



Hyperpolarization

Dr. Marie-Aline Neveu



Nuclear magnetic resonance (NMR)

- Non invasive tool to reveal tumor metabolites in vivo: ¹H, ³¹P, ¹³C
- Metabolic and functional tumor information

¹³C NMR

- Study organic molecules and follow biotransformation
- Drawbacks: low sensitivity to detect endogeneous compounds in vivo

$$^1\text{H SNR} \gg \gg \gg \gg ^{13}\text{C SNR}$$

$$\text{SNR} \propto \gamma P c$$

Nuclei	<i>m</i> (spin)	Natural abundance (%)	γ (rel to ¹ H)	$\Delta\delta$ (ppm)	<i>T</i> ₁ range	Example biomedical application
¹ H	1/2	99.98	1	13	0.1–2 s	Total body MRI and MRSI
² H	1	0.02	0.1535	13	<1 s	Metabolic tracer injection using MRSI
¹³ C	1/2	1.11	0.2515	200	0.1–100 s	Metabolic tracer injection using MRSI
¹⁵ N	1/2	0.37	0.1013	900	0.1–400 s	Metabolic tracer injection using MRSI
¹⁷ O	5/2	0.04	0.1355	1160	5–50 ms	Oxidative metabolism using MRSI
¹⁹ F	1/2	100.00	0.9409	700	0.1–1 s	Tracer injection of therapies using MRSI
²³ Na	3/2	100.00	0.2645	72	10–50 ms	Neurodegeneration and cardiac using MRI
³¹ P	1/2	100.00	0.4048	430	0.05–2 s	Bioenergetics and pH using MRSI

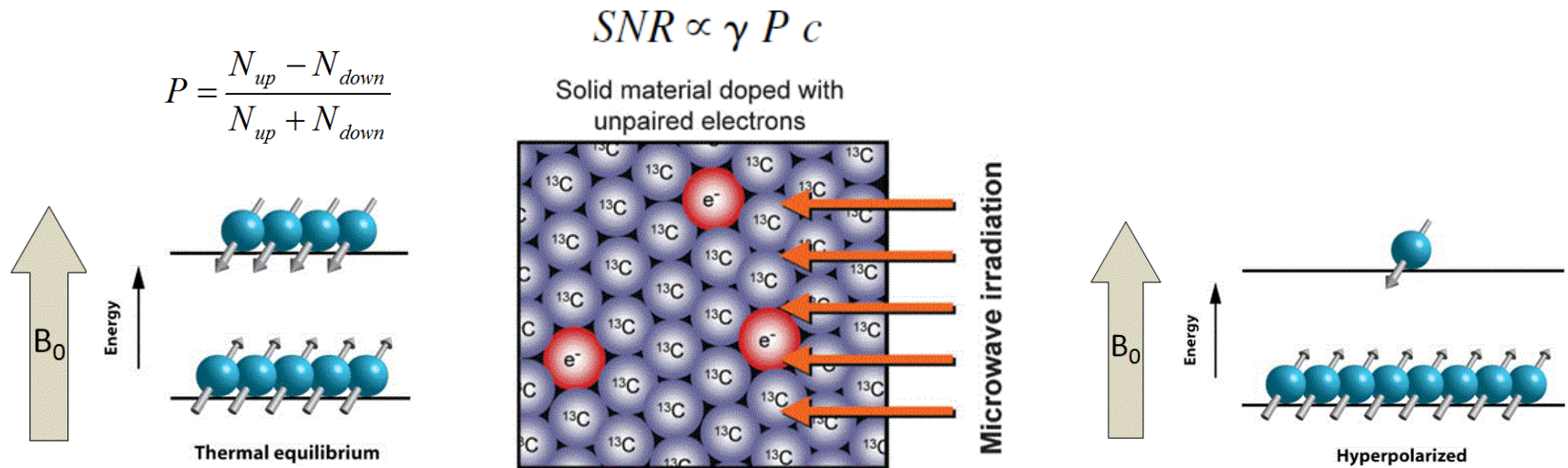
Keshari & Wilson, Chem Soc Rev 2014

Hyperpolarization techniques

- Optical pumping (OP):
 - Hyperpolarization of noble gases (³He and ¹²⁹Xe)
 - Low-radiation imaging of the lungs
- Parahydrogen-induced polarization (PHIP):
 - Parahydrogen used to create highly polarized nuclei (¹³C/¹⁵N)
 - Limited to unsaturated molecules
- Dynamic nuclear polarization (DNP):
 - Radical compounds used to create highly polarized nuclei
 - Small organic molecules
 - Detection of the introduced tracer and its metabolic products in real-time



DNP Principle : Polarization



Polarizing material boosted with a free radical
placed at high field (~3-5T) and low temperature (~1K)
Microwave irradiation at electron resonance frequency



