Dynamic Nuclei Polarization

from the Nucleon Structure to Medical Applications

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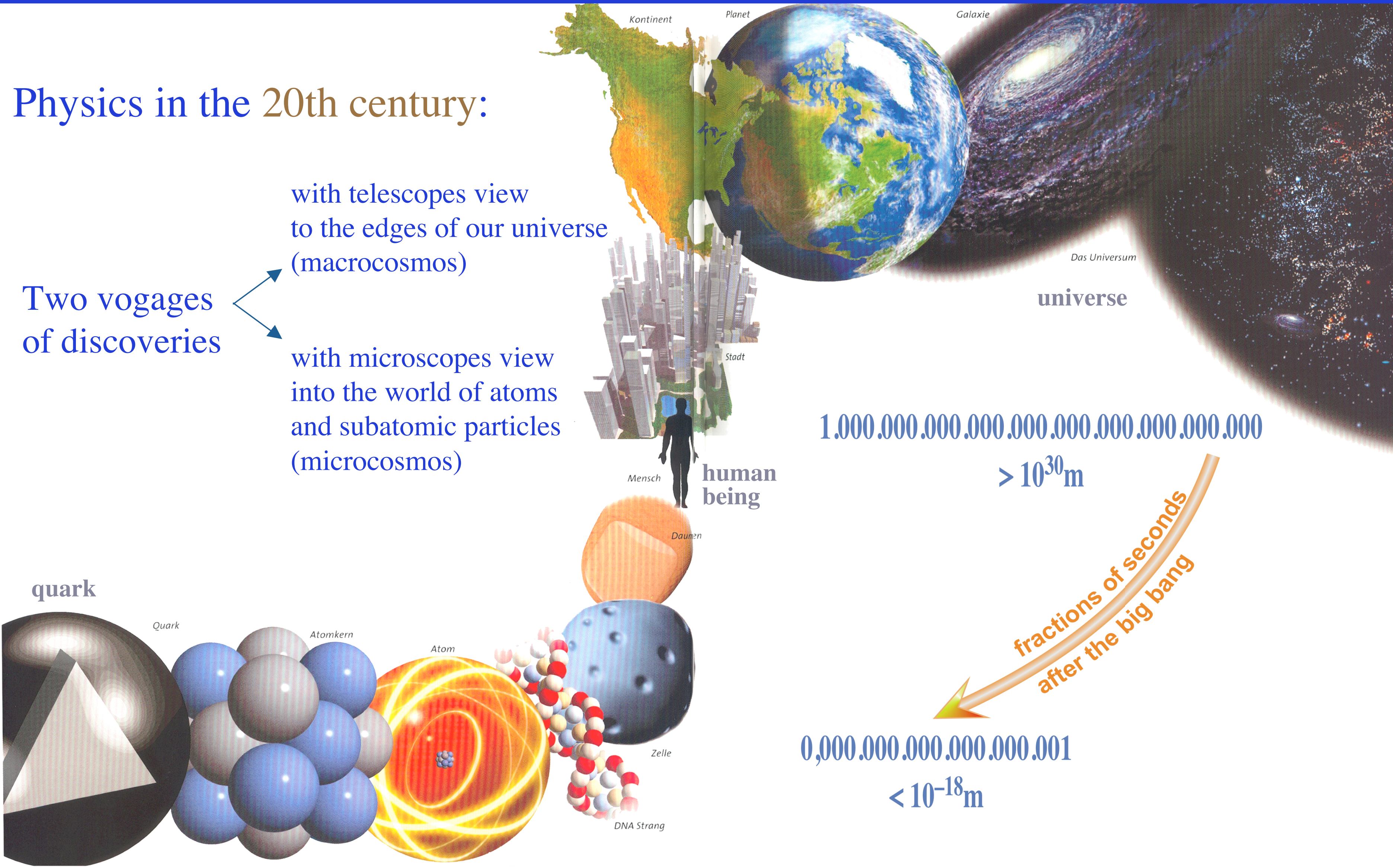
Tiny and Large World

Physics in the 20th century:

Two vogages of discoveries

- with telescopes view to the edges of our universe (macrocosmos)
- with microscopes view into the world of atoms and subatomic particles (microcosmos)



universe

human being

quark

1.000.000.000.000.000.000.000.000.000.000

$> 10^{30}$m

fractions of seconds after the big bang

0,000.000.000.000.000.000.001

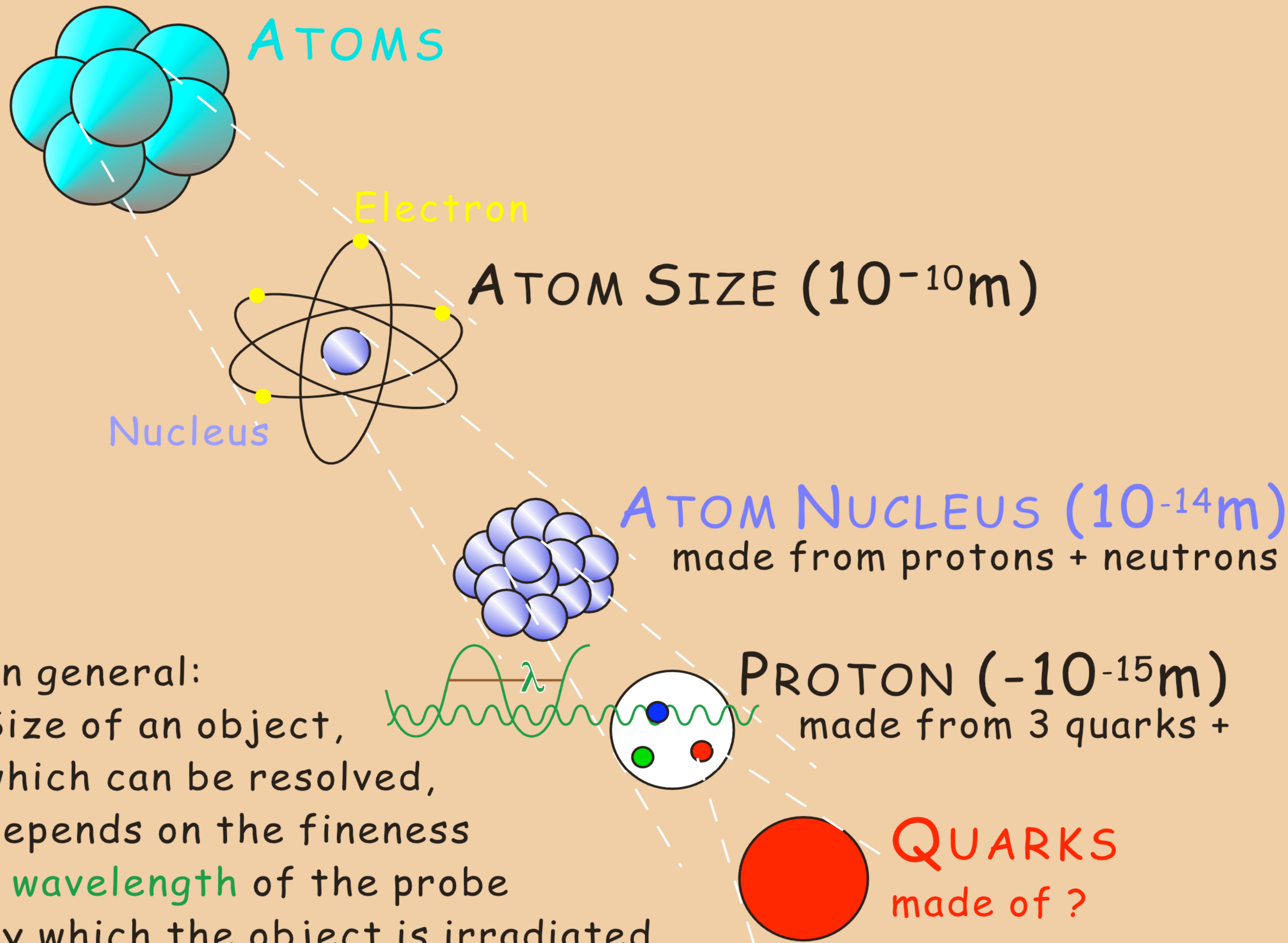
$< 10^{-18}$m

Quarks and Leptons build our World

Leptons		Quarks	
Electron Mass 0.0005 GeV	**Electron-Neutrino** Mass unknown	**Up** Mass 0.004 GeV	**Down** Mass 0.007 GeV
Myon Mass 0.1 GeV	**Myon-Neutrino** Mass unknown	**Charm** Mass 1.5 GeV	**Strange** Mass 0.15 GeV
Tau Mass 1.8 GeV	**Tau-Neutrino** Mass unknown	**Top** Mass 174 GeV	**Bottom** Mass 4.7 GeV

