BEYOND THERMAL SNR: EFFICIENT USE OF HYPERPOLARIZED MAGNETIZATION

PROF. JAN ARDENKJÆR-LARSEN

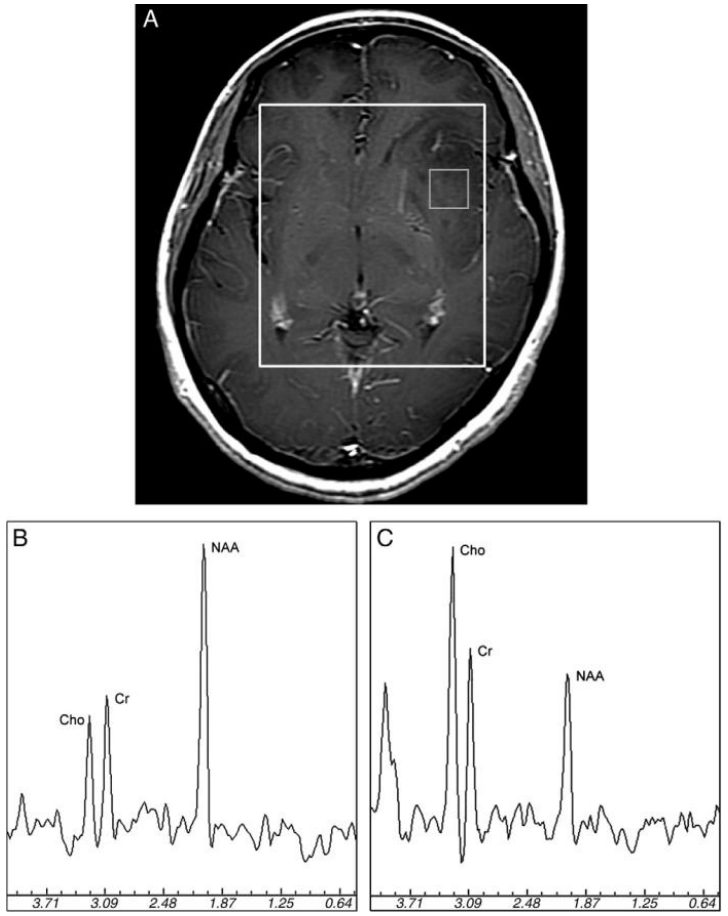
Disclosure: Owner of Polarize that manufactures instrumentation for hyperpolarization

AGENDA

- Where does the signal come from (magnetization, noise, induction, …)
- Relaxation: where does it go?
- How do we use the signal most efficiently?
  - Flip angle
  - Temporal resolution
  - Acceleration

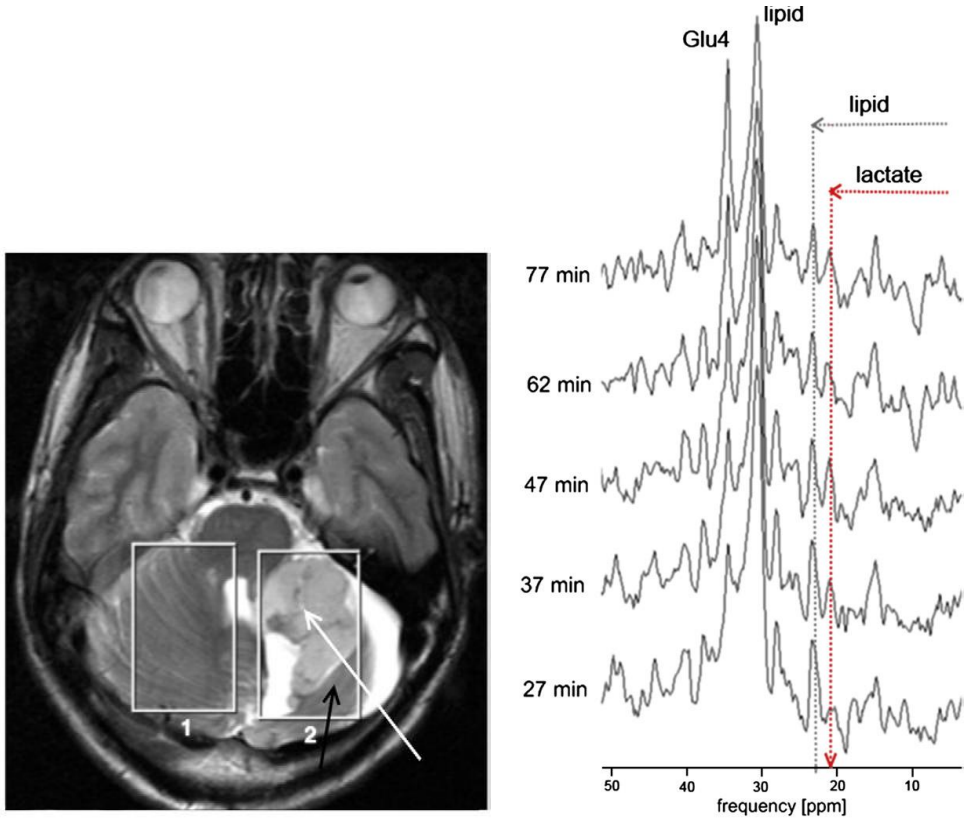
MR IS A NEVER-ENDING QUEST FOR SIGNAL

And has led to increased magnetic field strength, optimized pulse sequences and detection coils



~9 min acquisition with 10 cm³ voxel size

Zeng et al, Magnetic Resonance Imaging 29 (2011) 25–31



>12 g of [1-^{13}C]glucose infused during examination. 10 min acquisition time and ~50 cm³ voxel size

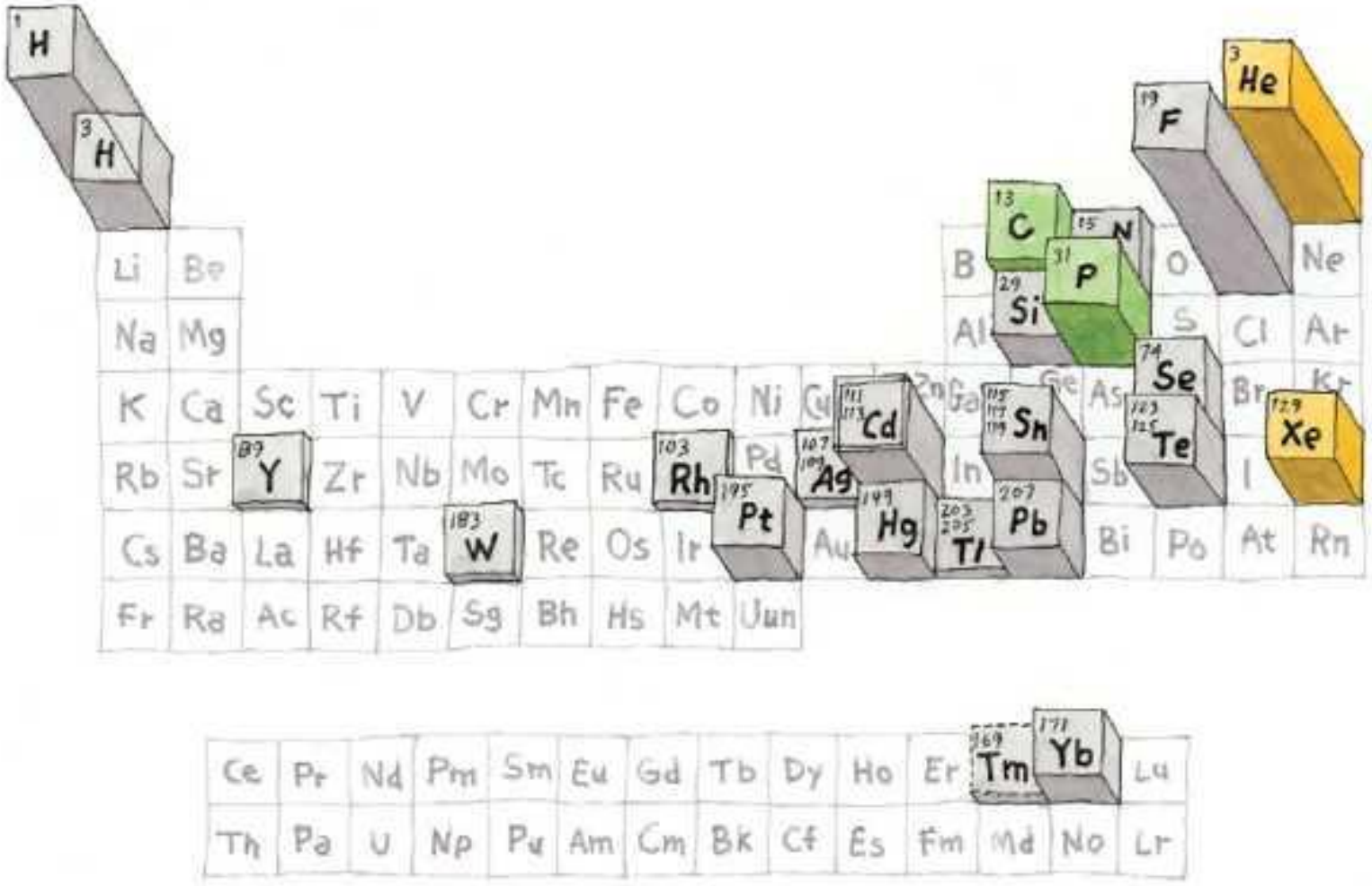
Wijnen et al, Magnetic Resonance Imaging 28 (2010) 690–697

NMR PERIODIC TABLE

Group	I	II		IIIa	IVa	Va	VIa	VIIa	VIIIa	VIIIb	VIIIc	IB	IIB	III	IV	V	VI	VII	VIII
Period																			
1	1 H																		2 He
2	3 Li	4 Be												5 B	6 C	7 N	8 O	9 F	10 Ne
3	11 Na	12 Mg												13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
4	19 K	20 Ca		21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
5	37 Rb	38 Sr		39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
6	55 Cs	56 Ba	*	71 Lu	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
7	87 Fr	88 Ra	**	103 Lr	104 Unq	105 Unp	106 Unh	107 Uns	108 Uno	109 Mt	110 Uun	111 Uuu	112 Uub	113 Uut	114 Uuq	115 Uup	116 Uuh	117 Uus	118 Uuo
*Lanthanides			*	57 La	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb		
**Actinides			**	89 Ac	90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No		

