How to investigate soft matter using Variable Field NMR Relaxometry

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My ties to the University of Bari:

(i) The last-in-the-World 80 MHz Tesla instrument I have serviced for a decade (now being decommissioned) $\Rightarrow$

(ii) One of two research-grade greenhouses my late father-in-law build in the 70's $\Leftarrow$ (still in use!).

What is <u>Relaxometry</u> ?

Many systems, left alone, evolve towards a steady state.

They often exhibit fast, periodic (orbital) evolution features and,
superposed, much slower a-periodic (secular) evolution patterns.
Alternatively, some systems exhibit only a monotonous
a-periodic «settling» of some of their parameters.

All such slow, a-periodic components of a spontaneous evolution
of a physical system can be referred to as relaxation phenomena.

Since relaxation leads to a steady state,
to repeat a relaxation phenomenon, one must
jolt the studied system out of its equilibrium.

In general,
relaxometry is the art of studying relaxation phenomena.

How many types of relaxometry there are?

Simple answers: as many as …

- the types of systems of interest (application-based classification)
- the interactions which cause them (phenomenological classification)
- the methods to follow them (metrological classification)

Examples

- Astronomical (hundreds of relaxation phenomena in solar system alone)
- Mechanical, electric, optical, ultrasound, … relaxometric techniques pertinent to various molecular relaxation phenomena, among which
- NMR relaxometry, concerned with the evolution of molecular nuclear magnetization, generally in an unisotropic (axial) magnetic field.

General theory of Relaxation Phenomena (a glimpse)

Quantum version:

Terms:

- H … Hamiltonian with its
- H_0 … time-averaged part and
- S(t) … its stochastic part.
- C(τ) … **Correlation function**
- J(H_0) … **Spectral density**

C's and J's are quadratic in the involved interactions!

Given a stochastic [spin] Hamiltonian

$$\mathbf{H} = \mathbf{H}_0 + \mathbf{S}(t), \quad <\mathbf{S}(t)>=0,$$

under certain conditions (secular vs stochastic time scales) one obtains a secular equation for the density matrix

$$\frac{d}{dt}\boldsymbol{\sigma}(t) = -\tfrac{1}{2}\boldsymbol{J}(\mathbf{H}_0)\{\boldsymbol{\sigma}(t)-\boldsymbol{\sigma}_0\}$$

where

$$\boldsymbol{J}(\mathbf{H}_0) = \int_{-\infty}^{\infty} d\tau\, \boldsymbol{C}(\tau) = \int_{-\infty}^{\infty} <\mathbf{S}^*(0)\,\mathbf{S}^*(\tau)> d\tau$$

and

$$\mathbf{S}^*(0)=\mathbf{S}(0) \qquad \mathbf{S}^*(\tau)=e^{i\mathbf{H}_0\tau}\mathbf{S}(\tau)e^{-i\mathbf{H}_0\tau}$$

with the italics denoting commutation super-operators

Note: In terms of the Lagrange-Hamiltonian approach, the classical version of relaxation theory is much the same. Classical and quantum approaches to relaxation are actually very similar.

So, what is, specifically, __NMR__ Relaxometry?

Simple answer: just replace *Hamiltonian* with *__Spin__ Hamiltonian*

$$H = H_Z + H_{SR} + H_C + H_{DD} + H_{DE} + H_F + H_J + H_Q$$

$H_Z = -\hbar\gamma_i \mathbf{B}.\mathbf{I}_i$,   Zeeman term

$H_{SR} = \mathbf{M}.R_i.\mathbf{I}_i$,   Spin-rotation term

$H_C = \mathbf{B}.C_i.\mathbf{I}_i$,   Chemical shifts (screening) term

$H_{DD} = \mathbf{I}_i.D_{ij}.\mathbf{I}_j$,   Direct dipole-dipole interactions term

$H_{DE} = \mathbf{I}_i.E_{ij}.\mathbf{S}_v$,   Dtto between nuclei and free electrons

$H_F = \mathbf{I}_i.A_{iv}.\mathbf{S}_v$,   Hyperfine couplings term (with free electrons)

$H_J = \mathbf{I}_i.J_{ij}.\mathbf{I}_j$,   Indirect couplings term

$H_Q = \mathbf{I}_i.Q_i.\mathbf{I}_i$,   Quadrupole interactions term

The intrinsic nature of relaxation mechanisms

In general, being quadratic in spin-interactions, **every relaxation term combines** *two spin-interaction terms* **and** *two molecular dynamics modes* **which** *activate* it.

The terms in which there is a coincidence between the two spin-interaction terms, as well as between the dynamics modes, are **the principle relaxation channels**.

Principle relaxation channels tend to dominate the relaxation phenomena, while the remaining **cross-relaxation pathways** are often quantitatively negligible.

Example:

In proton MRR of many diamagnetic systems the dominant relaxation channel uses direct dipole-dipole interaction, activated by molecular reorientation.

Molecular dynamics models: huge complexity

- Ever-growing, amazing number of [equally amazing] models
- Sub-molecular, molecular, oligo-molecular, and collective motions
- Huge range of correlation times (from 1 Hz to tens of GHz)
- Observable by many methods which should be compared

Molecular motions are harder to describe than spin interactions:
They are the "weak link" of MR Relaxometry **Theory** but also …
… the principal goal of MR Relaxometry **Practice**

Wrapping it up

Interactions:

- DD   Dipole-dipole interaction between nuclei
- DE   Nucleus-electron dipole-dipole interaction
- CE   Nucleus-electron contact interaction (the Fermi term)
- NQ   Nuclear quadrupole interaction with local electric field gradients
- SR   Spin rotation interaction
- CSA   Chemical shift anisotropy (part of CS)
- CS   Chemical shift (isotropic part) when not constant (exchange)
- JA   J coupling anisotropy (part of J)
- J   Scalar part of J coupling when not constant (exchange)
- etc.   including interactions with SPIO's and other "exotica"

X

Motions:

- Rot   Rotational diffusion (global, unconstrained)
- IRot   Internal rotations (partial, tunnelling, kinks, you name it …)
- Rept   Reptations
- Libr   Librations
- Vibr   Vibtations with angular components (bending motions)
- Trans   Translations (free or constrained)
- Crawl   on surfaces, like Kimmich's caterpillars
- Hits   Collisions (like against pore walls)
- Jump   across barriers, between hydration shells, and the like
- Coll   Collective motions (like in liquid crustals)
- etc.   like Halle's flickering acquducts in proteins, …

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The Grid of MRR Formulas

Interactions versus types of motions:

	Rot	IRot	Rept	Libr	Vibr	Trans	…
DD	BPP	F_{1b}	F_{1c}	F_{1d}	F_{1e}	F_{1f}	…
DE	F_{2a}	F_{2b}	F_{2c}	F_{2d}	F_{2e}	F_{2f}	…
CE	F_{3a}	F_{3b}	F_{3c}	F_{3d}	F_{3e}	F_{3f}	…
NQ	F_{4a}	F_{4b}	F_{4c}	F_{4d}	F_{4e}	F_{4f}	…
SR	F_{5a}	F_{5b}	F_{5c}	F_{5d}	F_{5e}	F_{5f}	…
CSA	F_{6a}	F_{6b}	F_{6c}	F_{6d}	F_{6e}	F_{6f}	…
…	…	…	…	…	…	…	…

In each cell there is a formula!
Only the principle channels need over 100 of them.
The total count would exceed 1000!

The BPP formula

Combines **dipole-dipole interaction** with **molecular reorientations**

$$R_1 \equiv \frac{1}{T_1} = \frac{\hbar^2 \gamma^4}{5d^6} I\,(I+1)\,P_1(\tau,\omega),$$

$$P_1(\tau,\omega) = J(\tau,\omega) + 4J(\tau,2\omega),$$

$$J(\tau,\omega) = \frac{2\tau}{1+(\omega\tau)^2}$$

$$R_2 \equiv \frac{1}{T_2} = \frac{\hbar^2 \gamma^4}{11d^6} I\,(I+1)\,P_2(\tau,\omega)$$

$$P_2(\tau,\omega) = 6J(\tau,0) + J(\tau,\omega) + 4J(\tau,2\omega)$$

This is only one of the most important relaxation channels!

But it does have a central position among all NMR relaxation formulas
(it's the **mother of all relaxation formulas**)

Bloembergen N., Purcell E.M., Pound R.V.,
Relaxation Effects in Nuclear Magnetic Resonance Absorption,
Phys.Rev. 73, 679-712 (1948). DOI: 10.1103/PhysRev.73.679
This could be considered as the first NMR review.

A very practical note

$$R_1 \equiv \frac{1}{T_1} = \frac{\hbar^2 \gamma^4}{5d^6} I(I+1) P_1(\tau, \omega),$$

$$P_1(\tau, \omega) = J(\tau, \omega) + 4J(\tau, 2\omega),$$

$$J(\tau, \omega) = \frac{2\tau}{1 + (\omega\tau)^2}$$

$$R_2 \equiv \frac{1}{T_2} = \frac{\hbar^2 \gamma^4}{11d^6} I(I+1) P_2(\tau, \omega)$$

$$P_2(\tau, \omega) = 6J(\tau, 0) + J(\tau, \omega) + 4J(\tau, 2\omega)$$

Always use relaxation rates, not relaxation times!

Contributions to relaxation rates are **nicely additive** across different spin-interactions and different molecular motions.

The use of relaxation times is to be abhorred!

The Mother of All Questions:

After all this complex and messy theory, do you <u>really</u> think that NMR Relaxometry can be ever good for something ?$^\infty$

Answer: YES, …

1) Because the theory nevertheles provides a general guidance
2) Because the BPP formula is fairly representative of all of them
3) Because qualitatively different cases also form uniform families
4) Because of the known excellent additivity of relaxation rates
5) Because even without theory, the relaxation rate curves still have an intrinsic value as metrological material characteristics.

