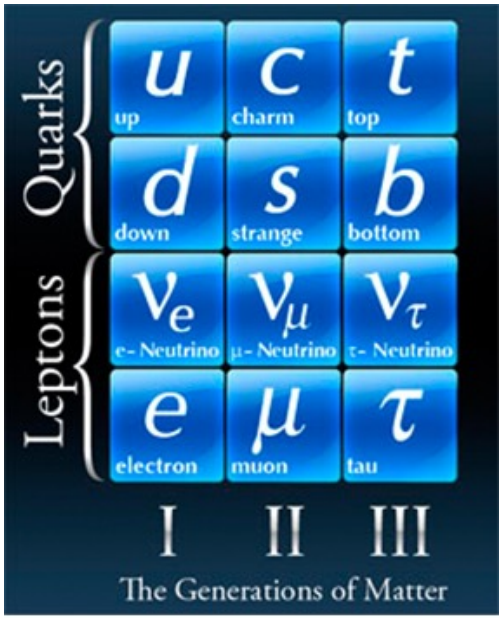
October 21st, 2022

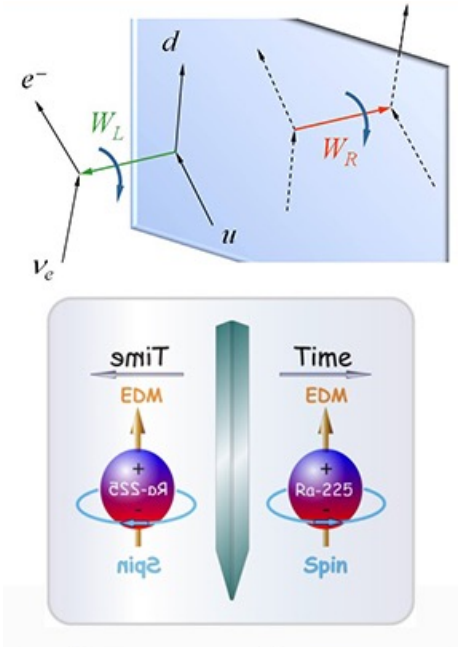
Hydrogen-based nuclear spin ordering: from fundamental symmetries to contrast agents in MRI

Danila Barskiy, PhD

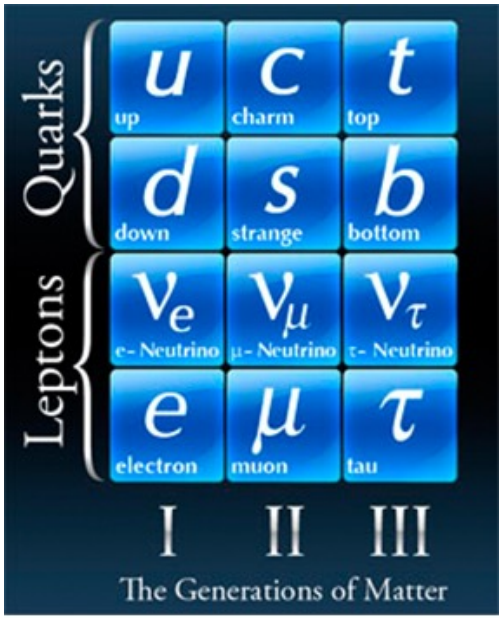
Helmholtz Institute Mainz
Johannes Gutenberg-Universität Mainz