Spin 1/2 – Particles : Fermions

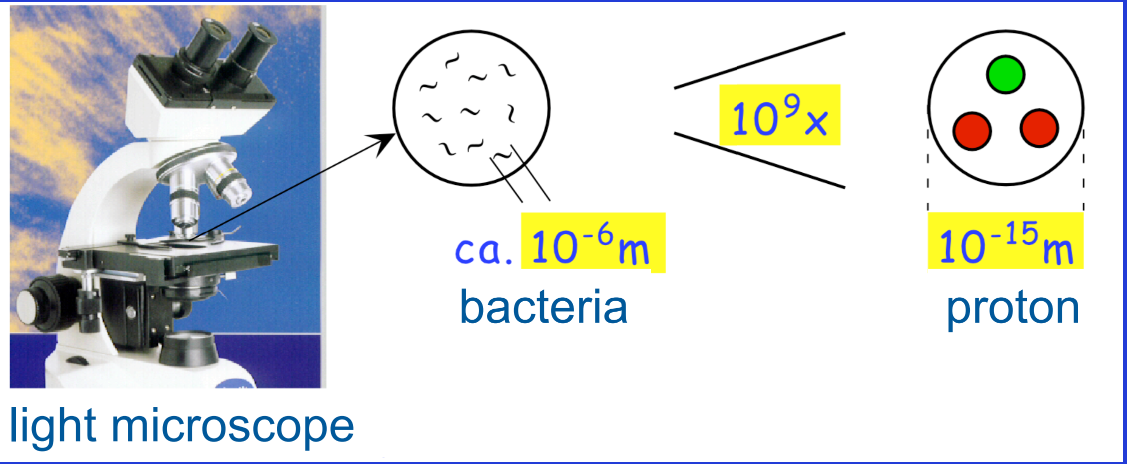
Deeper Insight into Matter



In general:
Size of an object,
which can be resolved,
depends on the fineness
= wavelength of the probe
by which the object is irradiated

$$E \approx \frac{h}{\lambda}$$

Generally:
the higher the beam energy or the smaller the wavelength, the **more structural details** can be resolved



$\lambda_{\text{visible light}} = 5 \cdot 10^{-7}$m $\qquad \lambda = 10^{-16}$m

$E = 2$ eV $\quad \Rightarrow \quad E > 10^9$ eV

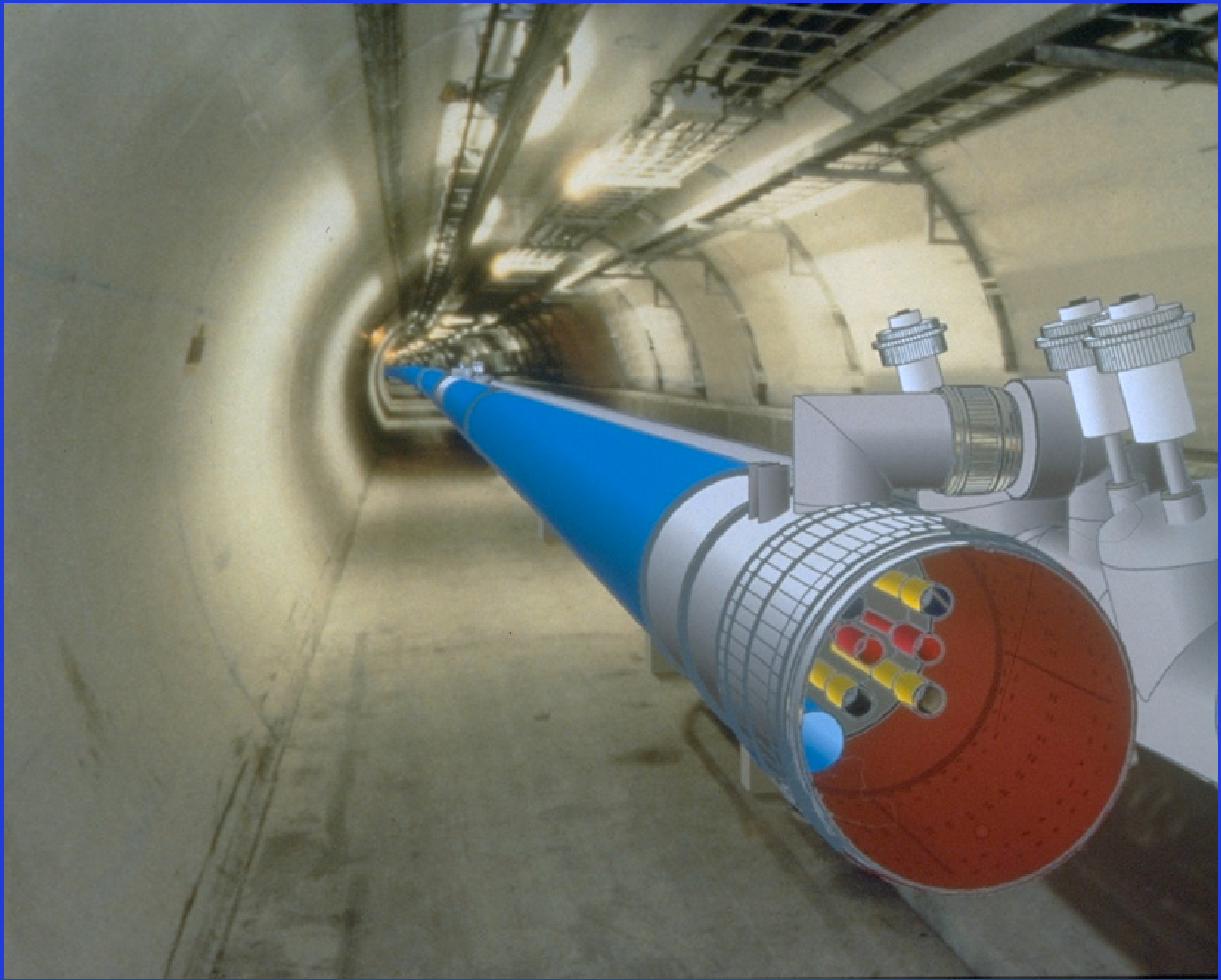
$\Rightarrow$ high energy accelerators

High Particle Energies ?

- Cosmic rays up to 10^{12}eV
  - ➥ uncontrollable
    accidentally
    low flux
    different energies
    cheap
- Accelerators (man made)
  - ➥ controllable
    adjustable energies
    expensive