The first four points actually enable the possibility of extensive educated-guess, semi-empirical "tinkering"

BPP: graphical representations
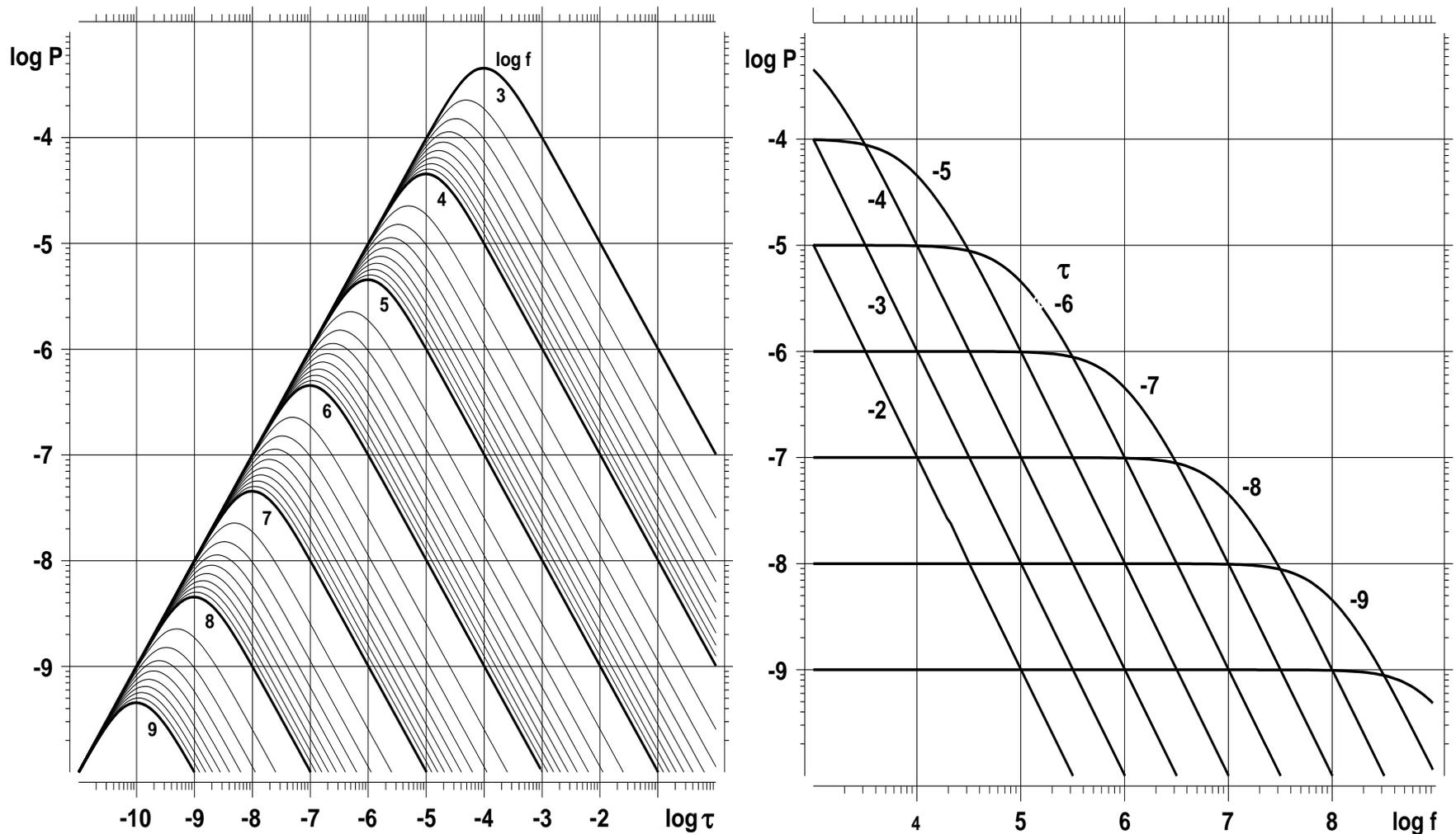
Another very practical note

Put any VF relaxation plots on a log(R) versus log(f) scale.

For a number of theoretical as well as practical reasons,
that is the only representation that really makes sense.

A few simulations based on BPP

The few slides that follow indicate an approach to simulating NMR R_1 relaxation-dispersion profiles (NMRD profiles).

Though based on BPP formula, this kind of semi-empirical approach is eminently suitable for quantitative investigations.

A simulated case of Variable Temperature MRR

The BPP factor $P(\tau,f)$ as a function of temperature for an Arrhenius process with $E_a = 10$ kJ/mol and $\tau_0 = 10^{-10}$ sec.

Note: A constant contribution of $P = 10^{-8}$ has been added
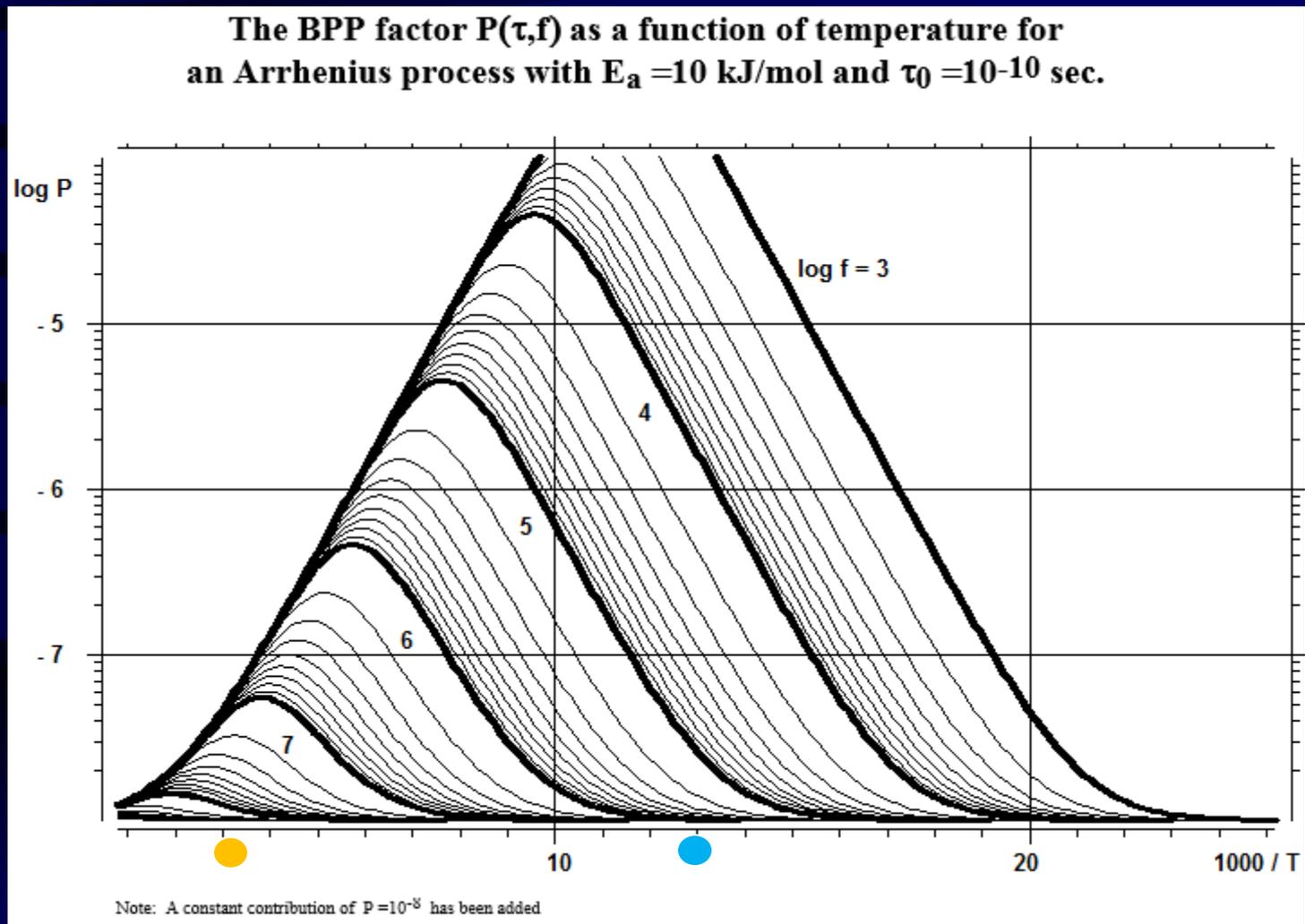
A corresponding Variable Field MRR approach

