(F)MRI Physics With Hardly Any Math

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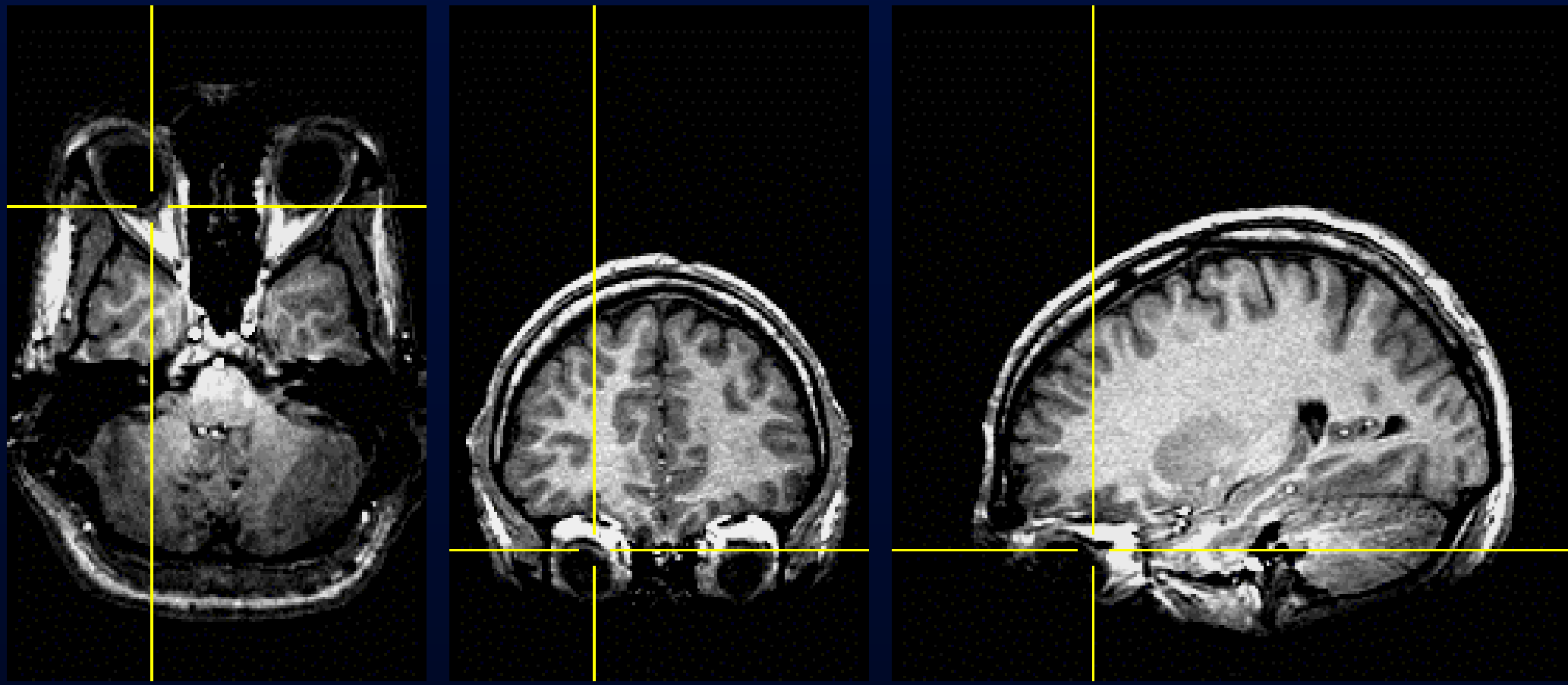
MRI ⇒ Cool (and Useful) Pictures



axial coronal sagittal

2D slices extracted from a 3D image

[resolution about 1×1×1 mm]