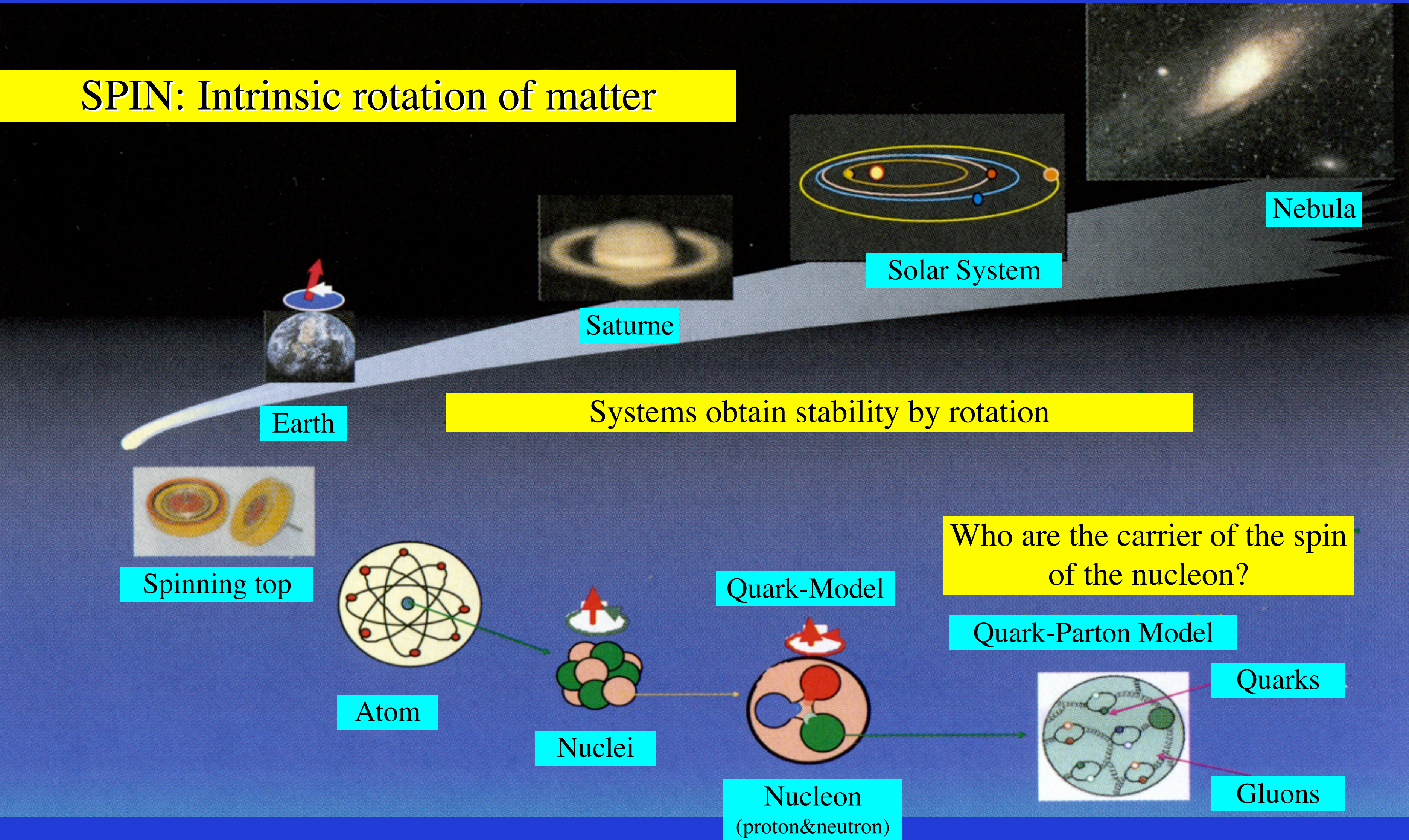
CERN

CERN (LHC-Ring)

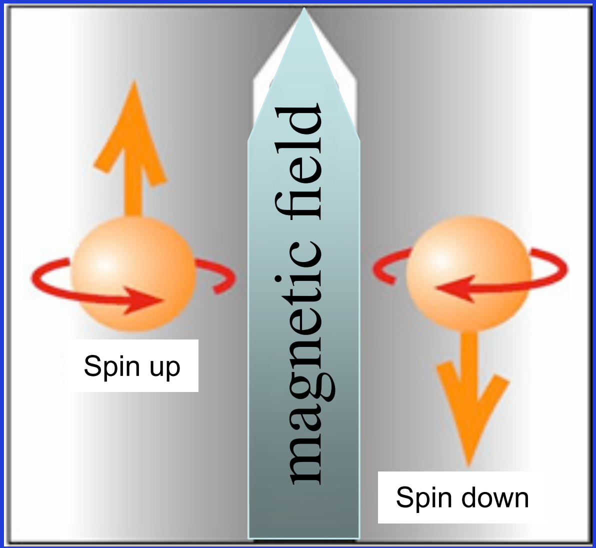


Concept: SPIN

What is SPIN ?


SPIN: Intrinsic rotation of matter
Nebula
Solar System
Saturne
Earth
Systems obtain stability by rotation
Spinning top
Who are the carrier of the spin of the nucleon?
Quark-Model
Quark-Parton Model
Atom
Nuclei
Quarks
Gluons
Nucleon
(proton&neutron)

What is SPIN ?



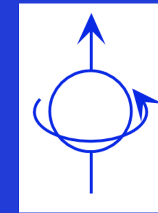
Internal angular momentum of particles
Picture: Spinning top which not tumbles during rotation
➥ but limits
description only by quantum mechanics

With Spin there is a magnetic moment, which acts in such a way, that particles in a magnetic field can be considered as small magnets, which can be aligned.

Proton has SPIN (fermion), but is composed from further objects with Spin:
Quarks and gluons – How do their Spins contribute?

➥ Polarized Target (our favoured apparatus)

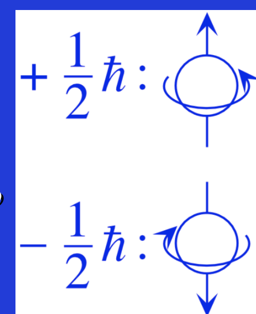
Concept: Spin ≙ Angular Momentum

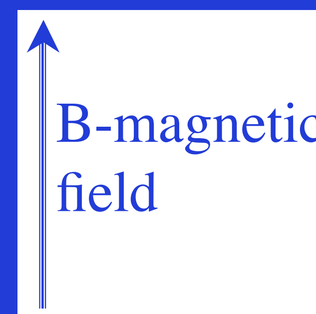


Picture: Particle with SPIN, that rotates around its center of gravity
Precise description: Only in the framework of quantum mechanics

W. Pauli was against the picture of a rotating electron
"It took quite a while, until N. Bohr was successfully, to convince his very critical pupil (W. Pauli) from the ingenuity of this new concept."
(Phys.-Blätter, April 2000)

e. g. for electron, proton, neutron
(Spin 1/2 - particles) 2 discrete numbers
in a magnetic field (orientation quantization,
energy quantization)

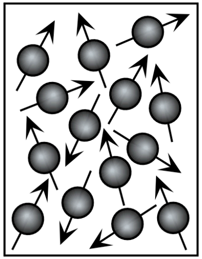




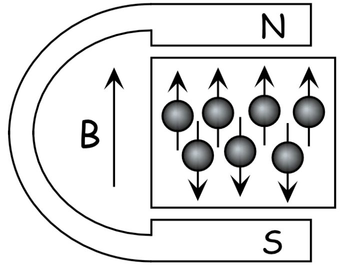
Particles with Spin can be manipulated with magnetic fields
(analogy: magnetic needle (compass) in the earth magnetic field)

Polarization

= Orientation of Spins in a magnetic field



Without magnetic field:
Randomly orientated spins

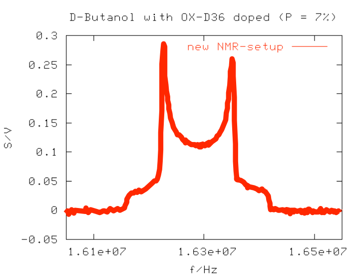


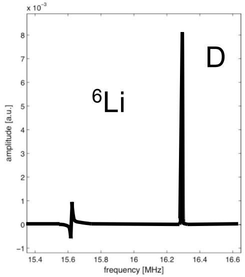
With magnetic field:
Orientation of spin

All Spins in magnetic field direction : 100 % Polarization

Change of polarization (e.g. destruction by HF-field) = energy change in the spin system measured by the **N**uclei **M**agnetic **R**esonance (**NMR**) method

⇒ resonance signal





⇒ ´visibility` of the particles with spin (mainly protons) by **M**agnetic **R**esonance **I**maging (**MRI**)

Dream: 100% polarization of a Spin ensemble

In reality not so easy to realize

Interplay between

polarizing force	≙	magnetic field B
and		
depolarizing force	≙	thermal motion of Spin particles (temperature T – relaxation)

Examples:

$B = 10^{-5}$ Tesla T = 25° Celsius	(earth magnetic field) (room temperature)	$P = 10^{-12}\%$
B = 5 Tesla T = -273° Celsius	(superconducting magnets) (refrigerators)	P = 100%NMR (particle physics)
B = 1 Tesla T = 37° Celsius	(superconducting magnets) (body temperature)	$P = 10^{-8}\%$ MRI (medicine)

Dynamic Polarized Solid Targets

Method:

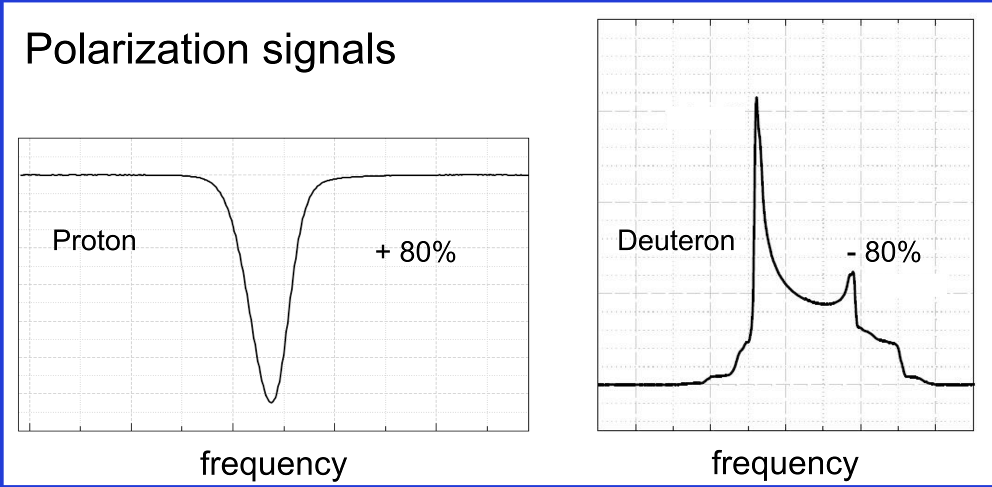
Production of a high degree of polarization in a suitable material with a high content of polarizable nucleons and 'free' electrons (radicals) by means of

– high magnetic field
– extremely low temperature

$$\left.\begin{array}{l}\\ \\ \end{array}\right\} P \sim \frac{\mu B}{kT}$$

– microwave irradiation → dynamic nuclei polarization (DNP)

Polarization detection by means of nuclear magnetic resonance technique (NMR)

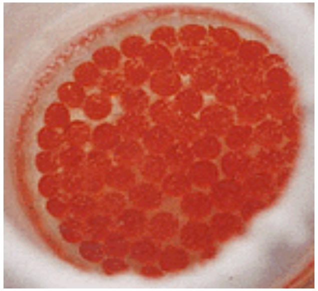


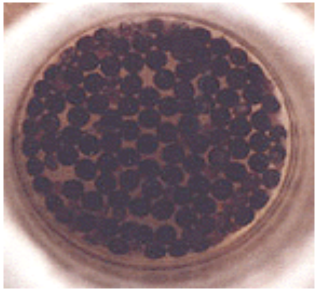
Additional qualities of target materials

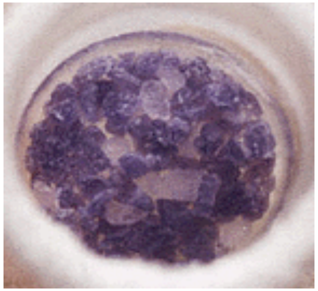
– degree of polarization resistant against radiation damage
– easy handling – quick target material exchange or refreshment of the polarization

Favor Materials for DNP Targets

	Name	Dopant	f	Radiation hardness	Polarization
–	Butanol, C_4H_9OH	chemically	0.13	moderate	80-85%
–	D-Butanol, C_4D_9OD	chemically	0.24	moderate	80%
–	Ammonia $^{14}NH_3$, $^{15}NH_3$	radiation	0.17	high	> 90%
–	Lithium Deuteride ^6LiD	radiation	0.50	very high	50-60%


Butanol with Porphyrexide

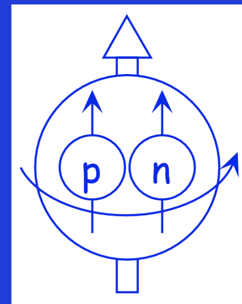

Butanol with CrV complex

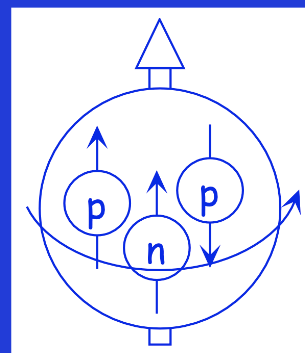

Ammonia


LiD or LiH

Polarized Neutrontarget

➢ Deuteron as Spin 1-particle





➢ ^{3}He as Spin 1/2-particle

^{3}He-gas highly polarizable (P ~ 50%)

by means of dynamic methods (laser)

at room temperature (300 K)

and small magnetic field (1 mT)

in glass cells

} polarized ^{3}He easily transportable

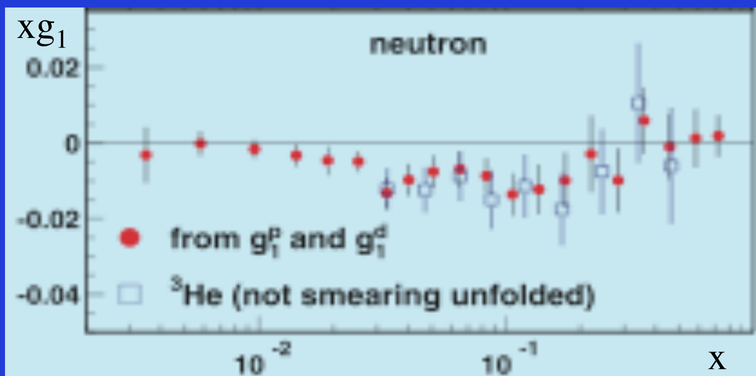
→ Deep inelastic scattering experiments e.g. at SLAC

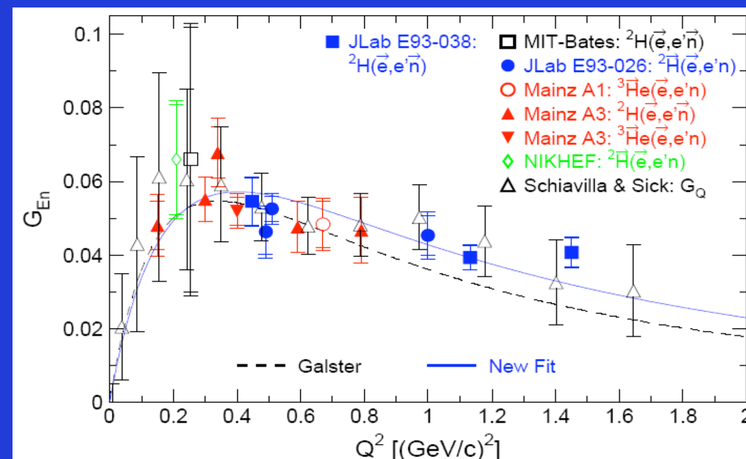
SPIN–OFF: Polarized ^{3}He-Gas

From basic research

– Structure function g_1^n, g_2^n (SLAC, DESY, JLab)

– Electrical formfactor G_{En} (Mainz, MIT - Bates, JLab)





to

Modern Lungdiagnostics

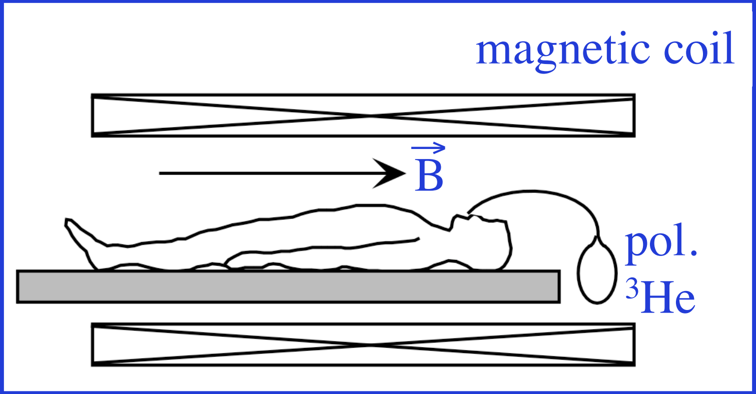
Air	(77% nitrogen 21% oxygen 2% +argon, ^{4}He ...)	no MRI-signal

Question: Information about lung and its ´airchannels´

pulmonary alveoli (about 400 million
diameter: 0.2 mm
area: ~10 m^2)