The BPP factor $P(\tau, f)$ as a function of temperature for an Arrhenius process with $E_a = 10$ kJ/mol and $\tau_0 = 10^{-10}$ sec.
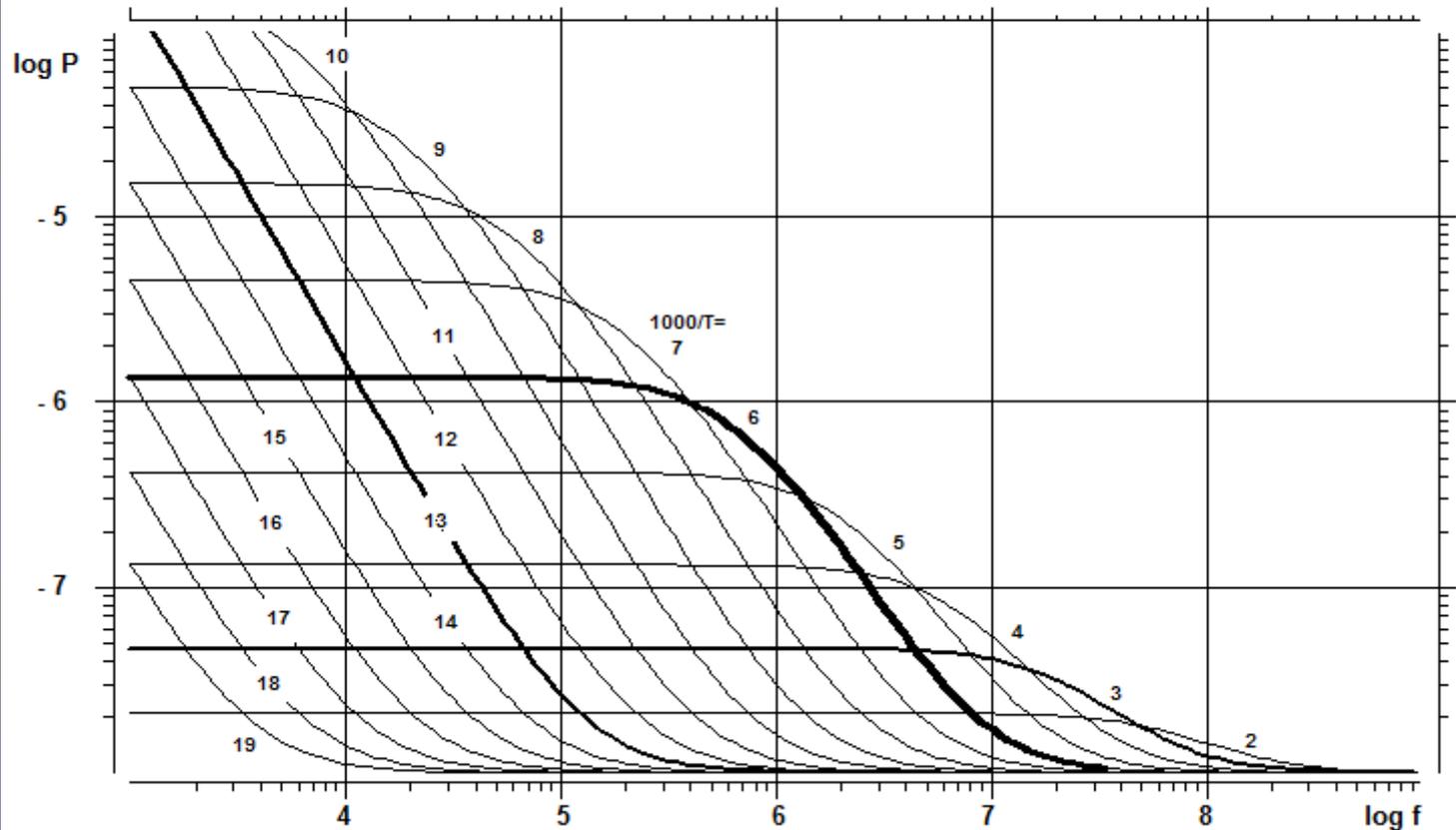
Note: A constant contribution of $P = 10^{-8}$ has been added

A more complex case: VT MRR

The BPP factor $P(\tau, f)$ as a function of temperature for two Arrhenius processes with $E_a = 6$ kJ/mol, $\tau_0 = 10^{-9}$ sec and $E_a' = 30$ kJ/mol, $\tau_0' = 10^{-12}$ sec and relative weights 0.2 and 0.8, respectively.

Note: A constant contribution of $P = 10^{-8}$ has been added
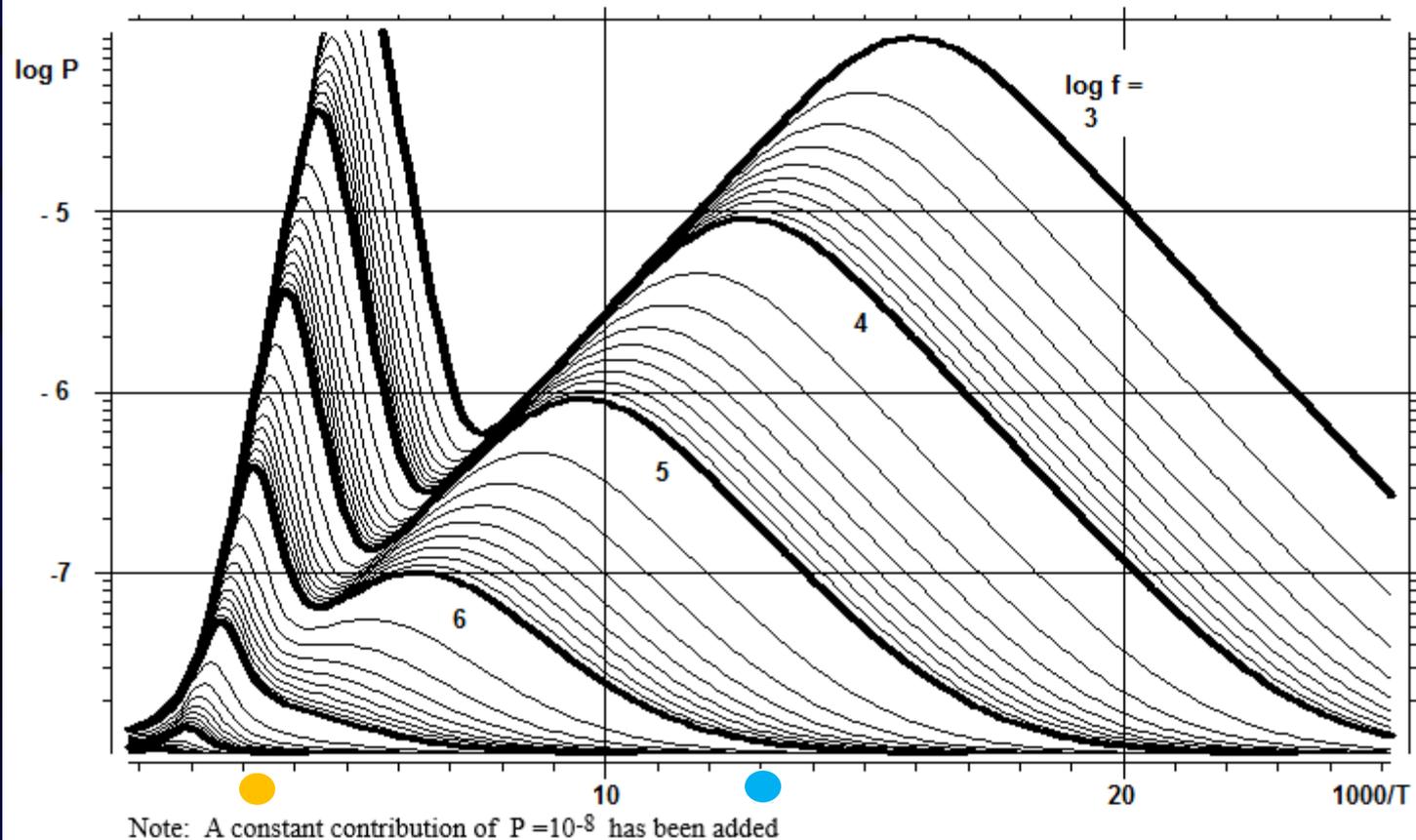
Fixed-frequency VT measurements cover just a small piece of a single curve

The same case in VF MRR format

The BPP factor $P(\tau,f)$ as a function of temperature for two Arrhenius processes with $E_a = 6$ kJ/mol, $\tau_0 = 10^{-9}$ sec and $E_a' = 30$ kJ/mol, $\tau_0' = 10^{-12}$ sec and relative weights 0.2 and 0.8, respectively.
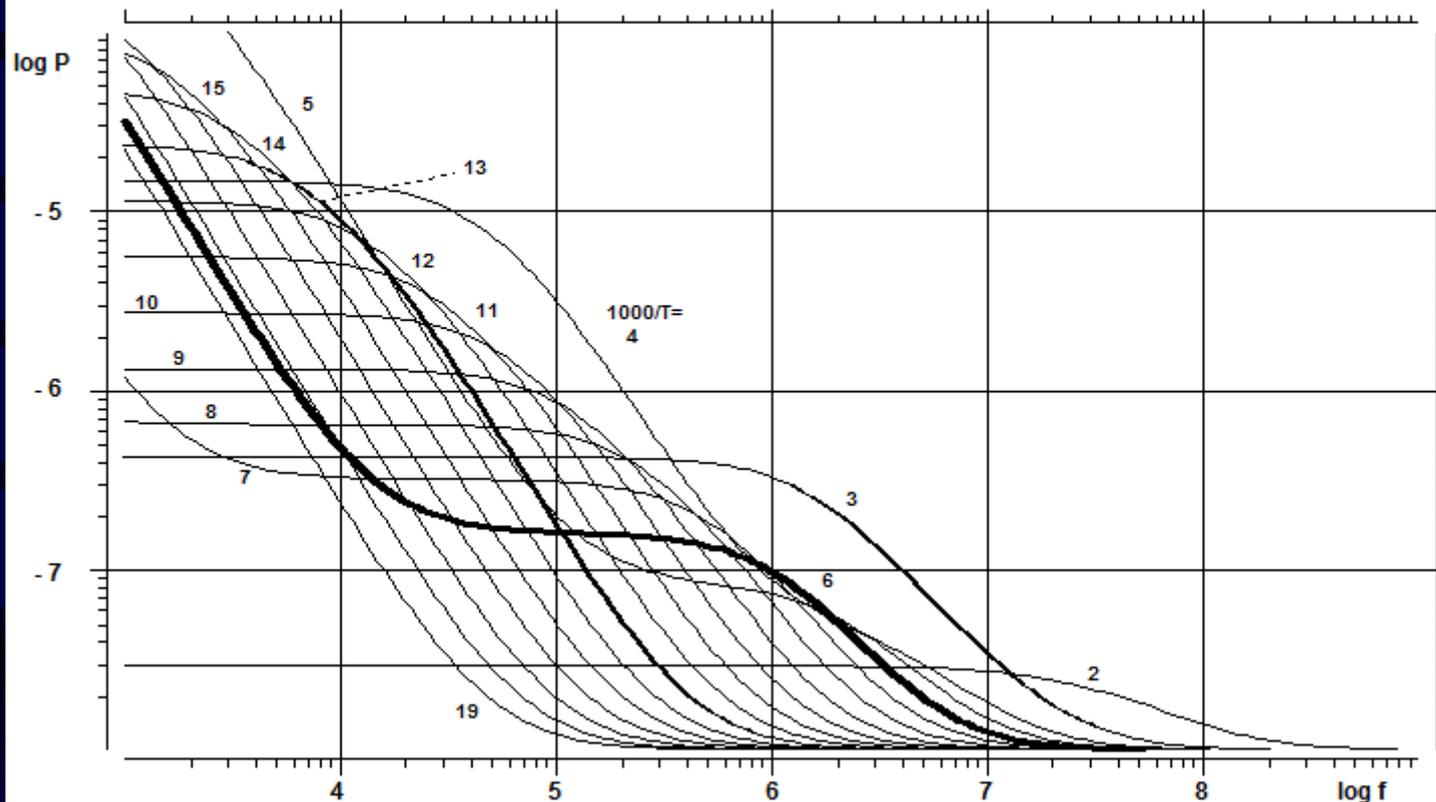
Note: A constant contribution of $P = 10^{-8}$ has been added

