

MR Physics for fMRI: From Quantum Spin to Brain Function

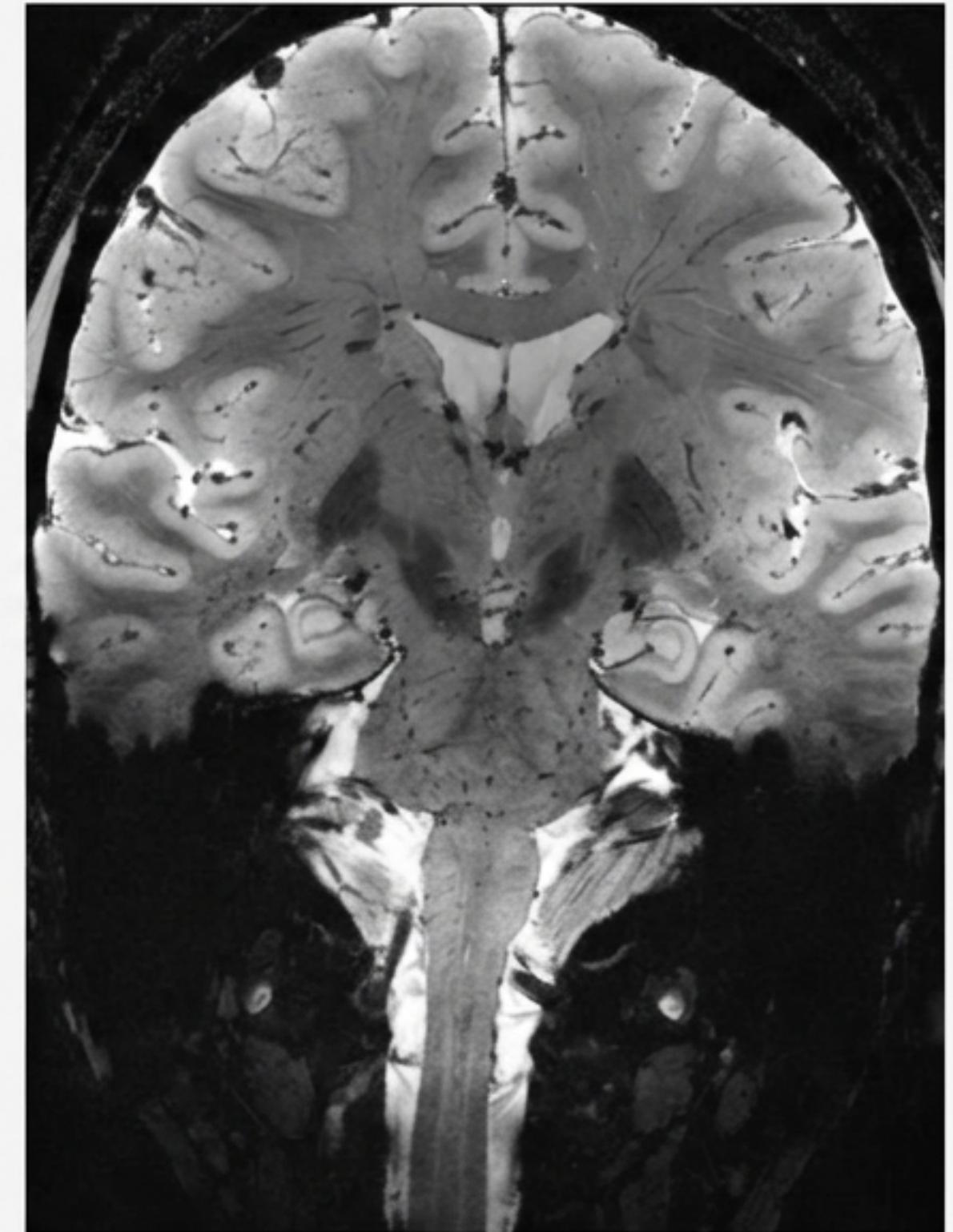
Lawrence L. Wald | HST.583 (Physics Lecture #1)



Massachusetts
Institute of
Technology

Disclosures

- Equity, consulting, SAB: Neuro42 Inc.
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- Equity: InnoCerebra, Reveal Pharma
- Equity: I Technical Fleem
- Research support: Siemens Healthcare
- Will discuss non-FDA approved devices



7T T2* image

Our Journey Today

MR Physics Lecture 1:

- Where the MR signal comes from
- T2*, T2, and T1 contrast mechanisms
- The basics of BOLD contrast

MR Physics Lecture 2:

- Encoding the image

MR Physics Lecture 3:

- Advanced topics: Fast imaging, artifacts, and alternatives to BOLD

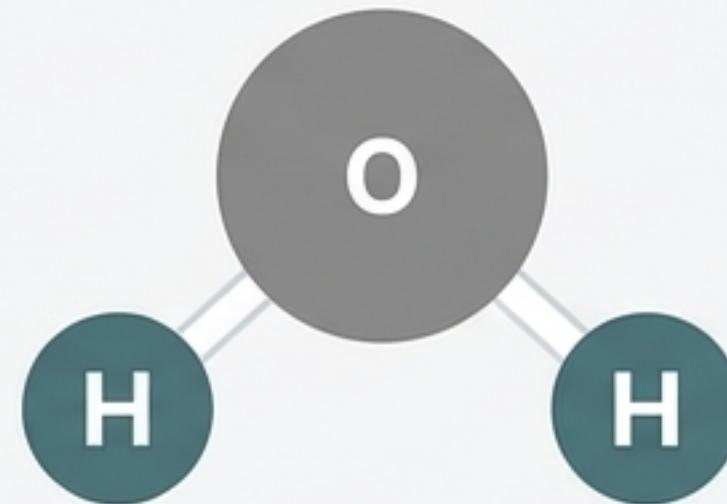


I wonder if the guy
on the stretcher
is okay...

The Three Pillars of Nuclear Magnetic Resonance

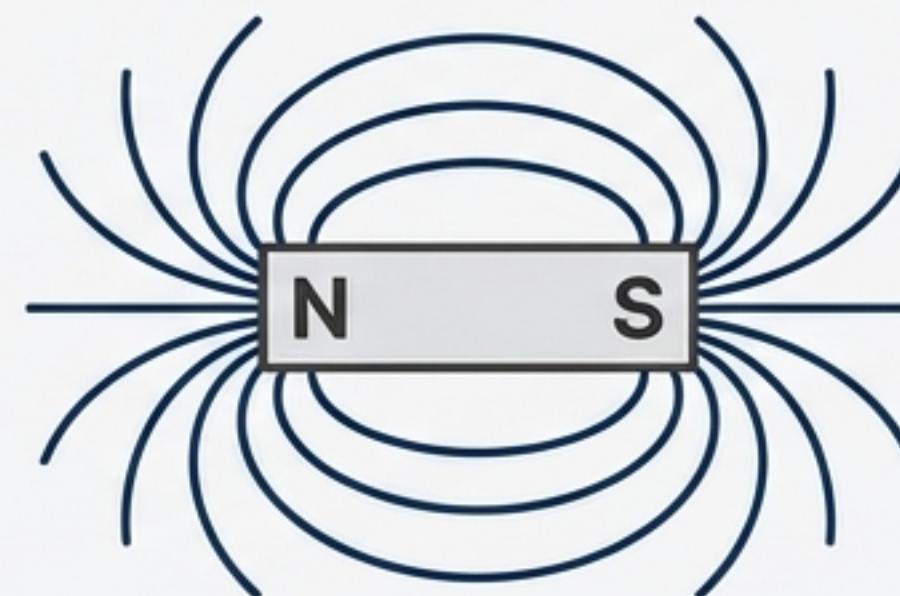
NUCLEAR

We are interested in the nucleus of the hydrogen atom—a single proton.



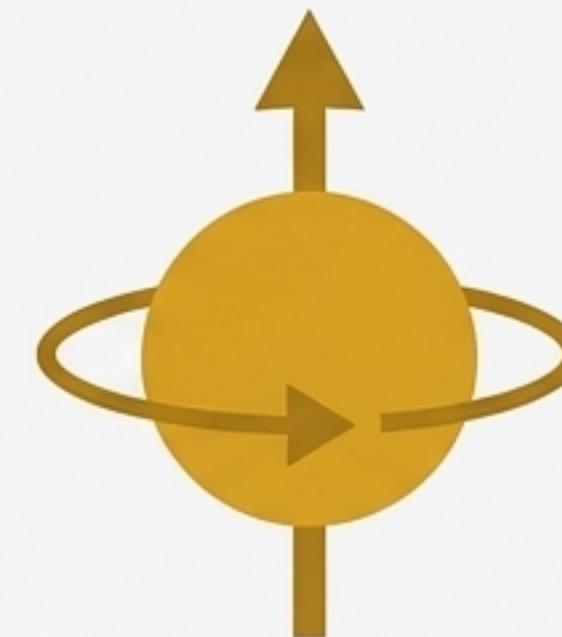
MAGNETIC

These protons act like tiny magnets and are placed in a powerful external magnetic field.



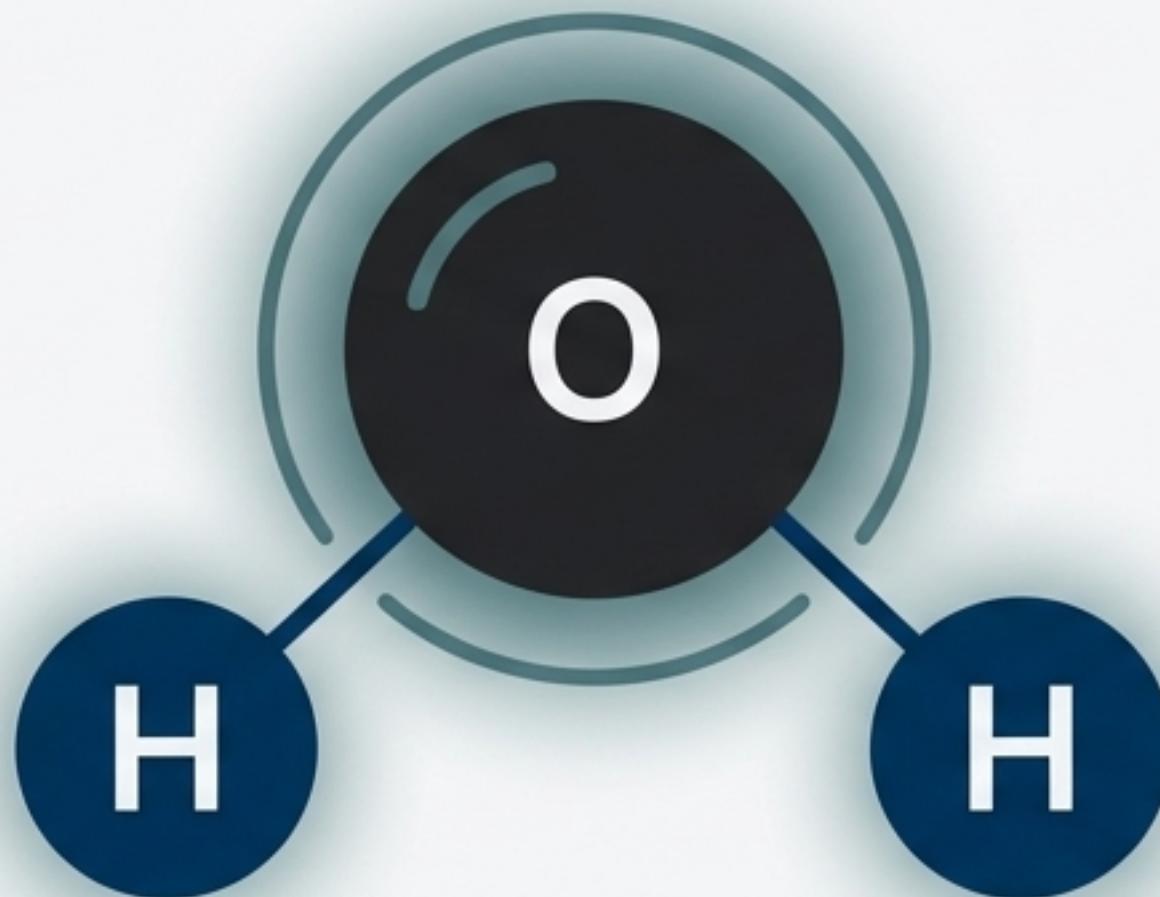
RESONANCE

We use a radio wave at a specific frequency to transfer energy to the protons.



At its heart, NMR is what happens when you take a glass of water, put it in a big magnet, and probe it with radio waves.

The Signal Originates from Water's Protons



- **Electron Magnetism:** In water, electron spins are paired, resulting in weak diamagnetism. This is not our signal source.
- **Nuclear Magnetism of Oxygen:** O^{16} has an even number of protons and neutrons, resulting in zero magnetic moment. It is invisible to us.
- **Nuclear Magnetism of Hydrogen:** The H^1 nucleus (a single proton) has a quantum property called 'spin $\frac{1}{2}$ ', which gives it a **magnetic moment**.

Conclusion: Water's magnetism, for our purposes, comes **entirely from its hydrogen protons**. These are the source of the MR signal.

From Trillions of Protons to One Net Magnetization Vector

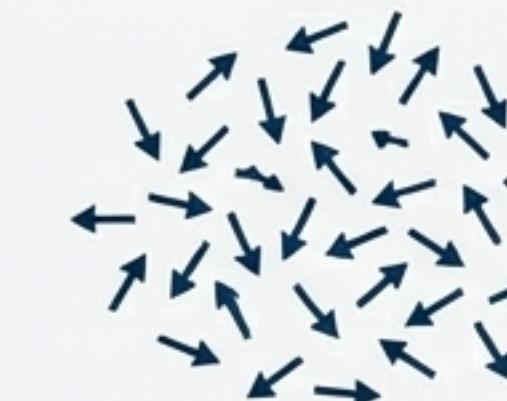
Microscopic View

A single proton is a **magnetic dipole**, like a tiny current loop or bar magnet.