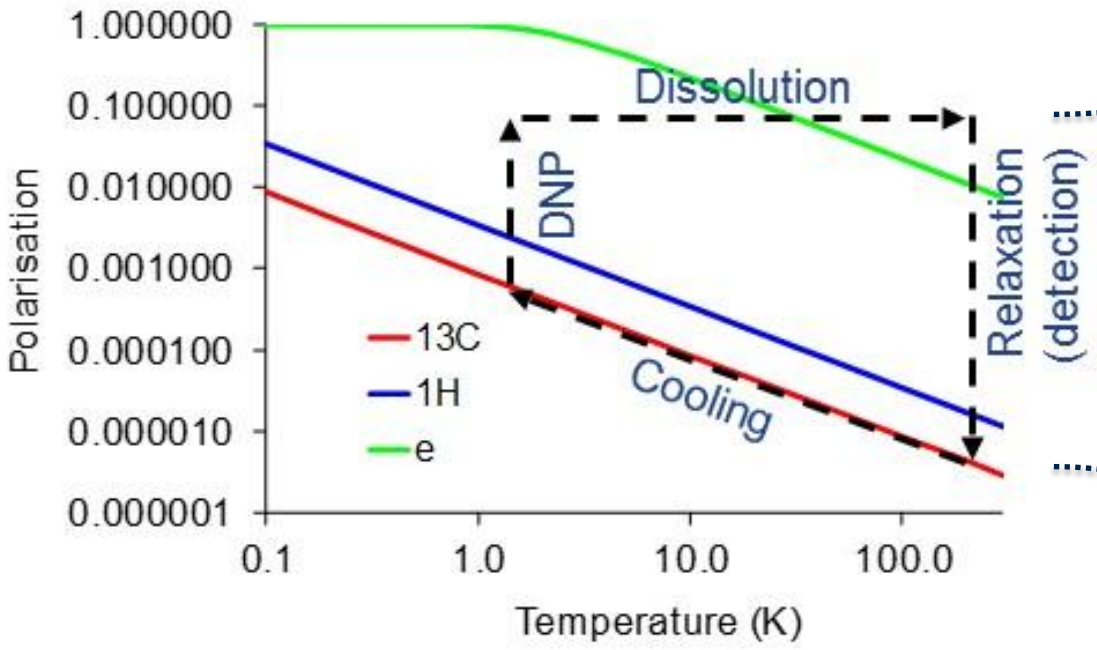
Nuclear Spins	1/2	1	3/2	5/2	7/2	9/2

NUCLEI OF INTEREST FOR HYPERPOLARIZATION

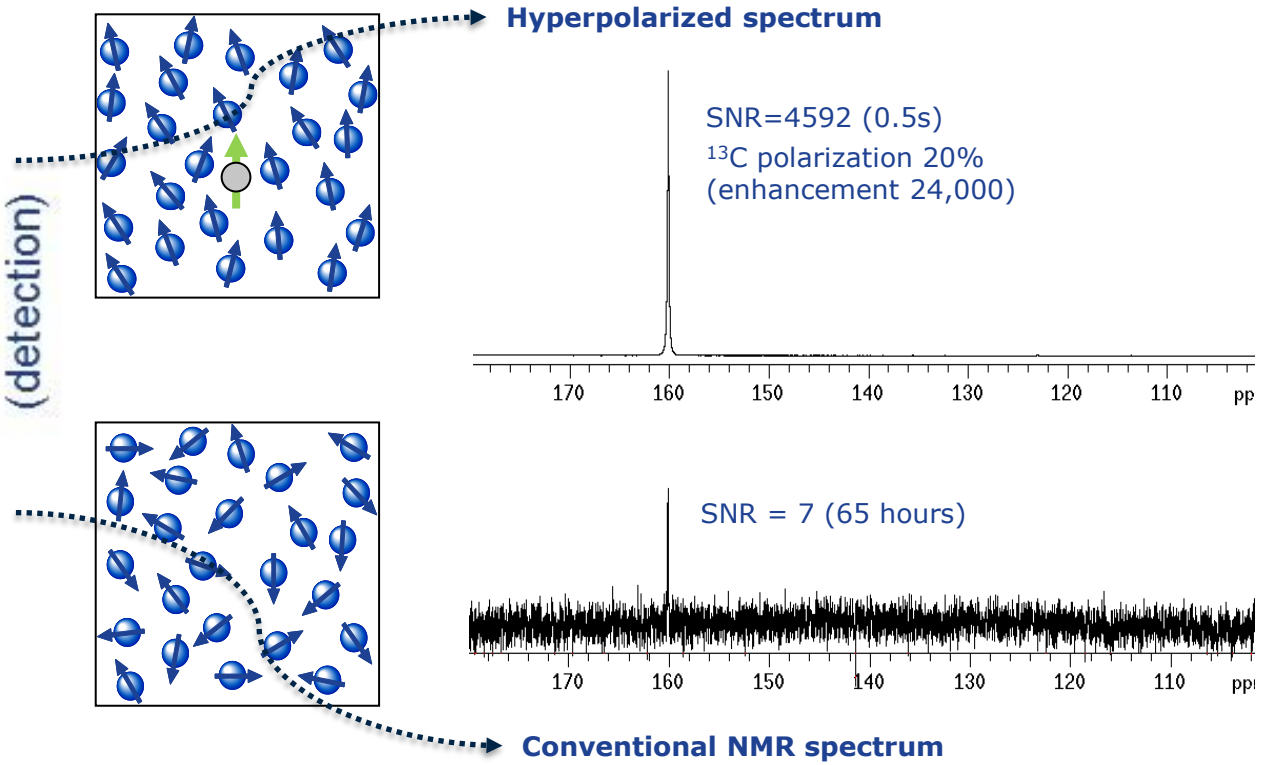


HYPERPOLARIZED MR

dissolution Dynamic Nuclear Polarization



Hyperpolarization



$$P_{thermal} = \tanh\left(\frac{\mu B_0}{k_B T}\right) \qquad M_0 = N\mu P \qquad SNR \propto \frac{f_o\, B_{1xy}\, M_o}{F\sqrt{4k_B T\, R}}$$

PNAS

Increase in signal-to-noise ratio of >10,000 times in liquid-state NMR

Jan H. Ardenkjær-Larsen*, Björn Fridlund, Andreas Gram, Georg Hansson, Lennart Hansson, Mathilde H. Lerche, Rolf Servin, Mikkel Thaning, and Klaes Golman

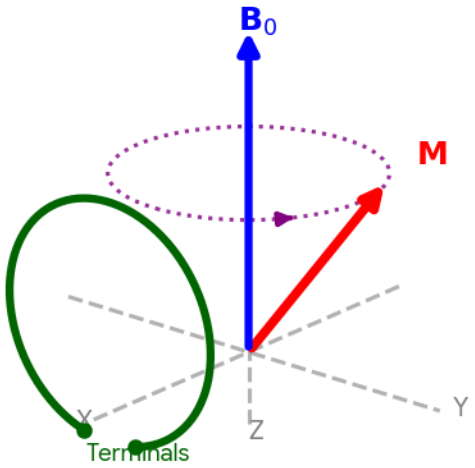
Amersham Health Research and Development AB, Medeon, SE-205 12 Malmö, Sweden

Communicated by Albert W. Overhauser, Purdue University, West Lafayette, IN, June 20, 2003 (received for review April 16, 2003)

INDUCTION, RECIPROCITY

The magnetization induces and electromagnetic force (voltage) in the receiver

$$E_{emf} = -\frac{\partial}{\partial t}\left(\int_{\mathbf{r}} \tilde{\mathbf{B}}_1(\mathbf{r})\cdot\mathbf{m}(\mathbf{r})d\mathbf{r}\right) = -\frac{\partial}{\partial t}\left(\int_{sample} \tilde{B}_{1xy} M_0 \sin\alpha\, e^{(-R_2^* + j\omega_0)t}\, dv\right)$$



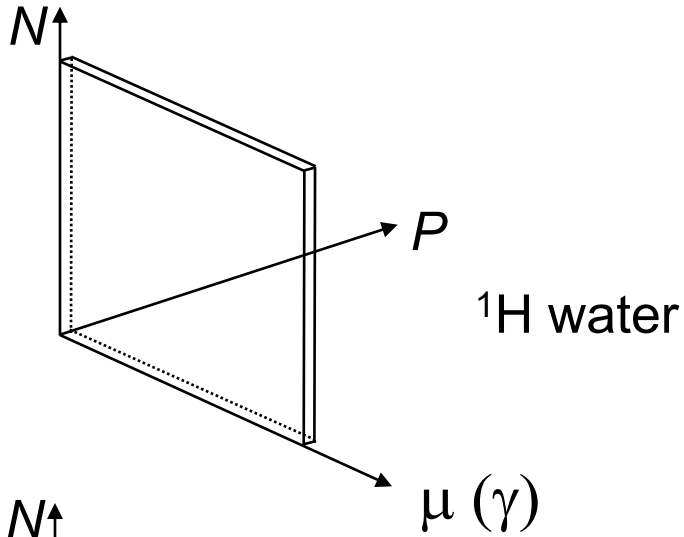
INDUCTION, RECIPROCITY

The magnetization induces and electromagnetic force (voltage) in the receiver

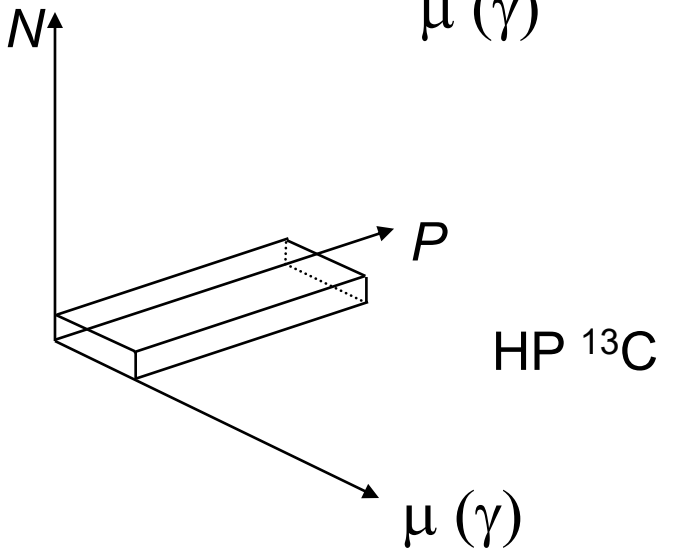
$$M_0 = N\gamma\hbar IP, \quad P = \frac{2I+1}{2I}\coth\left(\frac{2I+1}{2I}\frac{\gamma\hbar B_0}{k_B T}\right) - \frac{1}{2I}\coth\left(\frac{1}{2I}\frac{\gamma\hbar B_0}{k_B T}\right)$$

$$M_0 = N\gamma^2\hbar^2 B_0 \frac{I(I+1)}{3k_B T}$$

$$M_0 = \frac{1}{2}N\gamma\hbar\tanh\left(\frac{\gamma\hbar B_0}{2k_B T}\right)$$