Variable-field measurements cover a full cut through the 2D $R_1(\tau,f)$ surface

Another kind of situation: VT MRR

The BPP factor $P(\tau, f)$ as a function of temperature for two Arrhenius processes with $E_a = 1$ kJ/mol, $\tau_0 = 10^{-7}$ sec and $E_a' = 15$ kJ/mol, $\tau_0' = 10^{-12}$ sec and equal relative weights.
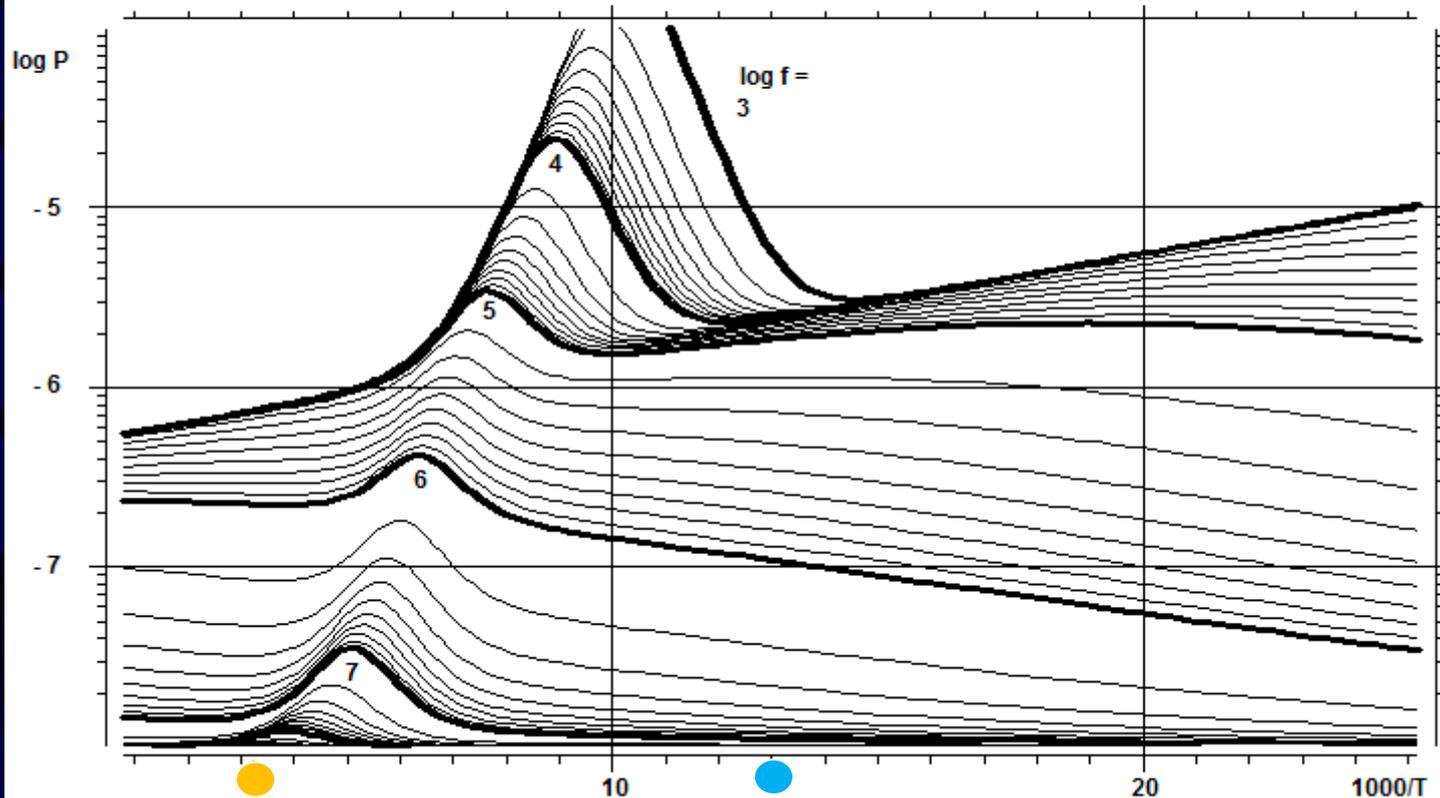
Note: A constant "other sources" contribution of $P = 10^{-8}$ has been added

Another kind of situation: VF MRR

The BPP factor $P(\tau,f)$ as a function of temperature for two Arrhenius processes with $E_a = 1$ kJ/mol, $\tau_0 = 10^{-7}$ sec and $E_a' = 15$ kJ/mol, $\tau_0' = 10^{-12}$ sec and equal relative weights.
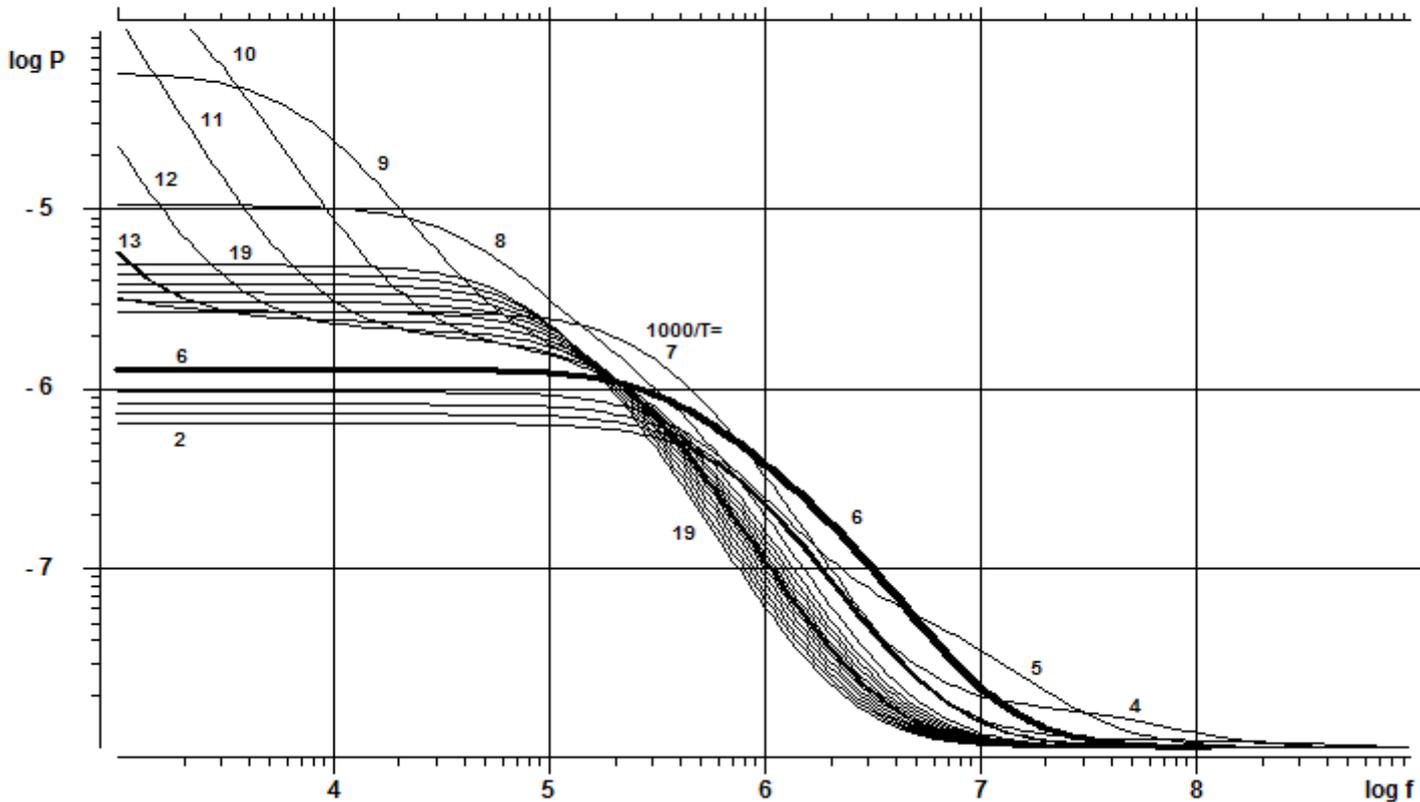
Note: A constant contribution of $P = 10^{-8}$ has been added