Synopsis of MRI

1) Put subject in big magnetic field (leave him there)
2) Transmit radio waves into subject [about 3 ms]
3) Turn off radio wave transmitter
4) Receive radio waves re-transmitted by subject
   - Manipulate re-transmission with magnetic fields during this *readout* interval [10-100 ms: MRI is not a snapshot]
5) Store measured radio wave data vs. time
   - Now go back to 2) to get some more data
6) Process raw data to reconstruct images
7) Allow subject to leave scanner (this is optional)

Components of Lectures

1) Magnetic Fields and Magnetization
2) Fundamental Ideas about the NMR RF Signal

} NMR Physics

3) How to Make an Image
4) Some Imaging Methods

} MRI Principles

5) The Concept of MRI Contrast
6) Functional Neuroimaging with MR

} Making Useful Images

Part the First

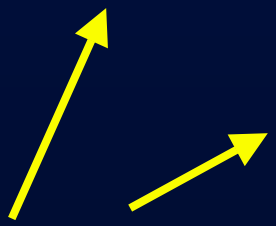
Magnetic Fields;
Magnetization of the Subject;
How the Two Interact

Magnetic Fields

- Magnetic fields create the substance we "see": *magnetization* of the H protons in H_2O
- Magnetic fields also let us manipulate magnetization so that we can make a map [or *image*] of its density inside the body's tissue
- *Static* fields change slowly (not at all, or only a few 1000 times per second)
  - Main field; gradient fields; static inhomogeneities
- *RF* fields oscillate at Radio Frequencies (tens of millions of times per second)
  - transmitted radio waves into subject
  - received signals from subject

Vectors and Fields

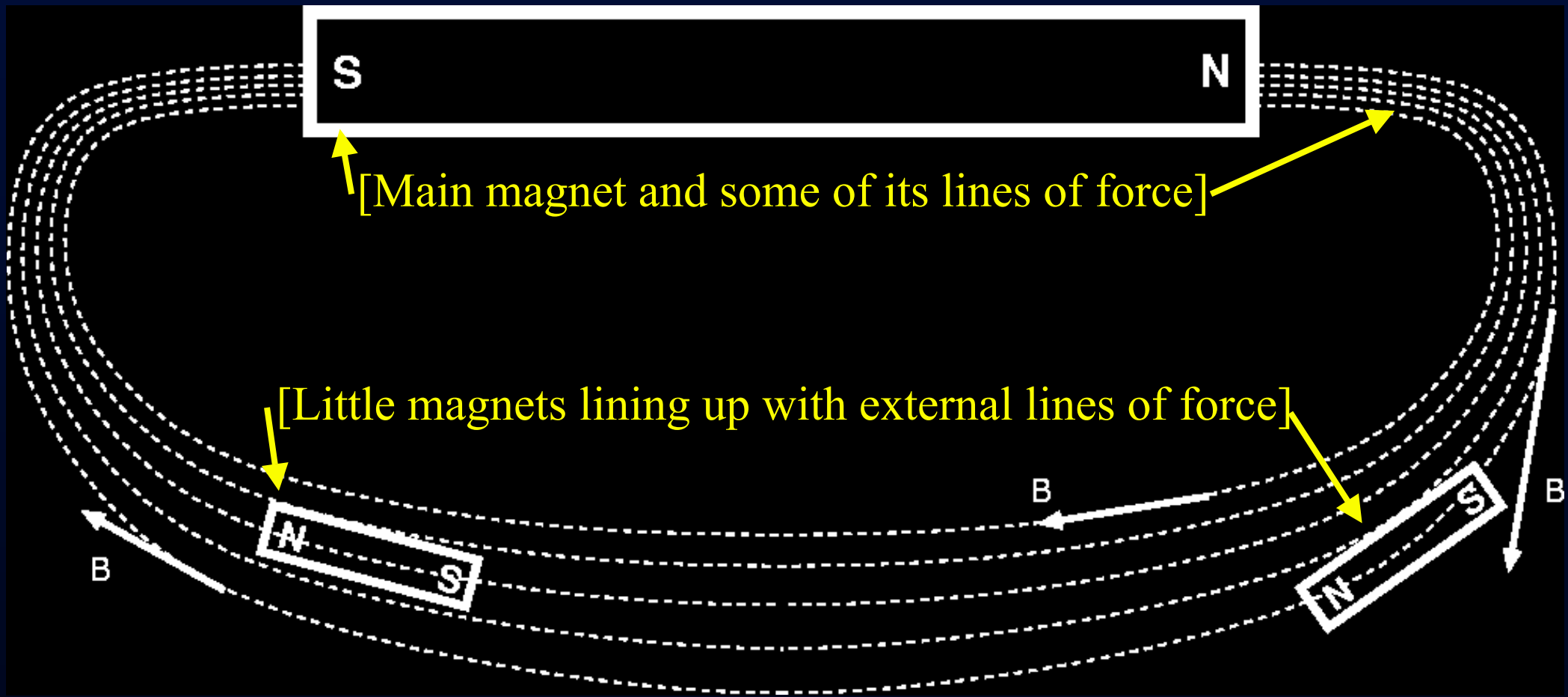
- Magnetic field *B* and magnetization *M* are *vectors*:
  - Quantities with direction as well as size
  - Drawn as arrows .....
  - Another example: velocity is a vector (speed is its size)