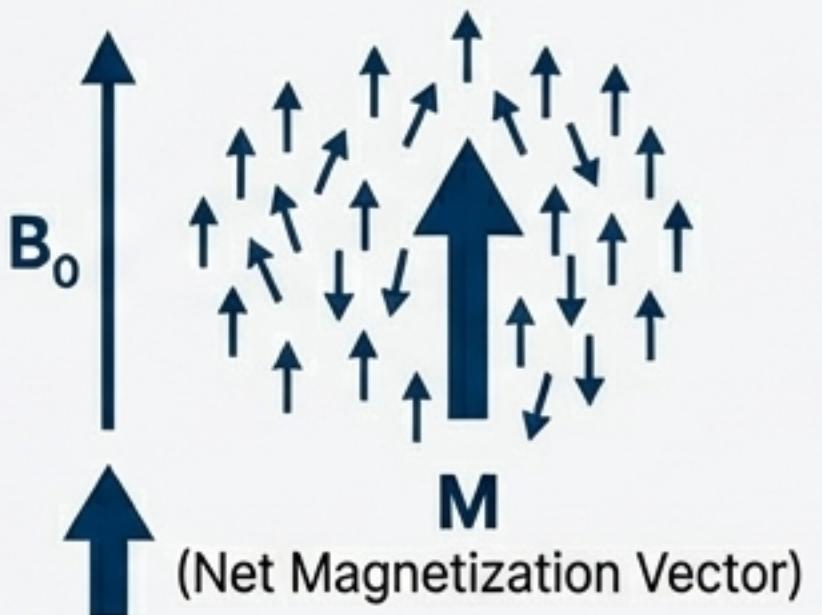
Macroscopic View

Without External Field ($B_0 = 0$)



Random orientations.
Net vector sum = 0

With External Field (B_0)



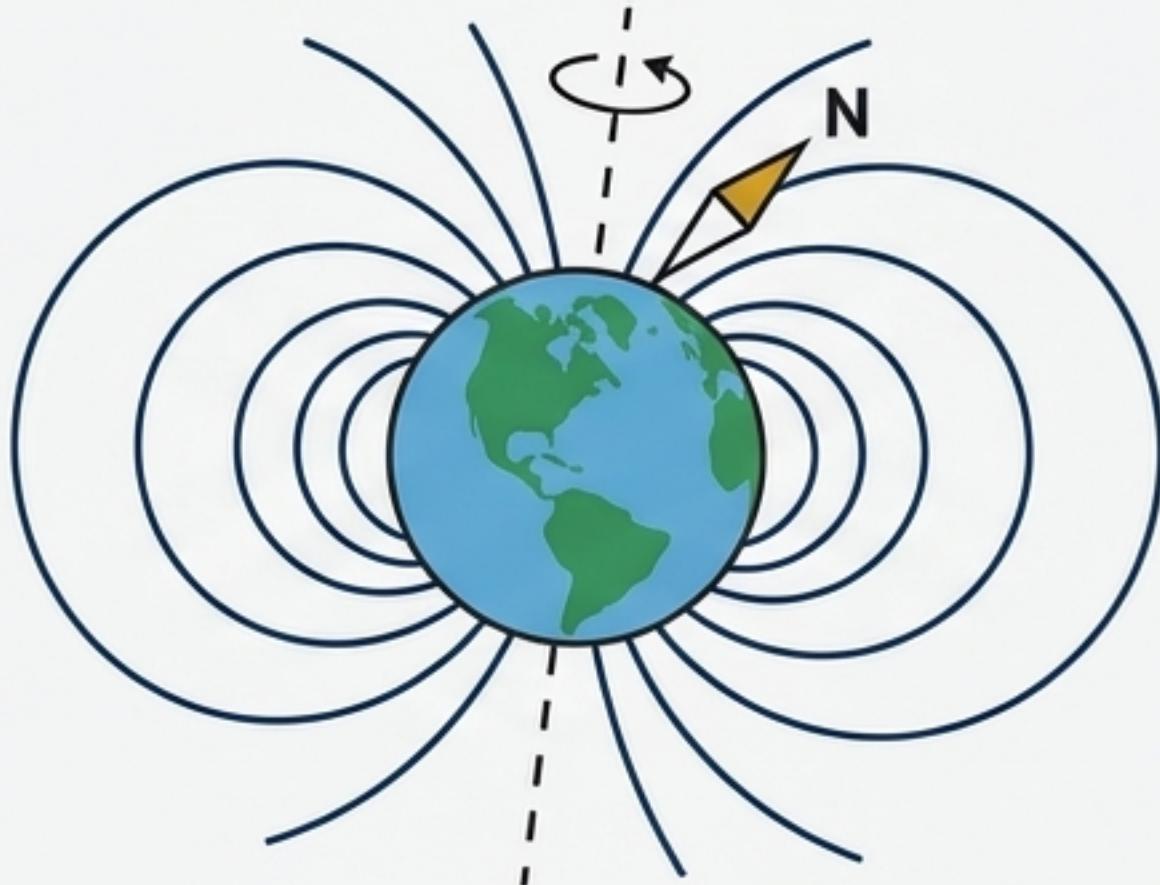
- In a voxel of tissue (e.g., 1 mm^3), there are $\sim 10^{18}$ protons.
- In a strong magnetic field (B_0), a tiny fraction achieve a net alignment.
- This creates a **macroscopic magnetization vector, M** .

$$\mathbf{M} = \sum \mathbf{m} \quad (\text{The net vector } \mathbf{M} \text{ is the sum of all individual magnetic moment vectors, } \mathbf{m}).$$

Takeaway: We manipulate and observe this macroscopic ensemble vector, \mathbf{M} .

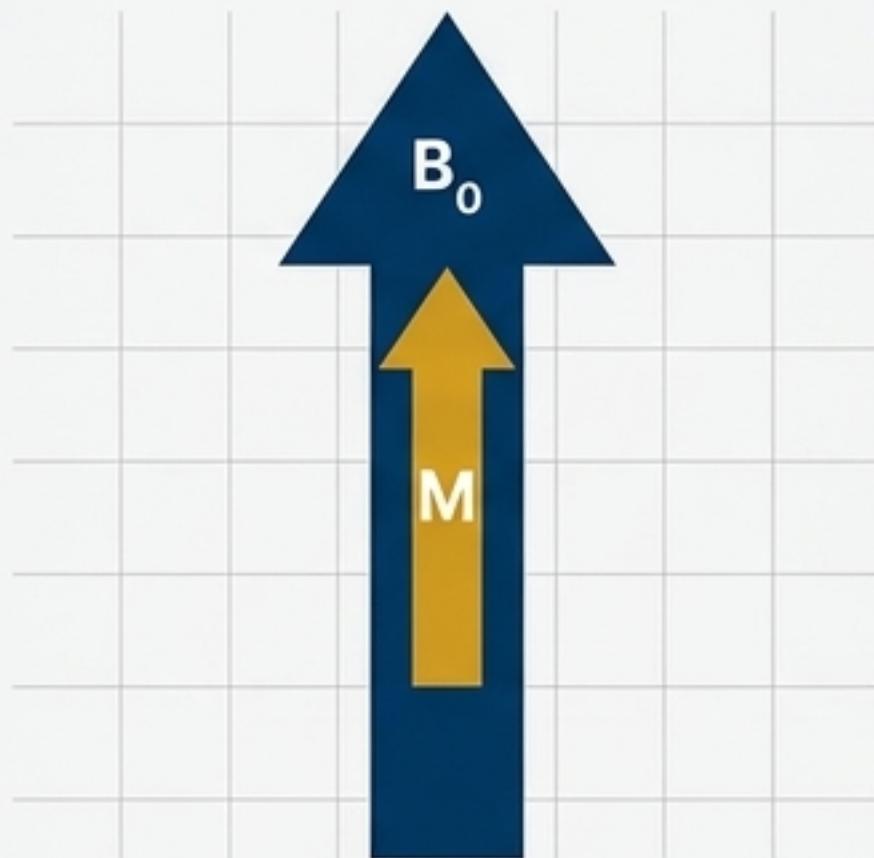
At Equilibrium, Magnetization Aligns with the Field

The Compass Analogy



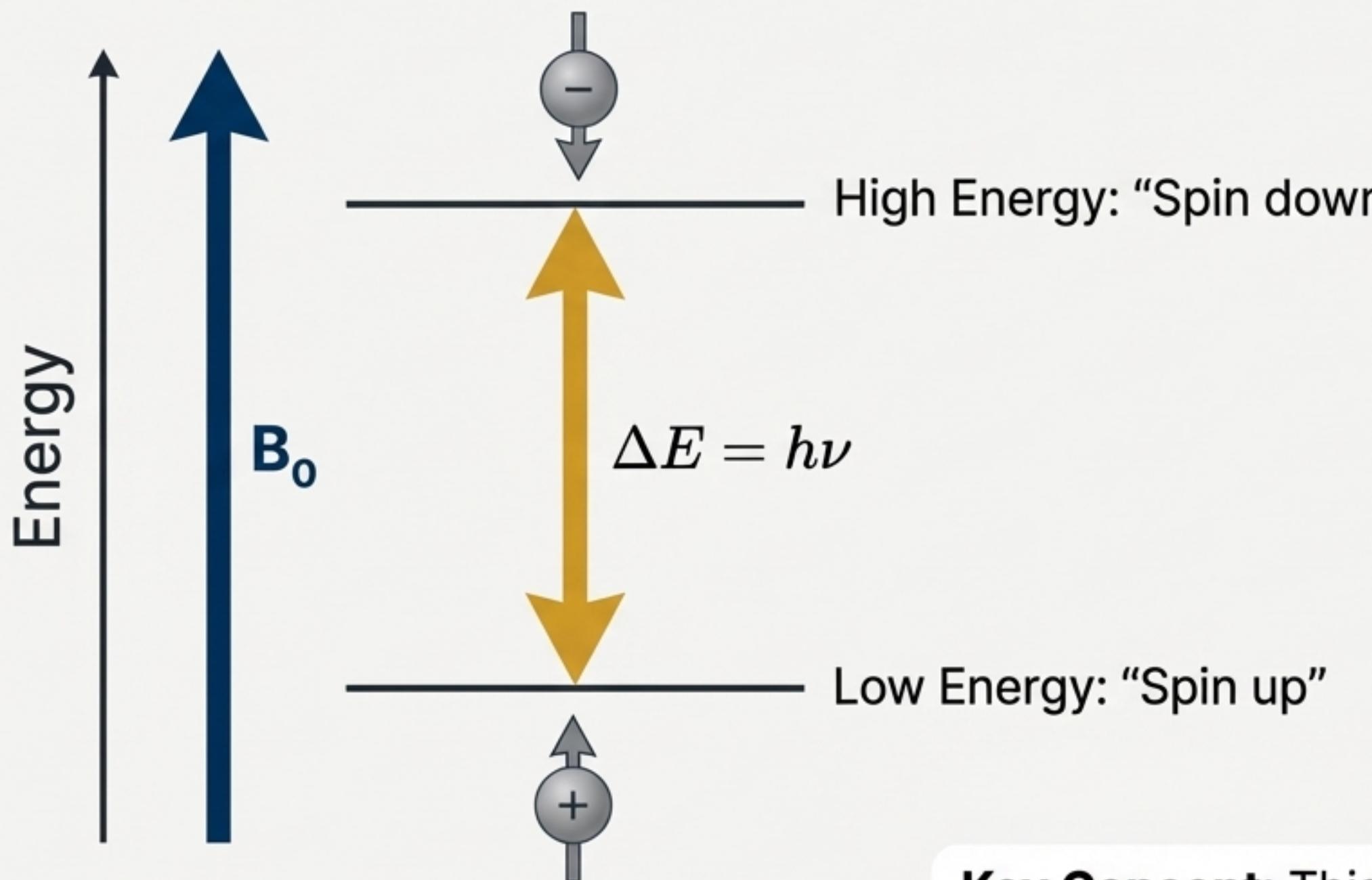
- A compass needle is a small magnet in the Earth's magnetic field.
- It naturally aligns with the field, pointing North.
- This is its **equilibrium**, or lowest potential energy, state. It takes energy to push it away from North.

The MRI Analogy



- The Net Magnetization (M) in the strong scanner field (B_0) does the same.
- At equilibrium, M is aligned with B_0 (along the z-axis) and is stationary.

