

超高極化核種的 MRI
Hyper-polarized Gas MRI

吳明龍

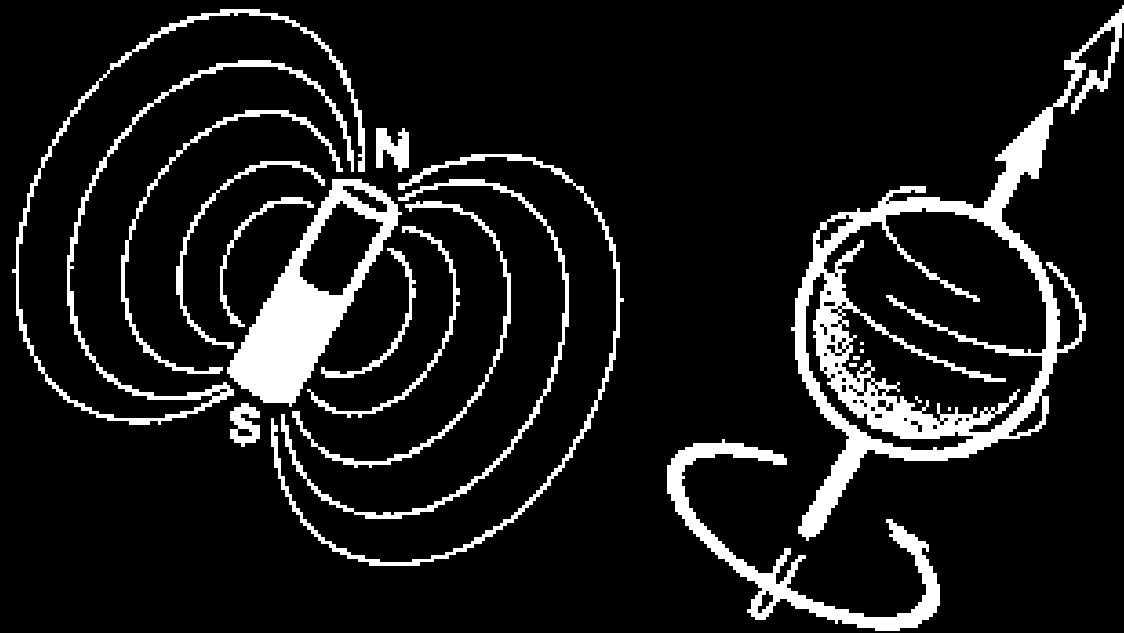
在開始之前,我要 confess

- 大部分投影片來自鍾老師
- 很多內容我也不是完全了解
- 紙上談兵,完全沒有實戰經驗

回顧：MRI 的信號源

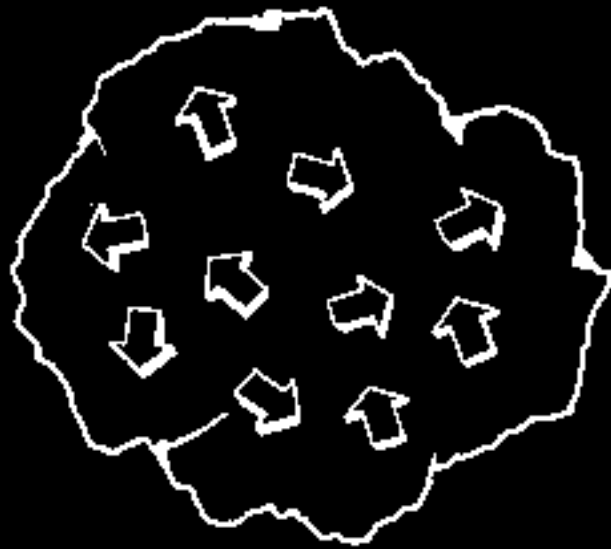
- 含有一個質子 (proton)
- 質子帶有電荷，並且不斷旋轉
 - 電荷旋轉 = 電磁鐵
- 外加磁場下，氫原子核整齊排列

人體內的 MRI 信號來源

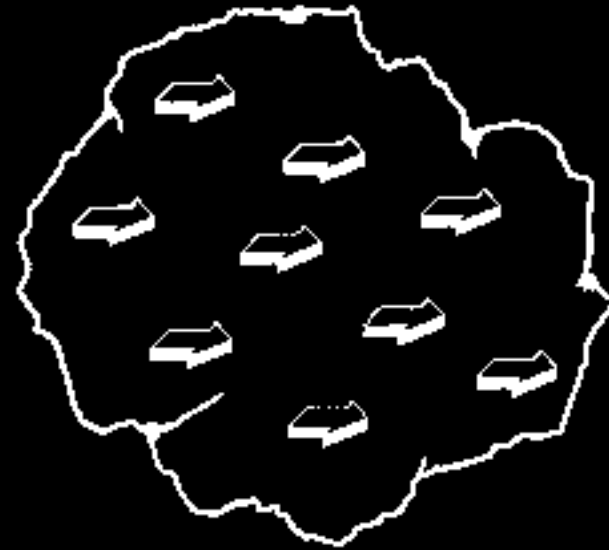


器官內的氫原子核酷似小磁鐵

外加磁場對氫原子核小磁鐵的影響



不規則排列

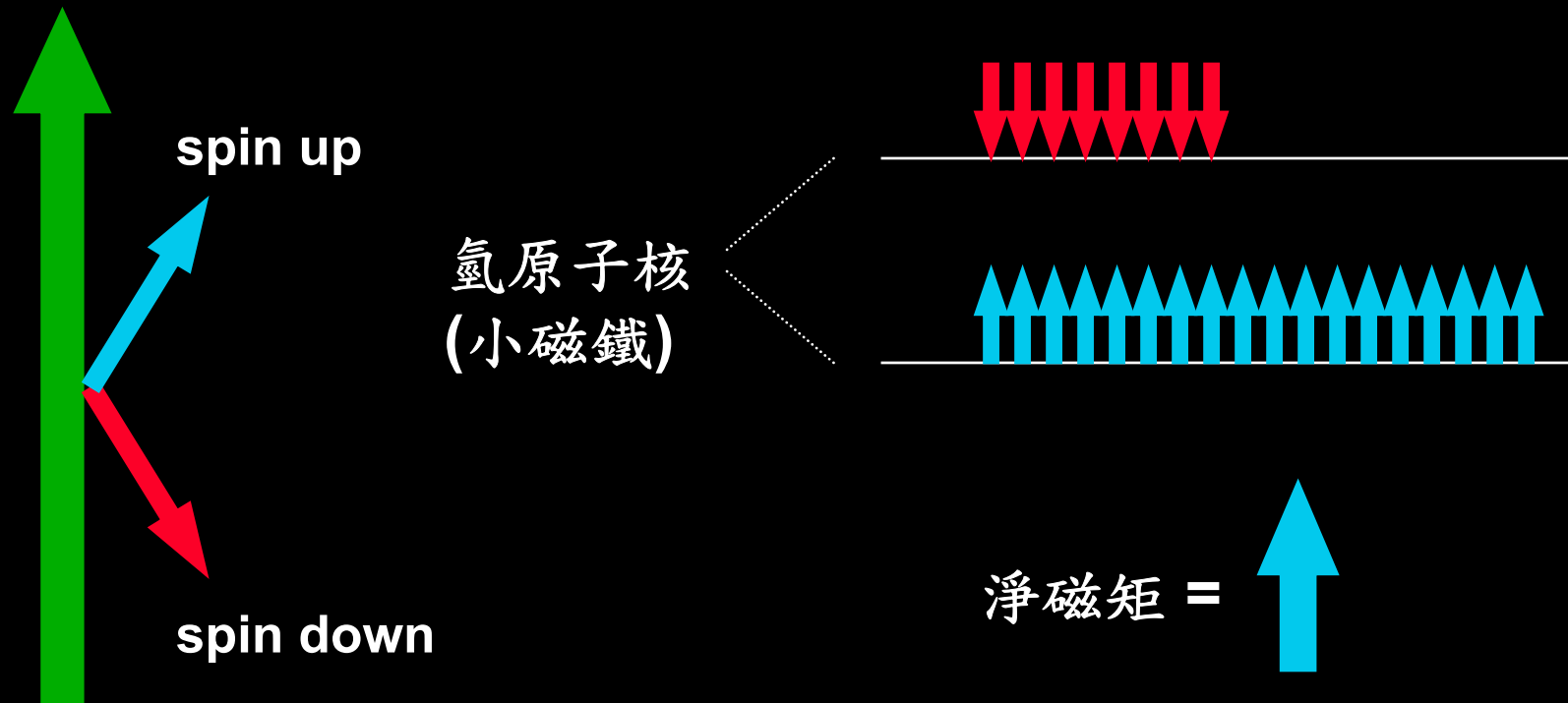


主磁場

規則排列



所謂整齊排列其實不見得很整齊



磁化向量大小 = 向量和 ~ 上下人口差

回顧：人體磁性的大小

- 外加磁場 = 1.5 Tesla = 地磁三萬倍
- 氫原子核排列仍然不甚整齊
- 每一百萬個之中只多了 5 個左右
 - 量子物理加上統計力學

人口差異符合「波茲曼分佈定理」

$$\frac{\text{spin up 人口數}}{\text{spin down 人口數}} = e^{\frac{\Delta E}{k T}}$$

$\Delta E = \gamma h \mathbf{B}_0$ (h : 浦朗克常數)