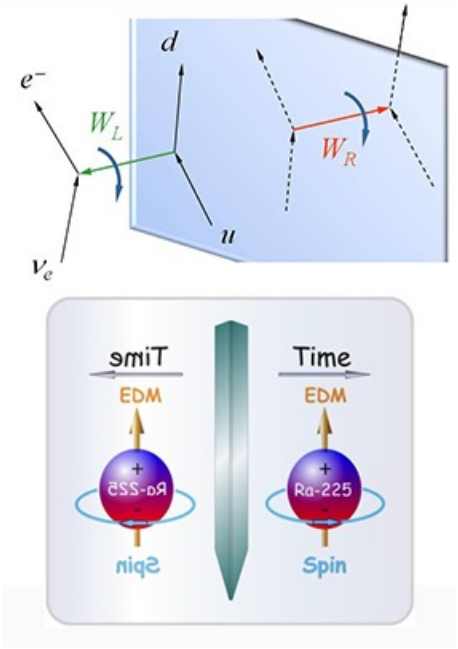
Fundamental Symmetries: Pauli Principle





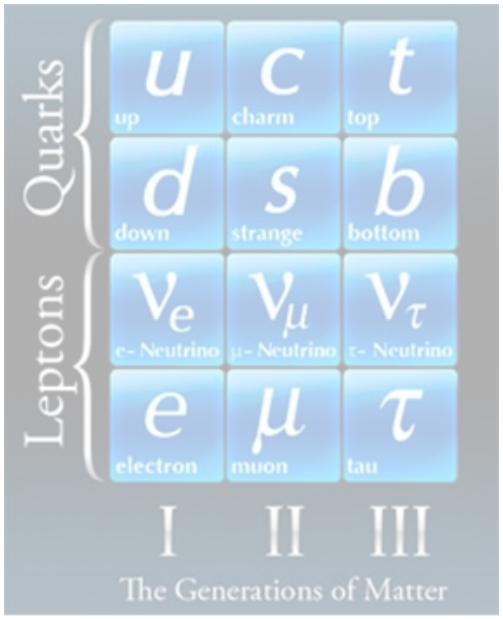
Fundamental Symmetries: Pauli Principle

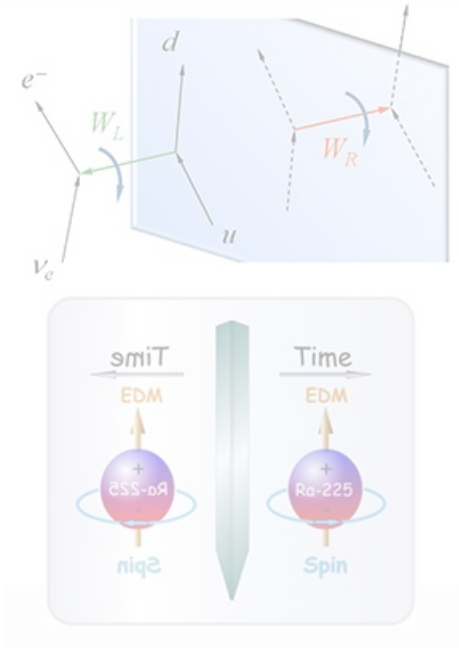




"Wavefunction of the quantum system is antisymmetric with respect to the permutation of two fermions"

Fundamental Symmetries: Pauli Principle



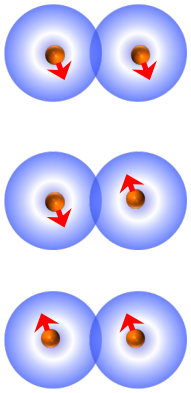


"Wavefunction of the quantum system is antisymmetric with respect to the permutation of two fermions"

https://smart-h2.de/

Parahydrogen

Orthohydrogen
(Triplet state)

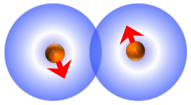


$$|\beta\beta\rangle$$

$$\frac{1}{\sqrt{2}}|\alpha\beta+\beta\alpha\rangle$$

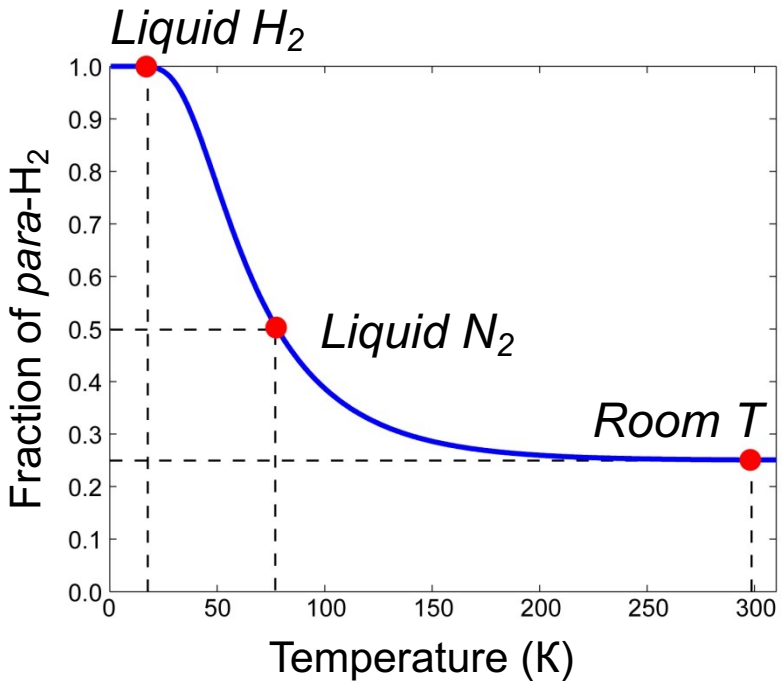
$$|\alpha\alpha\rangle$$

Parahydrogen
(Singlet state)



$$\frac{1}{\sqrt{2}}|\alpha\beta-\beta\alpha\rangle$$

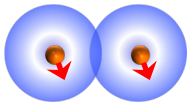
Once obtained, parahydrogen may be stored for a long time (weeks) without back conversion to ortho-isomer



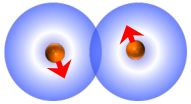
- Equilibrium at 295 K
  – *ortho*-H_2 : *para*-H_2 = 3:1
- Equilibrium at 77 K (liquid N_2)
  – *ortho*-H_2 : *para*-H_2 = 1:1
- Equilibrium at 20 K – 100% *para*-H_2

