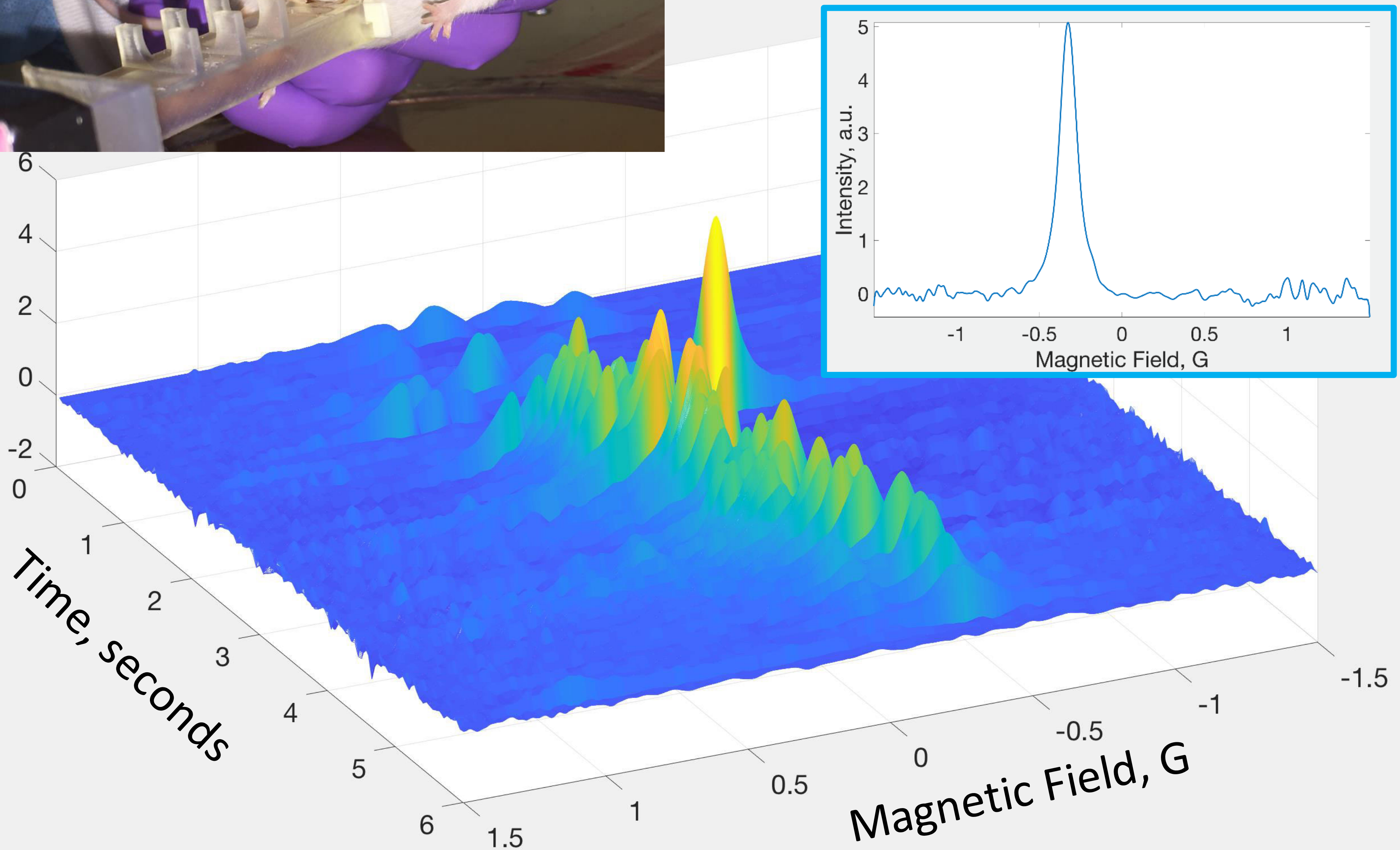
Tseytlin et al. Phys Med Biol. 2018 May 16;63(10)