A few NMRD profiles …
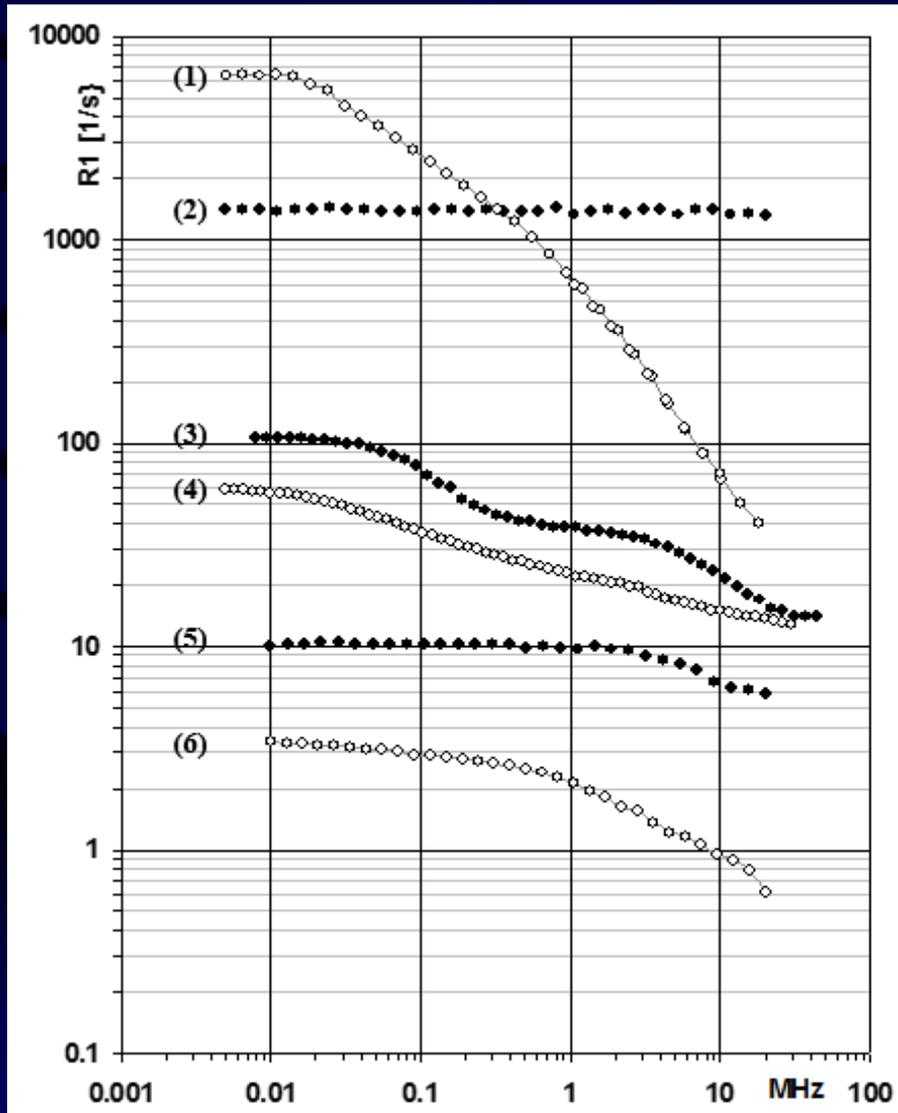
(1) Parafilm M
(2) 2.1M $Dy(ClO_4)_3$ in H_2O
(3) 2mM $MnCl_2$ in H_2O
(4) Egg yolk
(5) 10 mM Gd^{3+} in D_2O
(6) Egg albumen

Notice the enormous range of relaxation rates across a broad range of Larmor frequencies.

Ferrante G., Sykora S., Technical Aspects of Fast Field Cycling in Advances in Inorganic Chemistry, Editors van Eldik R., Bertini I., Elsevier 2005, Vol.57

NMRD profiles of some elastomers
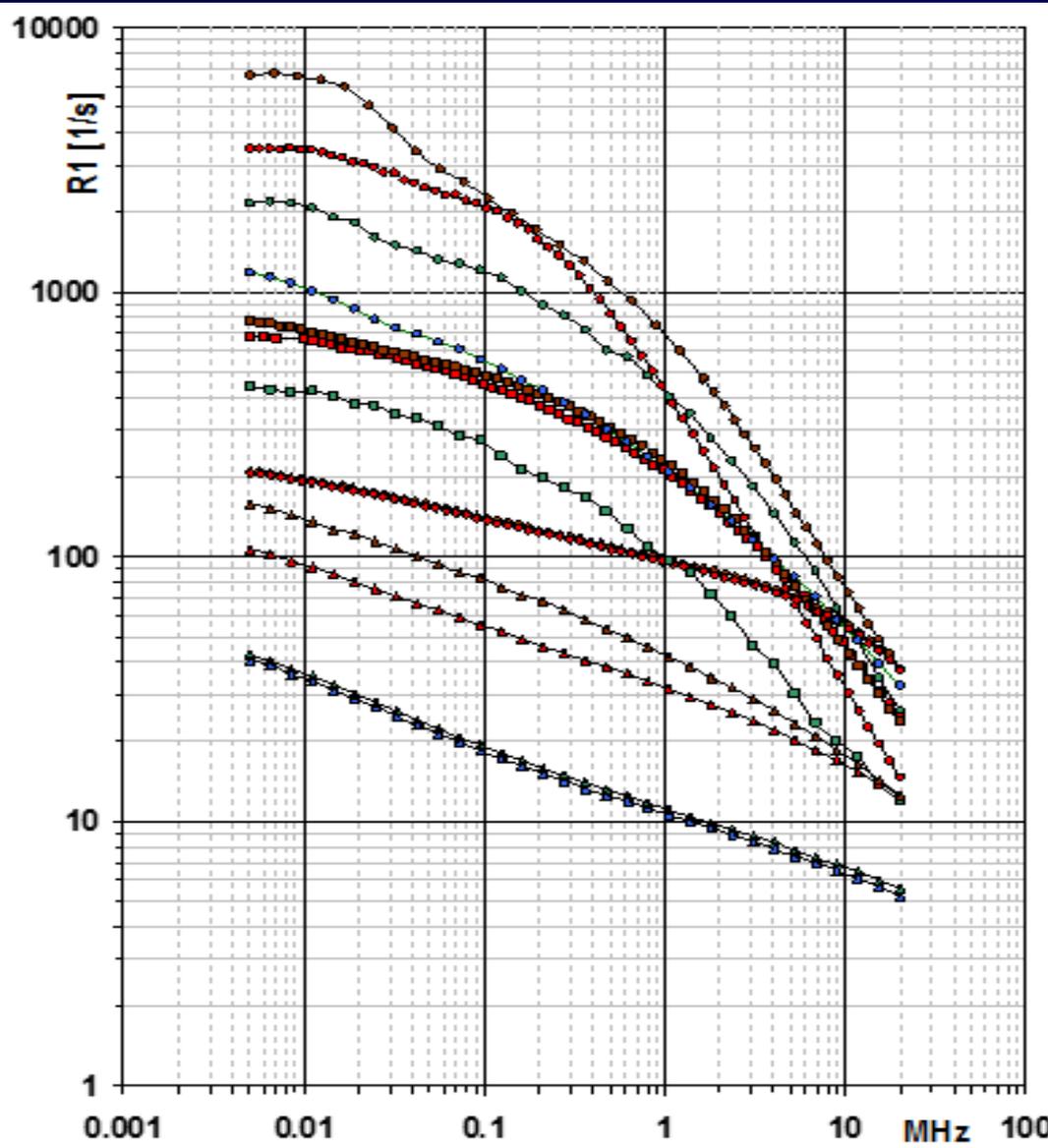
Listed from top down at 0.01 MHz:

Circles:
  Brown: Isobutylene-isoprene
  Red: Styrene-butadiene, anionic
  Green: Polychloroprene cis
  Blue: Ethylene-propylene rubber

Squares:
  Brown: Styrene-butadiene
  Red: Styrene-butadiene, radical
  Green: Polyisoprene trans

Diamonds:
  Brown: Polyisoprene 97%
  Red: Natural rubber

Triangles:
  Brown: SBS rubber
  Red: Polybutadiene cis/trans
  Green: Polybutadiene 97%
  Blue: Polybutadiene 97.5%

NMRD profiles of some polystyrenes & polycarbonate
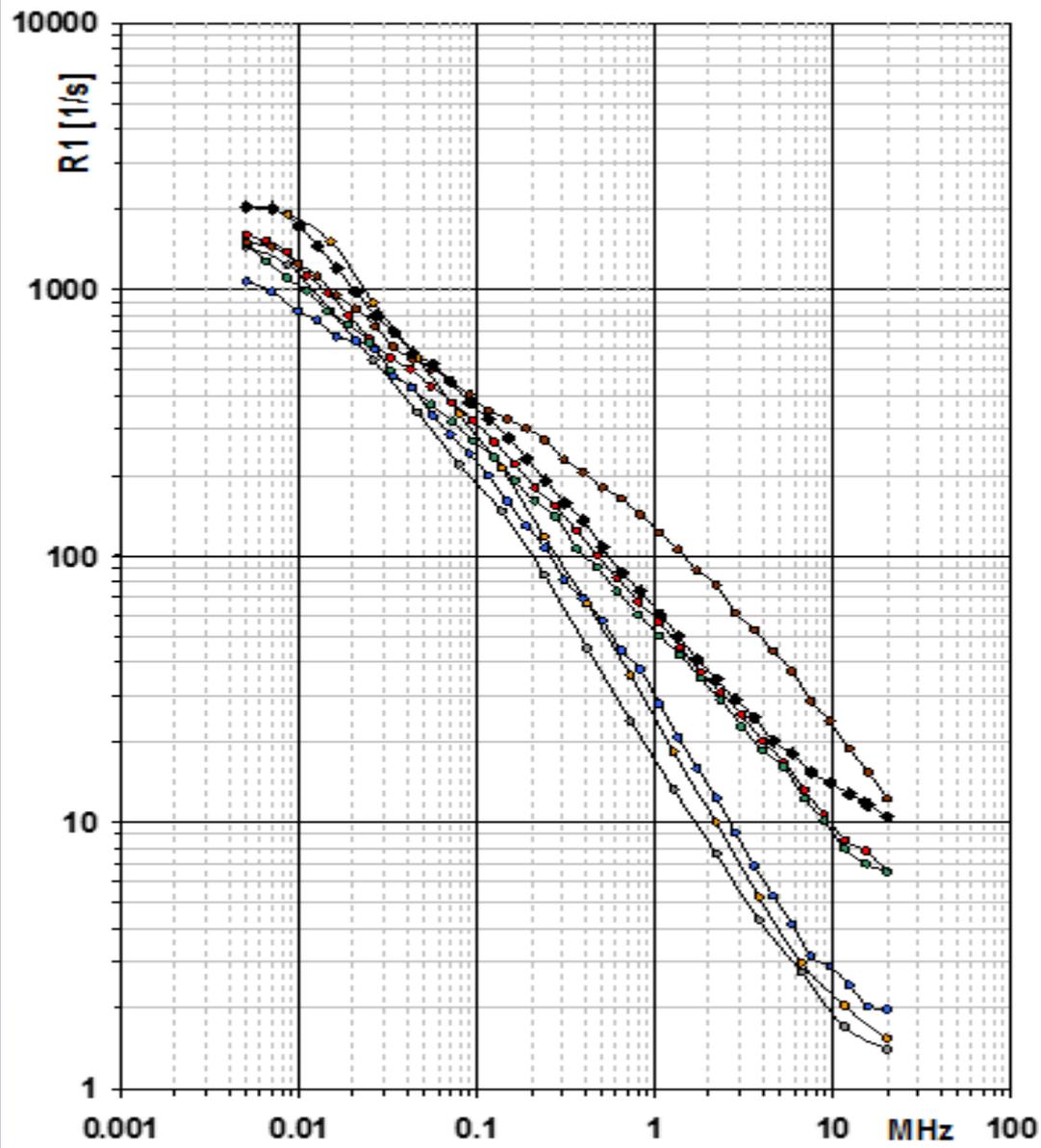
Circles (styrenes)
from top down at 20 MHz:

Brown: Poly-α-methyl-styrene
Red: Styrene-butadiene copolymer I
Green: Styrene-butadiene copolymer II
Blue: HIPS (I) antishock polystyrene
Orange: Styrene homopolymer
Gray: Styrene-acrylonitrile (SAN)

Diamonds:
 Black: Polycarbonate

NMRD profiles of some nylons
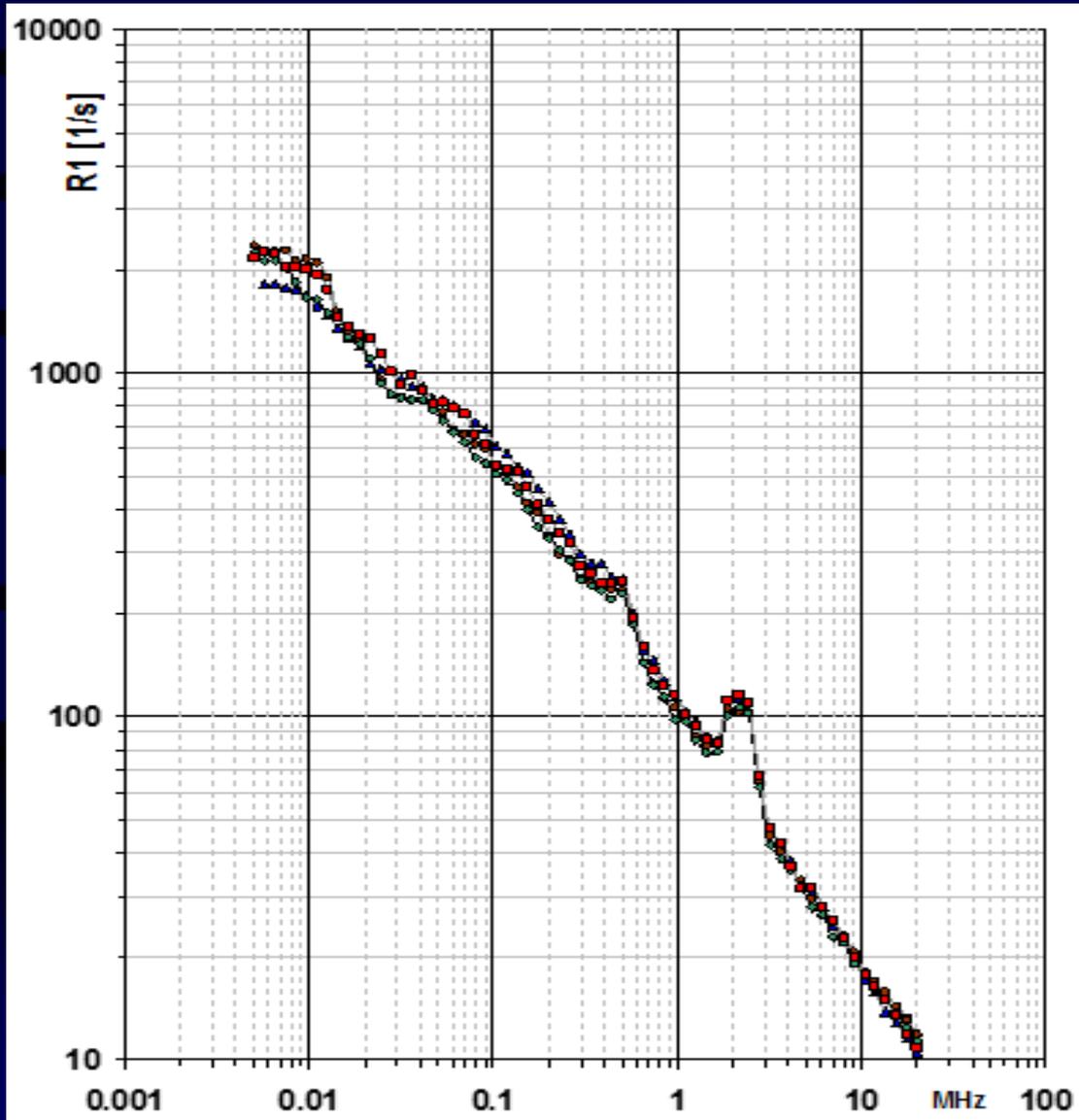
Blue triangles: Nylon 6
Red squares: Nylon 6-6 Corean
Brown disks: Nylon 6-6 Rhone-Poulenc
Green diamonds: Nylon ICI

NMRD profile of solid BSA
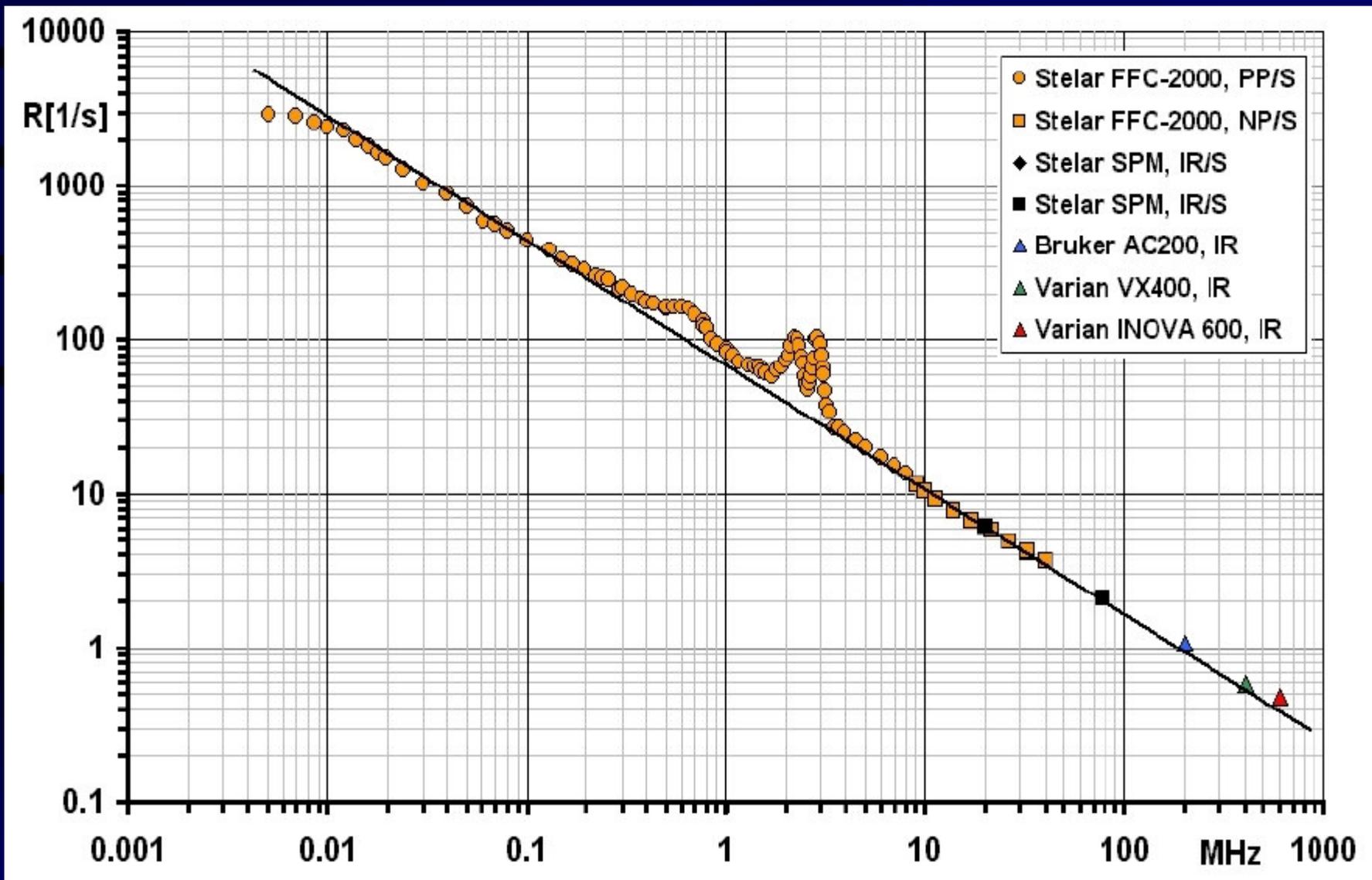
NMRD profile of a 30% cross-linked BSA solution
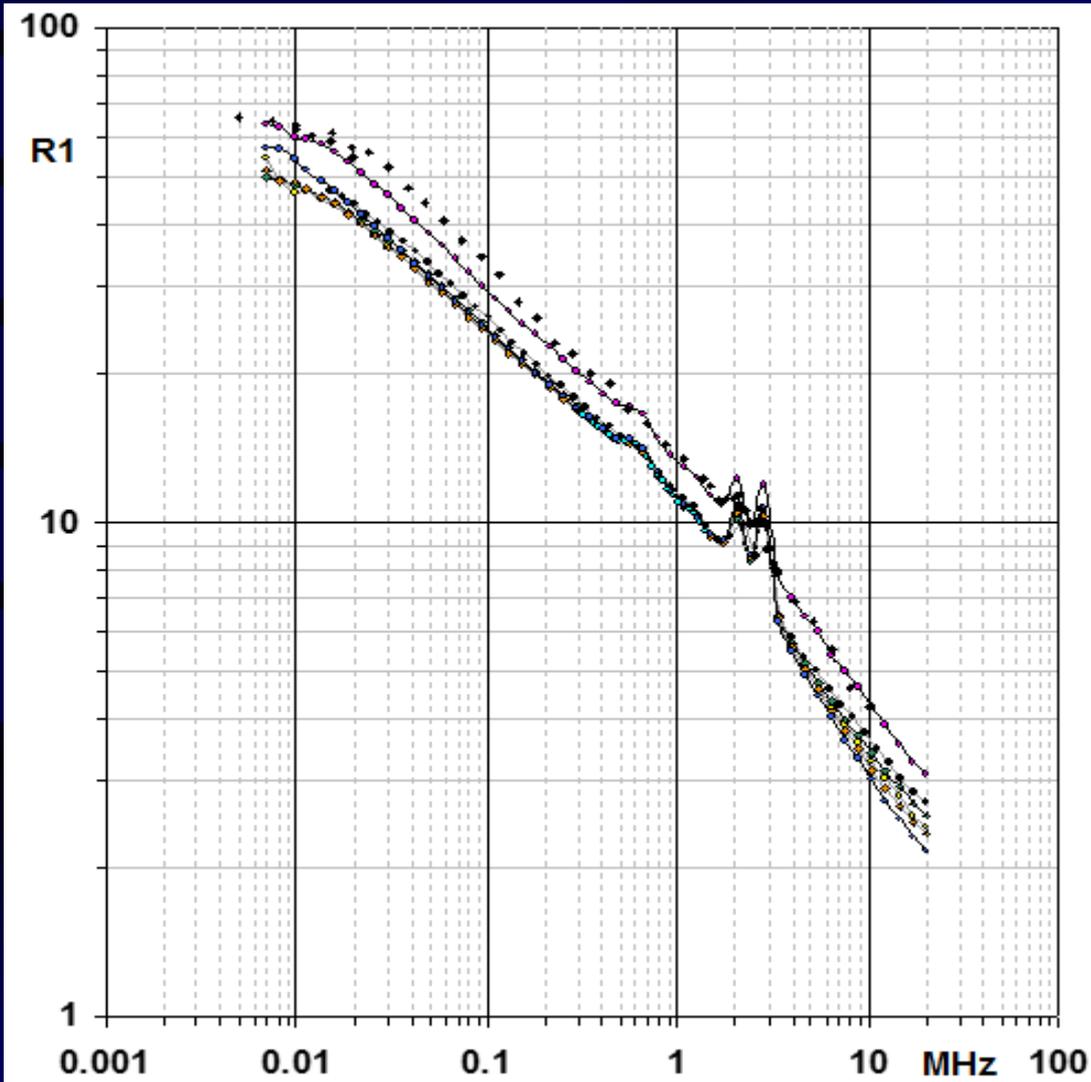
Black dots   20°C
Green diamonds   25°C
Yellow dots   30°C
Orange diamonds   35°C
Light blue circles   35 °C
Violet dots: denaturated, 30 °C