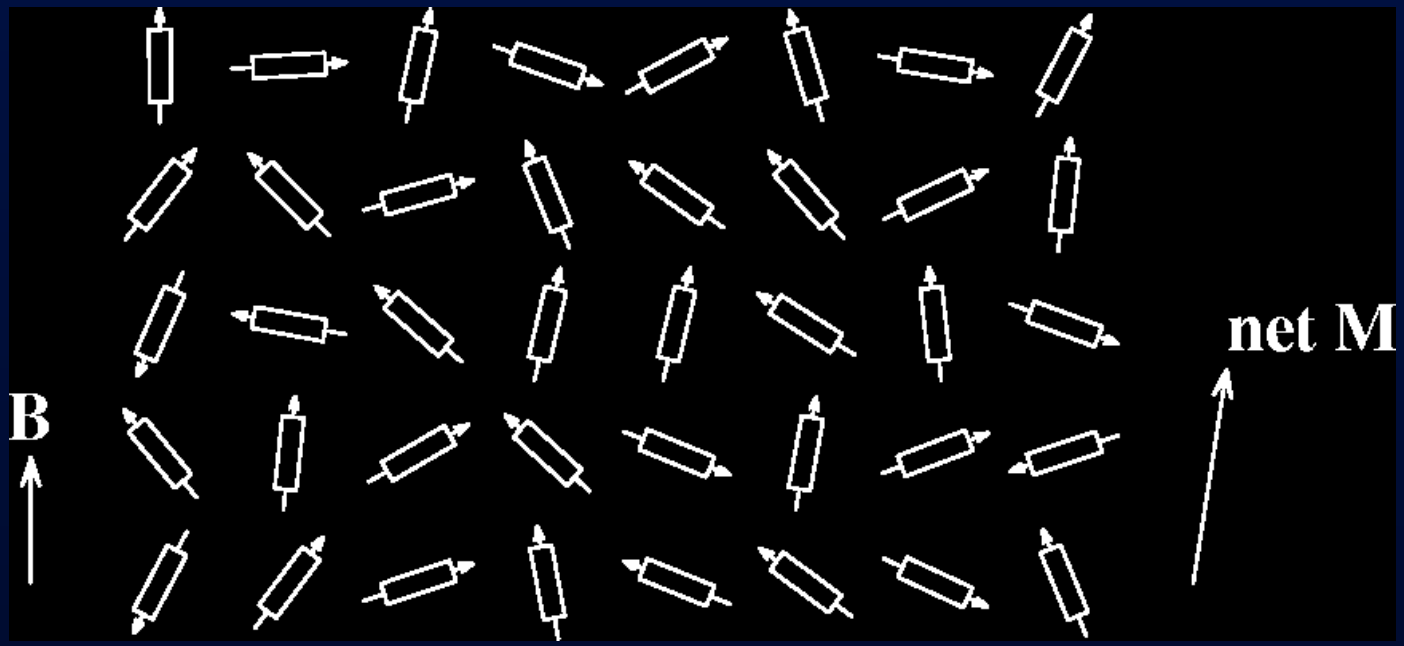


- A *field* is a quantity that varies over a spatial region:
  - e.g., velocity of wind at each location in the atmosphere
- Magnetic field exerts torque to line magnets up in a given direction