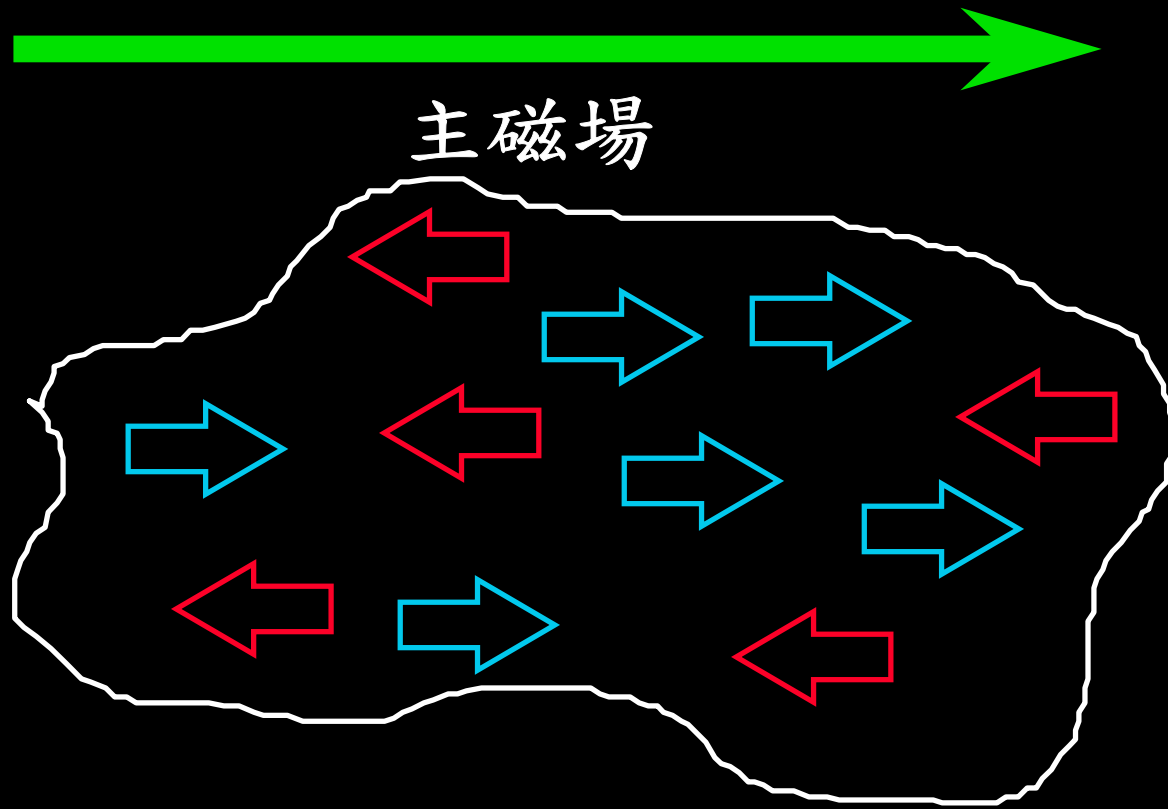
$k =$ 波茲曼常數

$T =$ 絕對溫度 (攝氏溫度 + 273)