Note: The black diamonds show the profile of 35% solution of natural BSA (no cross-linking) in H_2O, measured at 25°C.

Water in pietra Serena:
UPEN T_1 distribution curves at different field strengths
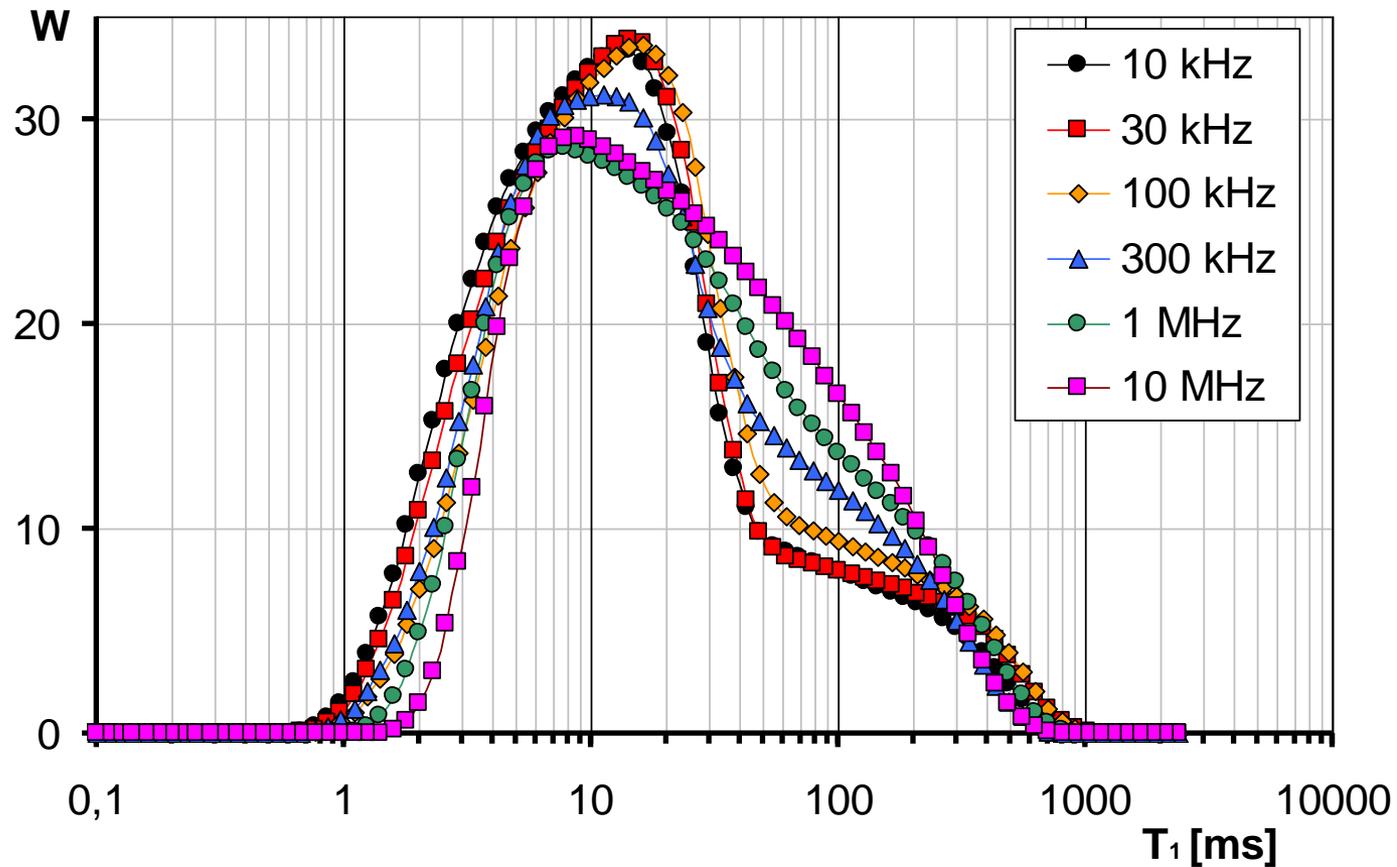
What we did not talk about: the instruments …

SPINMASTER - FFC
Fast Field Cycling NMR relaxometer

These are old, historic hardware slides (1997).
for more recent stuff, visit Stelar Srl

The Magnet ...

Magnet cutting

coil	1	2	3	4	5	6	7	8	9	10
layer 1	0.2253	0.2356	0.2129	0.2088	0.2051	0.2030	0.2045	0.2015	0.2013	0.2004
layer 2							0.2007	0.2005	0.2027	0.2035
coil	11	12	13	14	15	16	17	18	19	20
layer 1	0.2033	0.2071	0.2005	0.2019	0.2009	0.2011				

DB/B in homog.

| | | | 0.2028 | 0.2020 | 0.2058 | 0.2033 |
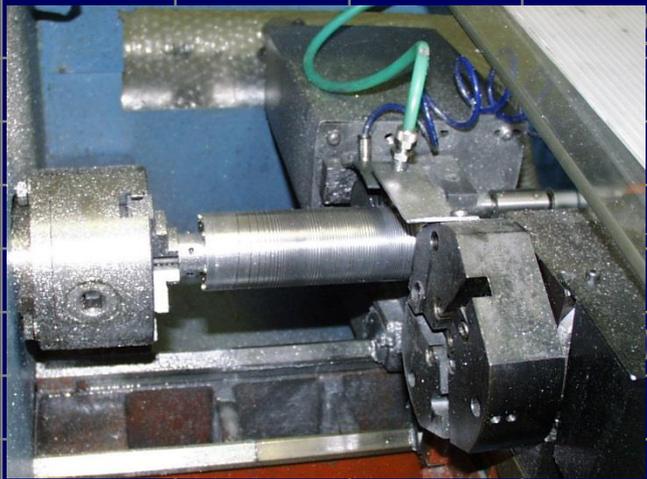
coil	61	62	63	64	65	66
layer 2	0.2003	0.2030	0.2026	0.2016	0.2014	0.2027
coil	71	72	73			
layer 2	0.2085	0.3019	0.2776			