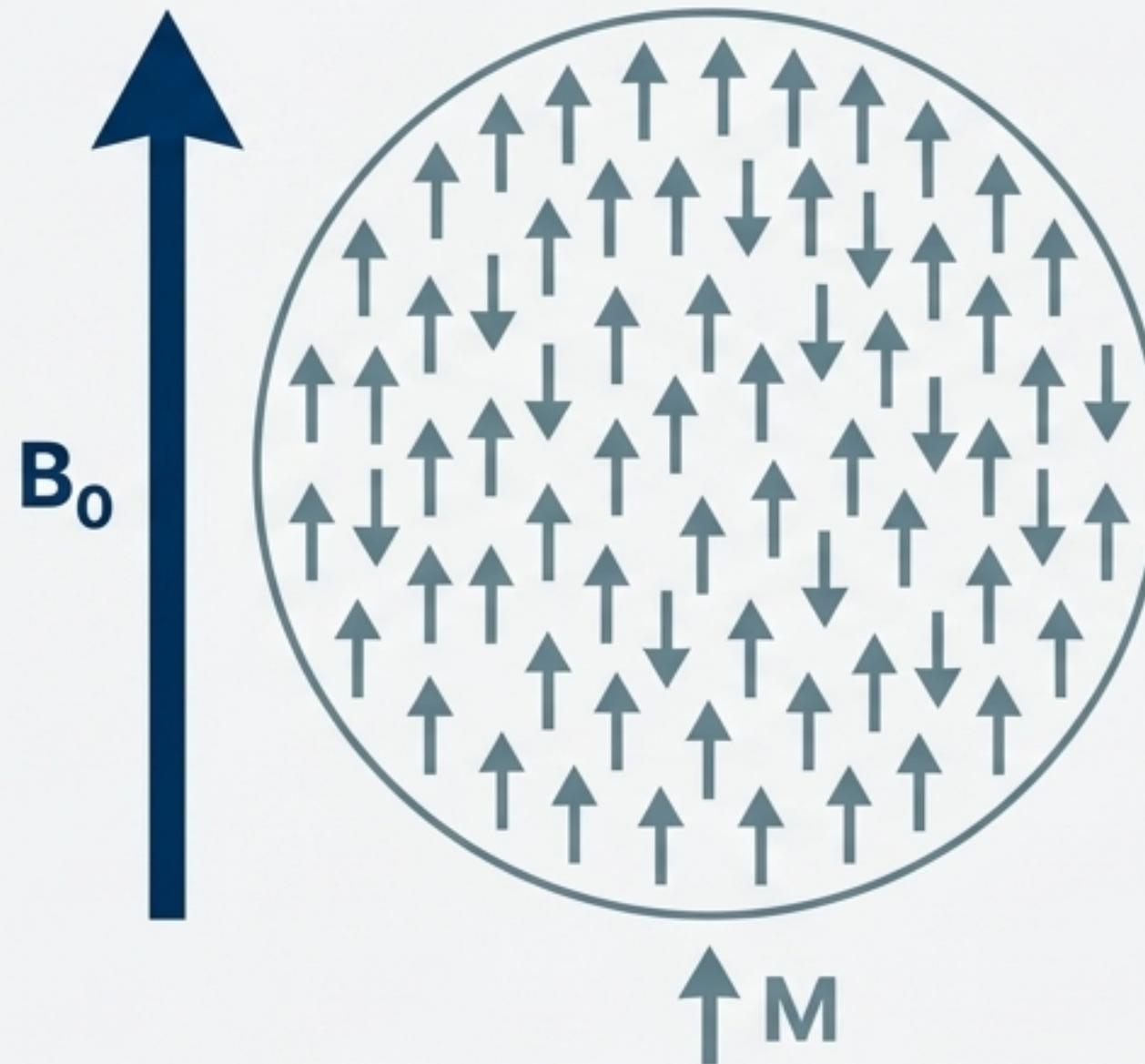
The Quantum Twist: Only Two Allowed Energy States



- Unlike a compass, a spin- $\frac{1}{2}$ particle in a magnetic field can only occupy one of **two** distinct energy states.
- The energy difference (ΔE) between these states is directly proportional to the magnetic field strength, B_0 . The stronger the field, the larger the energy gap.

Key Concept: This quantization of energy is the foundation of the “Resonance” phenomenon.

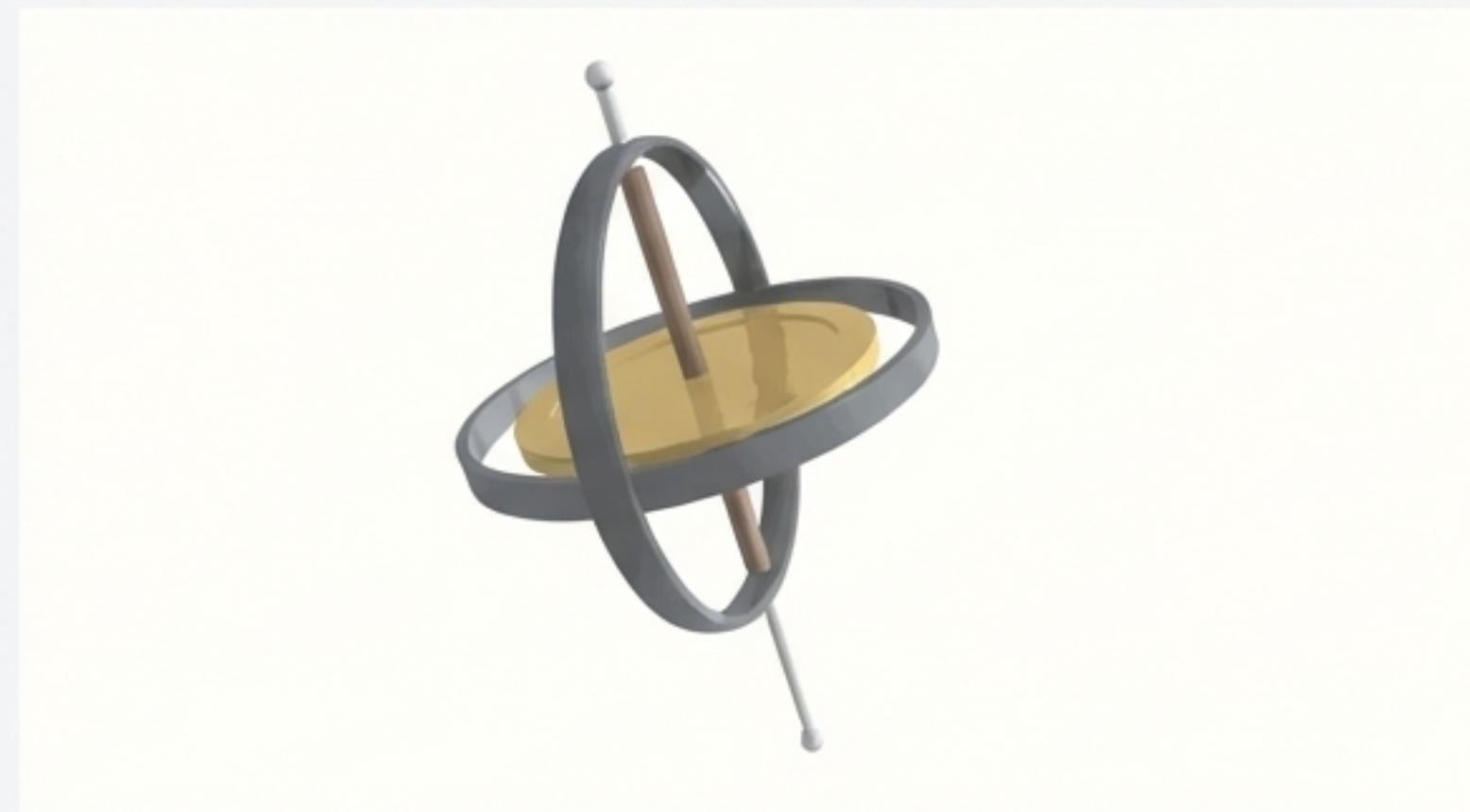
Thermal Energy and the Origin of Net Magnetization



- At body temperature, thermal energy (kT) is constantly jostling protons, causing them to jump between the 'spin up' and 'spin down' states.
- However, there is always a slight excess population in the lower energy 'spin up' state, governed by the **Boltzmann distribution**.
- This population difference is tiny: at 3T, the excess is only about **10 parts per million**.
- This small surplus of 'spin up' protons is what creates our net longitudinal magnetization, M .

Takeaway: Stronger magnets increase the energy gap (ΔE), which increases the population difference and thus the available signal.

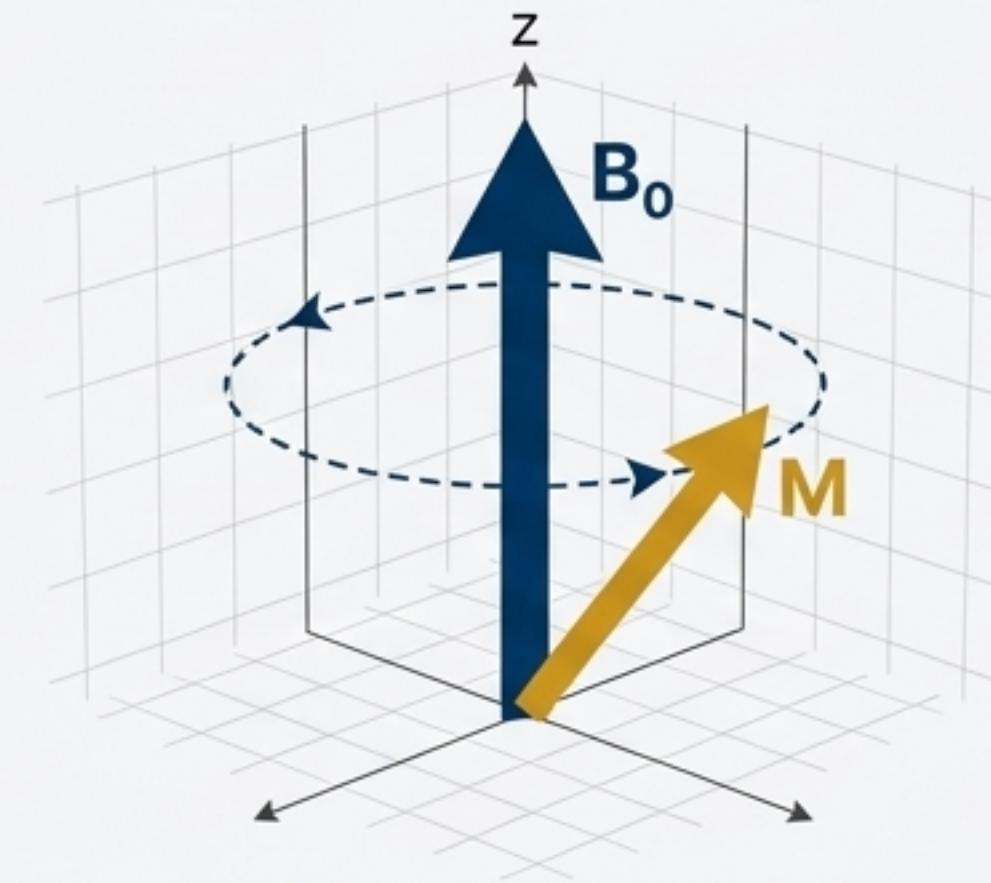
The Larmor Dance: Protons Precess Like Gyroscopes



The Physics:

The animation shows a gyroscope precessing like a gyroscope.

- A particle with angular momentum (spin) in a magnetic field experiences a torque.
- This torque does not cause simple alignment; it causes **precession**. The magnetization vector (**M**) sweeps out a cone shape around the B_0 axis.



The Equation:

The frequency of this precession is the **Larmor Frequency**, and it is the most important equation in MRI:

$$\nu = \gamma B_0$$

ν : Larmor Frequency (MHz)

γ : Gyromagnetic Ratio (a constant, 42.58 MHz/Tesla for protons)

B_0 : Magnetic Field Strength (Tesla)

Key Insight: The precession frequency is directly and precisely proportional to the magnetic field strength.

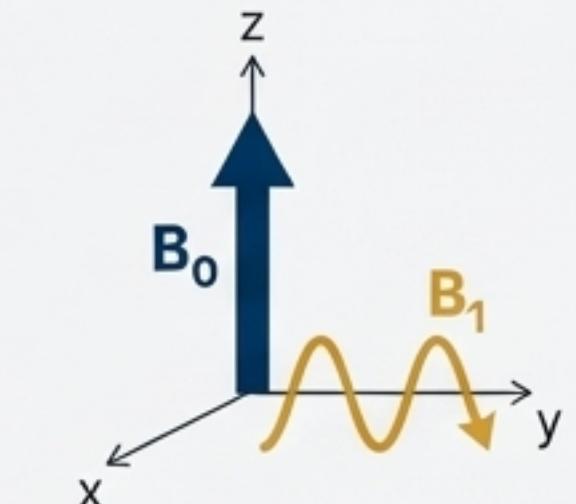
Excitation Through Resonance

The Goal:

To detect a signal, we must tip the magnetization **M** away from the z-axis.

The Method:

- We apply a second, weaker magnetic field, **B₁**, perpendicular to **B₀**.
- **B₁** is an **oscillating** magnetic field, applied as a **radiofrequency (RF) pulse**.