$$= 1.0000049$$

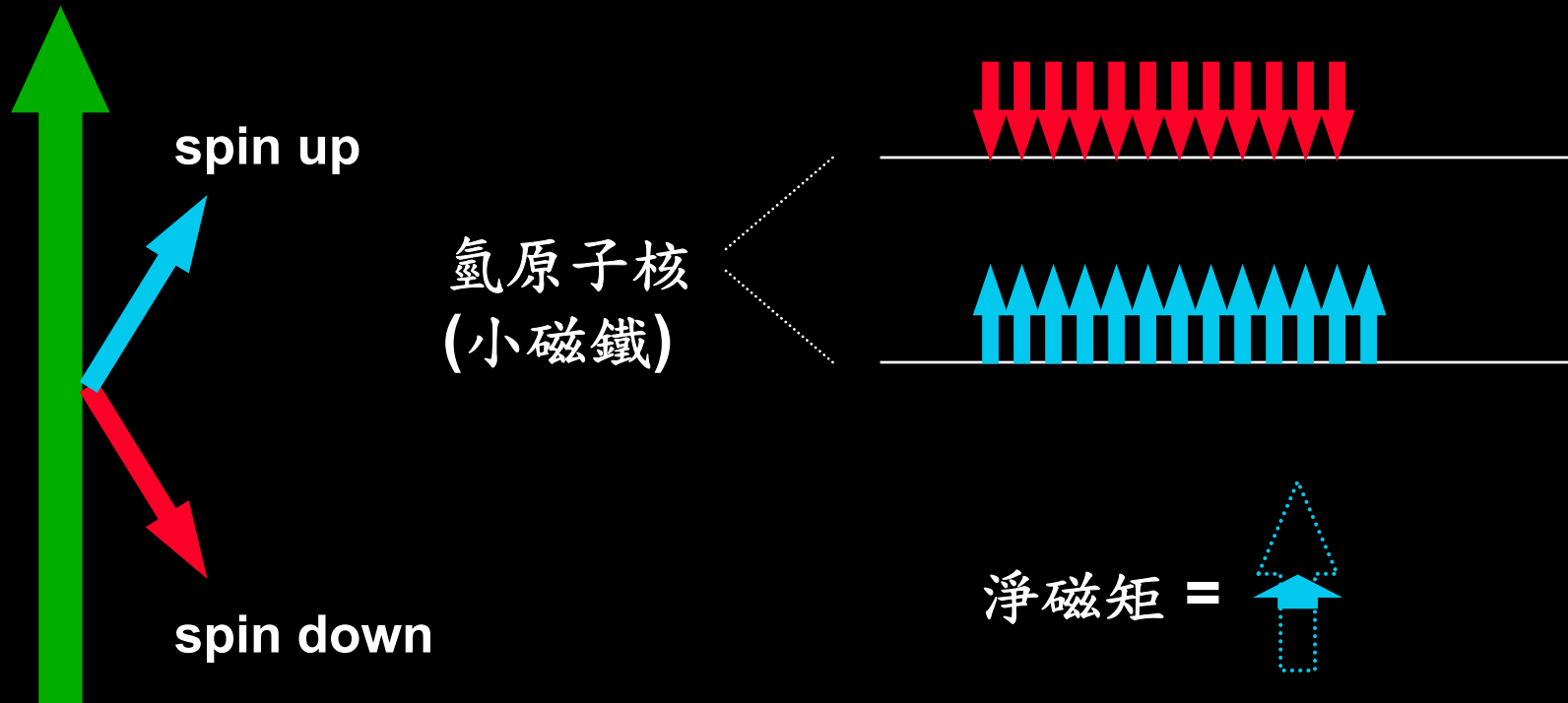
除了主磁場之外，沒有一項可以更動

實際的排列沒那麼整齊



每一百萬個氫原子核，只多五個左右

比較正確的畫法



磁化向量大小 = 向量和 ~ 上下人口差

回顧：給一個概念

- 外加磁場 = 1.5 Tesla = 地磁三萬倍
- 人體引發的磁鐵 ~ 0.05 Gauss ~
地磁十分之一
- 而且離體表愈遠，磁性愈小

才這麼一點點哪！

- 沒錯！MRI 先天上信號就非常微弱
 - 電壓信號約為百萬分之一伏特
- 但是隨著儀器的進步，要測到氫原子核的信號已經沒什麼問題了

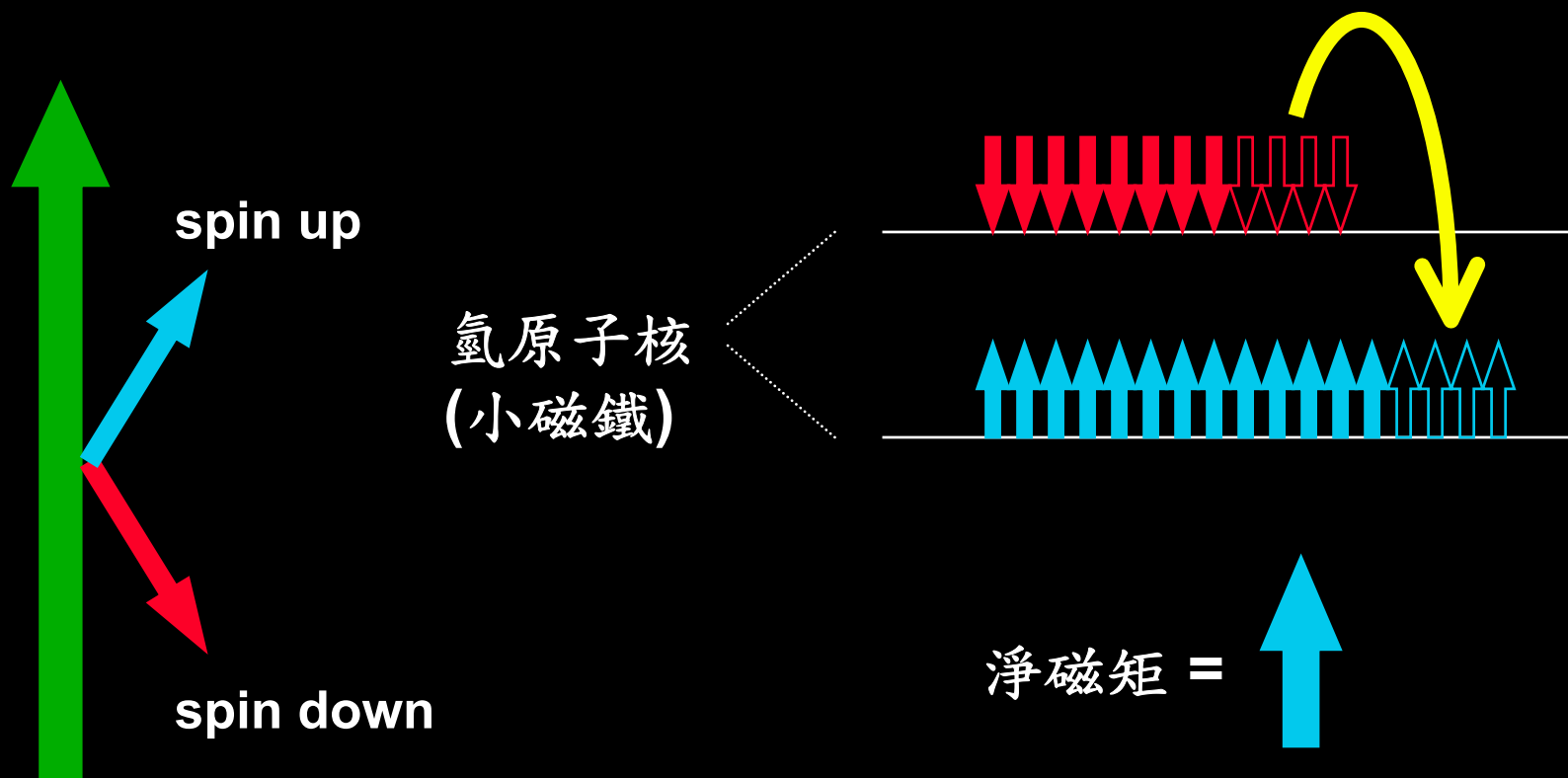
再說人體內 ^1H 特多

- 人體 (70 Kg) 內大部分成分是水
- 每 18 公克的水就有 $2 \times 6 \times 10^{23}$ 個
氫原子核
- 1.5T : 10^{22} 個氫原子核的磁性總和

那什麼叫做「超高極化」？

- **Hyper-polarization**
- 打破波茲曼定律，增加人口差異
- 淨磁矩 正比於 人口差異
- **MR** 信號因而成比例增加

磁性大小 ~ 上下人口差異



可不可以把一些高能階原子核 送到低能階？

如果做得到 ...

- 只要低能階人口比高能階多 10%
- **MR 信號就比熱平衡高 20,000 倍！**
 - $0.1 / 0.0000049 = 20,000$
- **MRS、EPI、fMRI、... 都不再困難**

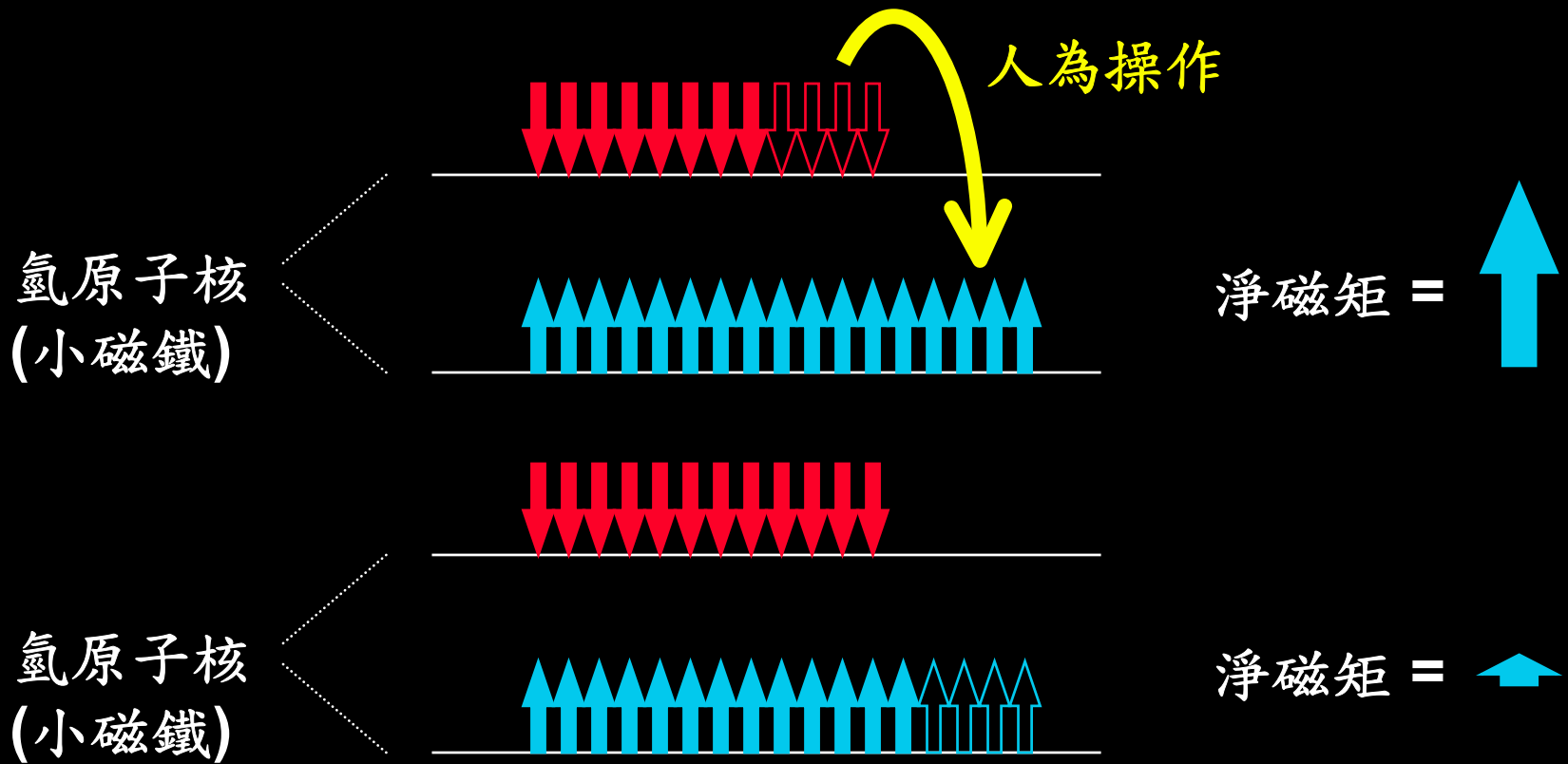
為什麼要談超高極化？

- 為了要高 **SNR**！
 - 尤其在水含量很少的部位，如 **pulmonary system**
- 而且並非藉由提高磁場而來
 - 有機會在低場下得到不錯的影像

但是您也立刻知道一件事

- 既然「波茲曼分佈」是指平衡狀態
- **Hyper-polarization** 就算能做到，也必然只是暫時的
- 時間一久，磁性便回復到熱平衡值

暫態 與 平衡狀態



時間一久，超高極化便消失了

如何做到超高極化？

- 那就沒那麼直接了
- 選擇鈍氣作為超高級化的核種
- 利用光抽運的方式達到超高極化
 - **Optical pumping**

如何做到超高極化？

- 經由碰撞，將鹼金族元素電子的超高極化，傳送到惰性氣體上
 - **Spin exchange via collision**
- 然後再吸入惰性氣體做 **MRI**

事情開始複雜了 ...

- **Optical pumping**
 - History, from 1960
 - **SEOP** (**S**pin **E**xchange **O**ptical **P**umping)
 - **MEOP** (**M**etastasis **E**xchange **O**ptical **P**umping)
- 需要用簡單的量子物理來解釋 ...