^{1}H water



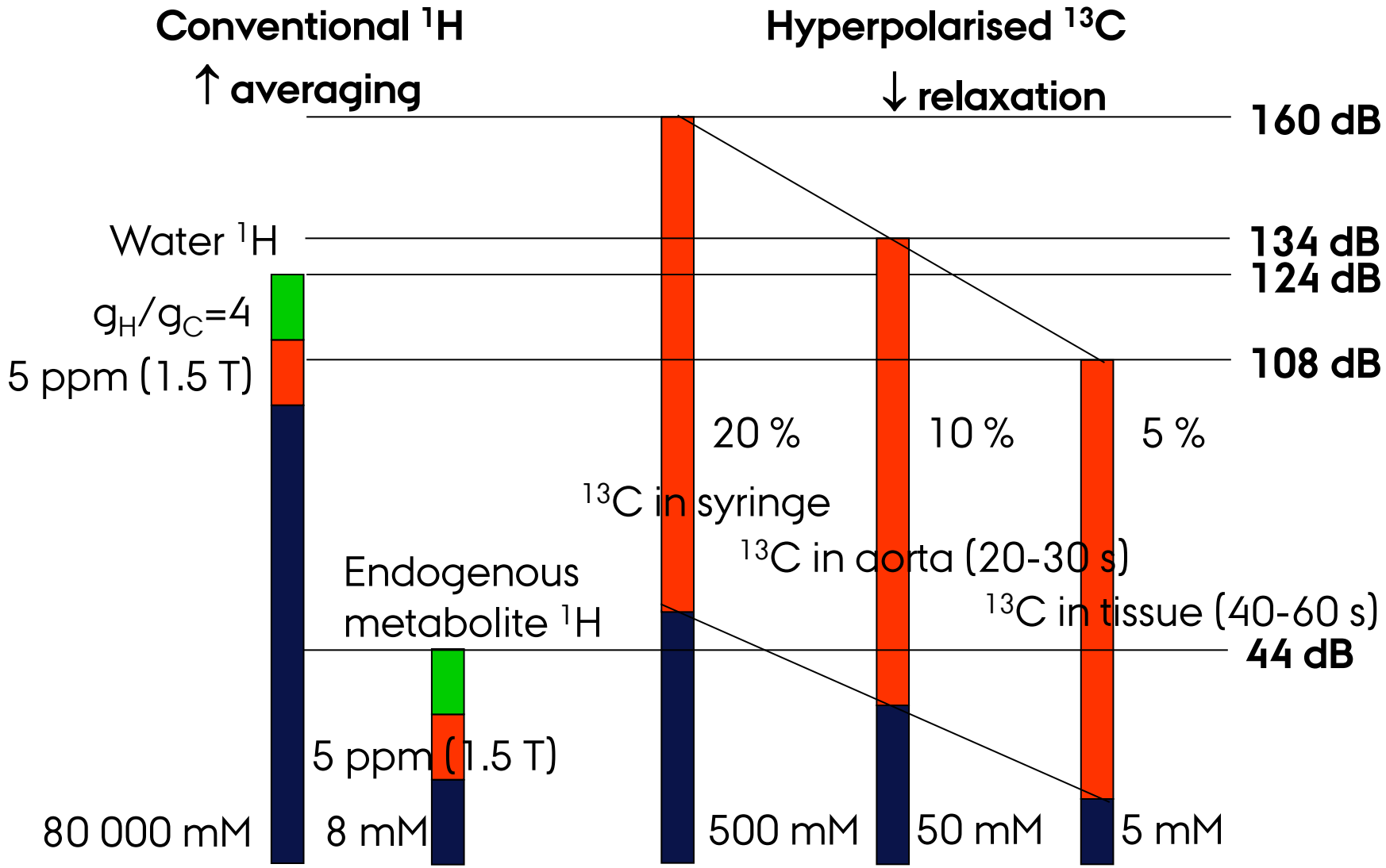
HP ^{13}C

INDUCTION, RECIPROCITY

The magnetization induces and electromagnetic force (voltage) in the receiver

$$E_{emf} = \omega_0 \tilde{B}_{1xy} M_0 V_S \sin \alpha e^{(-R_2^* + j\omega_0)t}$$

SIGNAL IN MRI



NOISE

F: noise figure of the pre-amplifier

R: Equivalent resistance of noise contributions (sample noise should be dominant)

T: Temperature of the noise resistor

$\Delta\nu$: Bandwidth

$$n_{rms}^{FID} = F \cdot \sqrt{4 R k_B T \Delta \nu}$$

THE COIL



Coil 1



Coil 2



Coil 3

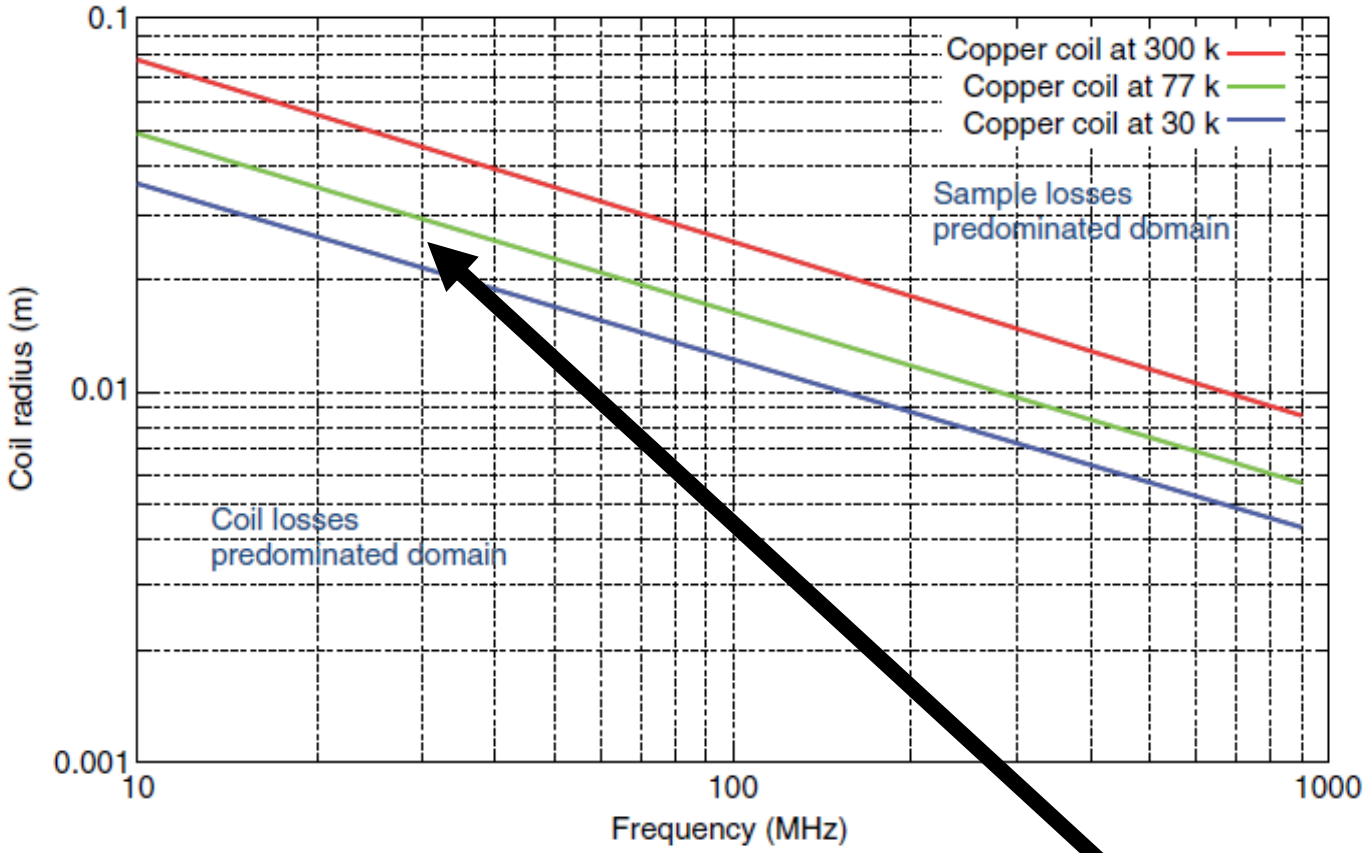
Measured Q-factor (coil unloaded):

	Measured Q		Simulated Q	
Loop Configuration	300K	77K	300K	77K
Coil 1	259	611	361	970
Coil 2	182	459	242	615
Coil 3	246	525	346	889

- In our simulations the capacitors and transmission lines are ideal, so losses are not taken in account for them → That explains the lower measured Q.
- Measured Q-factor, consistently lower than simulations (≈ 40% difference).