The sequences …
PP: basic Pre-Polarized sequence
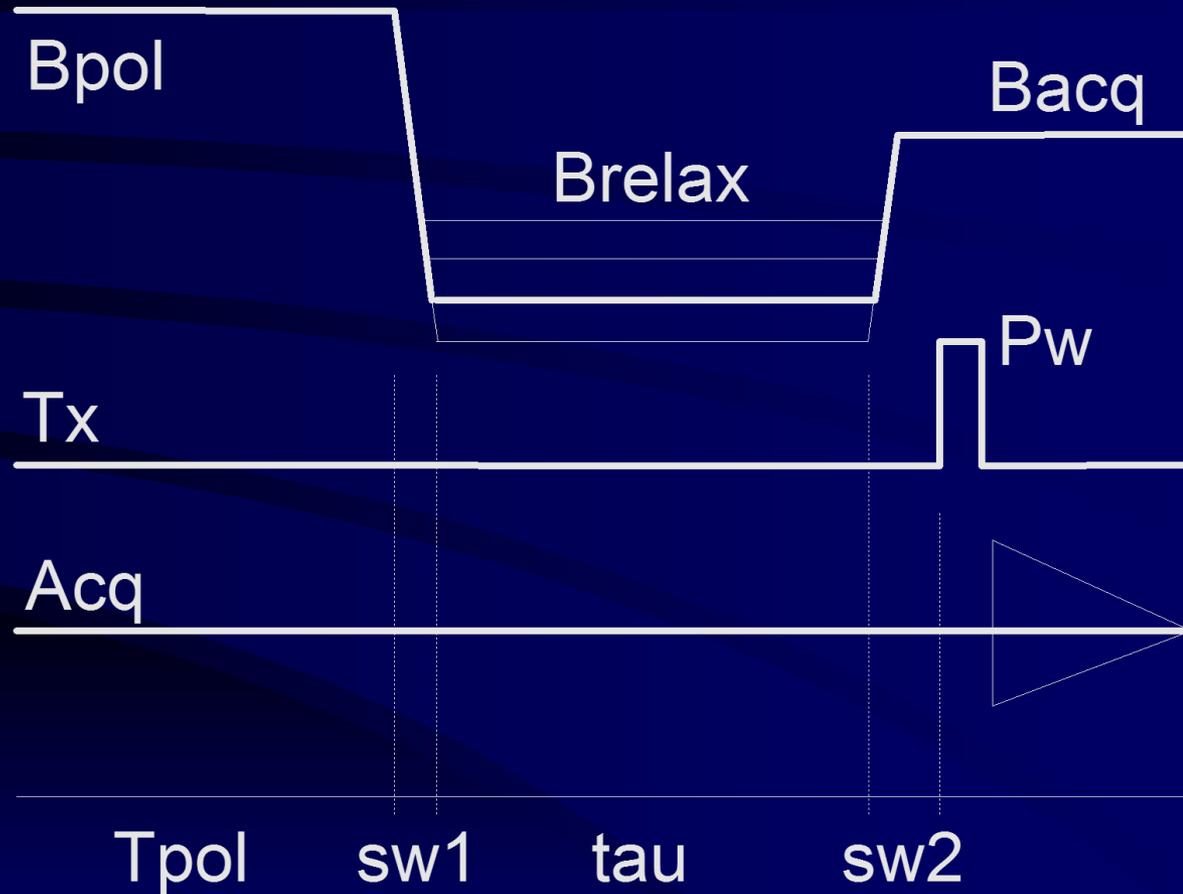
NP: basic Non-Polarized sequence
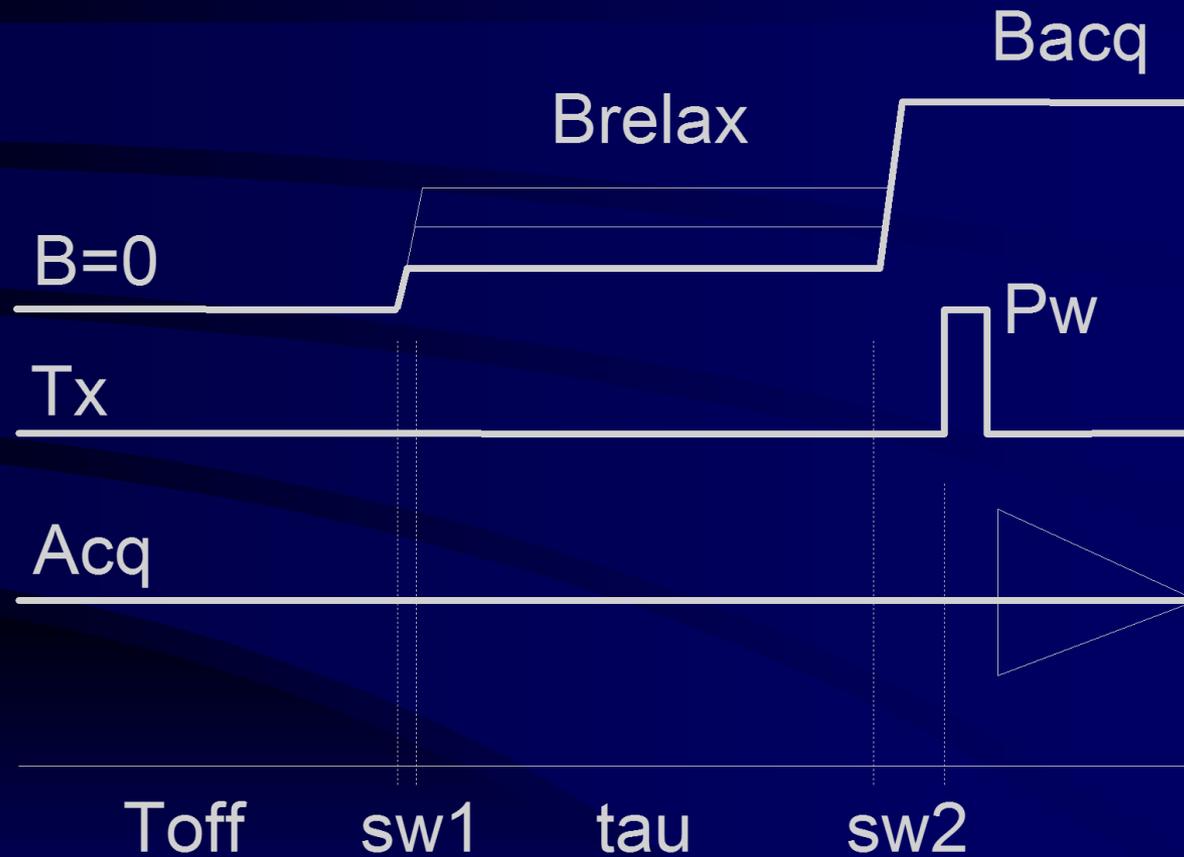
The way the actual data look ...

NP
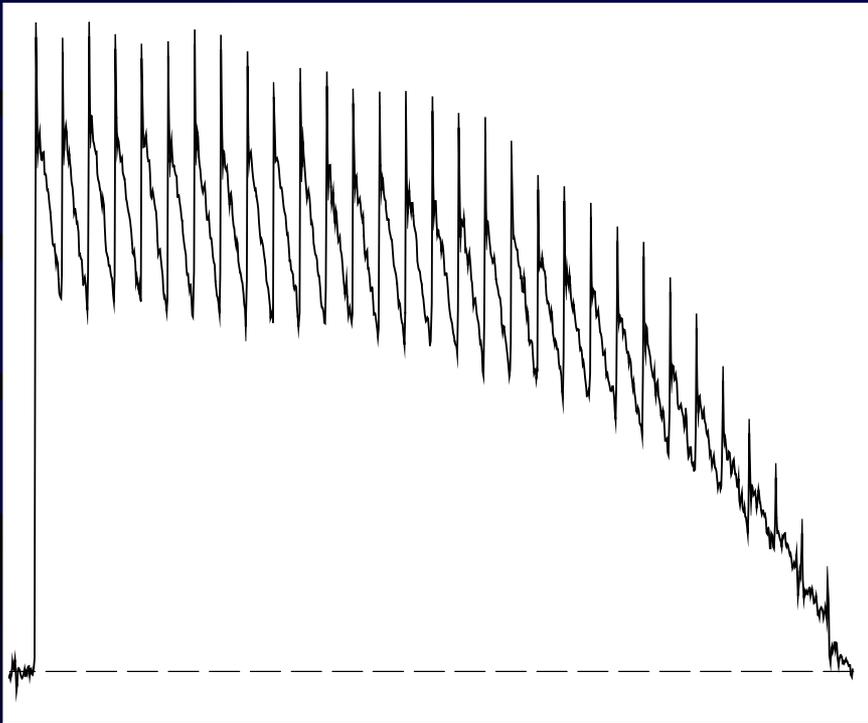
PP
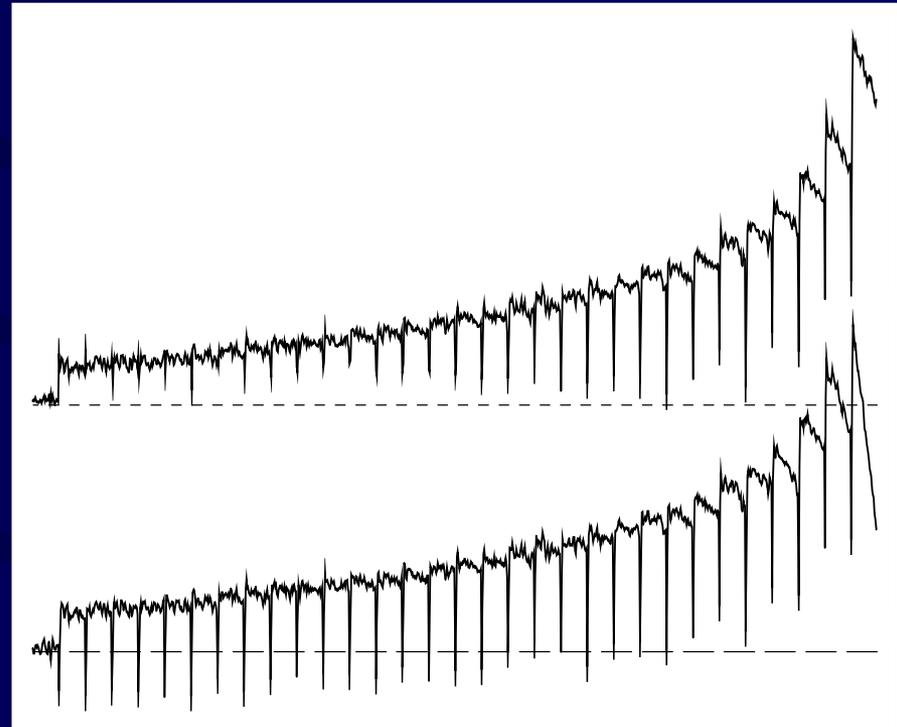
Arrayed parameter: tau (decreasing)

… and many, many other things!

**But my allocated time is finite
and therefore**

Thank You for your **Attention**

All slides will appear online under

DOI 10.3247/SL4Nmr13.008