  - direction of alignment is direction of *B*
  - torque proportional to size of *B* [units=*Tesla*, *Gauss*=10^{-4} T]

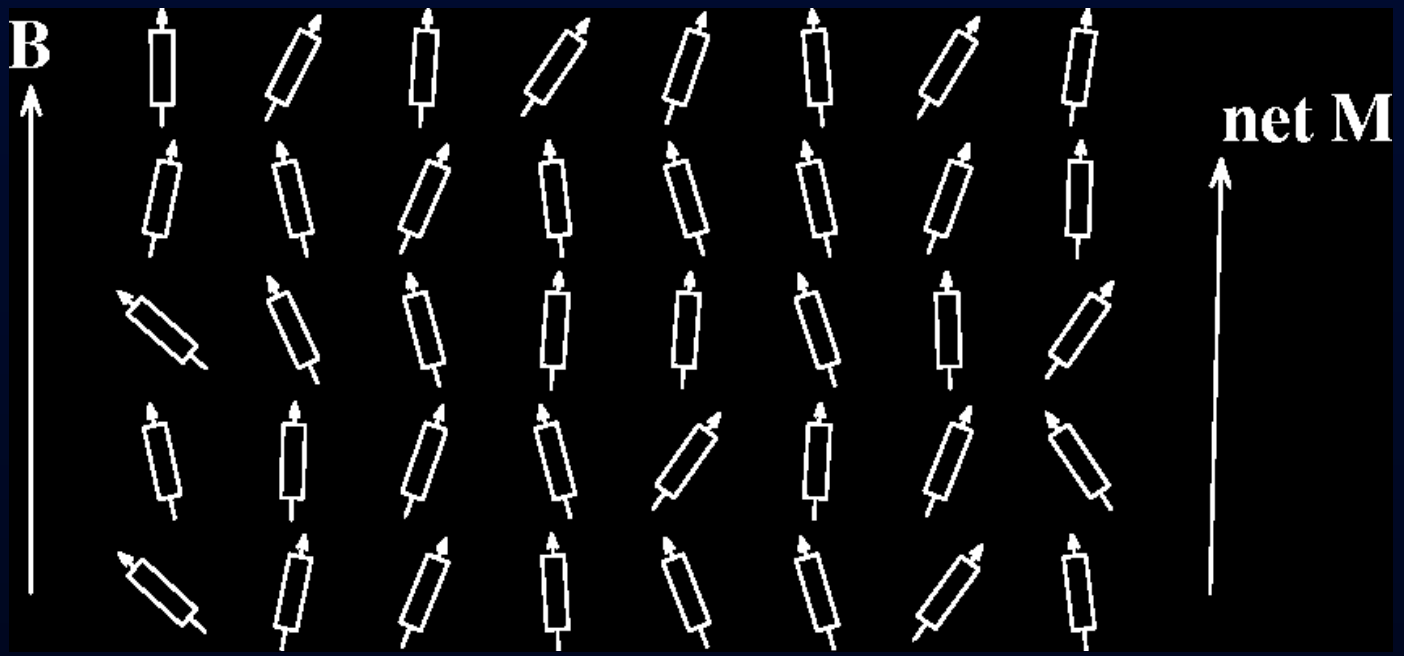
B_0 = Big Field Produced by Main Magnet

- Purpose is to align H protons in H_2O (little magnets)