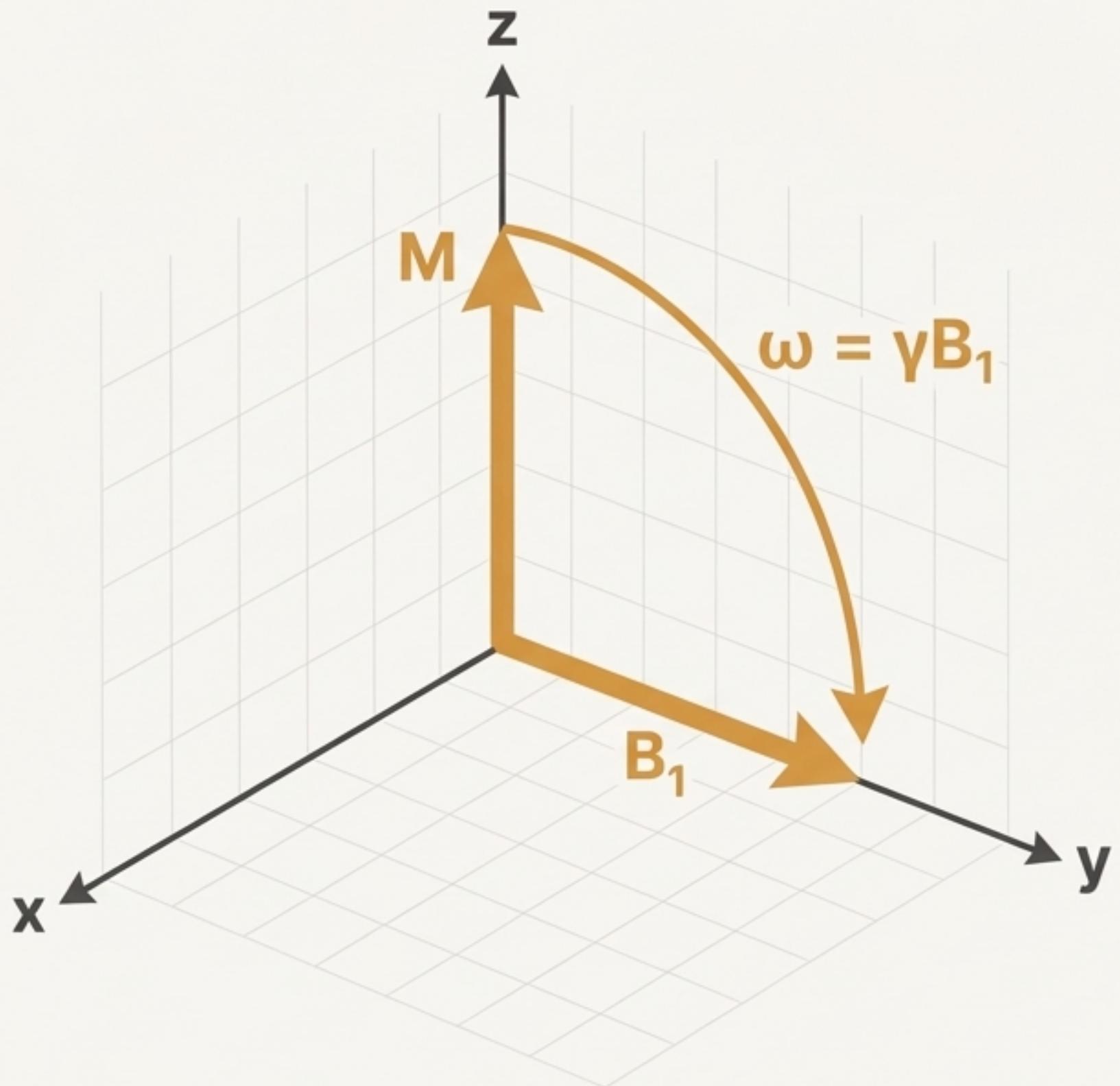
The Principle of Resonance:

- To be effective, the **B₁** field must **oscillate at exactly the Larmor frequency** of the protons.
- Like pushing a swing: if your **pushes match the natural frequency**, even small pushes **build up a large motion**. At any other frequency, your effort is wasted.

Conclusion:

When $\nu_{\text{RF}} = \nu_{\text{Larmor}}$, we efficiently transfer energy to the spins and tip **M away from the z-axis.**

Controlling the Tip Angle



A Simpler View: The Rotating Frame

- To simplify the complex spiraling motion, we view the system from a frame of reference that is rotating at the Larmor frequency.
- In this frame, the B_1 pulse causes **M** to perform a simple rotation around the B_1 axis.

Controlling the Rotation

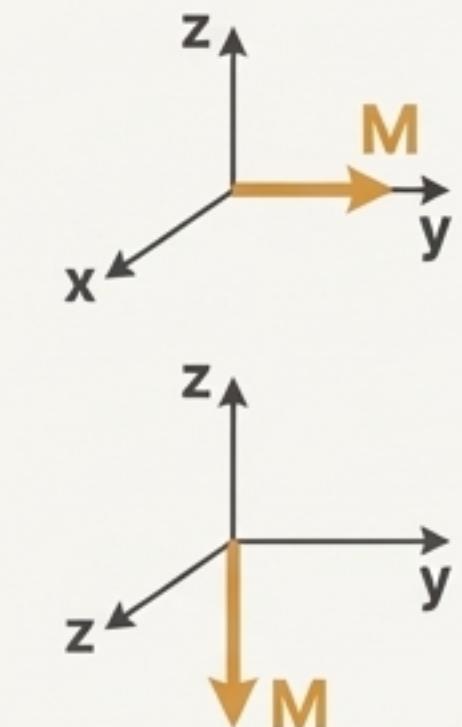
- By controlling the **duration** and **strength** of the B_1 pulse, we control the **tip angle**.

90° Pulse:

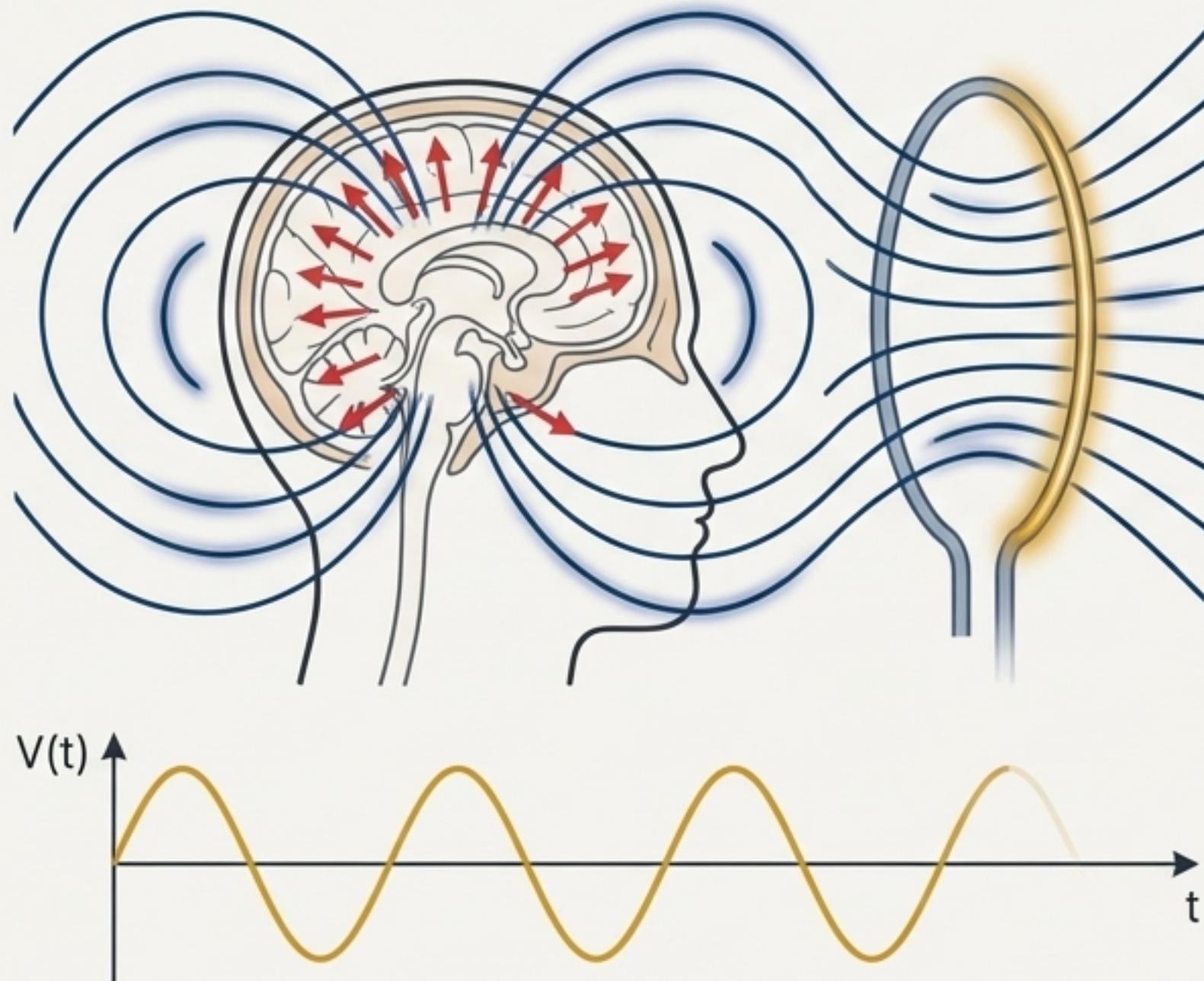
Tips **M** completely into the transverse (x-y) plane to maximize the detectable signal.

180° Pulse:

Inverts the magnetization completely. Used for creating specific types of contrast.



Detecting the Signal: Faraday's Law of Induction

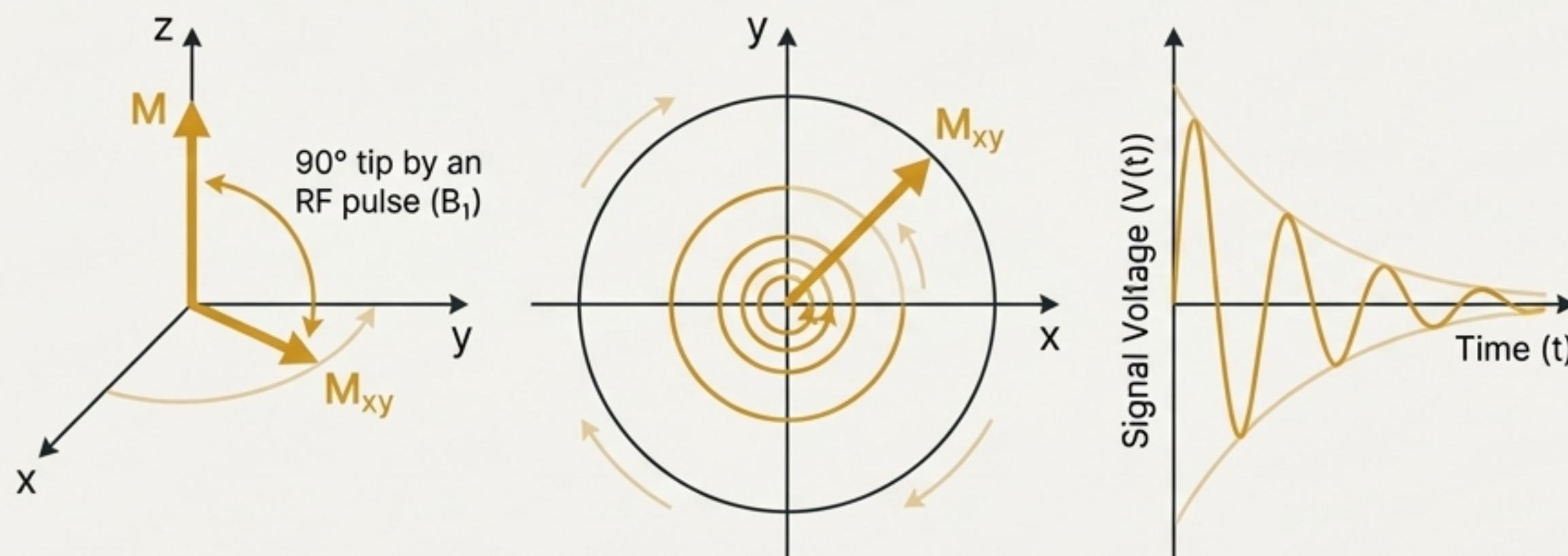


The Process:

1. After a 90° pulse, the transverse magnetization (M_{xy}) is rotating in the x-y plane at the Larmor frequency.
2. This rotating macroscopic magnet creates a changing magnetic flux outside the body.
3. **Faraday's Law:** A changing magnetic flux through a loop of wire (a receiver coil or antenna) induces a voltage.
4. This induced sinusoidal voltage, oscillating at the Larmor frequency, **is the MR signal.**

Takeaway: The precessing magnetization acts like a tiny electrical generator.

The Signal Decays Over Time: Free Induction Decay (FID)



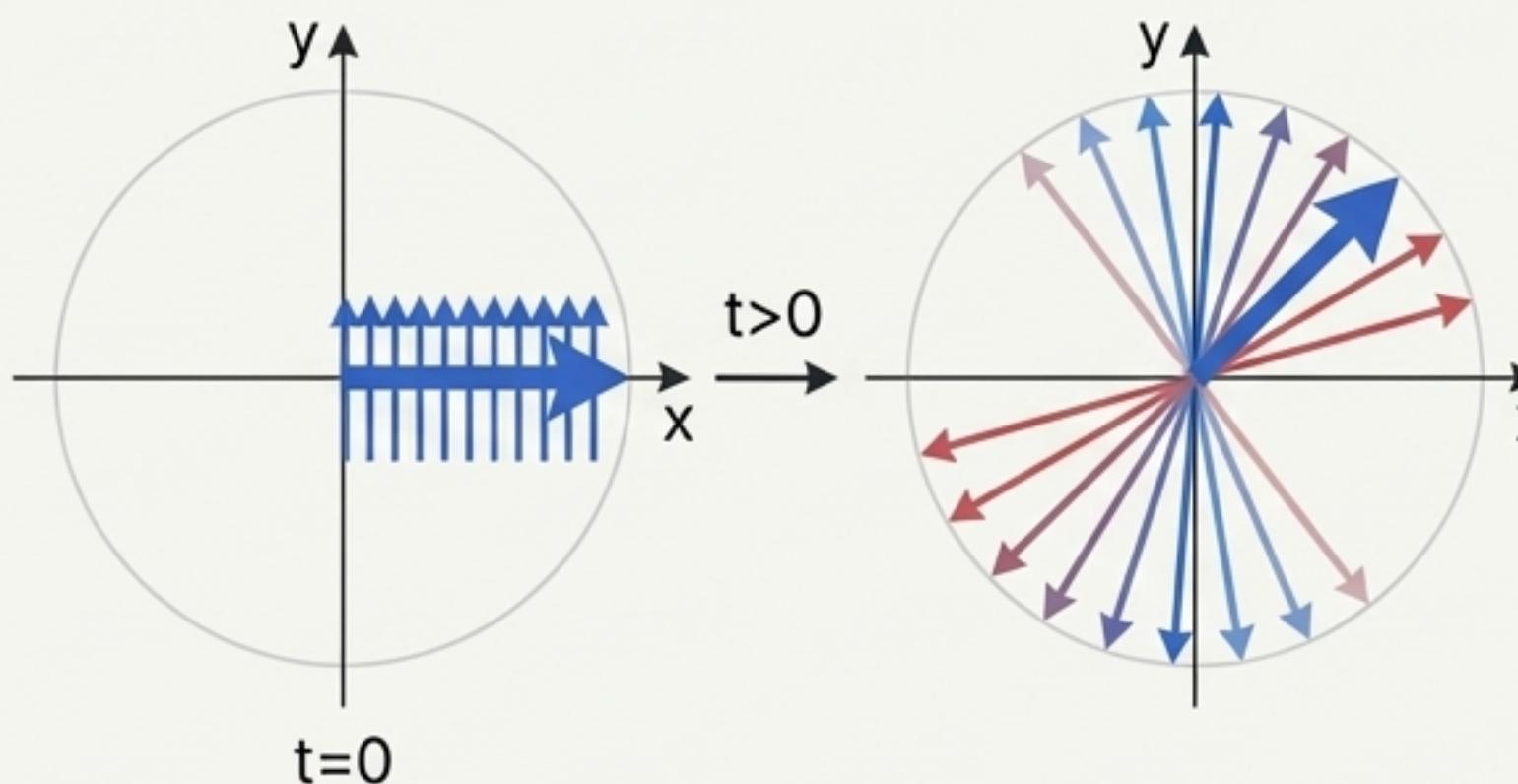
The Observation:

- Immediately after the 90° RF pulse, M_{xy} is at its maximum, and all the constituent proton spins are coherent (in phase).
- The resulting signal is strong, but it does not last. It rapidly decays away.
- This decaying signal is called the Free Induction Decay (FID).