THE COIL

When cooled to 77 K ρT decreases for copper a factor ~20

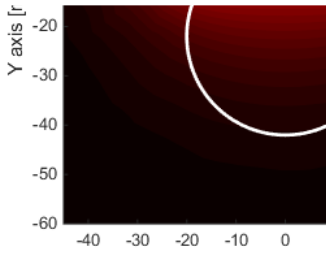


Potential 4.5-fold SNR enhancement (assuming low sample losses)

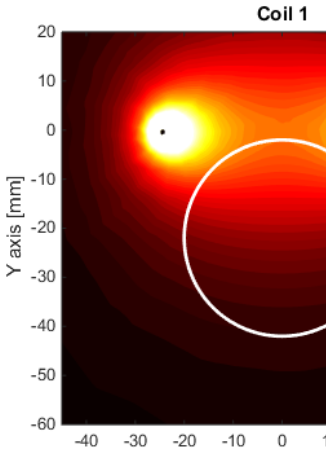
f = 32 MHz
coil radius = 25 mm

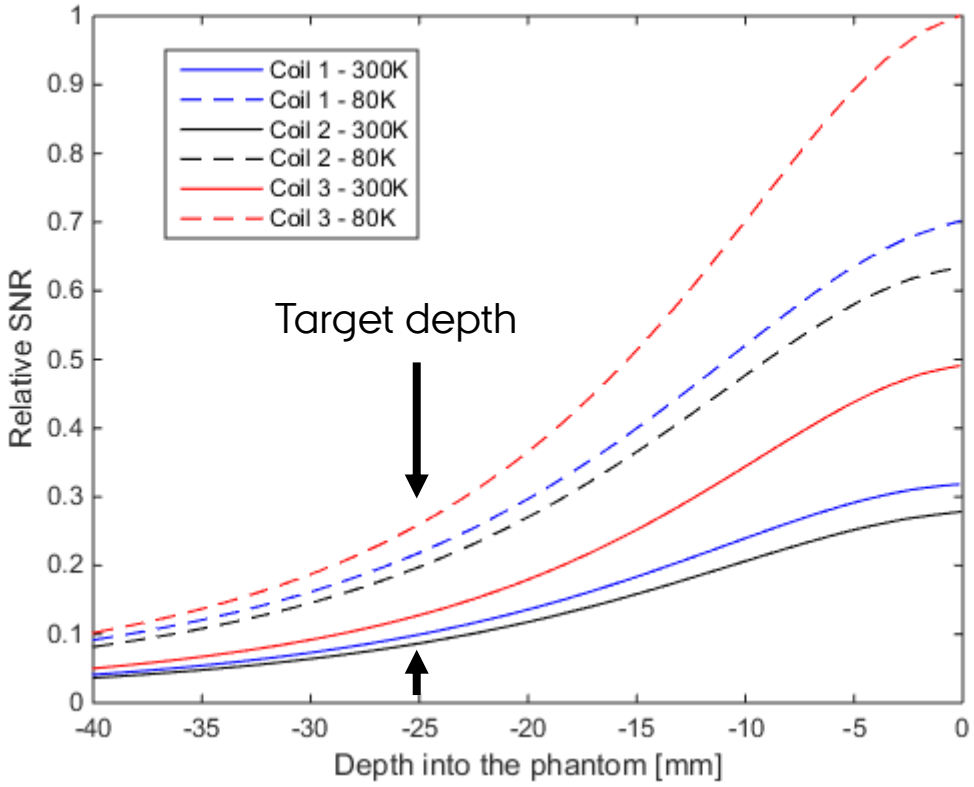
THE COIL

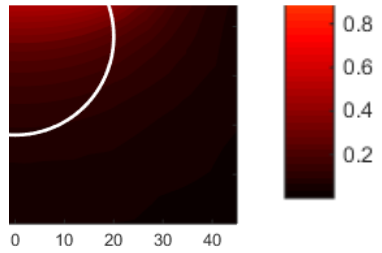
	Unloaded Q		Loaded Q		Loaded Q/ Unloaded Q		Δf_0 [MHz]	
Loop Configuration	300K	77K	300K	77K	300K	77K	300K	77K
Coil 1 (UT.085 Wire)	313	607	305	596	0.971	0.981	0.011	0.010

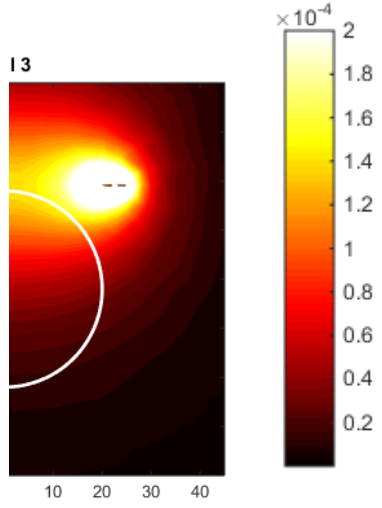


Simulated B_1^-









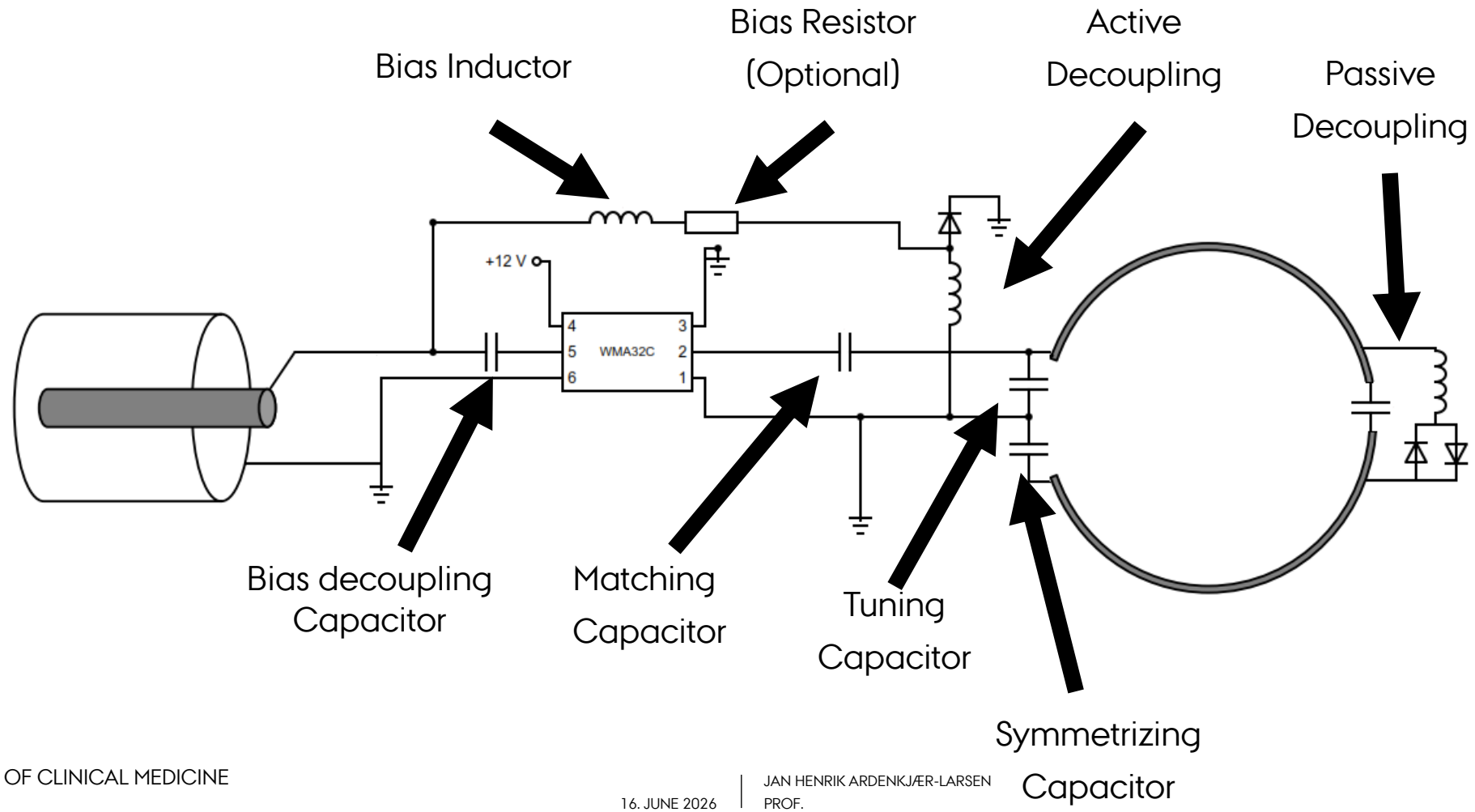
PREAMPLIFIER

- Commercially available: Wantcom WMA32C
  - Frequency of 32.19 MHz
  - 3.0 Ohm Input Impedance
  - 0.70 dB Noise Figure
  - 28.0 dB Gain
  - 1.22:1 Output VSWR
  - Unconditional Stable, k>1
  - Non-magnetic
- Low input impedance: can be used for preamp decoupling in phased arrays.
- Includes a High Electron Mobility Transistor (HEMT): Noise Figures below 0.05 dB reported in literature when cryogenically cooled*



COIL INTERFACING

Full circuit (coil + preamp)



PARALLEL IMAGING

Hyperpolarized agents:

- No remagnetization after RF excitation.
- Multidimensional space needs to be sampled in short time