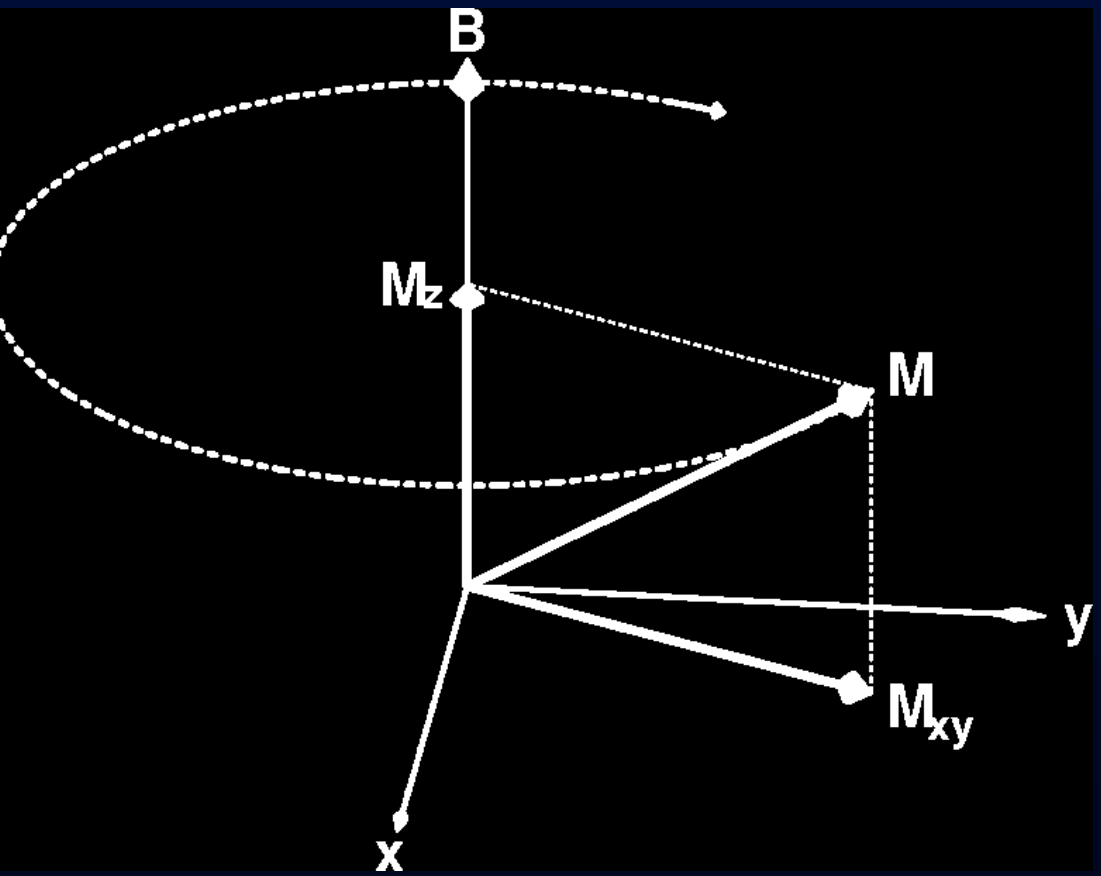
- Small B_0 produces small net magnetization M
- Thermal motions try to randomize alignment of proton magnets



- Larger B_0 produces larger net magnetization M, lined up with B_0
- Reality check: 0.0003% of protons aligned per Tesla of B_0