Parahydrogen

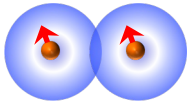
Orthohydrogen
(Triplet state)



$$|\beta\beta\rangle$$

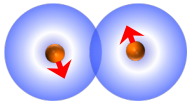


$$\frac{1}{\sqrt{2}}|\alpha\beta+\beta\alpha\rangle$$



$$|\alpha\alpha\rangle$$

Parahydrogen
(Singlet state)



$$\frac{1}{\sqrt{2}}|\alpha\beta-\beta\alpha\rangle$$

Once obtained, parahydrogen may be stored for a long time (weeks) without back conversion to ortho-isomer

Parahydrogen-Induced Polarization (PHIP)

Russell Bowers

Daniel Weitekamp

Parahydrogen and Synthesis Allow Dramatically Enhanced Nuclear Alignment

C. Russell Bowers and D. P. Weitekamp*

Contribution No. 7578, Arthur Amos Noyes Laboratory of Chemical Physics, California Institute of Technology Pasadena, California 91125

Received April 23, 1987

Recently we have predicted that very large nuclear spin magnetizations can be obtained on molecules formed by molecular addition of parahydrogen (p-H_2) such that the dihydrogen protons become magnetically inequivalent.[1] In this communication we report the experimental observation of this effect. The reaction studied is the hydrogenation of acrylonitrile, CH_2CHCN, to propionitrile, CH_3CH_2CN, catalyzed by tris(triphenylphosphine)rhodium(I) chloride (Wilkinson's catalyst[2]) at ambient temperature and pressure. Large transient proton nuclear mag-

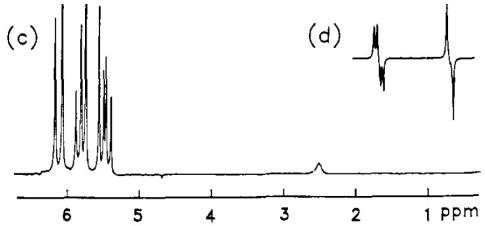


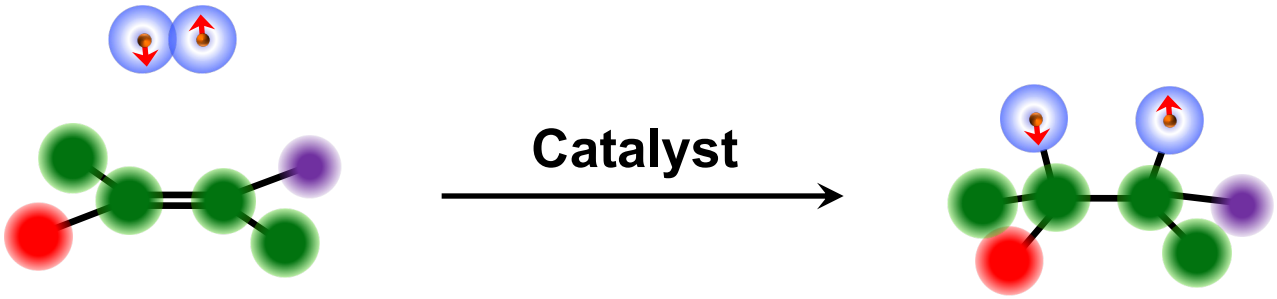
Figure 1. Demonstration that parahydrogen and synthesis allow dramatically enhanced nuclear alignment. Part (a) shows the proton NMR spectrum prior to the reaction. The intense lines are due to the acrylonitrile substrate. Part (b) was obtained subsequent to the hydrogenation to propionitrile but prior to spin-lattice equilibration. The large antiphase propionitrile multiplets in response to a $\pi/4$ pulse are observed only with para-enriched H_2 as reagent. Part (c) is the spectrum of the equilibrated sample and shows that the signal of (b) was a large transient enhancement. Part (d) is a line shape simulation demonstrating the agreement of the theory of ref 1 with the experiment of part (b). The line width is 3.5 Hz due to inhomogeneity of the field, which is degraded by the H_2 capillary.

a stable product, the transient nature of the enhanced NMR

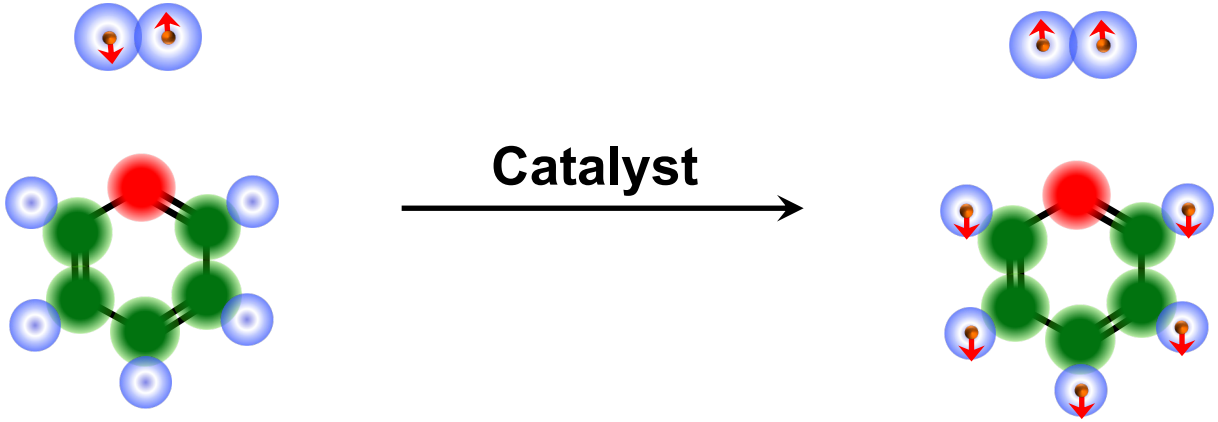
C. R. Bowers, D. P. Weitekamp *// **J. Am. Chem. Soc.,** **1987***