The Question:

- Why does it decay? The protons get out of phase with each other. This process is called dephasing.

T2* Decay: Dephasing from Local Field Differences



The Analogy:

Imagine runners on a circular track. They start together, but because they run at slightly different speeds, the group quickly spreads out.

The Physics:

- Each proton experiences a slightly different local magnetic field due to:
 1. **External Field Inhomogeneity:** The main B_0 magnet is not perfectly uniform.
 2. **Local Susceptibility:** Tissues contain substances (iron, deoxyhemoglobin) that create microscopic magnetic field variations.

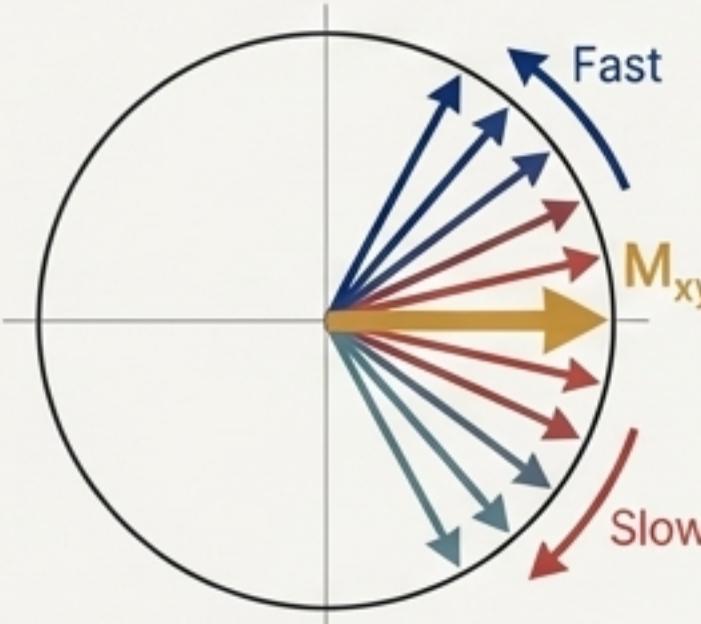
Since $\mathbf{v} = \gamma \mathbf{B}$, different \mathbf{B} fields mean different precession frequencies.

- Spins fan out, their vector sum (M_{xy}) shrinks, and the signal decays. This combined process is called **T2* decay**. It is the source of T2*-weighted contrast.

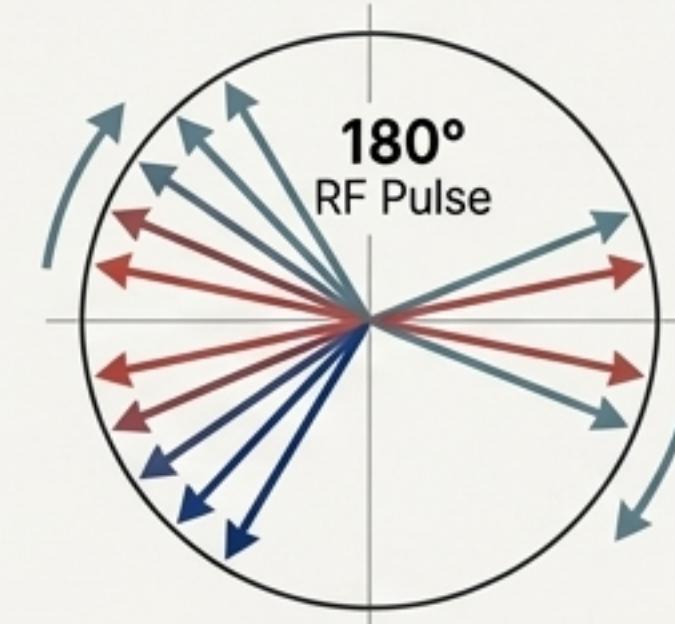
The Spin Echo: Reversing Dephasing with a 180° Pulse

SPIN ECHO SEQUENCE: TRANSVERSE PLANE (TOP-DOWN VIEW)

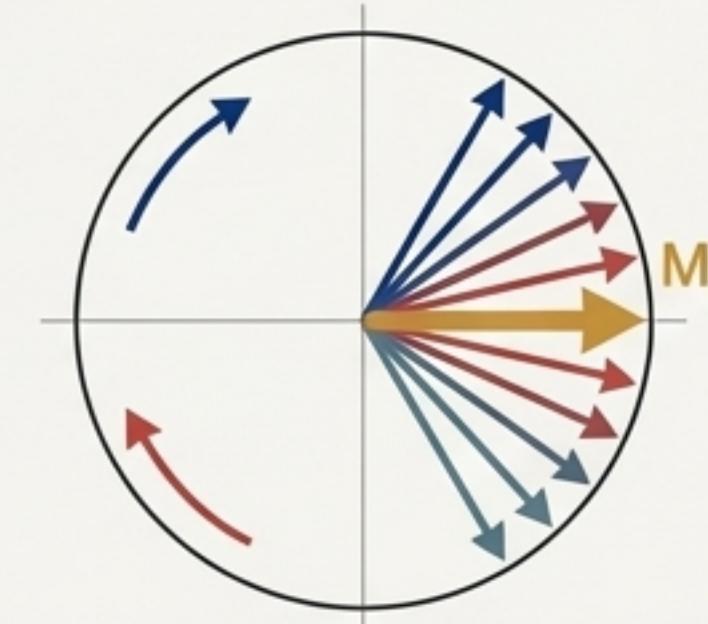
1. DEPHASE ($t=0$ to T)



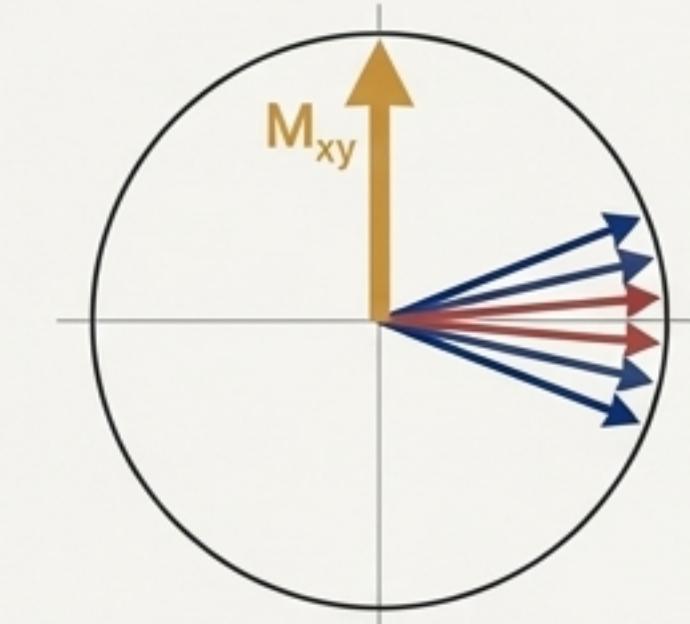
2. 180° PULSE (at $t=T$)



3. REPHASE ($t=T$ to $2T$)

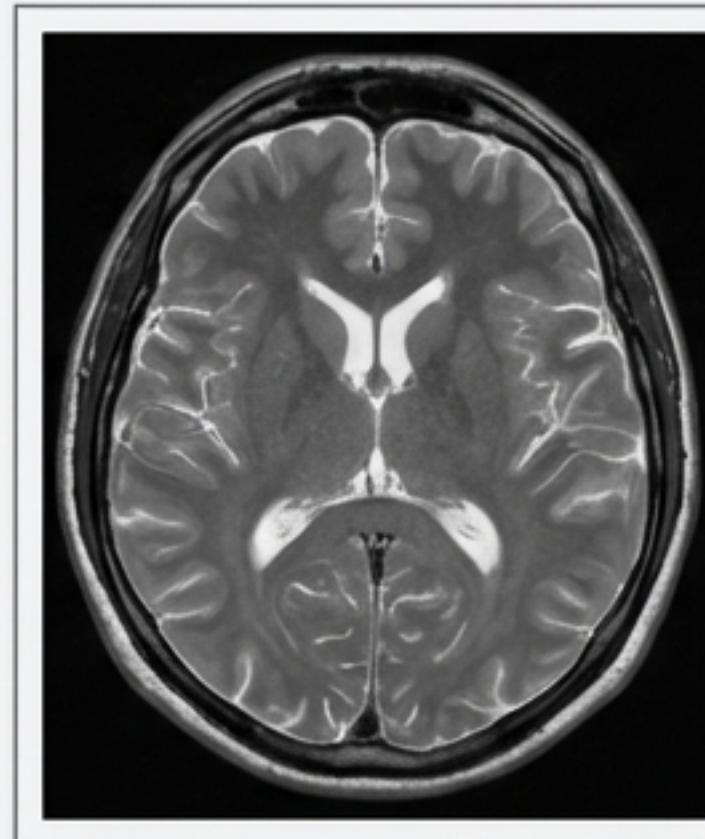
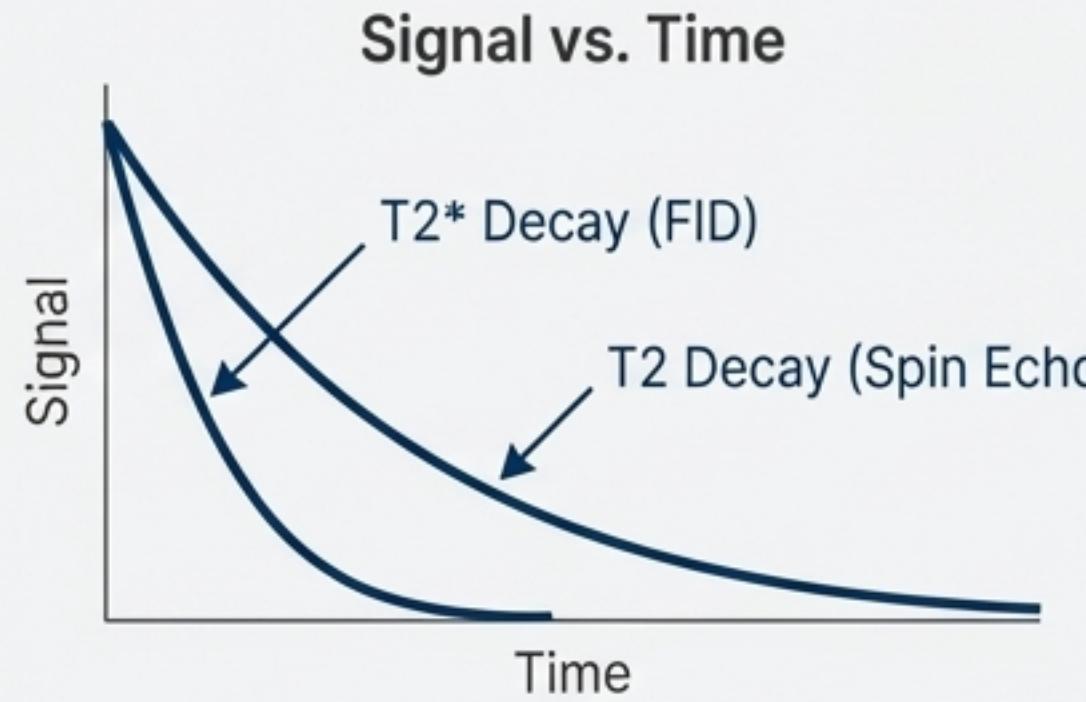


4. ECHO (at $t=T_E=2T$)



- **The Problem:** Dephasing from static field inhomogeneities (the main part of $T2^*$) is coherent and predictable. The “fast runners” stay fast, the “slow runners” stay slow.
- **The Trick:**
 1. After a 90° pulse, let the spins dephase for a time T .
 2. Apply a **180° RF pulse**. This flips the orientation of each spin in the transverse plane. The fast runners are now behind the slow ones.
 3. Let the spins evolve for another time T . The fast runners catch up to the slow ones, and all the spins come back into phase, forming a signal **echo**.
- **The Result:** The spin echo recovers signal lost to static field inhomogeneities.