Parallel Imaging can be implemented without SNR penalty for Hyperpolarized agents

$$SNR_{PI} = \frac{SNR_0}{g\sqrt{R}}$$

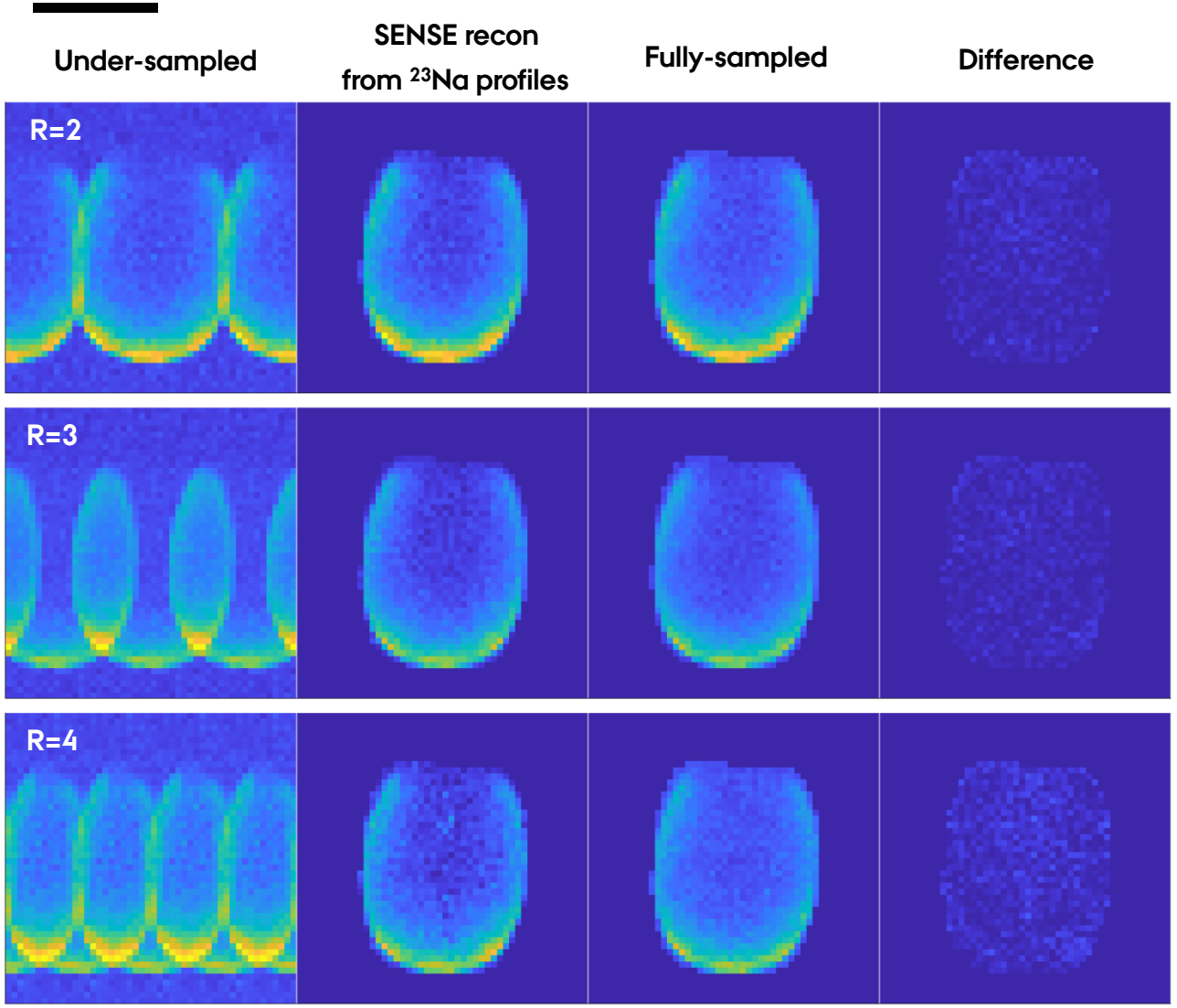
SNR0: Unaccelerated SNR
R: Acceleration Rate
g: geometric factor

$$SNR_{PI} = \frac{SNR(N)}{g}$$

N: Number of shots needed to encode an image
SNR(N): Inherent SNR of hyperpolarized agents

Parallel Imaging SNR for hyperpolarized agents not proportional to the acceleration rate!

THROUGH DEDICATED $^{13}C/^{23}NA$ COIL DESIGN



Retrospective undersampling of the fully sampled ^{13}C 2D GRE acquisition (lines in k-space removed uniformly)