Affordable Hyperpolarization

Parahydrogen-Induced Polarization (PHIP)

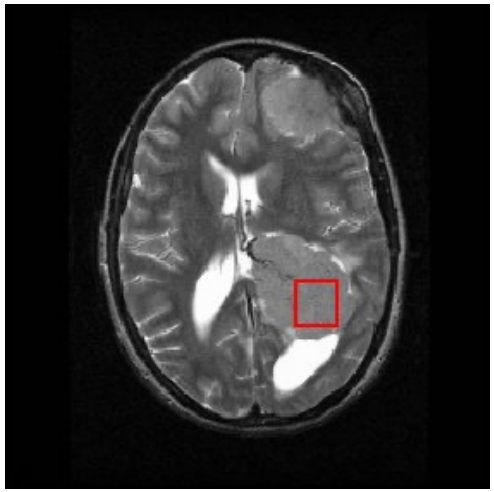


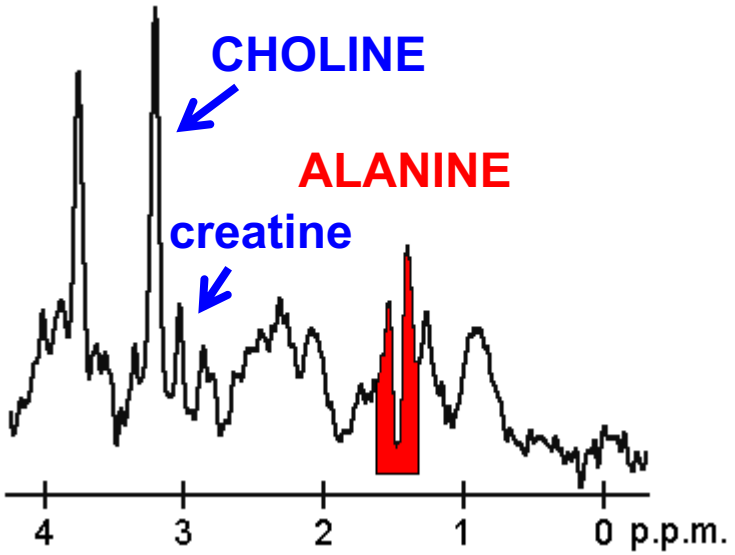
Signal Amplification By Reversible Exchange (SABRE)



Signal Enhancement for *in vivo* NMR/MRI

- Single Voxel Spectroscopy (SVS)
- Chemical Shift Imaging (CSI)