雖然是 **Advanced ...**

**I think I can safely say that nobody
understands quantum mechanics.**

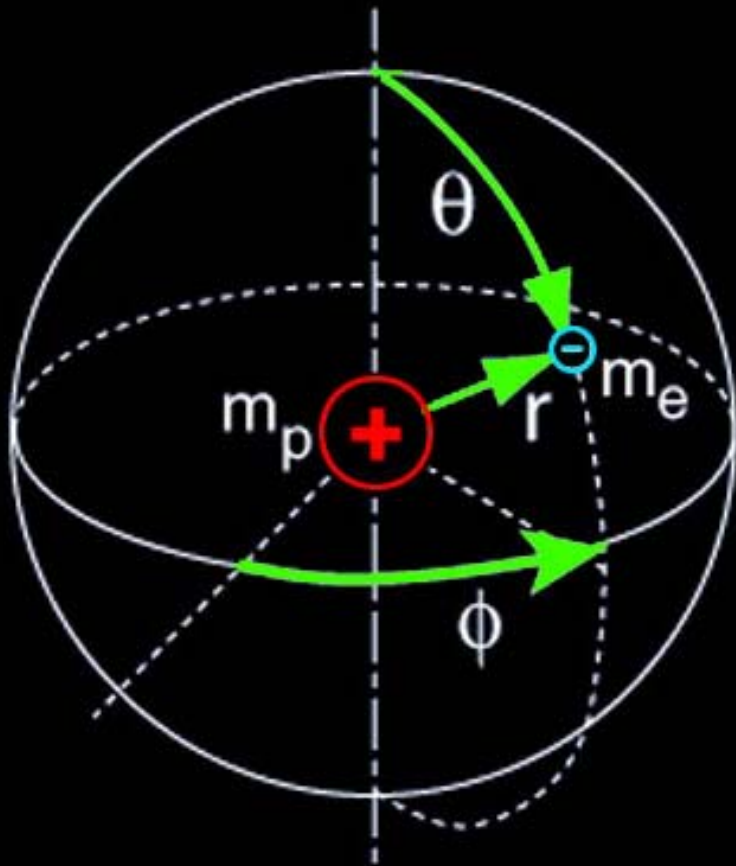
Richard Feynmann

我只能解釋我懂的一小部份...

先來複習大一普物

- 量子物理中描述原子核周圍電子雲
能量分布
 - 水丁格方程式(Schrodinger eq.)
 - 能量分布在固定的能階
(Quantized energy)

氫原子電子雲



Schrodinger Equation

$$\Psi(r, \theta, \phi) = R(r)P(\theta)F(\phi)$$

n

principal
quantum
number

l

orbital
quantum
number

m_l

magnetic
quantum
number

Quantum number

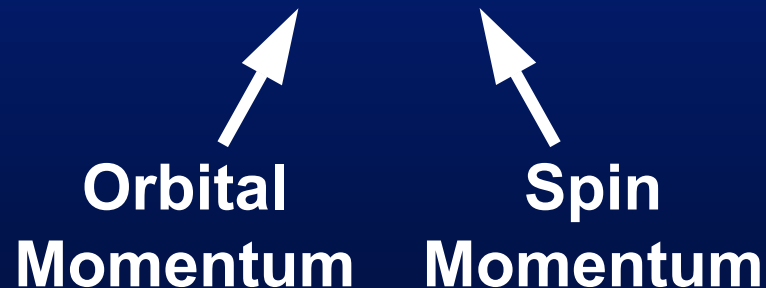
- **Principal quantum number**
 - $n = 1, 2, 3 \dots$
- **Orbital quantum number**
 - $l = 0, 1, 2, \dots, n-1$
- **Magnetic quantum number**
 - $m_l = -l, -l + 1, \dots, l$

Total Angular Momentum

- Spin quantum number
 - electron : $s = \pm \frac{1}{2}$
- Total momentum quantum number

$$- j = l + s = l \pm \frac{1}{2} \text{ (for electron)}$$

Orbital Momentum Spin Momentum



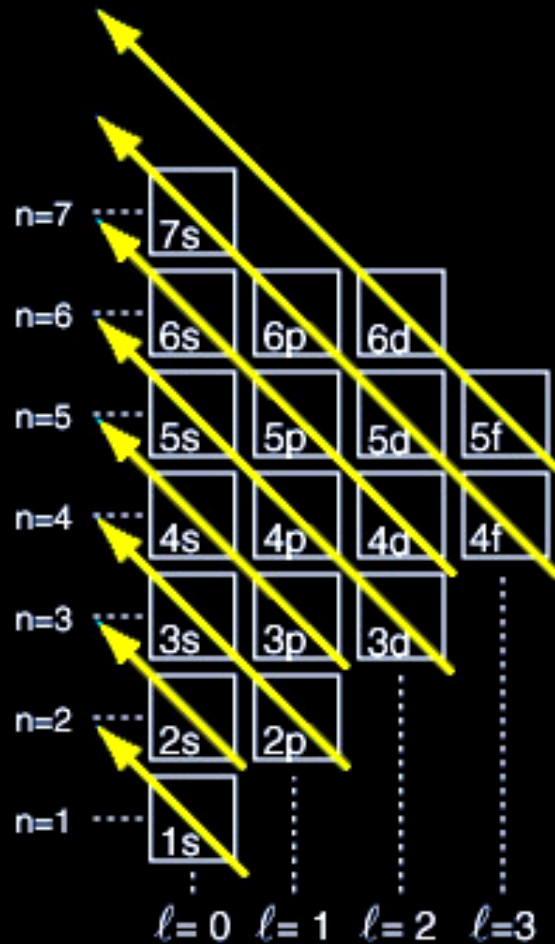
Nucleus spin number

- 原子核
 - 有質子和中子
 - 比較像是整個一起自旋
 - spin number: i

Nucleus spin number

- 決定 nucleus spin number
 - 質子(偶) + 中子(偶) $\rightarrow i = 0$
 - 質子(奇) + 中子(奇) $\rightarrow i = 1, 2 \dots$
 - [質子 + 中子](奇) $\rightarrow i = 1/2, 3/2, \dots$

填入電子軌域的順序



<i>state</i>	<i>n</i>	<i>l</i>	<i>m_l</i>	<i>s</i>	# <i>e</i>
1s	1	0	0	$\pm 1/2$	2
2s	2	0	0	$\pm 1/2$	2
2p	2	1	-1,0,1	$\pm 1/2$	6
3s	3	0	0	$\pm 1/2$	2
3p	3	1	-1,0,1	$\pm 1/2$	6
3d	3	2	-2,-1,0,1,2	$\pm 1/2$	10

由能量低的開始填

把元素週期表拿出來翻一翻吧

Periodic Table of the Elements

I	II	Transition Metals										III	IV	V	VI	VII	0
H ¹																	He ²
Li ³	Be ⁴											B ⁵	C ⁶	N ⁷	O ⁸	F ⁹	Ne ¹⁰
Na ¹¹	Mg ¹²	IIIB	IVB	VB	VIB	VII B	VIII B			IB	IIB	Al ¹³	Si ¹⁴	P ¹⁵	S ¹⁶	Cl ¹⁷	Ar ¹⁸
K ¹⁹	Ca ²⁰	Sc ²¹	Ti ²²	V ²³	Cr ²⁴	Mn ²⁵	Fe ²⁶	Co ²⁷	Ni ²⁸	Cu ²⁹	Zn ³⁰	Ga ³¹	Ge ³²	As ³³	Se ³⁴	Br ³⁵	Kr ³⁶
Rb ³⁷	Sr ³⁸	Y ³⁹	Zr ⁴⁰	Nb ⁴¹	Mo ⁴²	Tc ⁴³	Ru ⁴⁴	Rh ⁴⁵	Pd ⁴⁶	Ag ⁴⁷	Cd ⁴⁸	In ⁴⁹	Sn ⁵⁰	Sb ⁵¹	Te ⁵²	I ⁵³	Xe ⁵⁴
Cs ⁵⁵	Ba ⁵⁶	57-71	Hf ⁷²	Ta ⁷³	W ⁷⁴	Re ⁷⁵	Os ⁷⁶	Ir ⁷⁷	Pt ⁷⁸	Au ⁷⁹	Hg ⁸⁰	Tl ⁸¹	Pb ⁸²	Bi ⁸³	Po ⁸⁴	At ⁸⁵	Rn ⁸⁶
Fr ⁸⁷	Ra ⁸⁸	89-103	Rf ¹⁰⁴	Ha ¹⁰⁵	106	107	108	109									

Lanthanides

57	58	59	60	61	62	63	64	65	66	67	68	69	70	71
La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu

Actinides

89	90	91	92	93	94	95	96	97	98	99	100	101	102	103
Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr



Metal



Metalloid



Nonmetal

Rubidium (Rb)

Atomic Data

Atomic number	37	Melting point	312.04 K
Atomic mass	85.4678 u	Boiling point	961 K
Atomic radius	2.98 Å	Electron	(Kr)5s

Nuclear Data

Z	A	Atomic Mass (u)	Natural Abund.	Half-life	Spin
37	83	82.915143	...	86.2d	5/2
37	85	84.911794	0.72165	stable	5/2
37	87	86.909187	0.27835	stable	5/2

Helium (He)

Atomic Data

Atomic number	2	Melting point	0.95 K
Atomic mass	4.0026 u	Boiling point	4.215 K
Atomic radius	0.49 Å	Electron	1s ²

Nuclear Data

Z	A	Atomic Mass (u)	Natural Abund.	Half-life	Spin
2	3	3.01603	1.38x10 ⁻⁶	stable	1/2
2	4	4.00260	.999999	stable	0
2	6	6.018886	...	0.807s	0
2	8	8.03392	...	0.119s	0