R=2, Total scan time 16 min

R=3, Total scan time 11 min

R=4, Total scan time 8 min

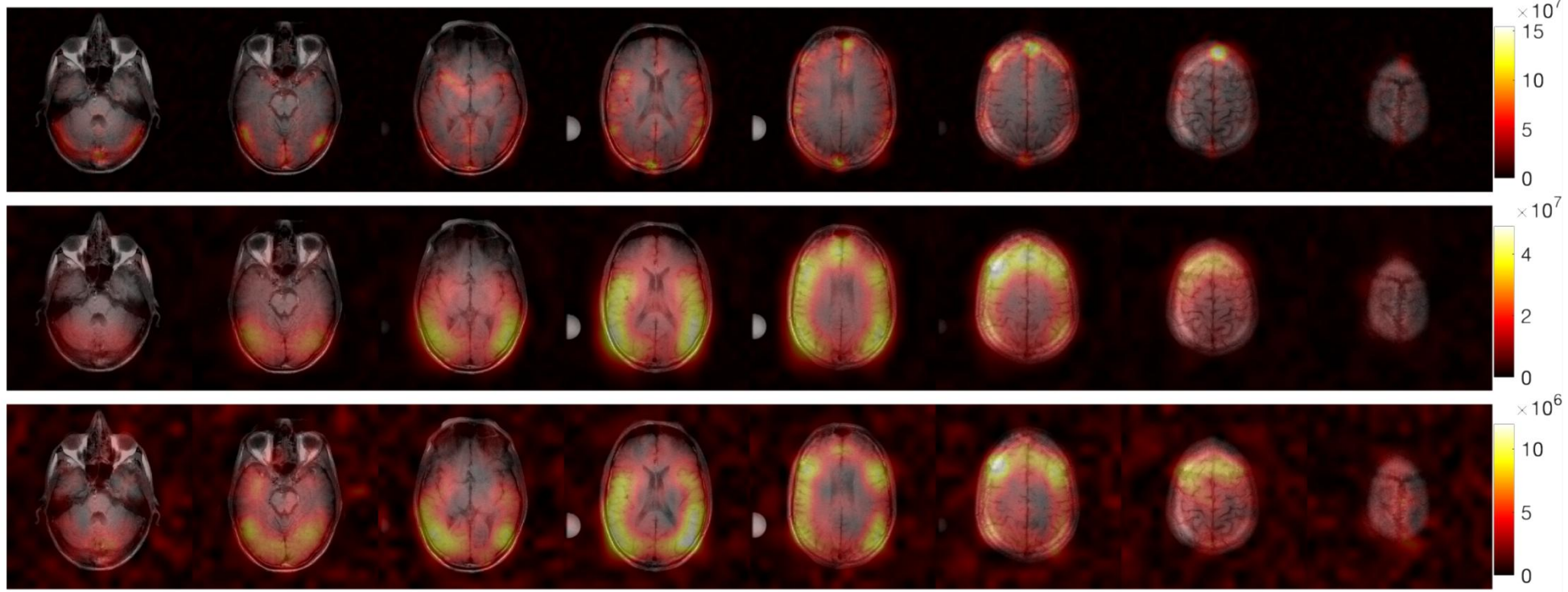


Olin, Sanchez et al, MRM 2022

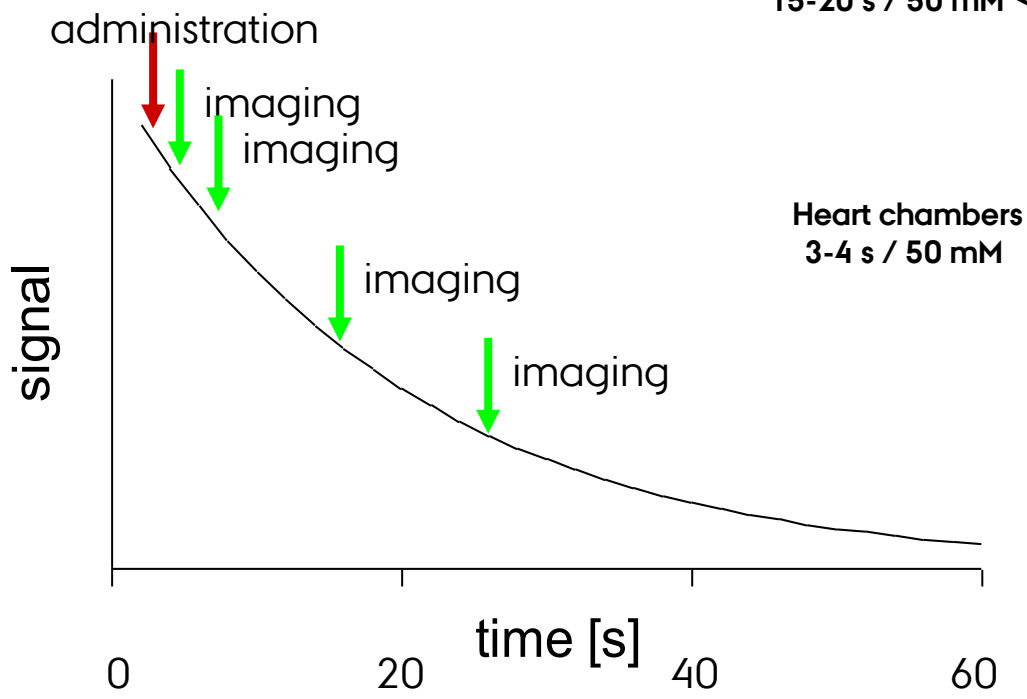
BRAIN METABOLISM

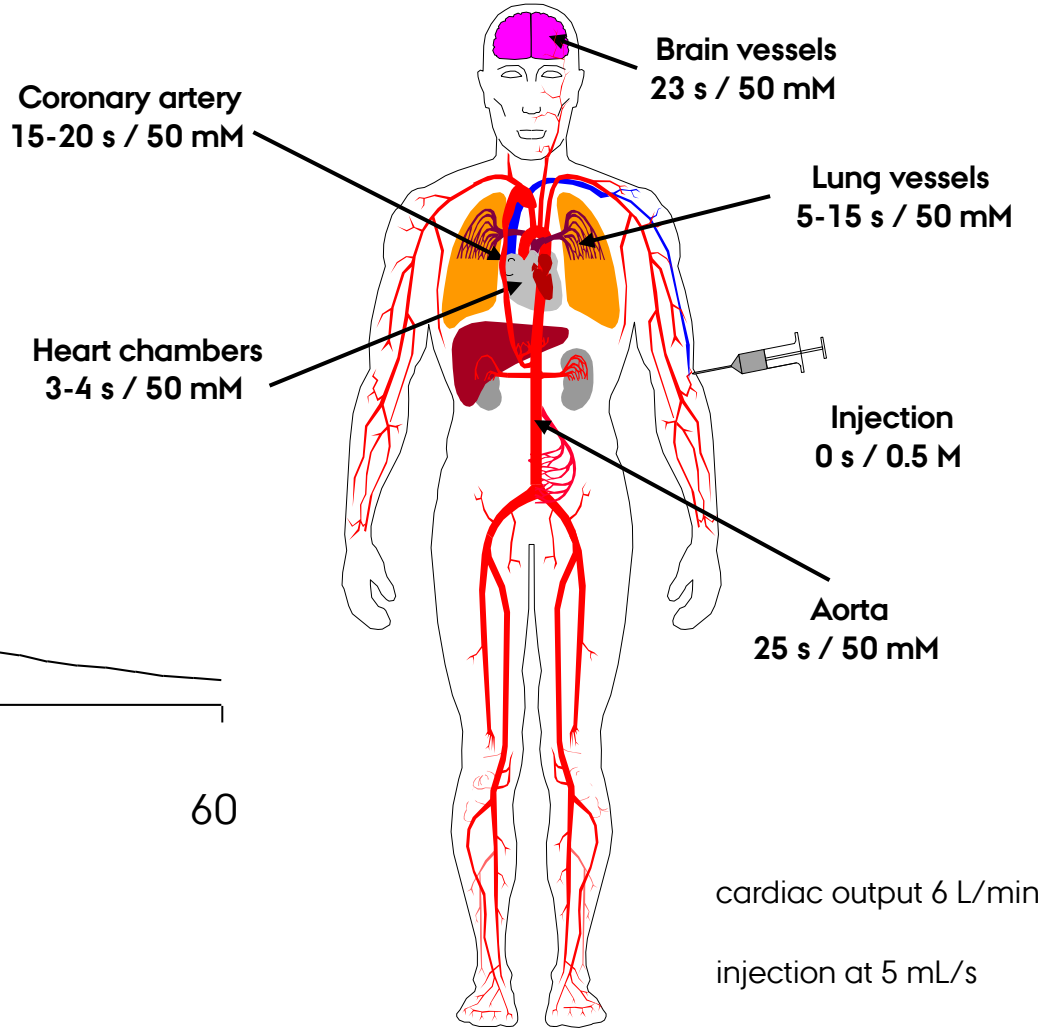
- 3D blipped stack-of-spirals with dual-resolution.
- FOV 28x28x12 cm^3, SPSP exc., TR/TE 80/9 ms, spiral readout duration 45 ms.
- Voxel size pyruvate = 7 x 7 x 15 mm^3.
- Voxel size metabolites = 14 x 14 x 15 mm^3.
- Acq. time pr. slice (4 exc.) = 320 ms.





THE SIGNAL DECAYS DUE TO RELAXATION AND DILUTION





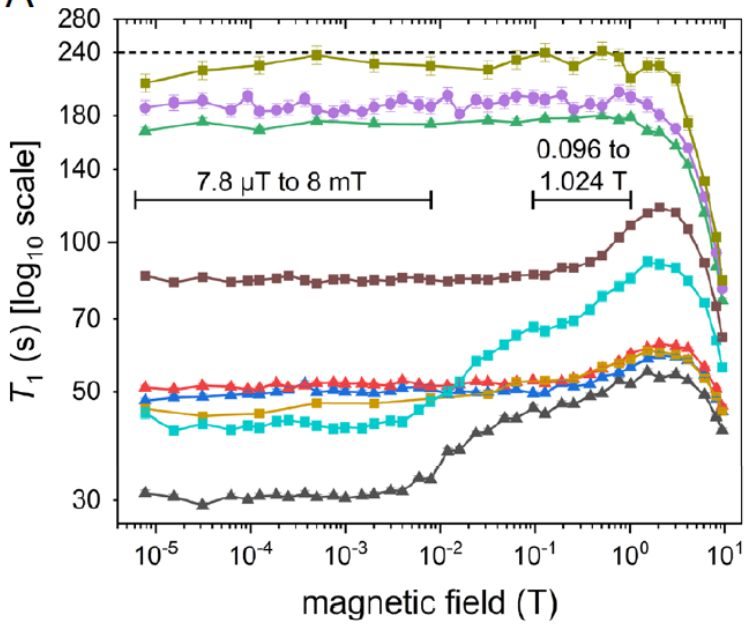
cardiac output 6 L/min

injection at 5 mL/s

RELAXATION

Peters et al, Nature Communications (2026) 17:4561

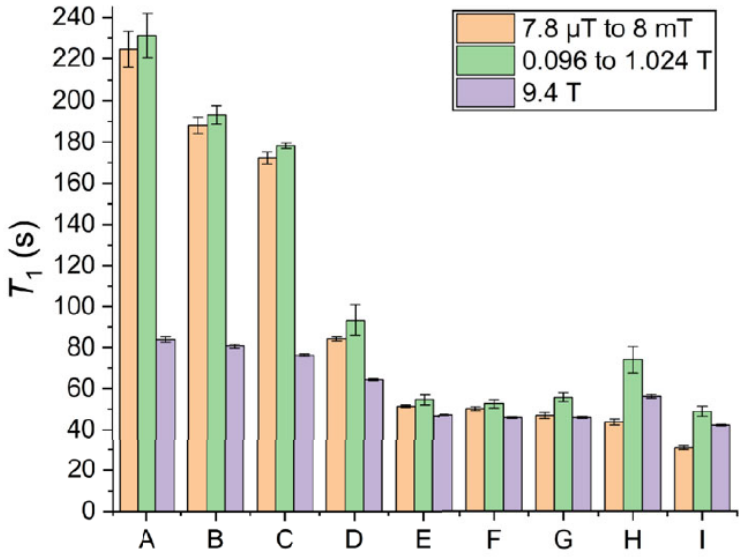
A



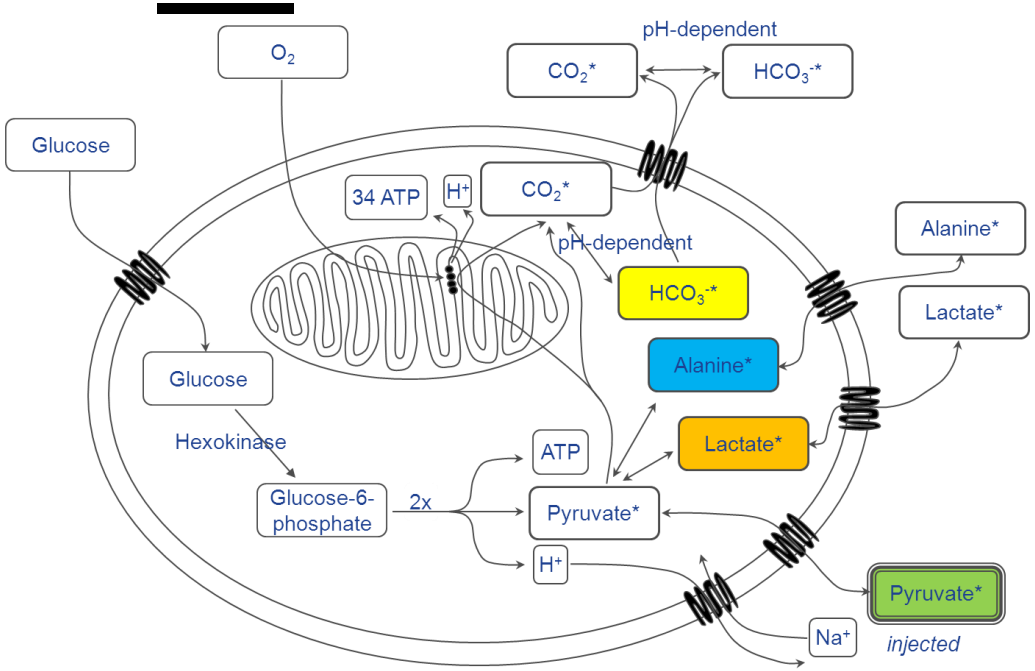
B

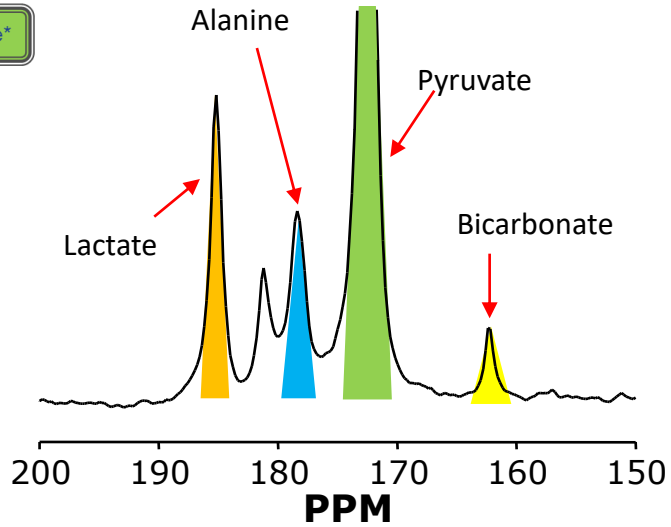
#	DNP	Tris	EDTA	D_2O	O_2	Pyr-d4
A	N	Y	Y	Y	N	Y
B	N	Y	Y	Y	N	N
C	Y *	Y	Y	Y	N	N
D	N	Y	Y	Y	Y	N
E	N	Y	Y	N	Y	N
F	N	Y	N	N	Y	N
G	Y	Y	Y	N	Y	N
H	N	N	N	Y	Y	N
I	N	N	N	N	Y	N