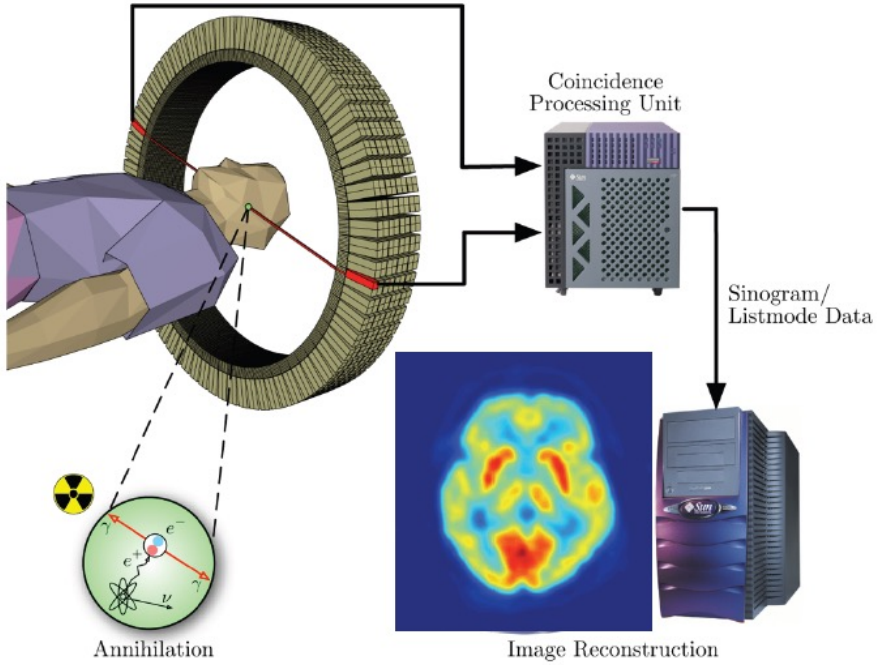




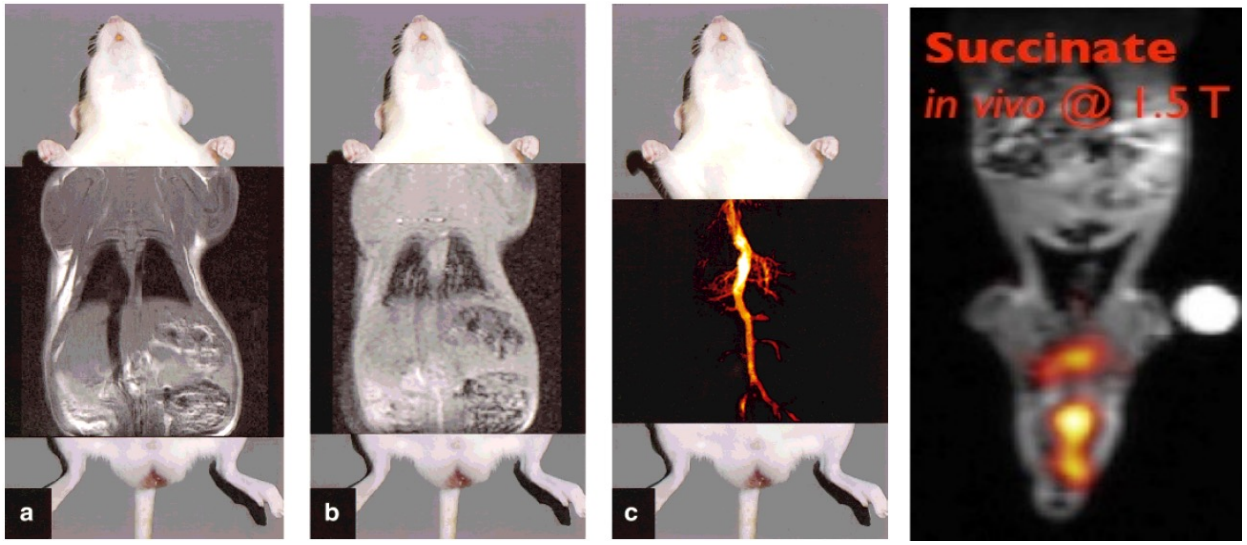
Motivation:

Use of molecular contrast agents,
in addition to Positron Emission Tomography (PET) for visualization of abnormal metabolic processes

Injection of the agent – uptake – visualization



Signal Enhancement for *in vivo* NMR/MRI

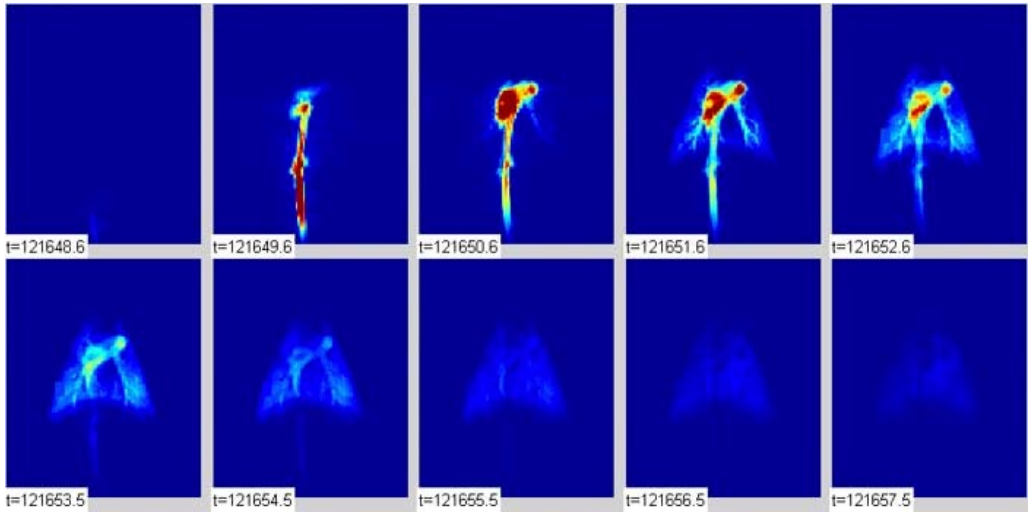


PHIP for MRI

In vivo ^{13}C image of a rat brain, after arterial injection of hyperpolarized succinate (in color); overlaid on a coronal ^{1}H fast gradient echo image.