Xenon (Xe)

Atomic Data

Atomic number	54	Melting point	161.36 K
Atomic mass	131.3 u	Boiling point	165.03 K
Atomic radius	1.24 Å	Electron	(Kr)4d ¹⁰ 5s ² 5p ⁶

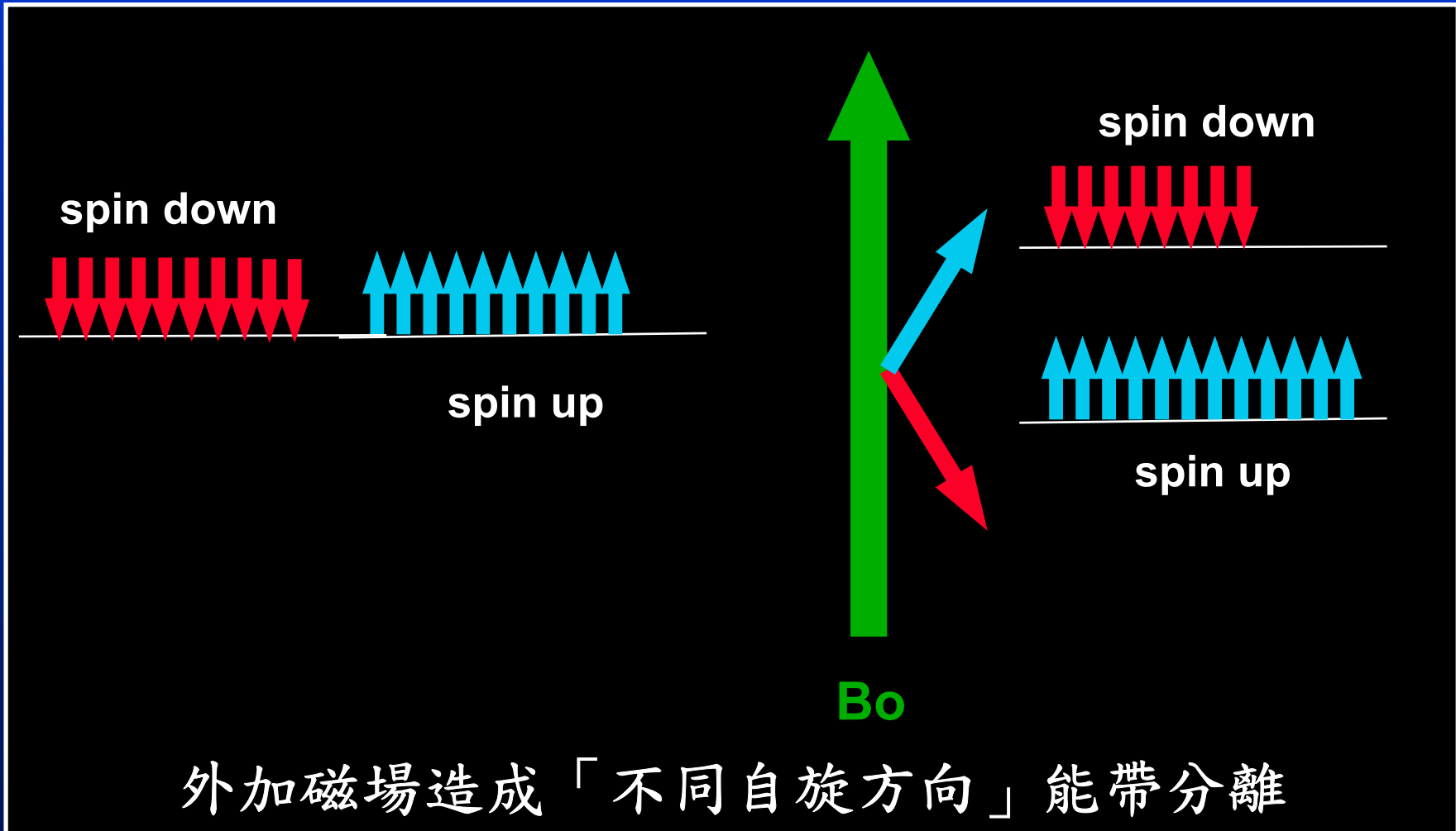
Xenon (Xe)

Z	A	Atomic Mass (u)	Natural Abund.	Half-life	Spin
54	124	123.905894	0.001	stable	0
54	126	125.904281	0.0009	stable	0
54	127	126.905182	...	36.2d	1/2
54	128	127.903531	0.0191	stable	0
54	129	128.904780	0.264	stable	1/2
54	130	129.903509	0.041	stable	0
54	131	130.905072	0.212	stable	3/2
54	132	131.904144	0.269	stable	0
54	133	132.905889	...	5.25d	3/2
54	134	133.905395	0.104	stable	0
54	136	135.907213	0.089	stable	0

Zeeman effect

- 不同自旋方向能量不同
- 磁場中, **spin energy split**
 - nucleus ($2i + 1$)
 - electron ($2s + 1$)

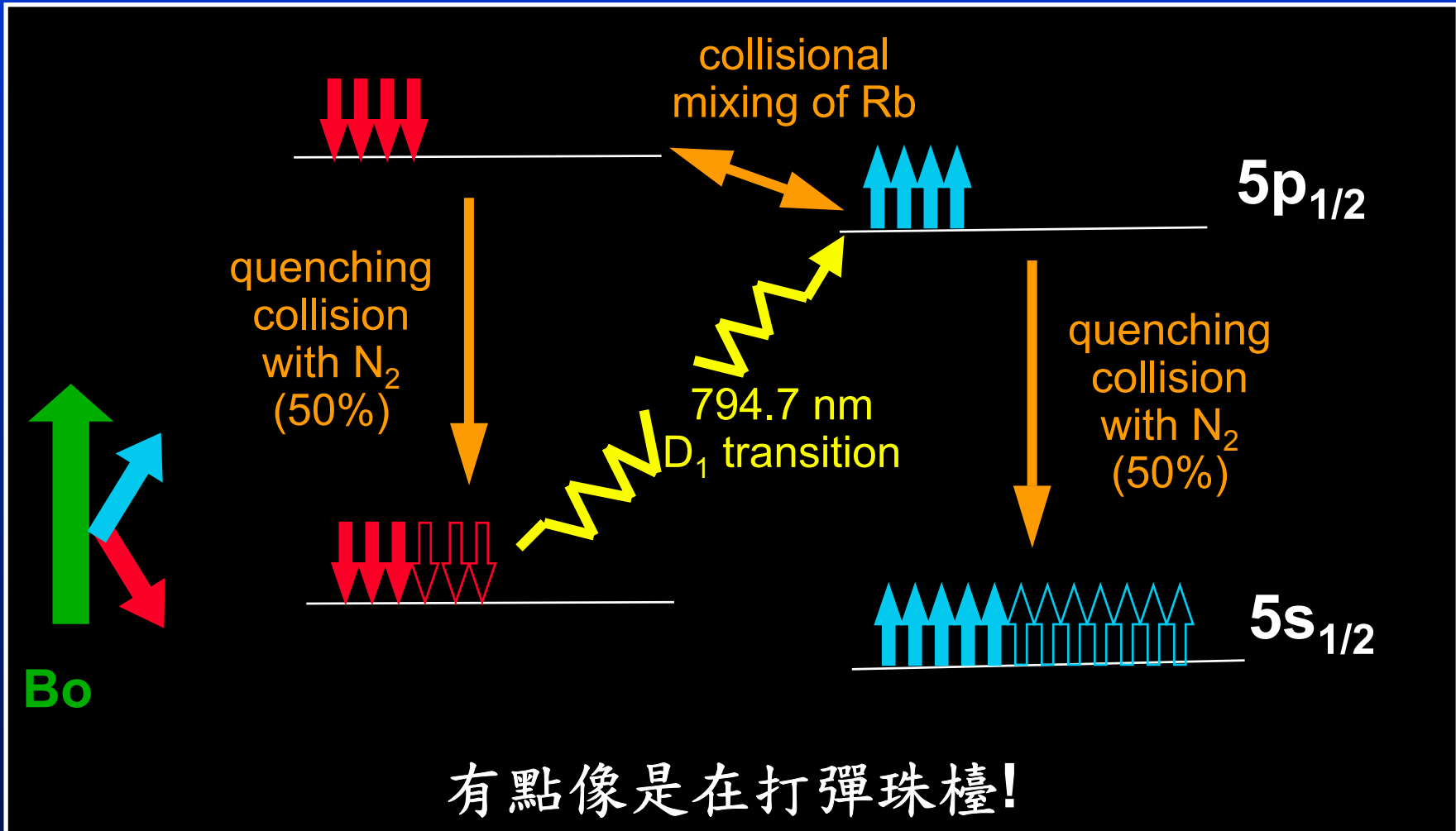
Zeeman effect



Optical pumping (SEOP)