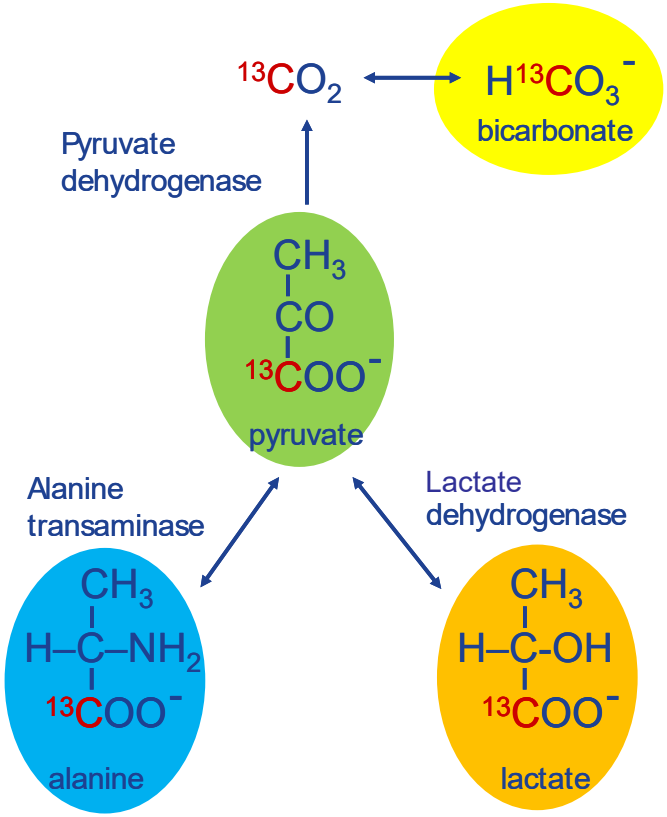
C



[1-^{13}C]PYRUVATE FOR *IN VIVO* IMAGING

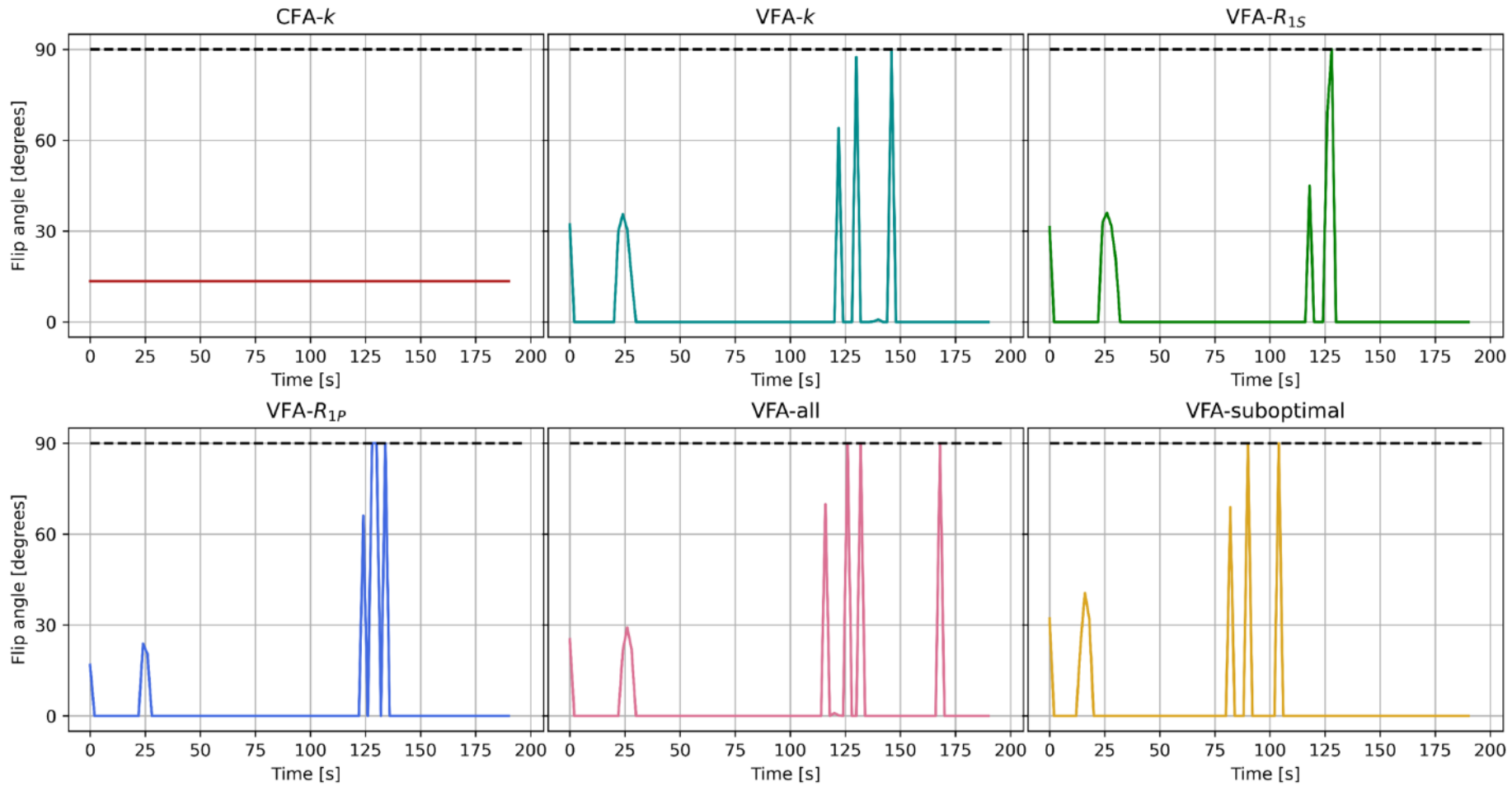






EFFICIENT USE OF THE SIGNAL

Garnæs et al, NMR in Biomedicine, 2025; 38:e70151

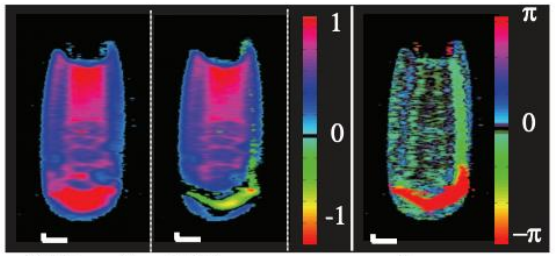


HYPERPOLARIZED WATER; ^1H IN D_2O

- Large magnetization due to high concentration
- Large gyromagnetic ratio for higher spatial resolution
- Signal detection with optimized ^1H MRI equipment and sequences

Applications

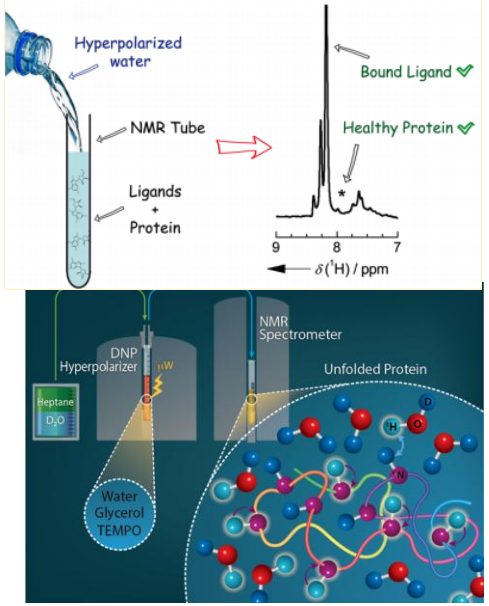
- Coronary MR angiography: high spatial resolution and fast acquisition to avoid motion artefacts. Eliminates the ionizing radiation from CTA and Gd-based contrast agents.
- Flow and perfusion.
- Proton exchange in proteins and chemical reactions, hydration reactions etc.



Hyperpolarized water as an authentic magnetic resonance imaging contrast agent

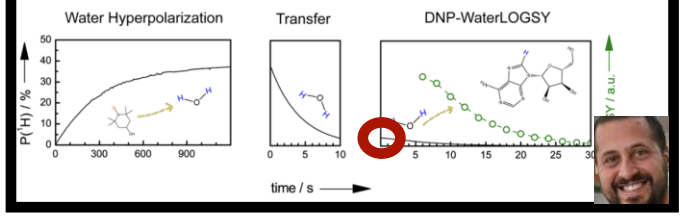
Evan R. McCarney*†, Brandon D. Armstrong§, Mark D. Lingwood*, and Songi Han*†‖

^1H signal enhancement of water by a factor o[illegible] −10 and −100 provides for an observation time of >4 and 7 s, respectively, upon its injection into fluids with a T_1 relaxation time of >1.5 s. The



Hyperpolarized Water to Study Protein–Ligand Interactions

Quentin Chappuis,† Jonas Milani,† Basile Vuichoud,† Aurélien Bornet,† Alvar D. Gossert,*,‡ Geoffrey Bodenhausen,†,§,⊥,# and Sami Jannin*,†,‖



On the Potential of Hyperpolarized Water in Biomolecular NMR Studies

Talia Harris, Or Szekely, and Lucio Frydman*

enhance the sensitivity of biomolecular nuclei. We find that water protons could be spin-aligned rapidly in a cryogeni[illegible] setup, delivering polarizations o[illegible] ~5% [illegible]fter their diss[illegible] and transfer to the NMR scanner. This enhancement c[illegible]

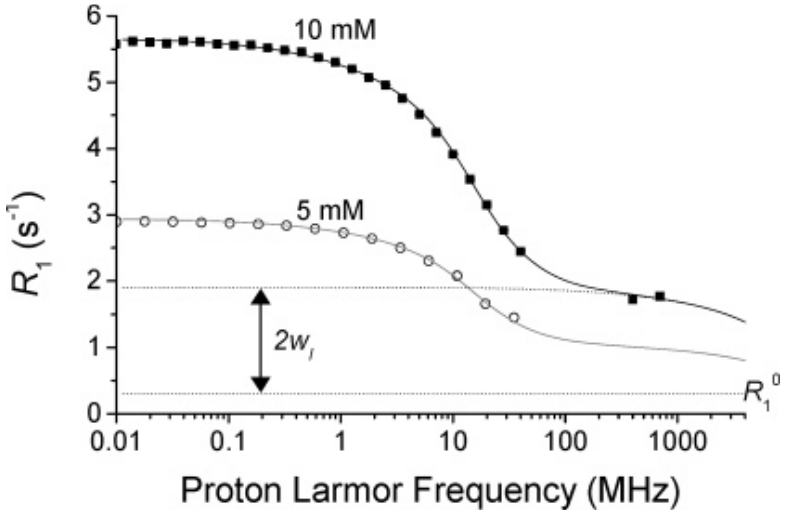
RELAXATION TIME OF ^1H IN H_2O/D_2O MIXTURES

Inversion recovery T_1 on thermal samples in Shigemi tube (deoxygenated)