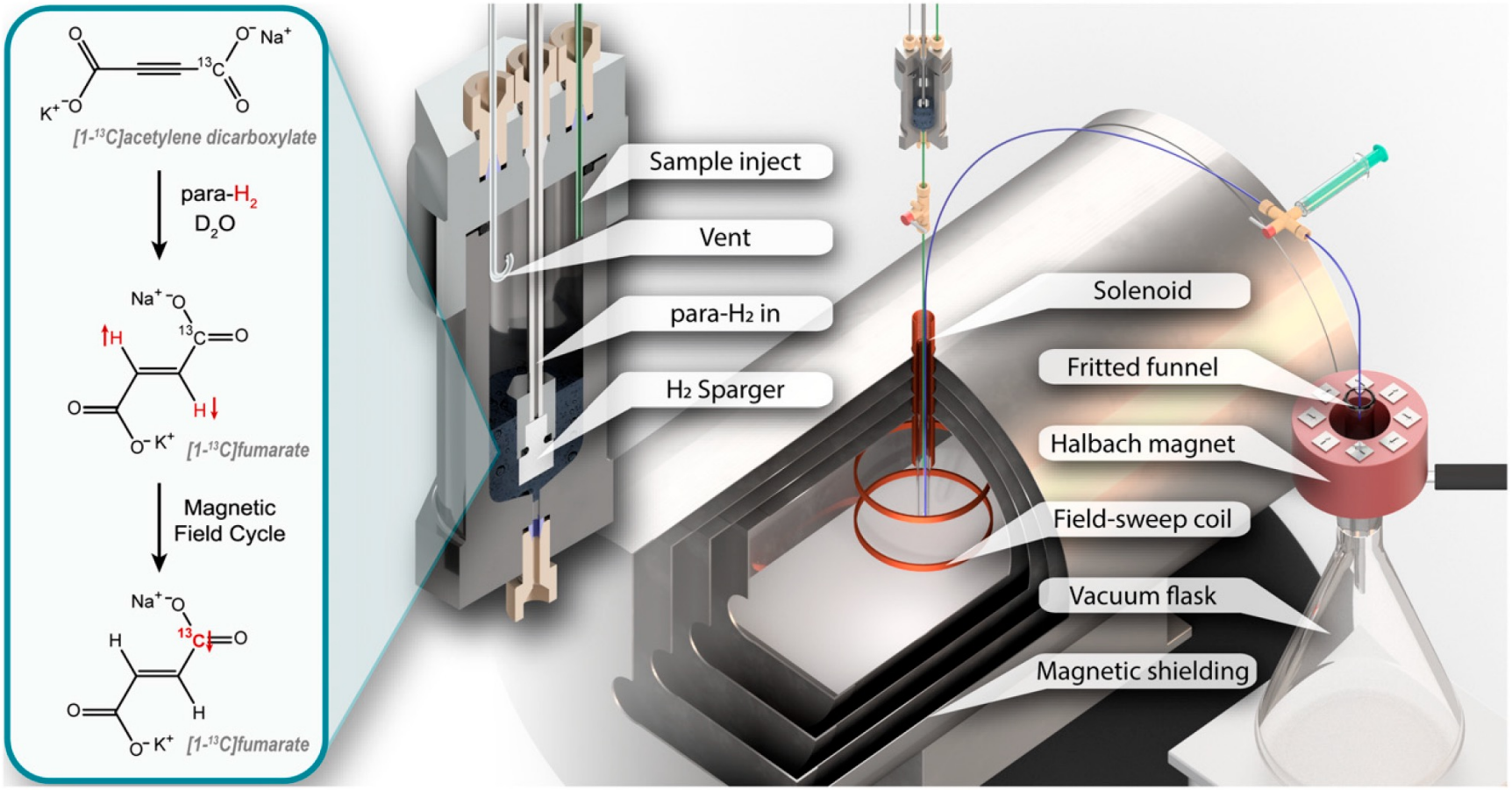
PHIP and polarization transfer to ^{13}C

TrueFISP ^{13}C images, showing the lungs of a pig after injection of a hyperpolarized ^{13}C imaging agent