- $S_{-1/2} D_1$ transition to $P_{1/2}$
- Collisional mixing of $P_{-1/2}$, $P_{1/2}$
- Quenching collision to ground state
- $S_{-1/2} D_1$ transition again

Optical Pumping (SEOP)



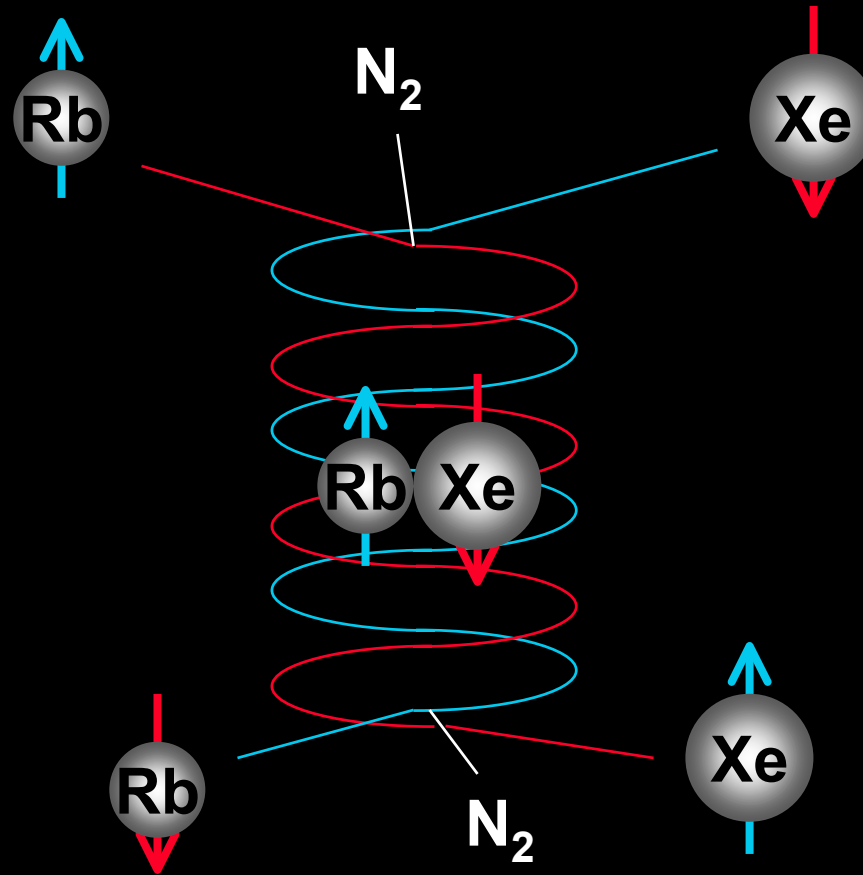
Optical pumping (SEOP)

- **Buffer gas (quenching gas)**
 - N_2 (or ^4He)
 - increase the tolerance of laser wavelength
 - avoid radiation trapping

Spin Exchange (SEOP)

- Rb electron spin exchange with noble gas nucleus spin

Collisional Spin Exchange 示意圖



經由碰撞把 Rb spin 轉移到 ¹²⁹Xe 上

MEOP

- **M**etastability **E**xchange **O**ptical **P**umping
- Directly pumping of ^3He electron
- Similar to SEOP, but much faster
(for ^3He : 數十秒 vs. 幾小時)

Spin Exchange (MEOP)

- **Electron pumped from 1s to 1p**
- **Depopulation (polarization) of 1s**
- **Collisional exchange of electron spin**
- **Self exchange of electron and nucleus spin**

MEOP

- **MEOP can occur only in low pressure (about 10 Torr)**
- **Need compression after pumping, technical difficulty**

(ps: 1atm = 760 Torr)

Wall Relaxation

- **Wall Relaxation (Surface Relaxation)**
 - **T1 relaxation near cell wall**
 - **Affects more on SEOP than MEOP**

^3He vs. ^{129}Xe

(SEOP)	^3He	^{129}Xe
Pumping time	hrs	mins
Temperature	170-200 °C	95 °C
Cell Pressure	8-10 atm	2-3 atm
Wall Relaxation	tens of hrs	hrs
Gas Cost	100 USD/L	20 USD/L 700 USD/L
Gyromagnetic Ratio (MHzT ⁻¹)	32.43	11.78
Biological Effect	Safe	Anesthetic

3He vs. 129Xe

	3He	129Xe
T1 (Pure Gas)	744 hrs	55 hrs
O ₂ relaxivity time k (S ⁻¹ Pa ⁻¹)	3.85 x 10 ⁻⁶	3.73 x 10 ⁻⁶
Self-diffusion coefficient (cm ² s ⁻¹)	2.05	0.061
Blood Solubility (L)	0.0085	0.17

其它超高極化方法

- **Brute force!**
 - 正在研究中,未必實用
 - 利用暴力法打破波茲曼平衡
 - 極低溫($T < 10\text{mK}$)
 - 高磁場($B_0 \geq 10\text{T}$)

人口差異符合「波茲曼分佈定理」

$$\frac{\text{spin up 人口數}}{\text{spin down 人口數}} = e^{\frac{\Delta E}{k T}}$$

$\Delta E = \gamma h \mathbf{B}_0$ (h : 浦朗克常數)

$k =$ 波茲曼常數

$T =$ 絕對溫度 (攝氏溫度 + 273)

$$= 1.0000049$$

除了主磁場之外，沒有一項可以更動

終於準備好要 imaging 了

- 什麼，軟硬體都需要調整？

Hardware Requirement

- **Broadband RF RX/TX**
- **Special tuned RX/TX coil**
 - ^3He : $\gamma = 32.43 \text{ MHz/T}$
 - ^{129}Xe : $\gamma = 11.78 \text{ MHz/T}$



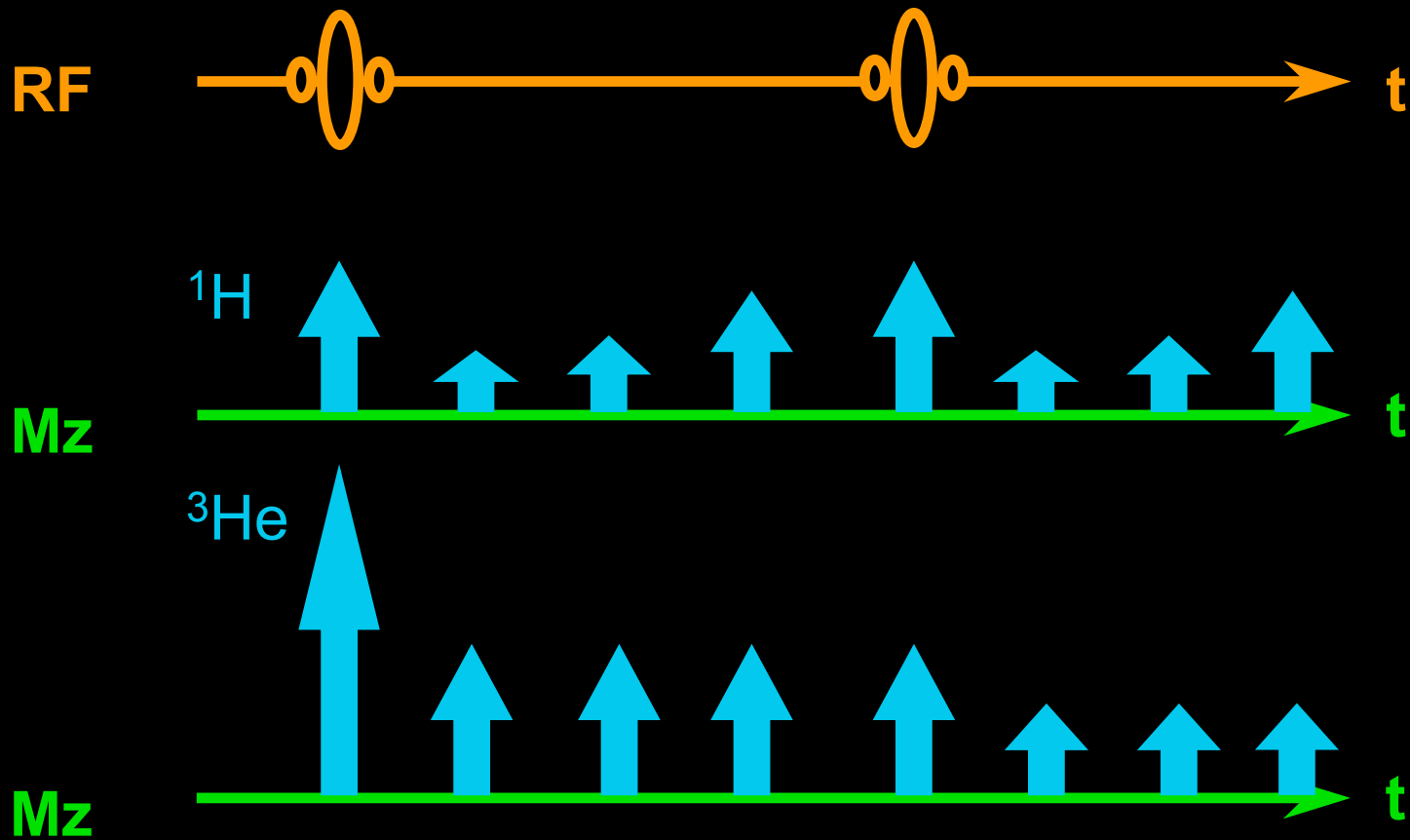
Nonequilibrium Imaging

- 注意, 磁矩不再源自於主磁場!
- 波茲曼平衡時磁矩反而接近零?
 - 上下人口差異只有幾個 ppm

Nonequilibrium Imaging

- 不會看到「以往的」T1 recovery
 - TR 可以儘量小
 - steady depletion of M_z
- 傳統 90° RF sequence 幾乎都不能用!
 - 磁矩就這麼多，一次用完就沒了