T2 Decay: Irreversible Dephasing



What the Spin Echo Reveals:

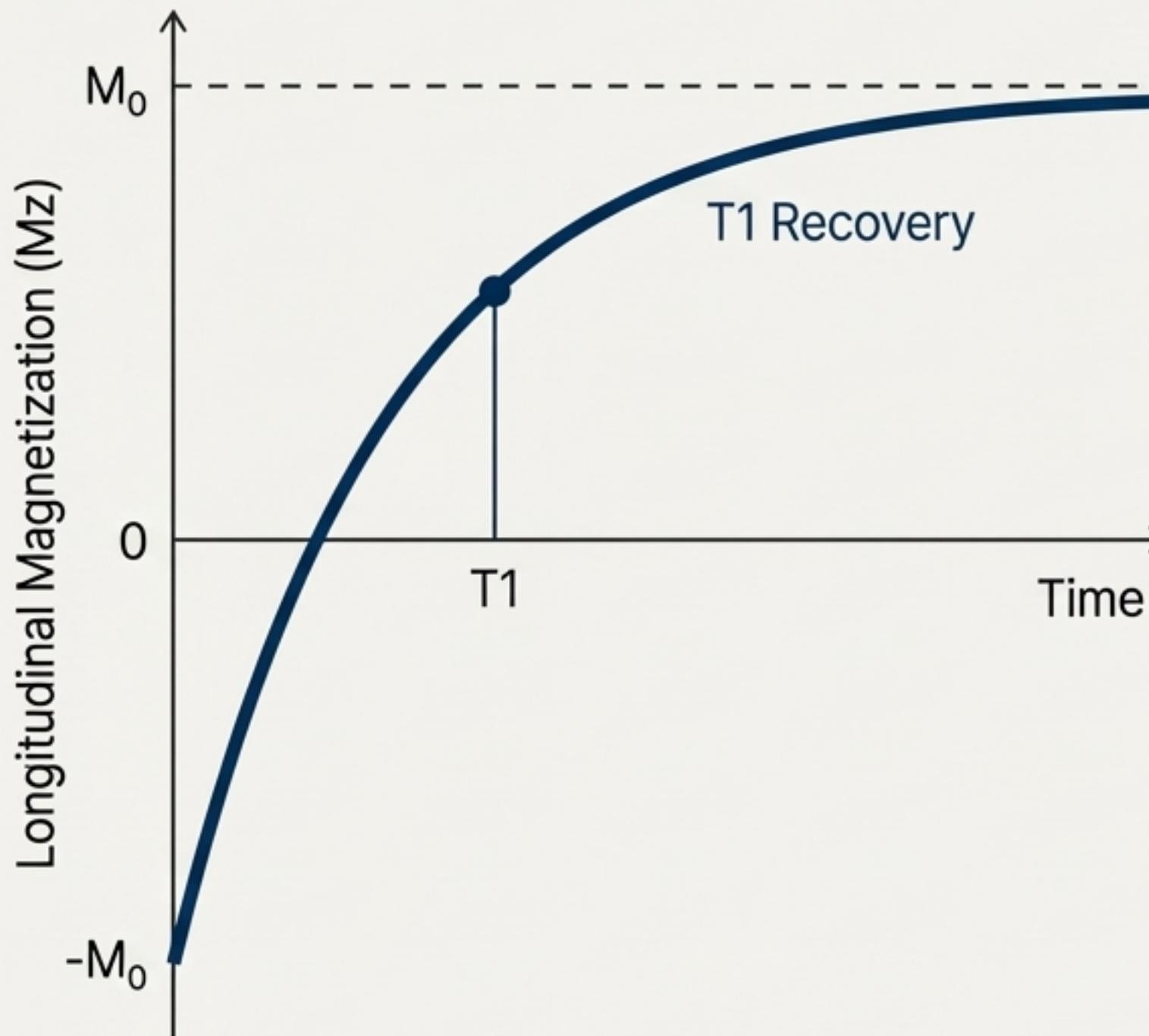
- The spin echo cannot correct for random, fluctuating field changes caused by **spin-spin interactions** (protons' magnetic fields interfering with each other).
- This irreversible dephasing is called **T2 decay**.
- The amplitude of the spin echo decays with the time constant T2.

The Relationship:

$$1/T2^* = 1/T2 + 1/T2' \text{ (from inhomogeneities)}$$

- T2 is an intrinsic tissue property, always longer than T2*.
- T2 contrast makes fluid-filled regions like CSF and pathology appear bright.

T1 Relaxation: Returning to Equilibrium



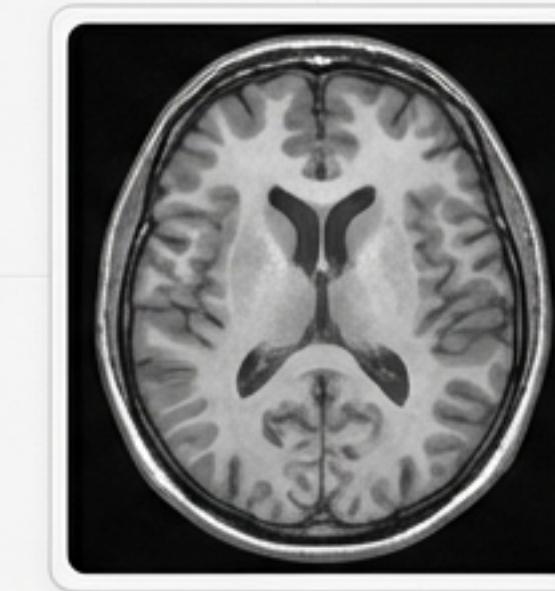
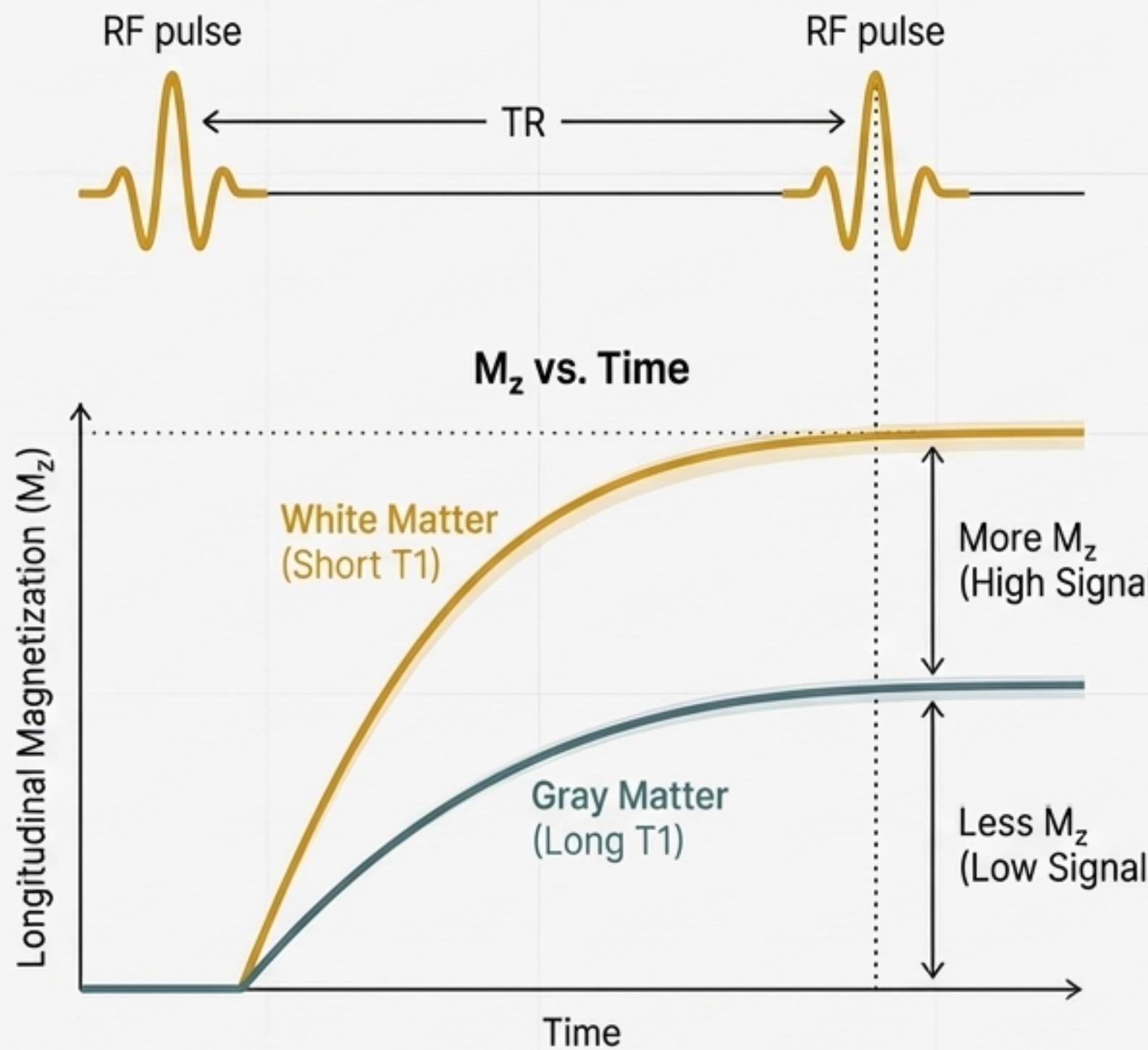
The Process:

- While M_{xy} is decaying, the longitudinal component (M_z) is **recovering**.
- This is called **T1 relaxation** or **spin-lattice relaxation**.
- It is the process of the excited 'spin down' protons giving their energy back to the surrounding molecular environment (the '**lattice**') and returning to the 'spin up' state.
- This re-establishes the net magnetization along the z-axis.

The Timescale:

- T_1 is the time it takes for M_z to recover to $\sim 63\%$ of its equilibrium value.
- T1 processes are much slower than T2 processes (e.g., $T_1 \approx 1\text{s}$, $T_2 \approx 100\text{ms}$ in brain tissue).

Creating T1 Contrast by Varying Repetition Time (TR)



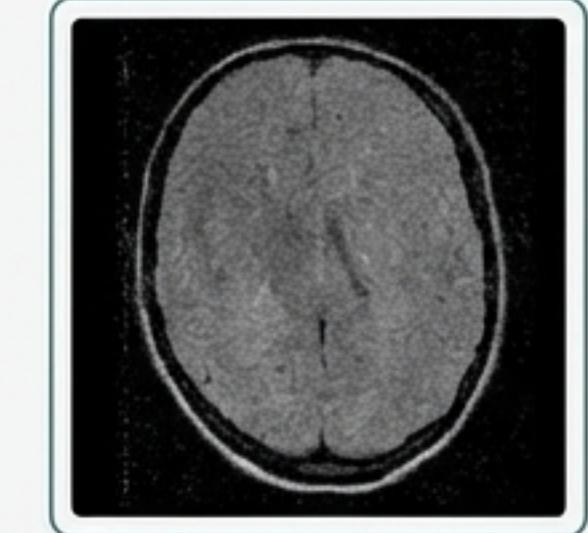
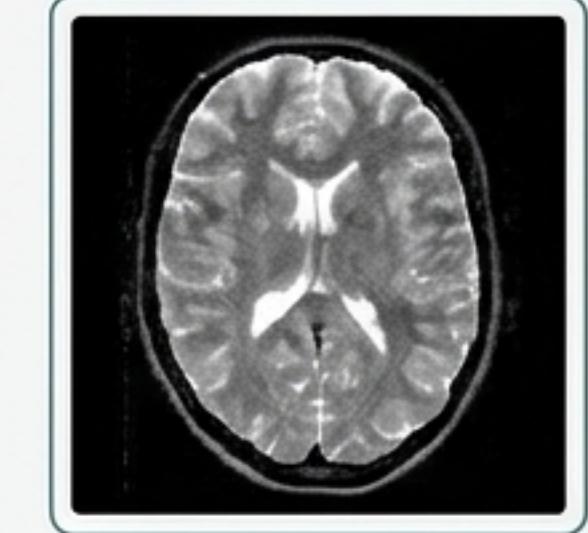
The Method:

- We repeatedly apply RF pulses to generate signal. The time between successive excitation pulses is the **Repetition Time (TR)**.
- If TR is short, tissues with long T1 times (like grey matter and CSF) will not have time to fully recover their M_z.
- Tissues with short T1 times (like white matter) will recover more M_z.
- The next RF pulse will therefore generate more transverse signal from the short T1 tissue.