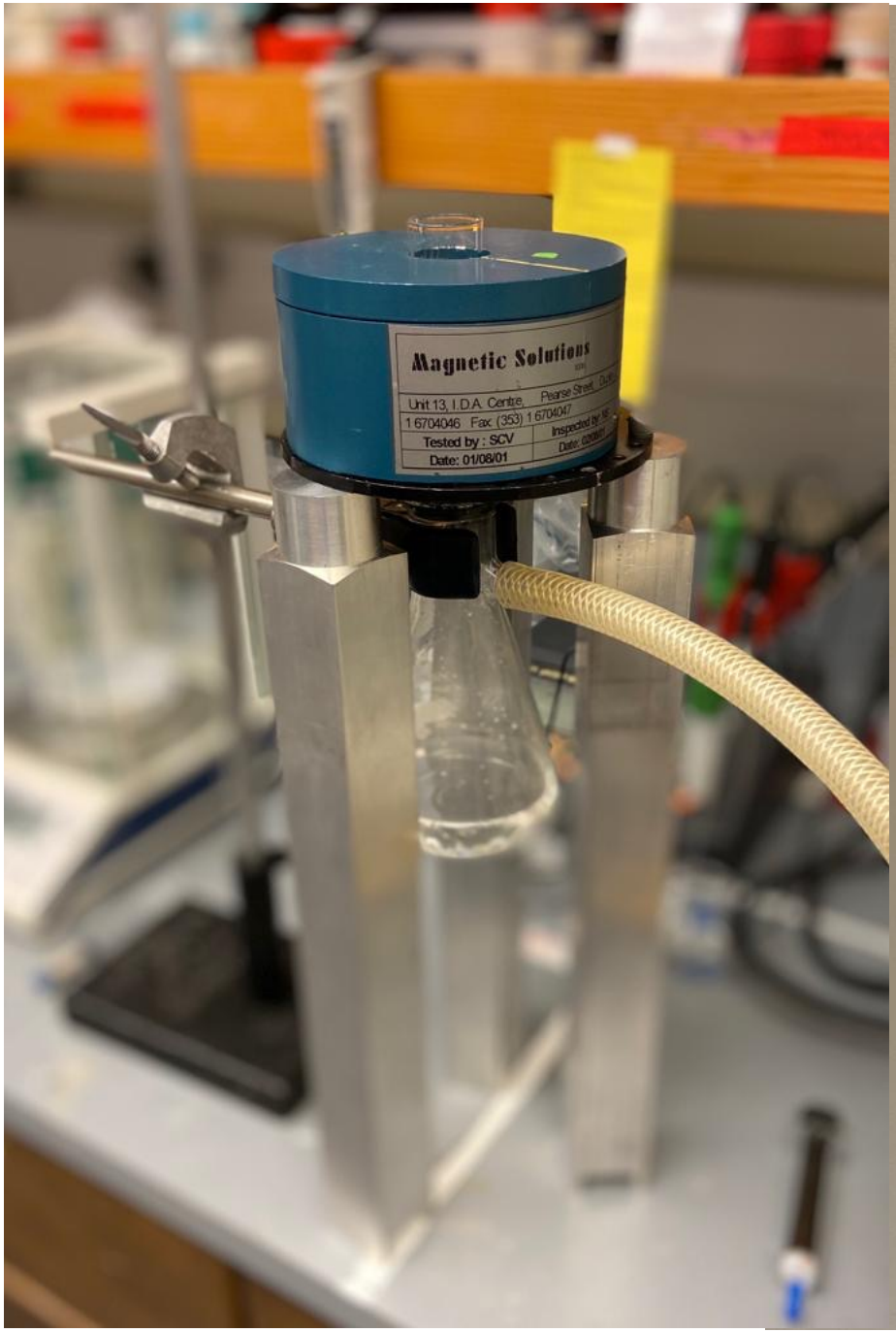


K. Golman et. al. // ***MRI in medicine*, 2001**; ***Br. J. Radiol.*, 2003**

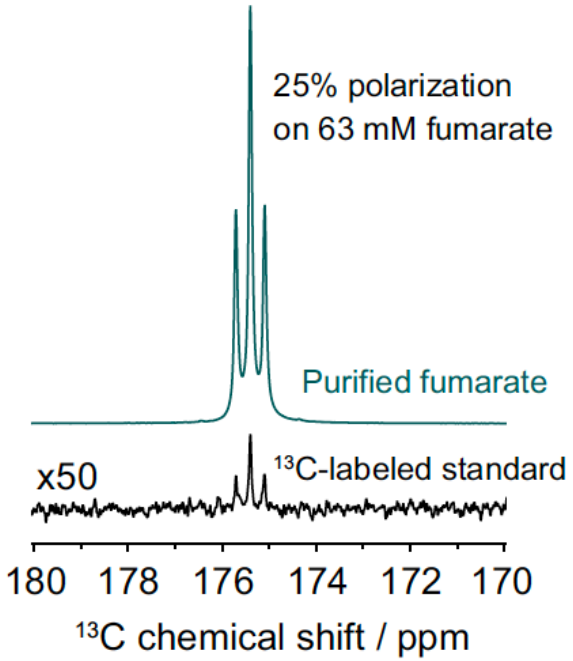
Production of Pure Hyperpolarized Fumarate

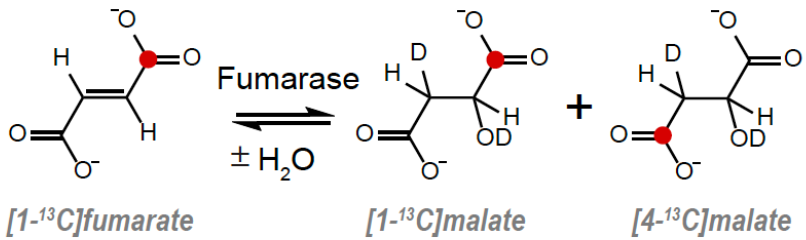


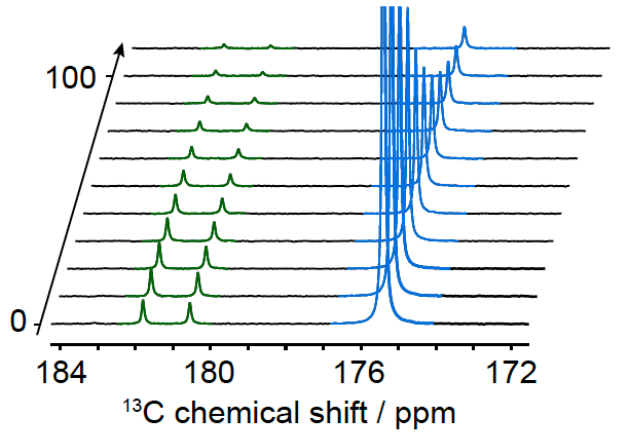
Knecht, Blanchard, Barskiy, et al. *PNAS*, **2021**