Compare with ^1H MRI



Nonequilibrium Imaging

- **Low flip angle**
 - 一次用掉一點磁矩
- **Fast acquisition**
 - EPI, Projection Reconstruction (PR),
RARE

In-vivo T1 relaxation

- **O₂ (paramagnetic) induced relaxation**
– $1/T_1 = k p_{O_2} \sim \text{sec}^{-1}$
- **in-vivo wall relaxation**
– T_1 10^2 sec order

O_2 Sensitive T_1

- T_1 largely reduced (to sec)
- T_1 in-vivo is time dependent
- Potential in regional p_{O_2} map
 - directly observe O_2 exchange!

T2 Relaxation

- Susceptibility dominate T_2^*
- ^3He in human lung
 - $T_2 = 8.9 \text{ sec (0.1T)}$
 - $T_2^* = 9.4 \text{ ms (1.5T)}$

Diffusion Characteristic

- **Much larger diffusion coefficient
(10^5 larger than water)**
- **Gas interaction**
- **Airspace size**
 - **of clinical potential**

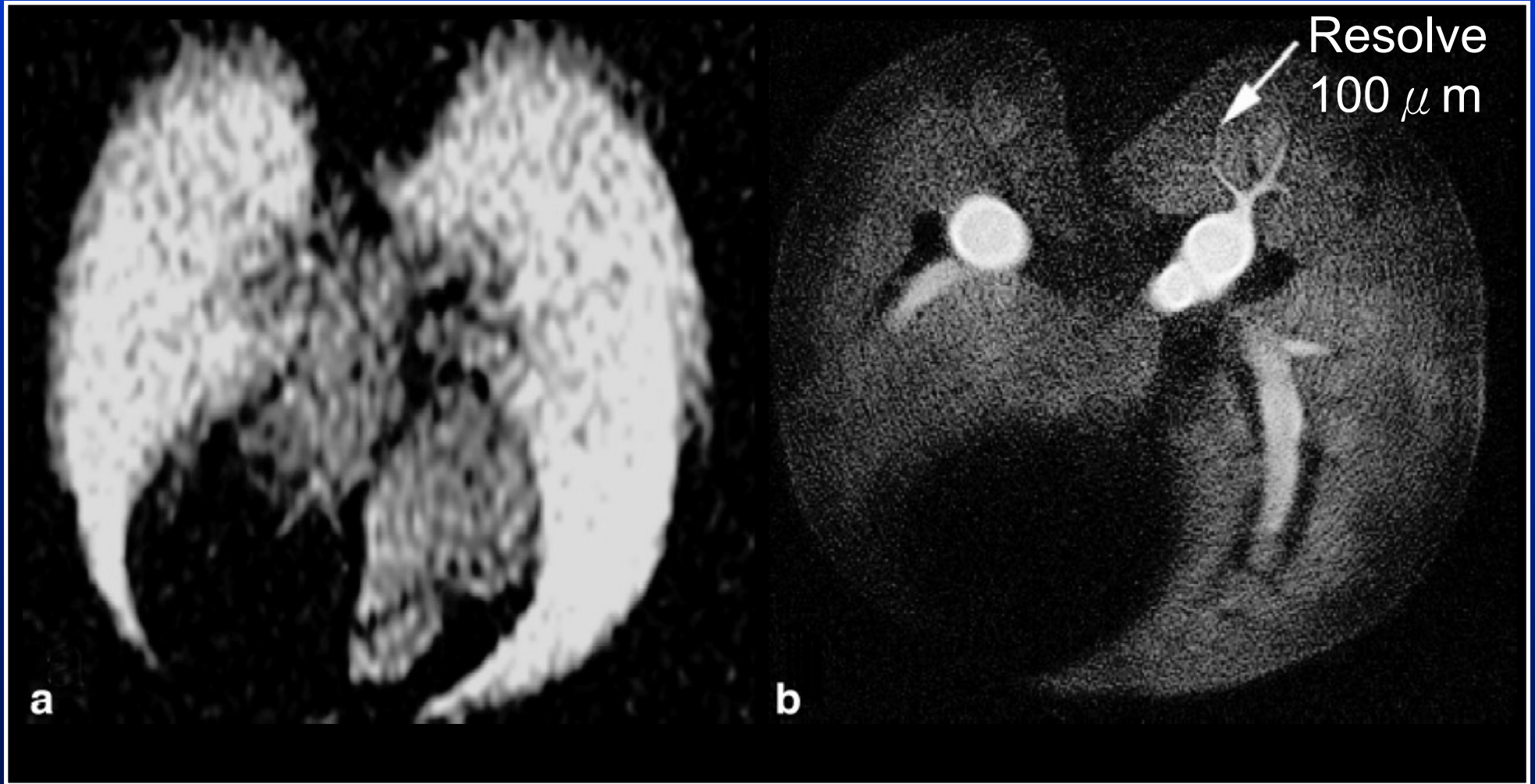
Ventilation & Perfusion

- **V/Q imaging possible**
 - **^3He density image**
 - **Supine or prone**
 - **perfusion bolus**

Other application

- **Intravascular delivery of HP gas**
 - **^{133}Xe in nuclear medicine**
 - **^{129}Xe /saline, lipid emulsion,
 ^3H emicrobubbles**