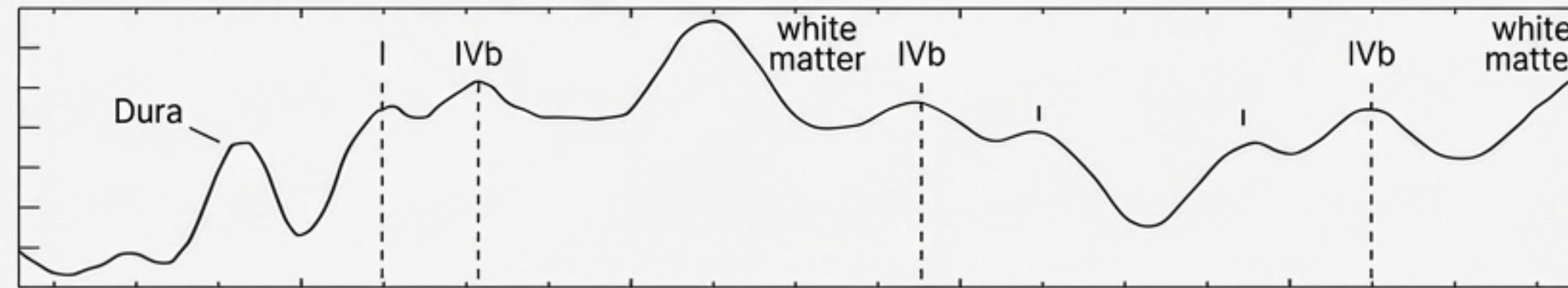
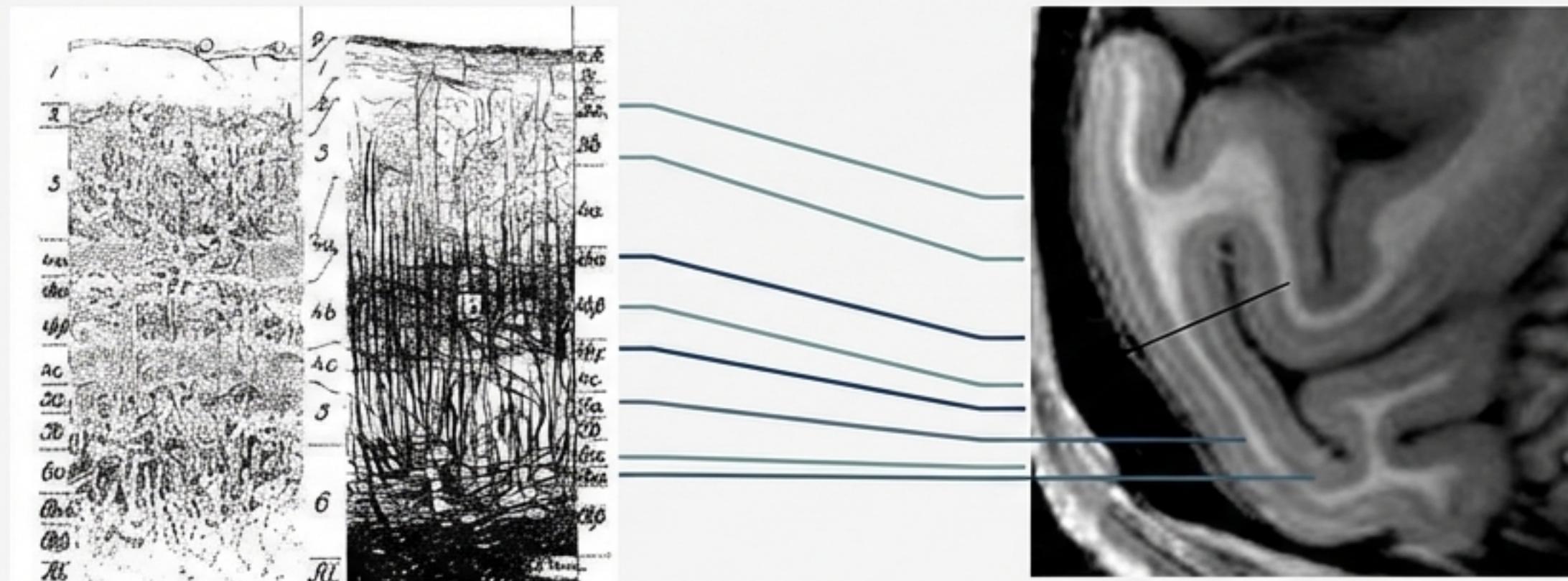
The Result:

- Short TR sequences produce **T1-weighted** images.
- Tissues with short T1 (fat, myelinated white matter) appear bright.
Tissues with long T1 (CSF, tumors) appear dark.

The MRI Contrast Palette: Controlled by Timing

		TE	
		Short	Long
Short		T1-Weighted Maximizes differences in T1 recovery.	Low Signal (not typically used)
TR	Short		
	Long	Proton Density (PD) Weighted Minimizes both T1 and T2 effects. Signal is proportional to the number of protons.	T2-Weighted Maximizes differences in T2 decay.
			

The Biological Source of Contrast: Myelin



The Correlation:

Differences in T1 and T2 values between gray matter, white matter, and even within cortical layers are primarily driven by **myelin content**.

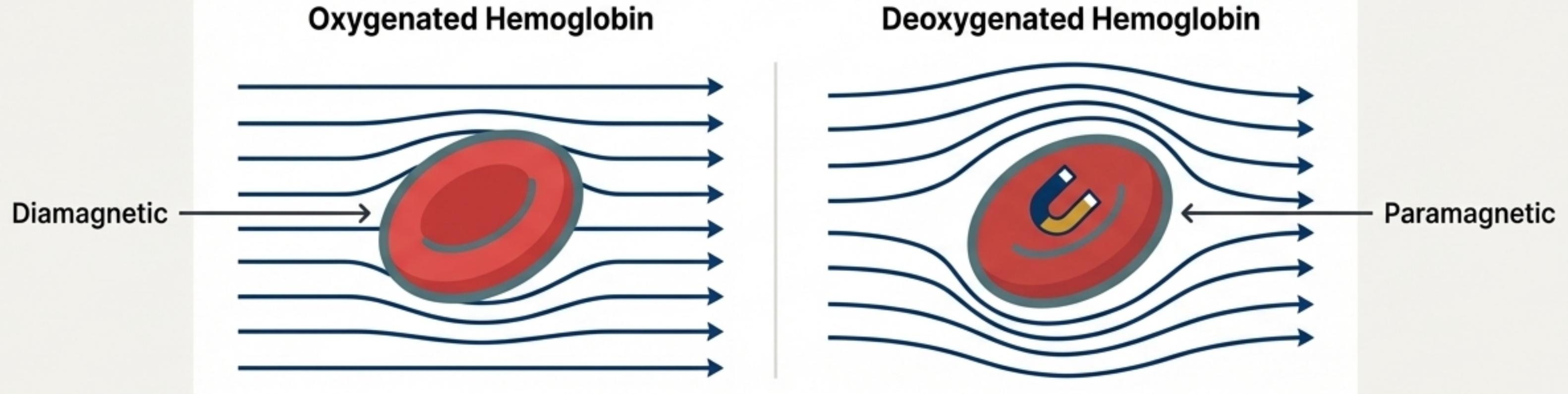
Myelin, the fatty sheath around axons, restricts water motion and creates an environment that facilitates T1 and T2 relaxation.

Highly myelinated tissue (like white matter and the Line of Gennari in V1) has a **shorter T1 and T2**.

The Implication:

High-resolution structural MRI can visualize the brain's cytoarchitecture based on its myeloarchitecture.

The Basis of fMRI: Blood Oxygen Level Dependent (BOLD) Contrast



The Key Ingredient: Deoxyhemoglobin

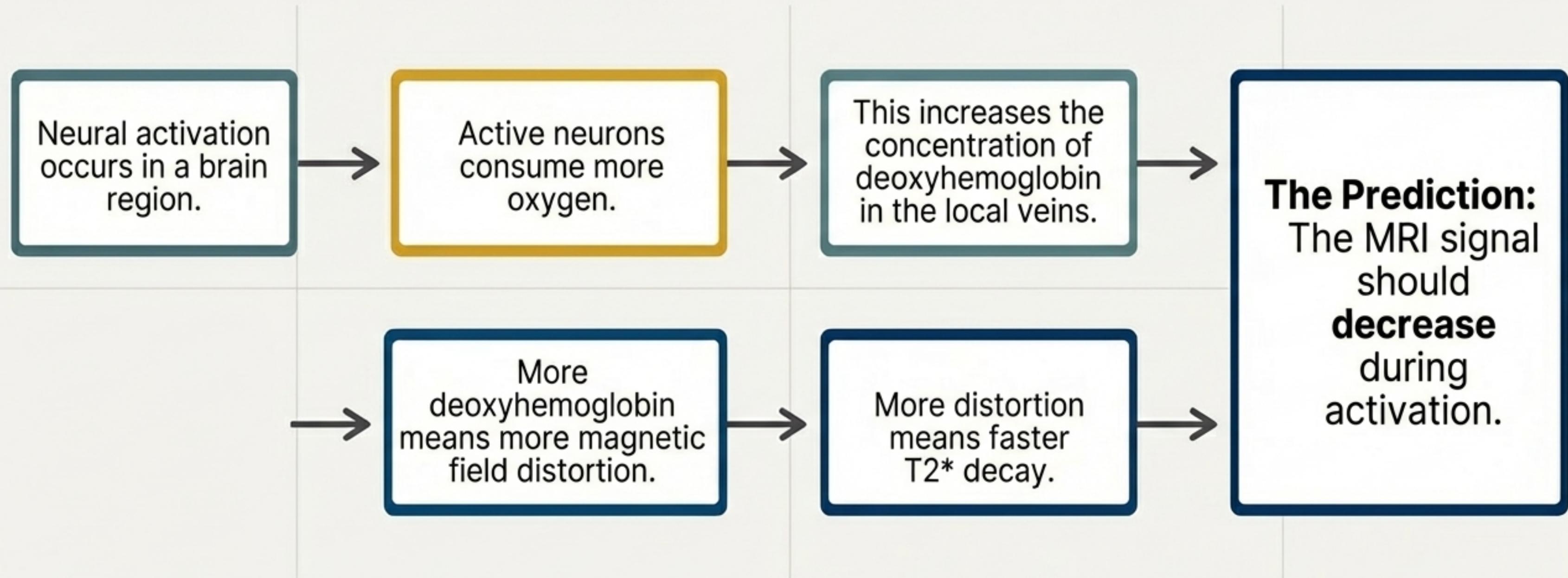
- Hemoglobin is the protein in red blood cells that carries oxygen.
- **Oxygenated hemoglobin (OxyHb)** is diamagnetic. It has no effect on the magnetic field.
- **Deoxygenated hemoglobin (DeoxyHb)** is paramagnetic. It acts like a tiny magnet and distorts the local B_0 field.

The Effect:

- The presence of DeoxyHb creates microscopic magnetic field inhomogeneities in and around blood vessels.
- This causes nearby water protons to dephase more quickly, leading to a **faster T2* decay** and a **lower signal** on T2*-weighted images.

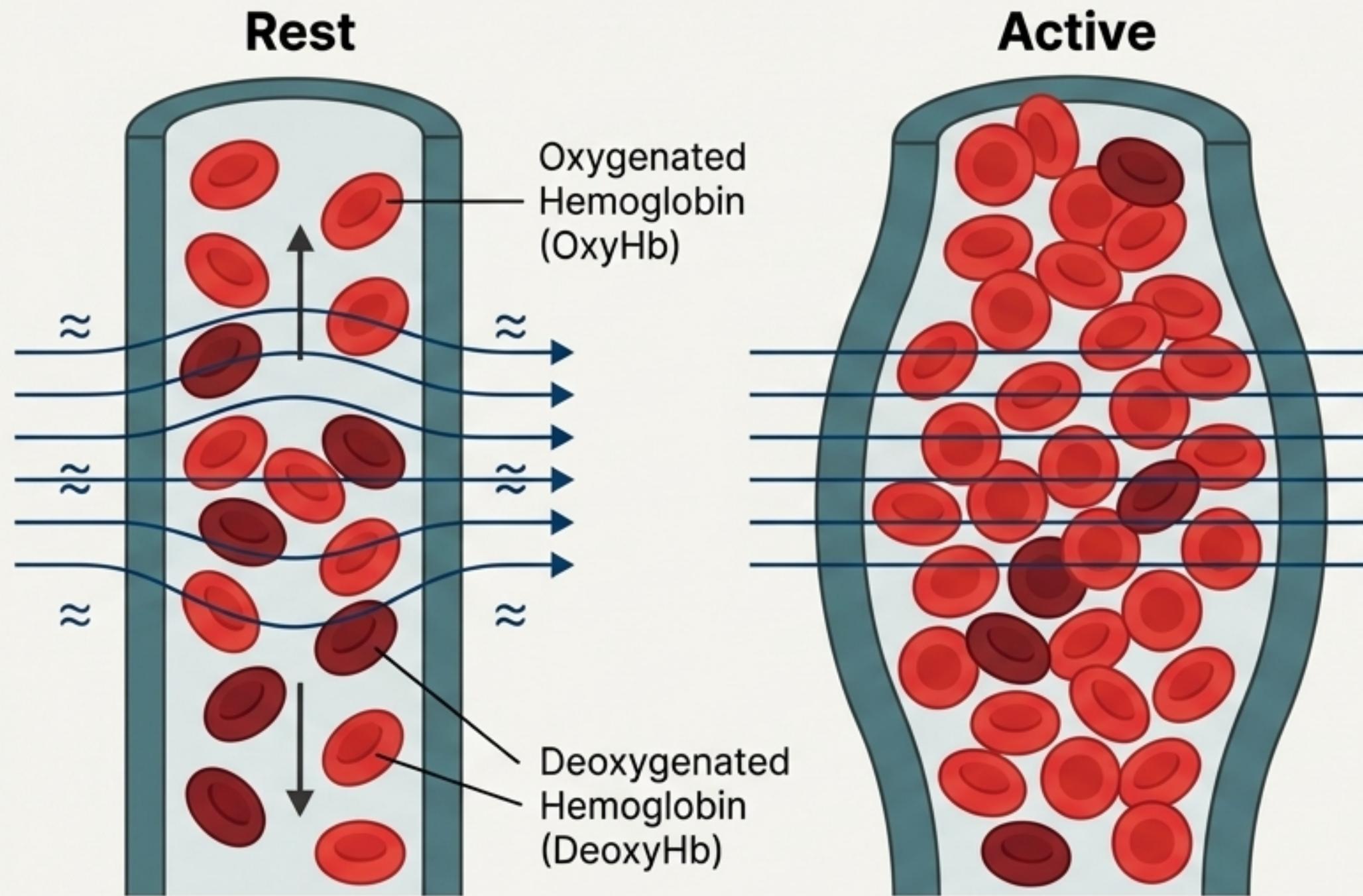
In short: Deoxyhemoglobin is an endogenous (naturally occurring) MRI contrast agent.