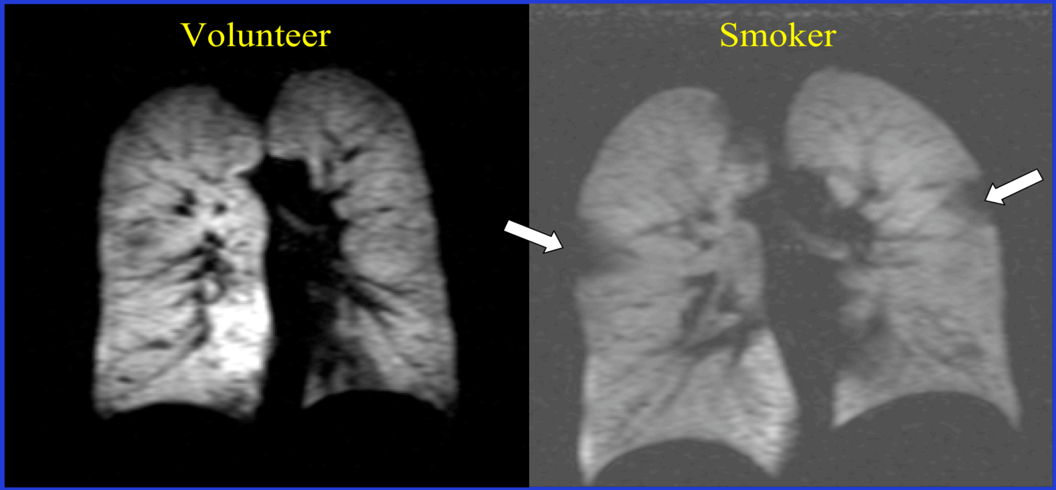
Inhale polarized ^{3}He-gas as patient in a MRI-tomograph

↪ ^{3}He-MRI ⇒ picture of lung

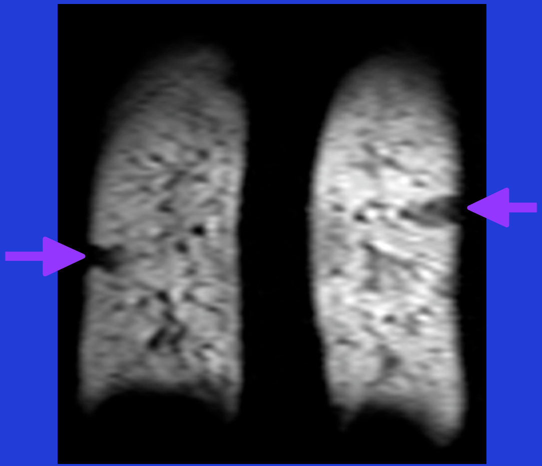


– Lung diagnostics by Magnetic Resonance Imaging (MRI)

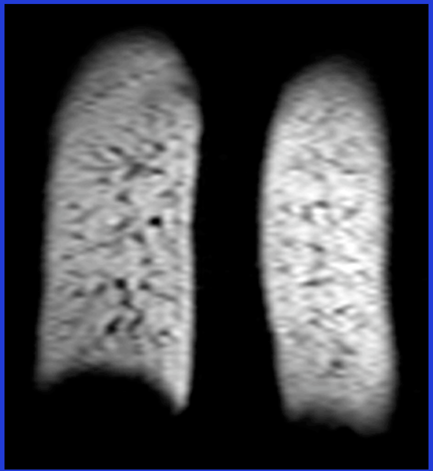
^{3}He spin density MRI



W. Heil, Univ. Mainz



before



after

inhalable beta blocker

asymptomatic asthmatic

T. Altes et al., University of Virginia

Polarized ^{3}He

Particle Physics: State-of-the-Art ^{3}He-Targets in Mainz and JLab

Medical use:

All technical problems solved

– Central ^{3}He production e.g. in Mainz (~80 bar · liter/day P=60%)

– Storage and transport (T_1 > 100h), polarimetry, ^{3}He-recovery

PHeLINet
Polarized Helium Lung Imaging Network

2007-2011

Research Partners

SIEMENS

Noble Gases Supplier

Spectra Gases

Tedlar Bags Supplier

Jensen Inert Products

Other Research Facilities Doing Similar Research

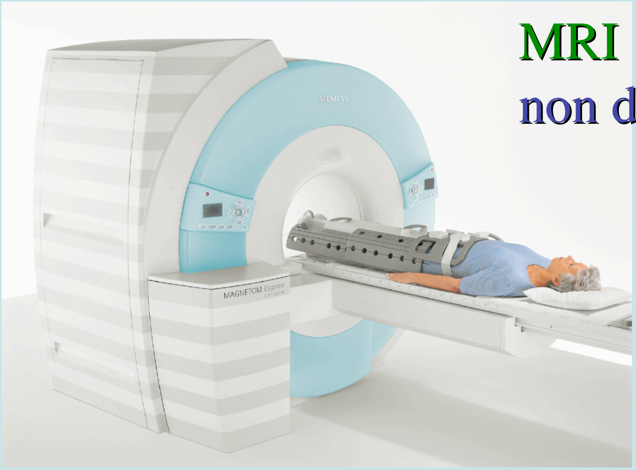
- Duke University (Center for Advanced MR Development)
- Duke University (Center for In Vivo Microscopy)
- Harvard Medical School
- Harvard University

- Laboratoire Kastler Brossel
- NIST Physics Laboratory
- Princeton University
- Royal Marsden NHS Trust
- UC Berkeley (Alex Pines)
- University of Mainz - Physics Department
- University of Mainz - Radiology Department
- University of Michigan (Magnetic Resonance Imaging)
- University of Michigan (Scott Swanson, PhD)
- University of Texas (Charles Martin,PhD)
- Washington
  Washington University in St. Louis

DNP ⇒ Medical Diagnostics

Polarized solid targets – DNP ⇨

SPIN as ‚Spin-off'

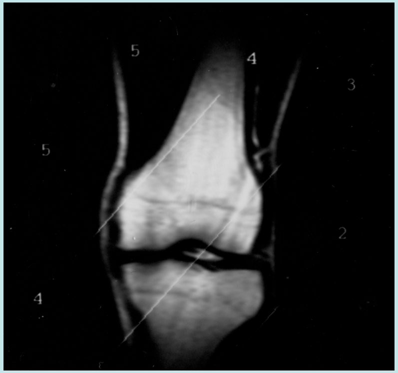


MRI

non destructive

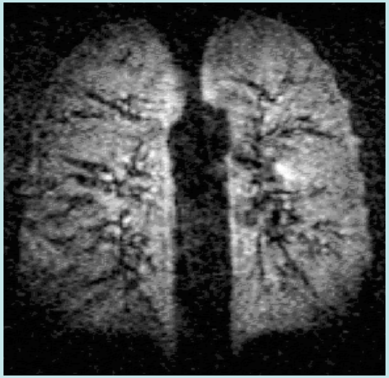
H_2O = proton spin

⇒ e.g. damage of meniscus



^{3}He = neutron spin

⇒ lung damage



DNP for all nuclei with spin

H, D, ^{6}Li, ^{14}N, ^{15}N, ^{13}C ...

$C_4 H_9 OH$

(Butanol)

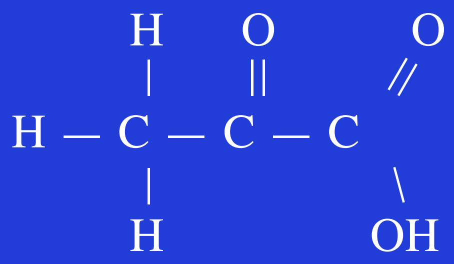
natural abundance

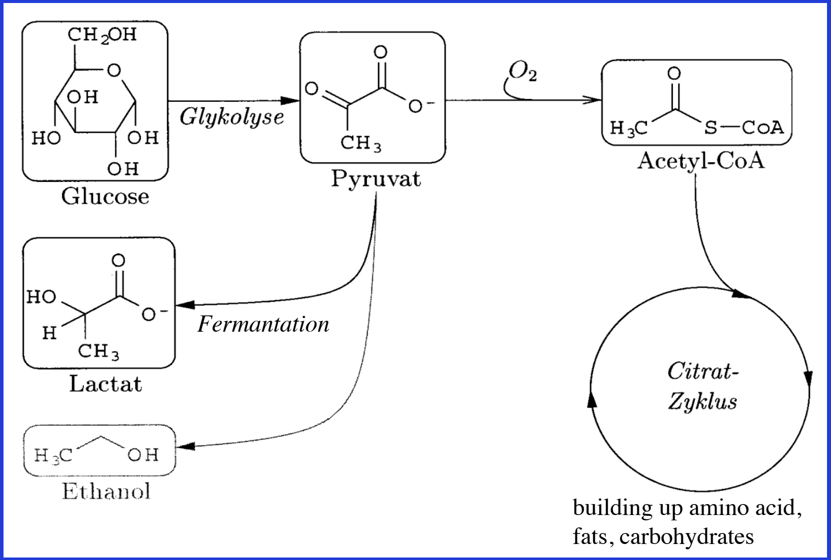
of ^{13}C : 1.1%

DNP ⇒ Medical Diagnostics

^{13}C-isotope marker, to detect molecules from metabolic processes with NMR/MRI-method

- carbohydrate-metabolism
  → pyruvic acid (C_3H_3OH)





<u>Limits</u>:

^{13}C has low sensitivity ⟺ DNP

($P_{^{13}C}$ ~ 0.0008% @ 300K, 9.4T) ($P_{^{13}C}$ ~ 10-35% @ 1.2K, 3.5T)

↳ at low temp. ⮥

Decisive Technical Step:

Dissolution of a frozen polarized sample at ~ 1 K with hot H_2O

Transfer of the hyperpolarized liquid out of the low temperature refrigerator to the MRI-apparatus

and the liquid is still polarized during the injection (to animals) (speed is needed!)