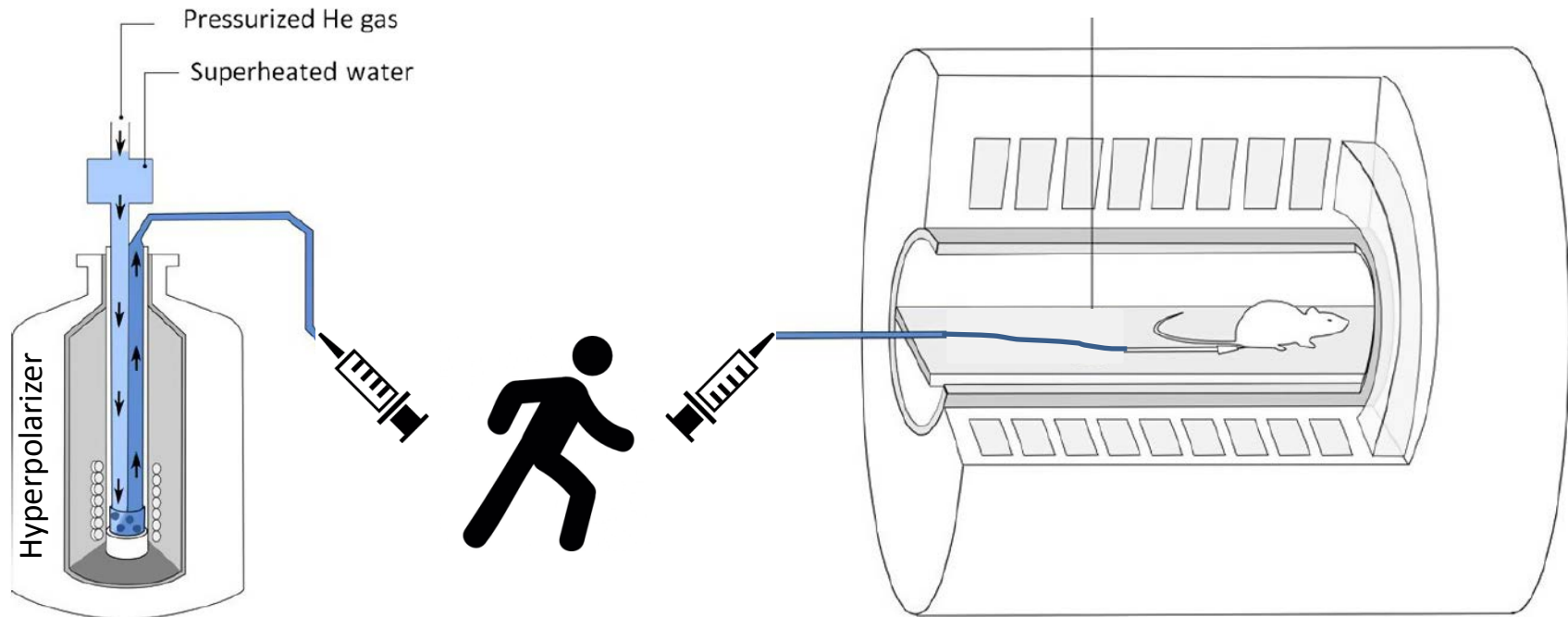
Enhanced spin polarization of nuclei by pumping electron spin

Hyperpolarization does not change any chemical or physical properties of the substance



Hyperpolarized ^{13}C MRS : Multi-step Process

- 1) Hyperpolarization of ^{13}C -tracer at solid state in a polarizer
- 2) Dissolution
- 3) Fast injection in vivo (signal loss)
- 4) Magnetic Resonance Spectroscopy (MRS) measurement
Real-time metabolic transformation *in vivo*



Comment, JMR, 2016

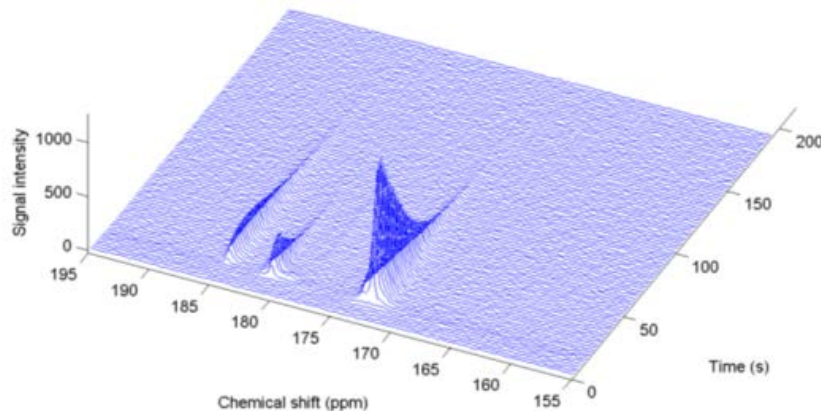


Hyperpolarized ^{13}C MRS : Multi-step Process

- 4) Magnetic Resonance Spectroscopy (MRS) measurement
Real-time metabolic transformation *in vivo*

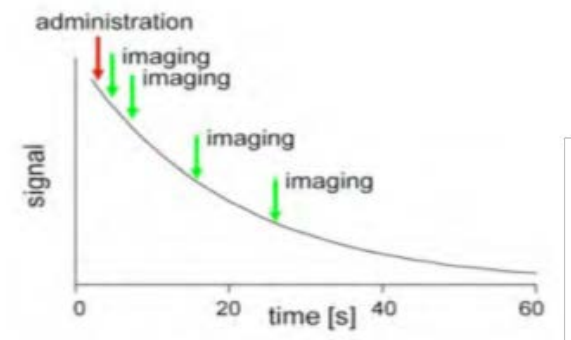
Tracer signal lifetime ~a few minutes

→ Ultra fast measurements necessary
to follow tracer arrival and biotransformation before signal loss



Signal decay mechanisms:

T1 process (tracer dependent)
RF pulse excitation (acquisition set-up dependent)



Typical acquisition set-up: low flip angle ($5\text{--}10^\circ$) pulse, 1-2 seconds repetition time, Bandwidth (ppm) to cover tracer and metabolites

Dynamic nuclear polarization = hyperpolarization technique

Used to improve ^{13}C NMR/MRS sensitivity
by boosting polarization of ^{13}C labeled molecules

Hyperpolarized compounds

Administered to study real time metabolism in vivo
Detected in vivo by spectroscopy (MRS) or spectroscopic imaging (MRSI)
! Limited time window for detection !
! Dedicated acquisition set-up (ultra fast measurements) !