Magnetic Solutions
Unit 13, I.D.A. Centre, Pearse Street,
1 6704046 Fax: (353) 1 670407
Tested by : SCV
Date: 01/08/01

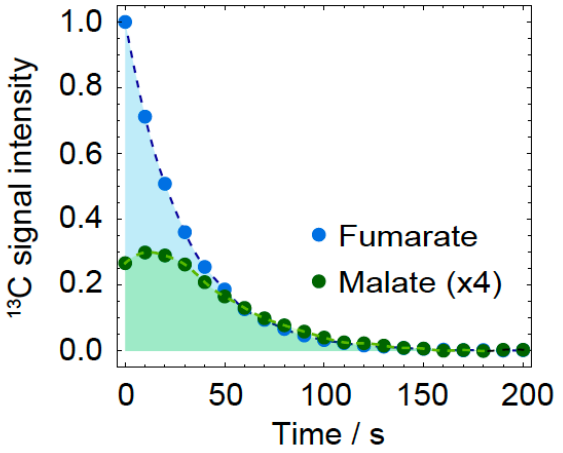
Production of Pure Hyperpolarized Fumarate







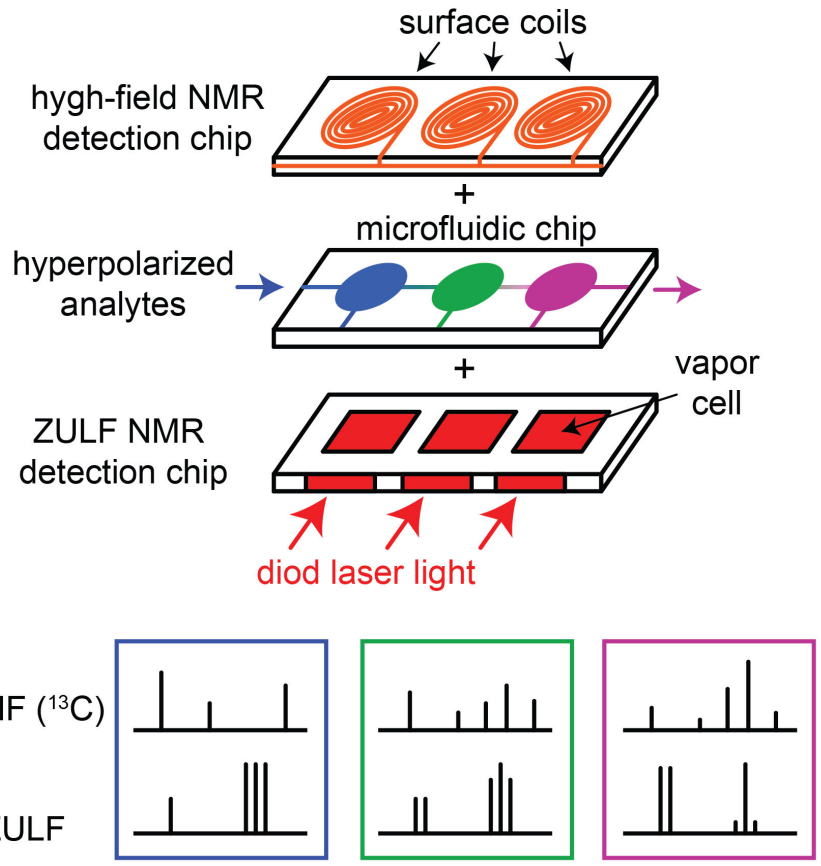
1. High levels of attainable polarization (~40%) is possible
2. Once produced, fumarate can precipitate from solution by adding the acid
3. The solution can be washed out of the catalyst, unreacted precursor, impurities etc.



Knecht, Blanchard, Barskiy, et al. *PNAS*, **2021**

Erwin Schrödinger Prize - 2021

Nuclear Spin Engineering for Advanced Chemo- and Biosensing



Nuclear Spin Chemistry

- Magnetization Transfer Catalysis
- Long-lived Spin States
- Interplay between Spin Dynamics and Chemical Kinetics

Nuclear Spin Physics

- Nuclear Spin Isomers
- Polarized Nuclear Targets

Optical Magnetometry

- OPMs
- NV Centers in Diamonds

Funding

Sofja Kovalevskaja Award

Unterstützt von / Supported by

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Helmholtz Institute Mainz, Germany

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**Roman Picazo-Frutos, James Eills,
Kirill Sheberstov, John Blanchard,
Dima Budker**

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