Ardenkjaer-Larsen et al., Proc. Math. Acad. Sci. USA 100 (2003) 10158
J. Wolber et al., NIM A526 (2004) 173

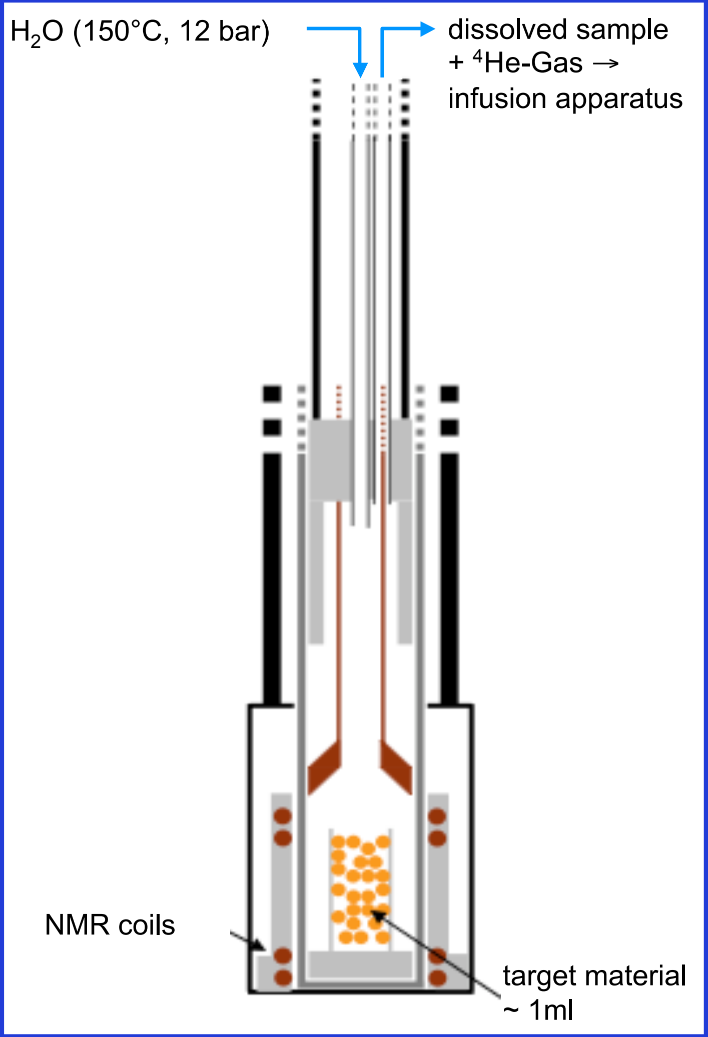
DNP-Polarizer

Apparatus e.g. EPF Lausanne/PSI

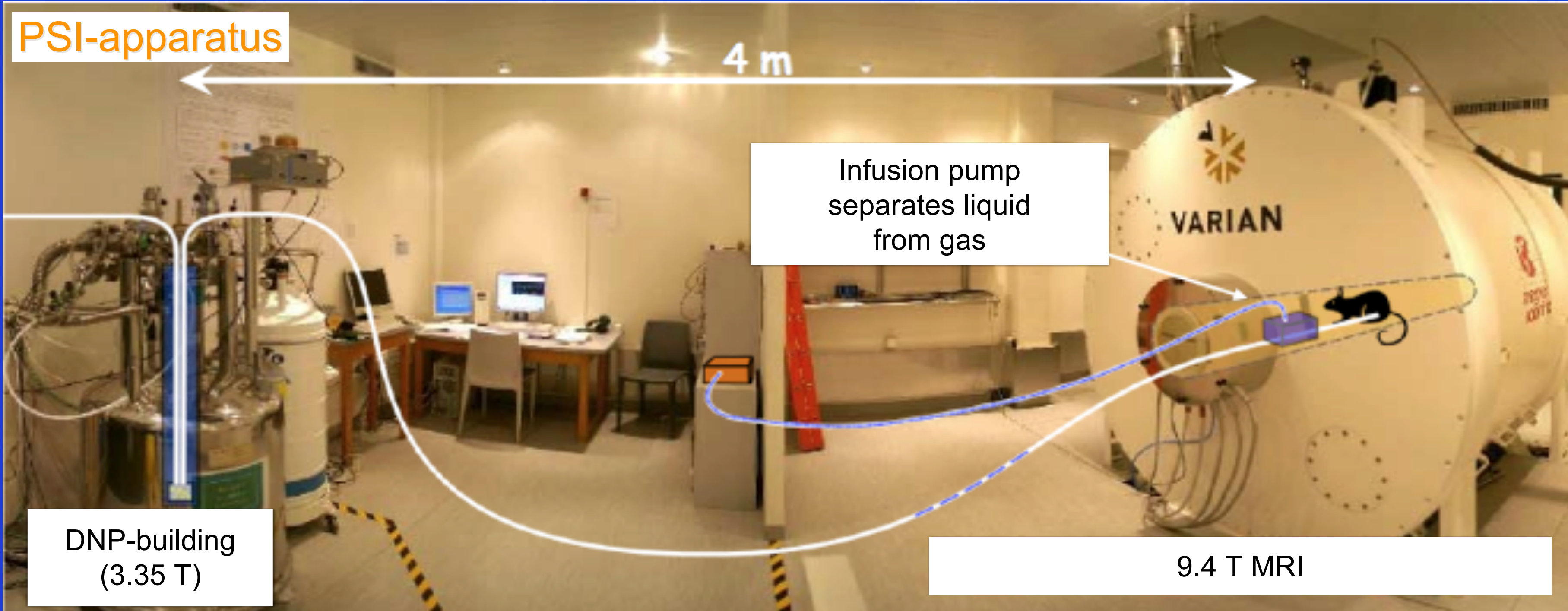
- Refrigerator in a standard NMR-magnet 3.35 T (∅ = 88 mm)
- Base temperature ~ 1.1 K with low liquid ^{4}He-consumption (~ 60 ℓ/week)
- 94 GHz microwave source ~ 50 mW → DNP
- Quick sample loading and fast polarization build-up in ~ 1 h

Dissolution Procedure

- DNP-insert replaced by ‘dissolution’ insert
- Dissolution of the solid material by water
  (some bar at ~ 150°C)
- Dissolution exit directly connected with the infusion apparatus



Liquid Sample Transfer



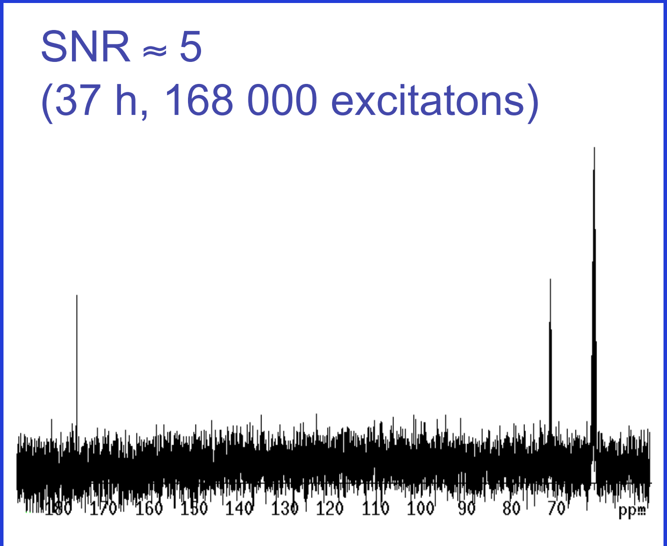
- ➢ Dissolution, transfer and infusion in ~ 15 s (lost ~ 50% of the starting polarization)
- ➢ Remaining enhancement factor ~ 5000-10000
- ➢ DNP and MRI at different magnetic fields