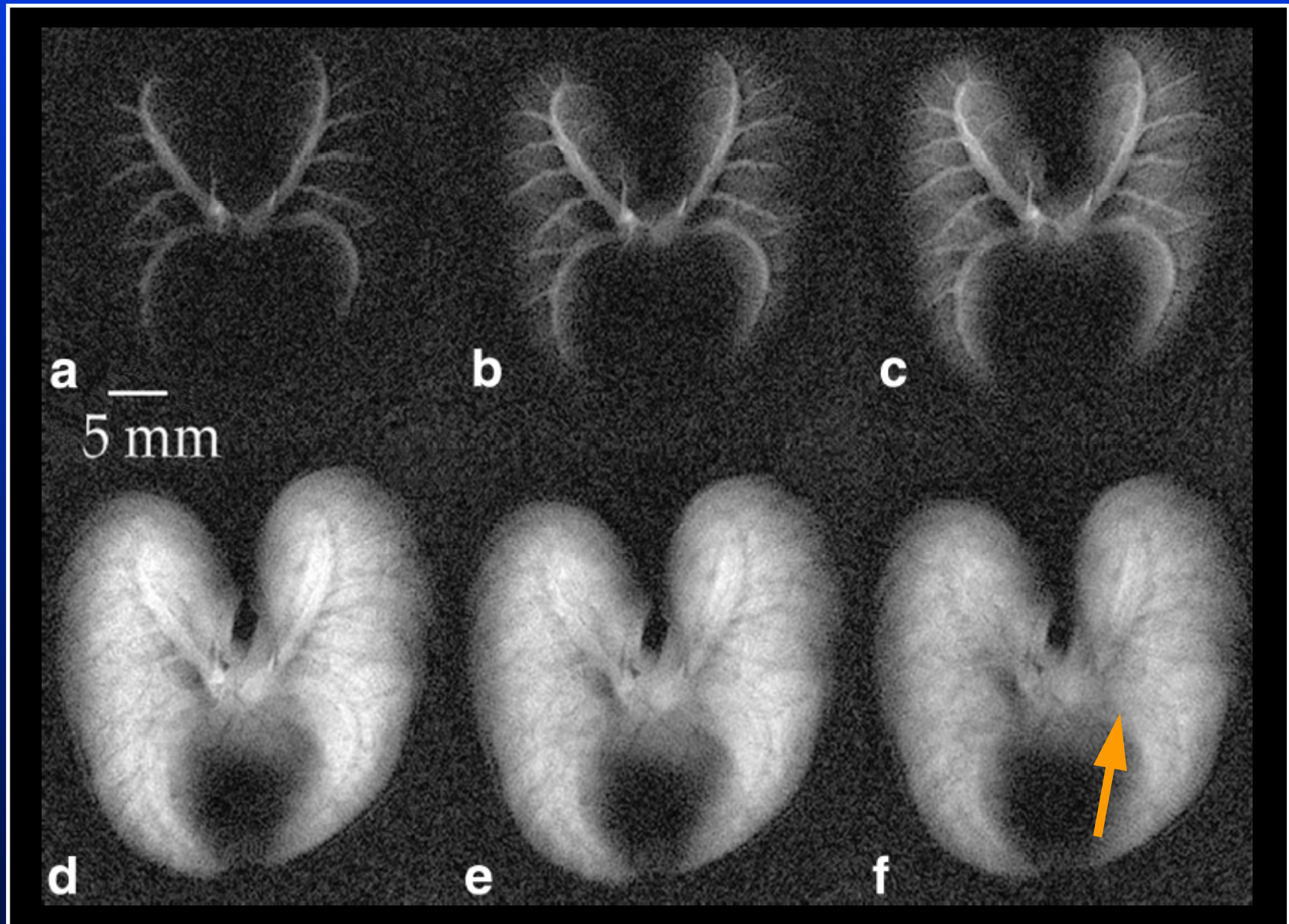
Image Development



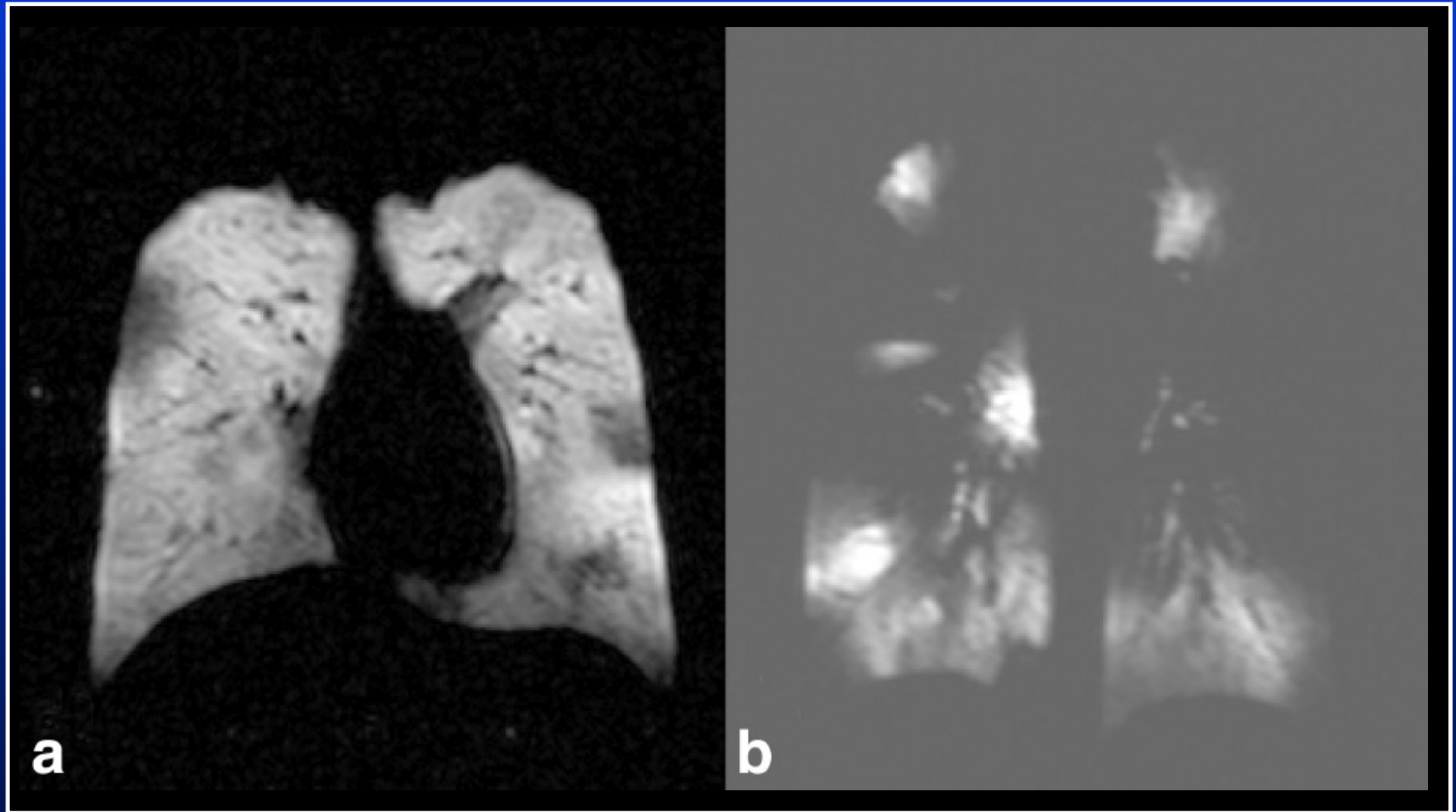
1995 / $280 \times 560 \times 10^4 \mu\text{m}$

2002 / $98 \times 98 \times 468 \mu\text{m}$

Dynamic Image



Cystic Fibrosis



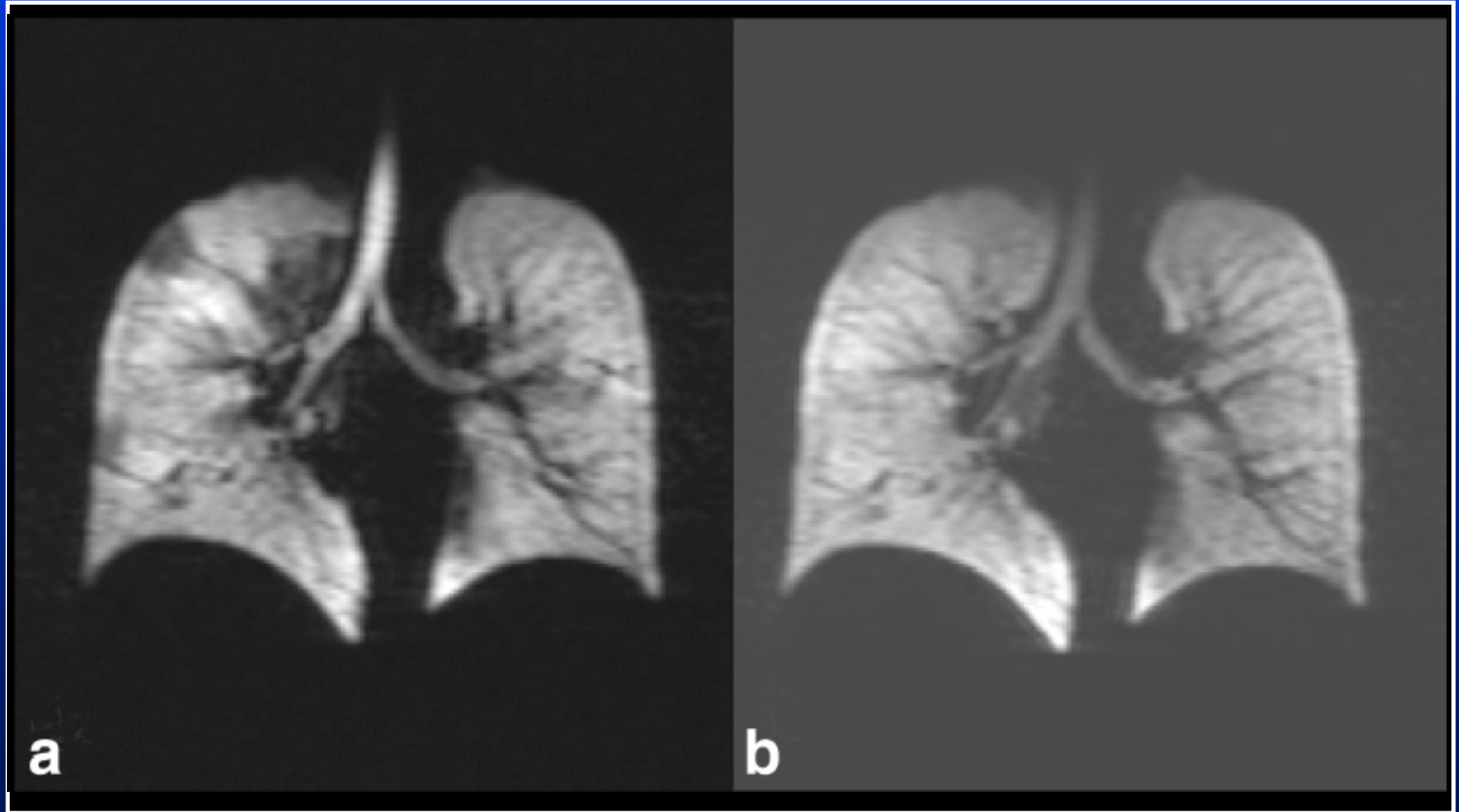
a

$FEV_1 = 91\%$

b

$FEV_1 = 41\%$

Asthma



$FEV_1 = 100\%$

Bronchodilator inhaled

Conclusion

- **HP noble gas is a matured**
- **Research going on**
 - **large quantity production**
 - **Clinical pulmonary application**
 - **In-vivo wall, T_1 , T_2 relaxation**
 - **Intravascular delivery ...**

終於結束了...

問問題吧!

雖然我也不太懂...😊