The BOLD Effect: A Physicist's Prediction



(Spoiler: This prediction is incorrect.)

The Reality: Blood Flow Overcompensates for Consumption



The Biologist's Analysis:

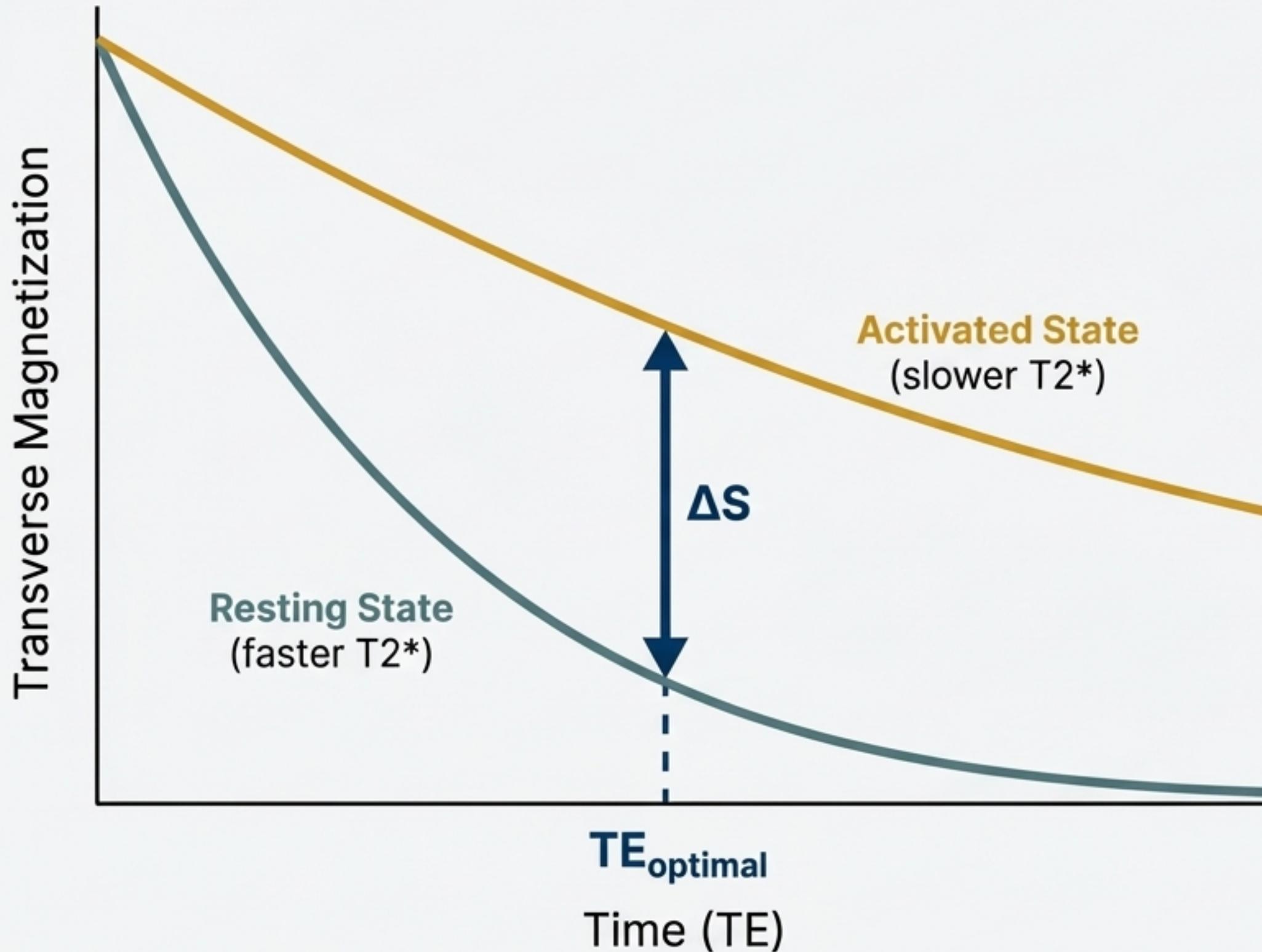
- During activation, the brain's vascular system reacts dramatically.
- There is a massive **increase in local blood flow (CBF)** that far exceeds the small increase in oxygen consumption.
- This oversupply of oxygenated blood "flushes" the deoxyhemoglobin out of the capillaries and veins.

The Result:

- The net concentration of deoxyhemoglobin in an activated voxel **decreases**.
- This leads to less dephasing and a **slower T₂* decay.**

The Correct Conclusion: The MRI signal **increases** during activation.

Optimizing BOLD Contrast with the Right Echo Time (TE)



The Goal: We want to maximize the Contrast-to-Noise Ratio (CNR), which is the **signal change (ΔS)** between the active and resting states.

The Method:

$$S_{\text{rest}} = S_0 * \exp(-TE/T2^*_{\text{rest}})$$

$$S_{\text{active}} = S_0 * \exp(-TE/T2^*_{\text{active}})$$

The difference between these two signals (ΔS) is a function of the **Echo Time (TE)**.

The Optimal Choice:

Calculus shows that the maximum signal difference occurs when the **TE** is **approximately equal to the $T2^*$ of the tissue**.

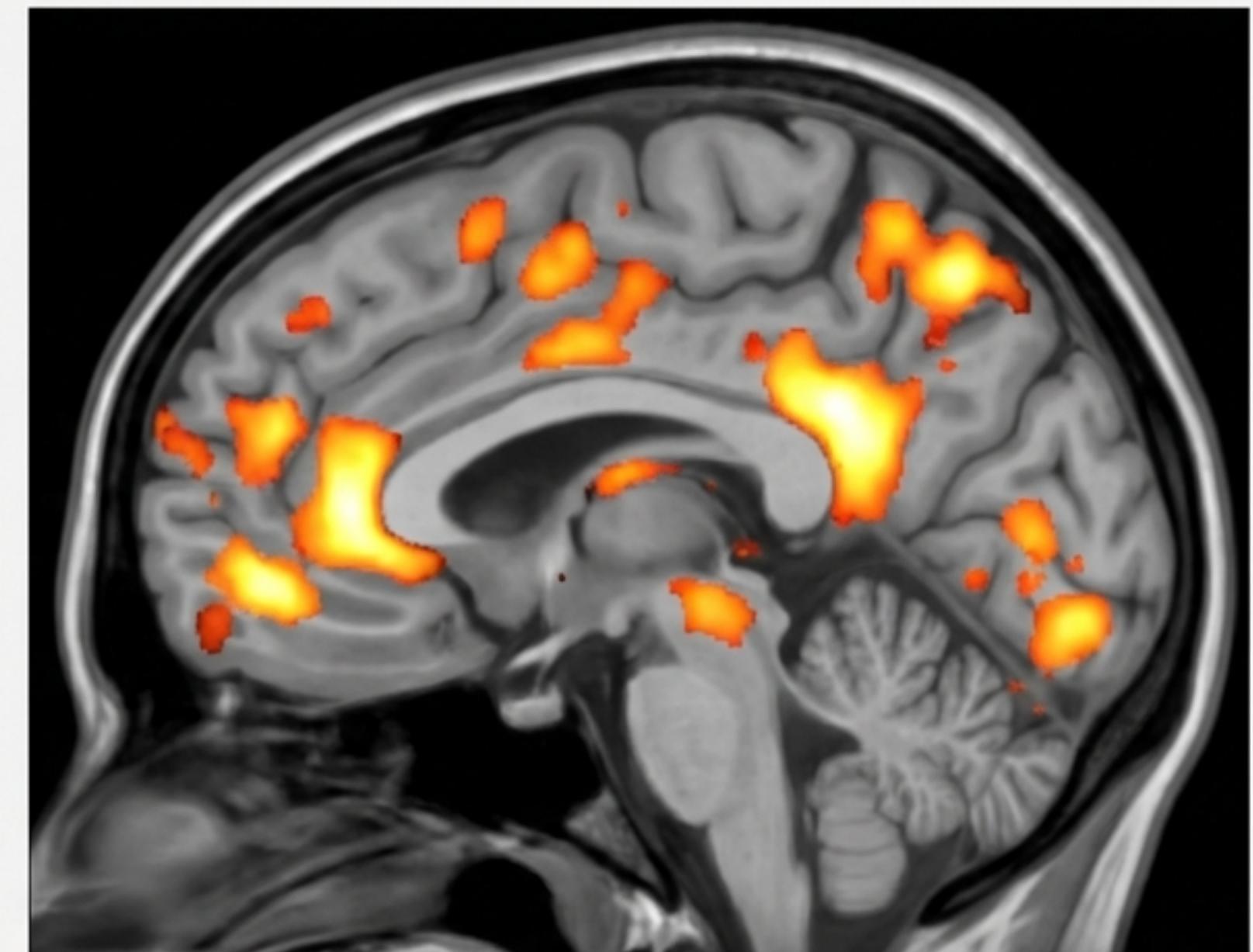
$$TE_{\text{optimal}} \approx T2^*$$

This is why fMRI is performed with $T2^*$ -weighted sequences (like Gradient Echo EPI) with a carefully chosen TE.

From Quantum Physics to Brain Function

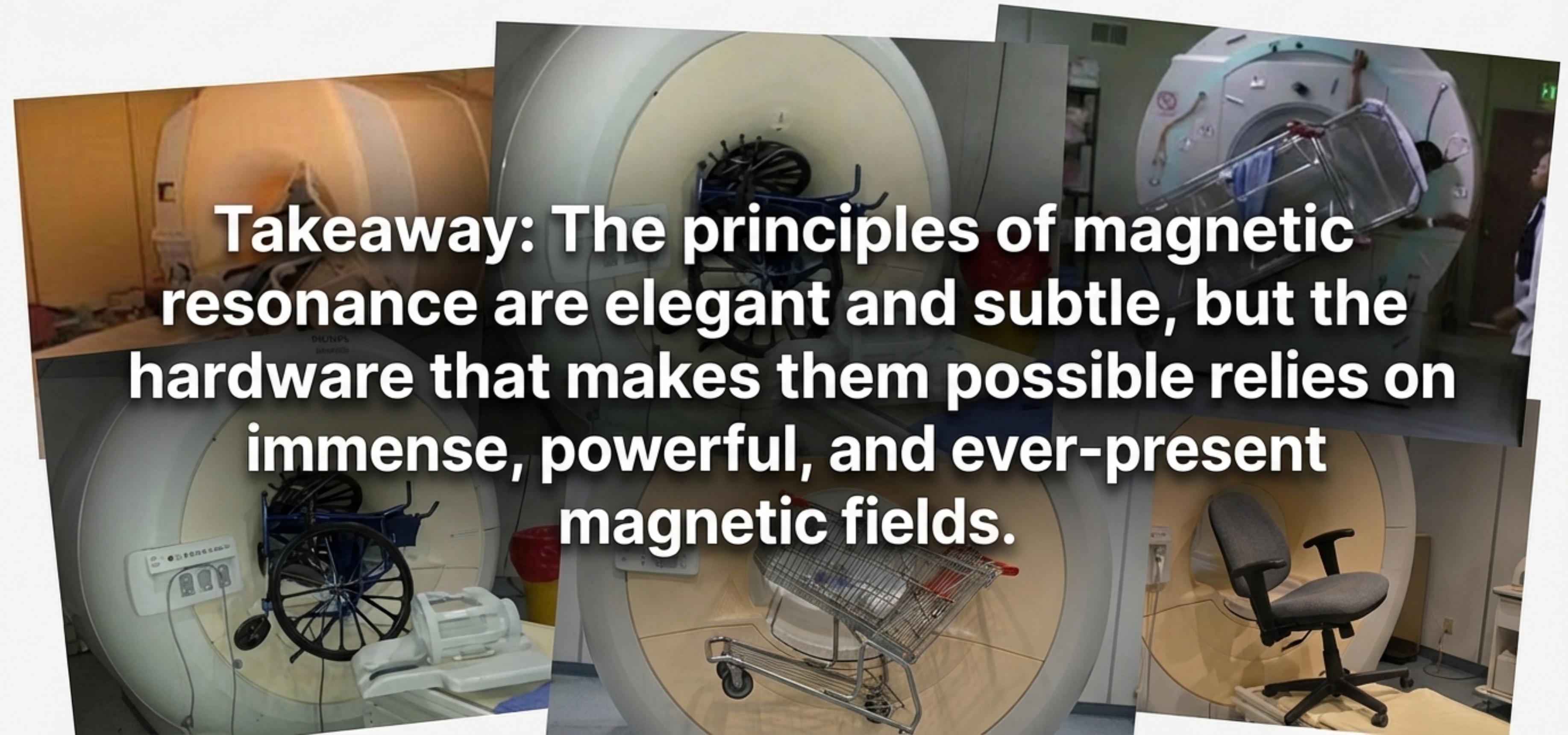
Putting It All Together:

1. We harness the magnetic spin of protons in water.
2. We place them in a strong magnetic field (B_0) where they precess at the Larmor frequency.
3. We excite them with a resonant RF pulse (B_1).
4. We create a $T2^*$ -weighted image by waiting a specific Echo Time ($TE \approx T2^*$) before collecting the signal.
5. We repeat this imaging process rapidly while a subject performs a task.
6. The small signal increases we detect are correlated with the task, revealing the patterns of brain activation.



The Result: We can non-invasively map brain activity by observing the magnetic properties of blood.

A Final Reminder: The ‘M’ is for ‘Magnetic’



Takeaway: The principles of magnetic resonance are elegant and subtle, but the hardware that makes them possible relies on immense, powerful, and ever-present magnetic fields.