Compound	Mol M	Solvent	H_20 (vol.%)	TEMPO (mM)	DNP %	τ_{BU}, sec.	A_{liq}ti mes	DT sec.	τ_{rel}, sec.
1-^{13}CNa acetate	4.5	D_2O/eth.-d6	67	33	7.3	360	3000	15	21
1-^{13}CNa puruvate	2.0	D_2O/eth.-d6	82	33	6.9	560	-	-	-
^{13}C urea	8.0	glycerol	0	33	8.2	1200	-	-	-
1-^{13}C glucose	4.5	D_2O/eth.-d6	67	33	5.9^{SA}	2500	~19	6	1.0
1-^{13}C glycine	1.5	D_2O/gl.-d8	40	50	9.0	780	2500	15	15
^{6}LiCl	15.0	D_2O/eth.-d6	67	33	7.0	410	-	-	-
^{15}N urea	8.0	glycerol	0	16	3.0	6360	6000	20	94
^{15}N cholineCl	6.0	D_2O/gl.-d8	40	50	3.5	4700	5000	20	74

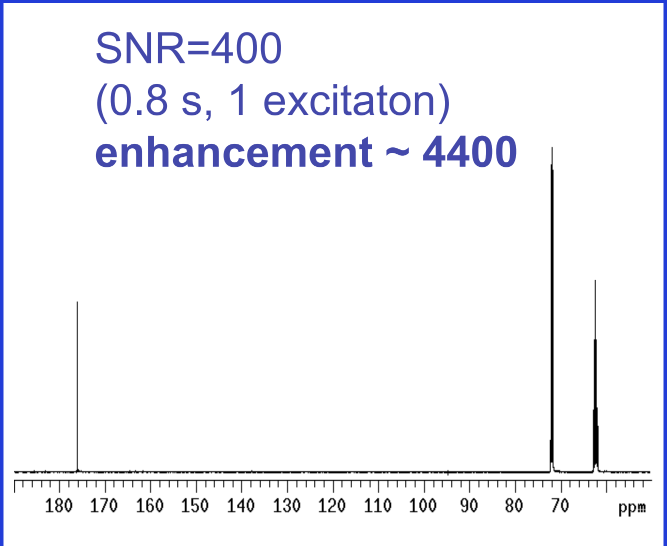
Hyperpolarization by DNP of Molecules in Solution

Ardenkjaer-Larsen JH et al, PNAS 103(30) (2003)
courtesy of GE Healthcare

Conventional MR



Hyperpolarized MR

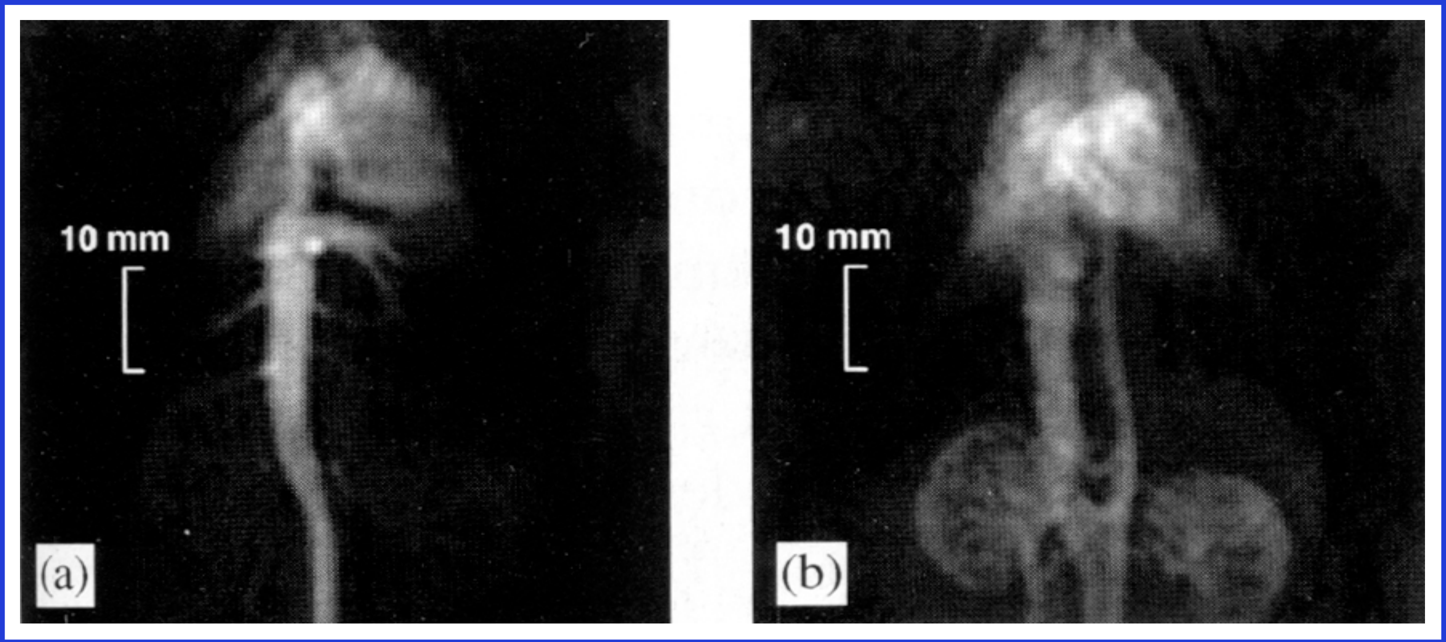


Pioneers: Amersham/Health Malmö now GE Healthcare

urea (CH_4N_2O) ➡ urea cycle (Krebs – Henseleit cycle)