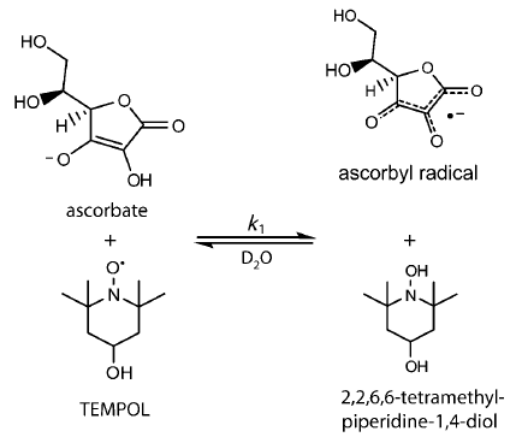
T (°C)	H_2O (s)	10% H_2O in D_2O	5% H_2O in D_2O	4.8% 1:1 glycerol:H_2O and 30 mM TEMPOL in D_2O
25	3.3	16	25	3.0
40	5.0	22	36	4.3
60	7.4	26	51	6.5
80	10	35	64	9.0
[H+]	**111**	**11.8**	**6.26**	**4.56**

When mixed with blood T_1 will quickly reduce to ~1 s

Harris et al, JMR 211 (2011), Dissolution DNP NMR with solvent mixtures: Substrate concentration and radical extraction



Höfer et al., JACS 130 (2008) 3254-3255

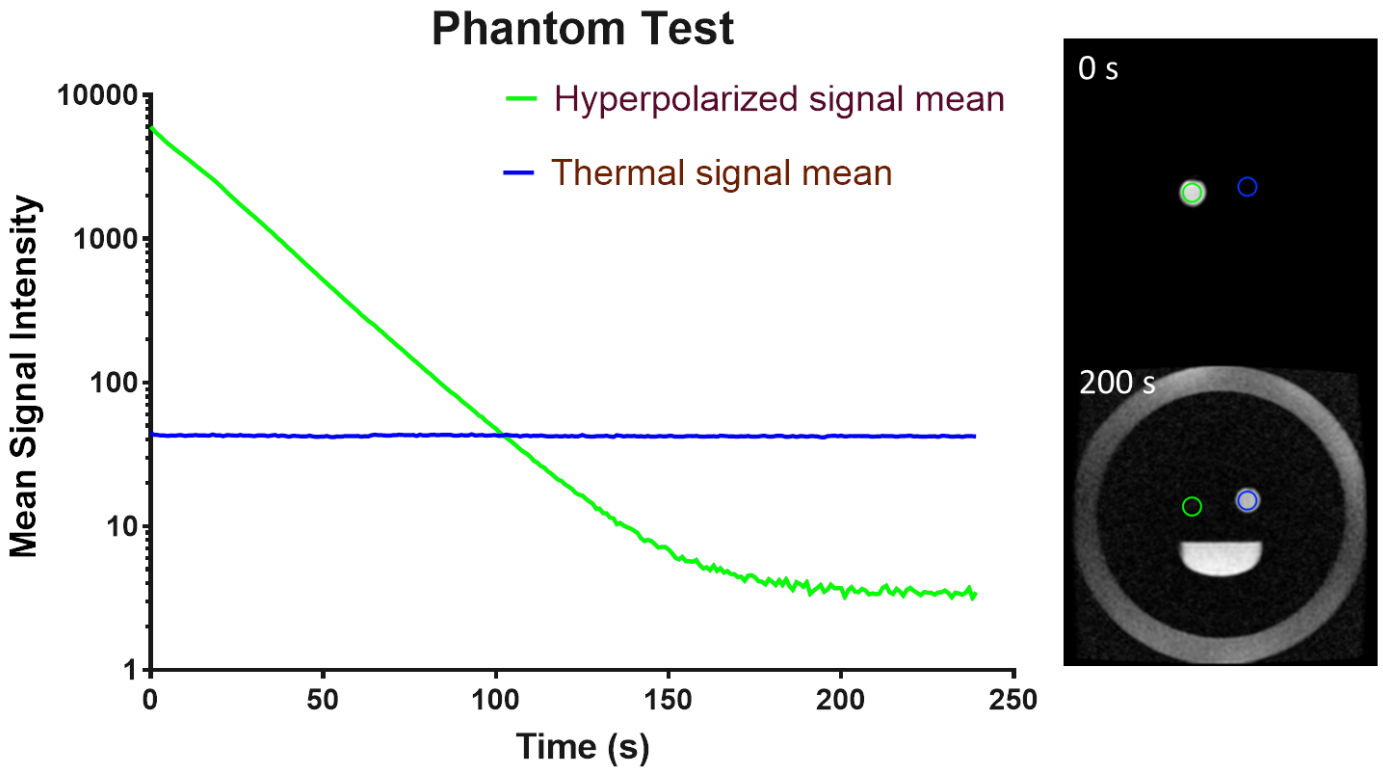


MAGNETIZATION OF ^{1}H

Nucleus	Initial conc. [M]	Polari-zation	Initial M_0 [mA/m]	T_1 [s]	Relaxation factor	Dilution factor	M_0 at imaging [mA/m]
^{1}H (H_2O/D_2O)	2	50%	4,895	10	$e^{-15/10}=0.2$	0.1	216
^{13}C agent	0.5	50%	615	60	$e^{-15/60}=0.8$	0.1	49
Thermal ^{1}H	80	10 ppm @ 3T	7.8	1	0.6	1	4.7

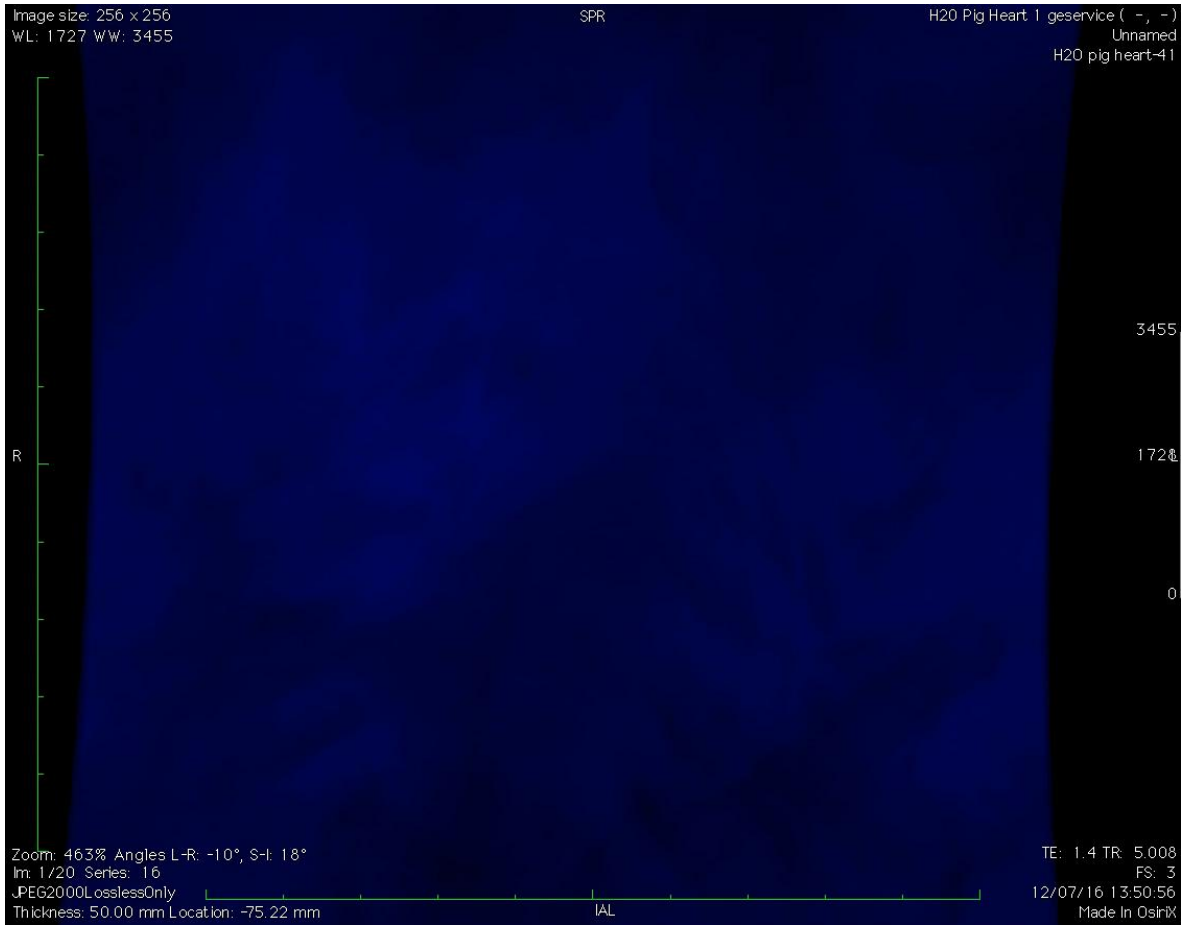
IMAGING OF HYPERPOLARIZED WATER

The hyperpolarized MR signal is initially 211 times stronger than the thermal H_2O signal, and the T_1 of the decay is 24 s. The hyperpolarized signal decays into the noise since the ^1H density is ca 20 times lower than the thermal H_2O sample.

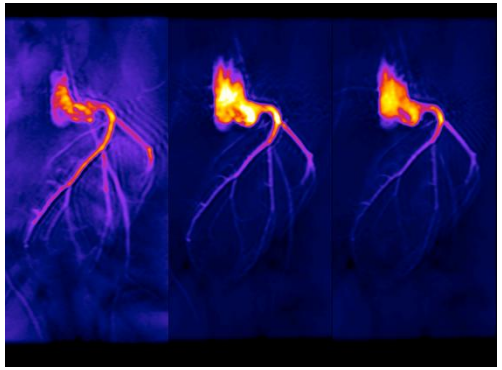


CORONARY ARTERY IMAGING WITH HYPERPOLARIZED WATER

Intra arterial injection in pig at 3 T with an 8-channel cardiac array receiver coil. Gradient echo sequence.



MRI parameters	
Flip angle	5°
Slice thickness	40 mm
TR	3.4 ms
TE	0.98 ms
Matrix size	256x256
FOV	$(140\ mm)^2$
Acquisition time	870 ms





DEPARTMENT OF CLINICAL