First clinical RS EPR measurements using OxySpot
Dartmouth, August 2017

Observed pO_2 reduction & measurement time a few milliseconds

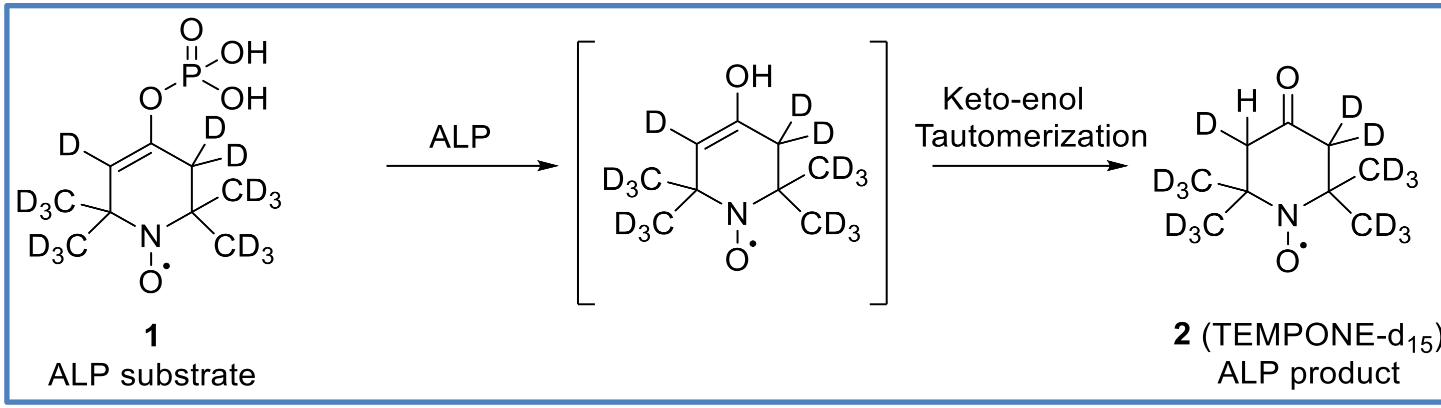
RS spectroscopy of conscious mice

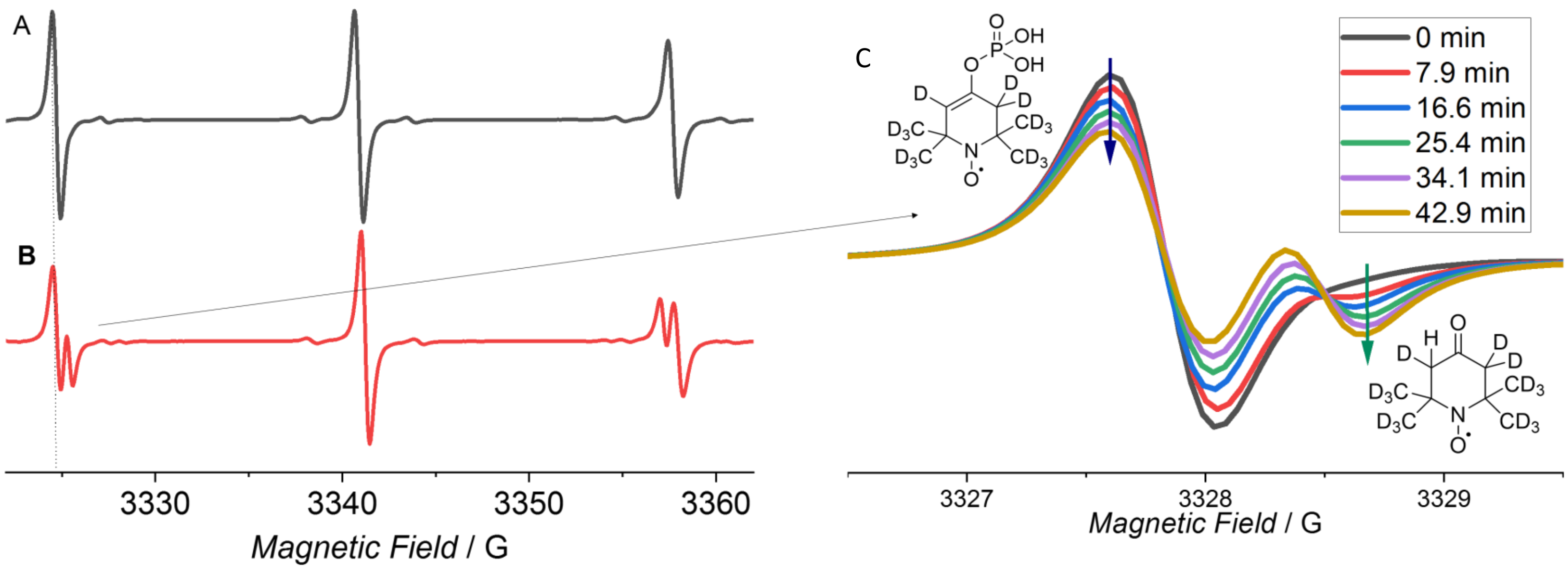
- Anesthesia may affect metabolism
- Permits repeated hourly measurements
- Not possible with the standard CW



1.4. Imaging of Enzyme Activity by Electron Paramagnetic Resonance

Phosphatase-sensitive Nitroxide spin probe:

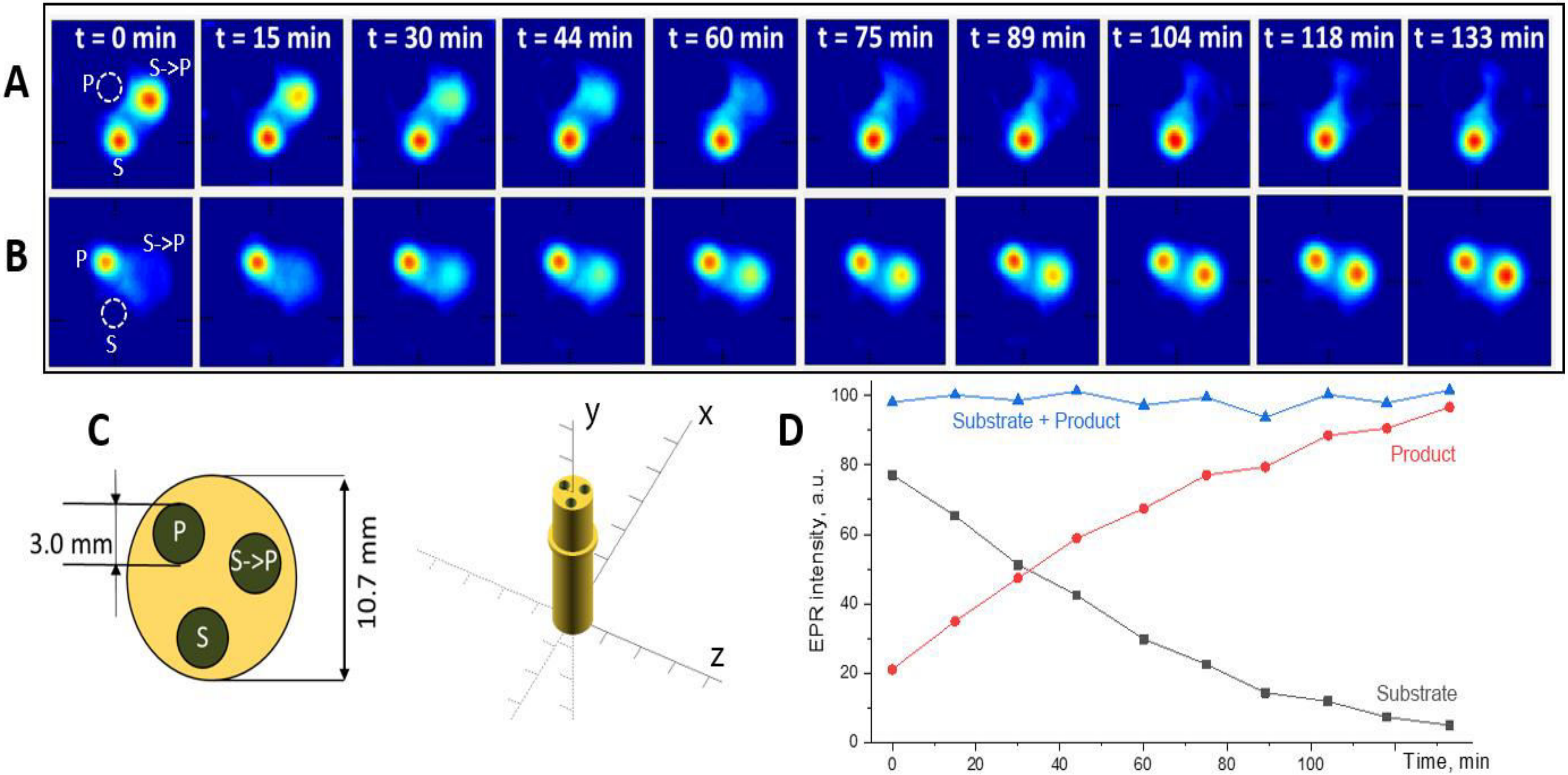




X-band EPR spectra of 200 μM **1** measured at 37°C in 10 mM Tris, pH=7.5, (A) before and (B) 50 min after incubation with 0.08 U/mL ALP, (C) Time evolution of the low-field EPR component.

U. Sanzhaeva; X. Xu; P. Guggilapu; M. Tseytlin; V. Khramtsov; B. Driesschaert, *Angew. Chem. Int. ed*. **2018**, 57(36):11701-11705.

In vitro Proof of Concept using a home made Rapid Scan Scanner (800 MHz)



First EPR image of enzymatic activity !!

U. Sanzhaeva; X. Xu; P. Guggilapu; M. Tseytlin; V. Khramtsov; B. Driesschaert, *Angew. Chem. Int. ed*. **2018**, 57(36):11701-11705.

Summary:

- RS (as of today) is an sensitivity-enhanced version of CW^{1h} EPR
- Narrowband CW excitation & broadband detection (as in pulse)
- Most of SNR gain comes using high power & fast scans
- Spin system remains linear (no saturation)
- No dead time
- However, high CW power may saturate the detector (LNA)
- Scan limitations (so far): Up-scan non-overlaps with down-scan
- Signal BW grows with scan rate => Q-factor becomes a

RS EPR is good for/when:

- ✓ High conversion power into B_1. e.g., small resonators
- ✓ Long relaxation times & inhomogeneous broadening
- ✓ High field EPR due to larger bandwidth

We use RS EPR for imaging. In comparison with pulsed EPR imaging

- Again, no dead-time (DT). Important if T2 $\cong$ TD, which may happen in the case of O_2 imaging.
- MUCH LESS bandwidth limited. As a result, multi-line multi-functional spin probes can be used.
- Spectral-spatial imaging is used / see lecture by Dr. Boris [illegible]