➥ Final product of egg metabolism ➟ liver ➟ blood ➟ kidney ➟ urine

Sample: urea (99% ^{13}C marked) | Glycerol + Tritylradical

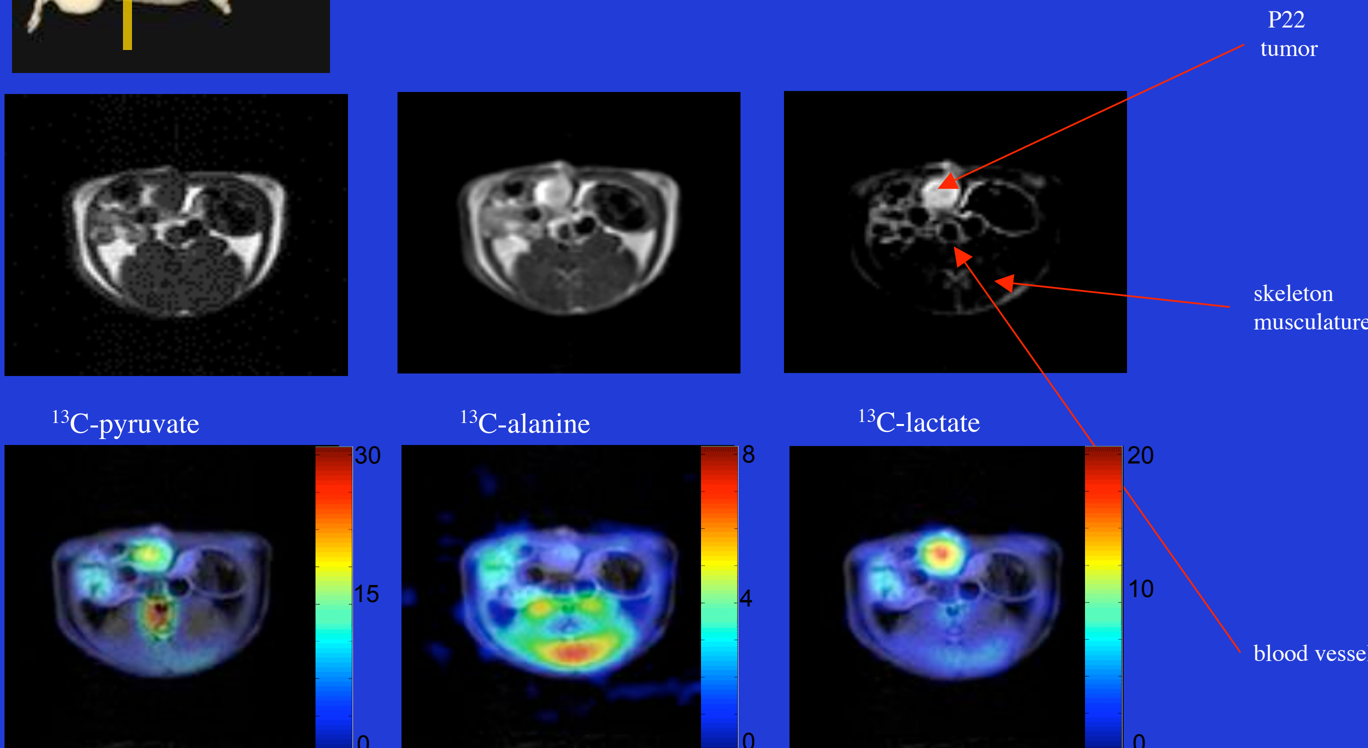


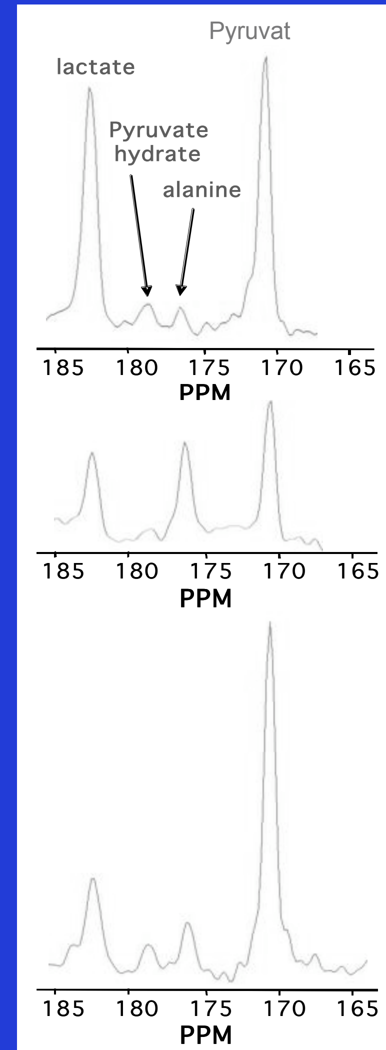
^{13}C coronal pictures of a rat

(a) after 1 s and (b) 3 s after injection of ^{13}C-urea

Metabolism Pictures from a Rat Tumor with Hyperpolarized [1-^{13}C]Pyruvat

Golman K et al, Cancer Res 66(22) (2006)
courtesy of von GE Healthcare





Cardiac Metabolism Measured Noninvasively by Hyperpolarized ^{13}C MRI, Klaes Golman et al.
Nature Medicine, Volume 13, Number 11, November 2007.
Detecting tumor responce to treatment using hyperpolarized 13C magnetic resonance imaging and spectroscopy, Sam E. Day et al.
Magnetic Resonance in Medicine 59:1005-1013 (2008).
Magnetic resonance imaging of pH in vivo using hyperpolarized 13C-labelled bicarbonate, F.A. Gallagher et al.
nature, Vol 453, 12 June 2008.

Bochum / GE Healthcare

Focus:

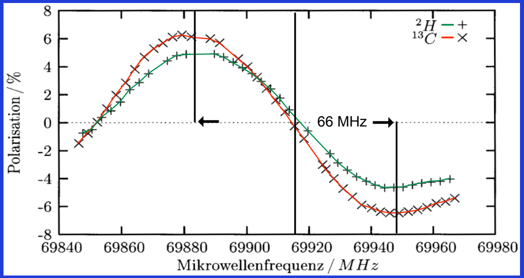
1) deut. pyruvic acid: C_3D_3OH + Triphenylmethyl radical (Trityl radical) AH 11501
→ DNP-Mechanism (Solid State Effect - EST)

2) Polarization enhancement of ^{13}C in C_3H_3OH + AH 11501

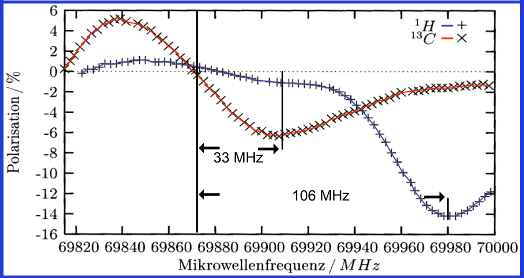
3.35 T / 1.2 K → 5.0 T / 1.0 K

$P_{^{13}C}$: 35% → 75%

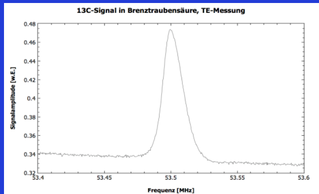
frequency curves for



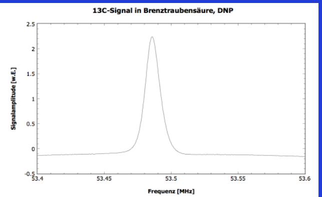
deuterons and ^{13}C



protons and ^{13}C



$P_{^{13}C}$ (T.E.) = 0.13%

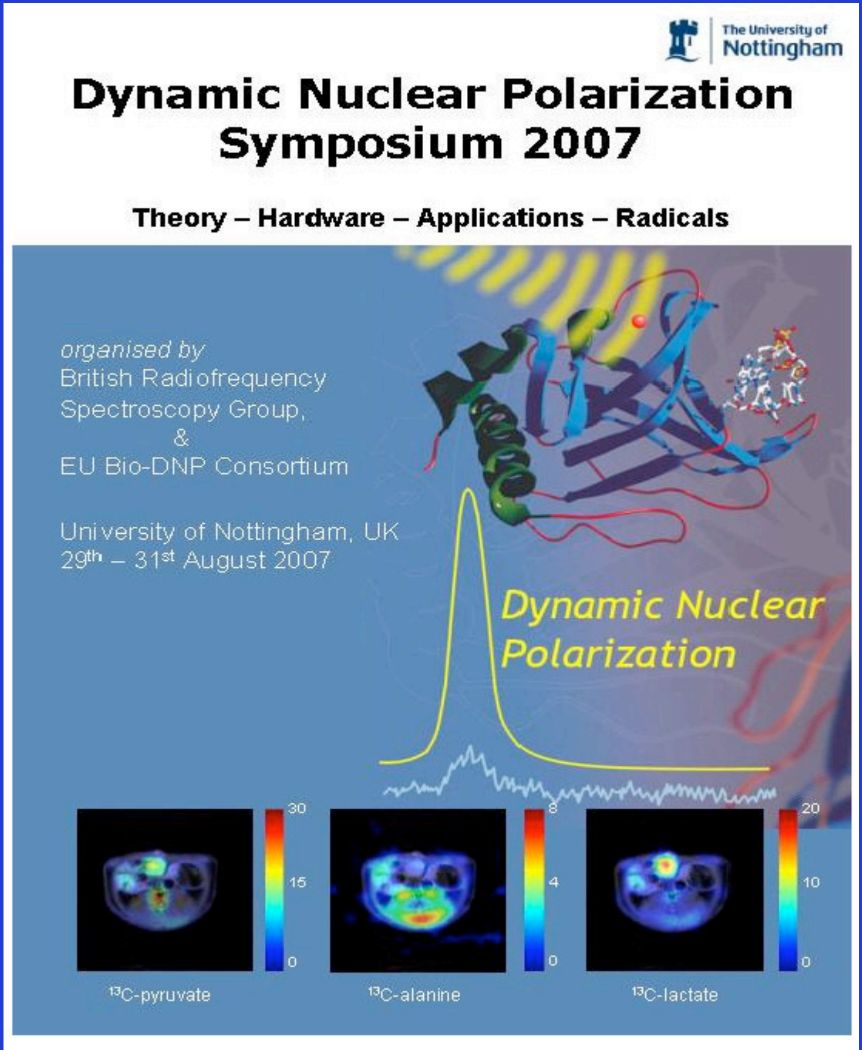


$P_{^{13}C}$ (DNP) = 75%

→ in vivo MRI → enhancement factor: 50000

Summary

Even after 45 years of DNP polarized solid targets for elementary particle physics
– (in the meantime often written off) –
the future is more than promising, especially by the new medical or biochemical applications



Proc. in Appl. Magn. Reson (2008)