Precession of Magnetization *M*

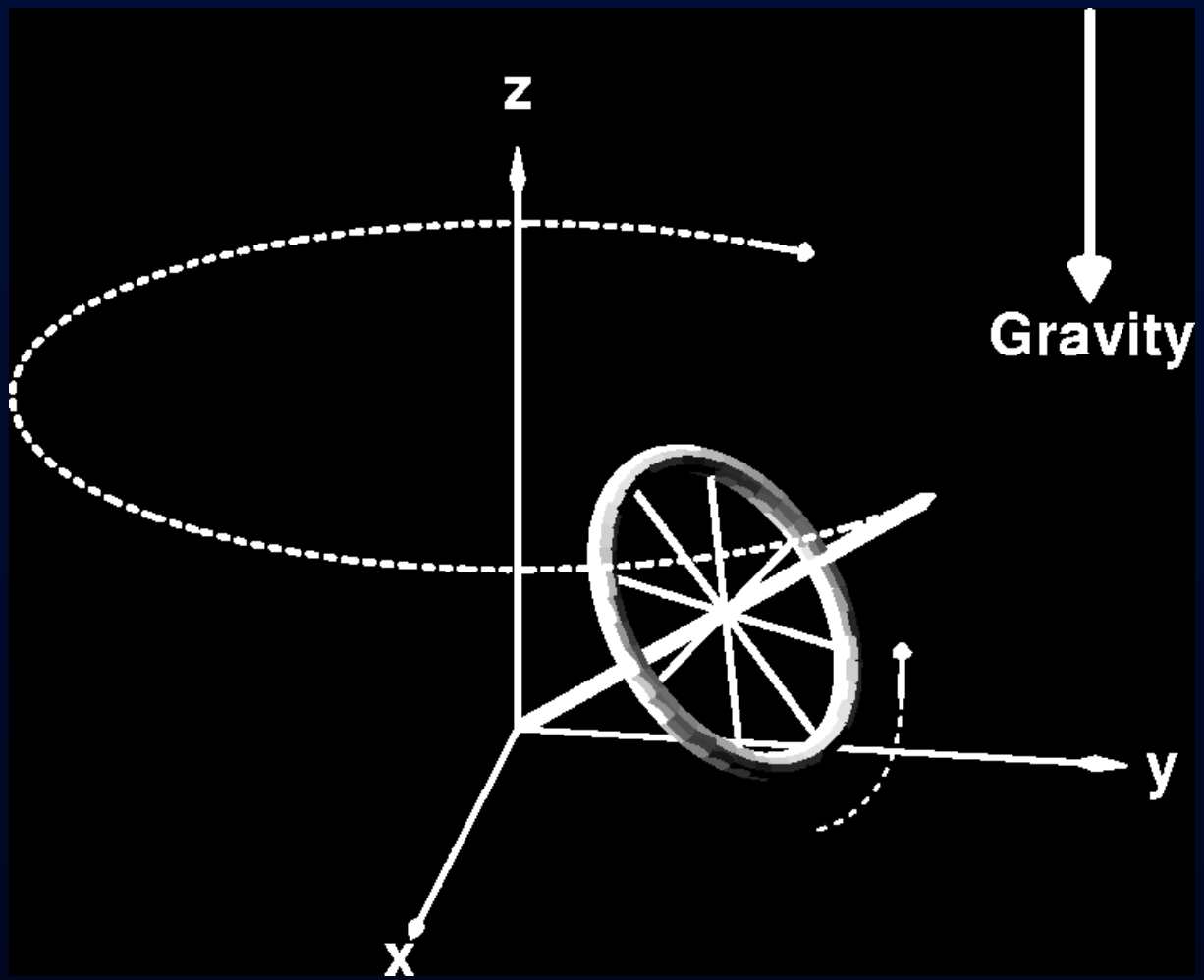
- Magnetic field causes *M* to rotate (or *precess*) about the direction of *B* at a frequency proportional to the size of *B* — 42 million times per second (42 MHz), per Tesla of *B*



- If *M* is not parallel to *B*, then it precesses clockwise around the direction of *B*.
- However, "normal" (*fully relaxed*) situation has *M* parallel to *B*, which means there won't be any precession
- N.B.: part of *M* parallel to *B* (M_z) does not precess

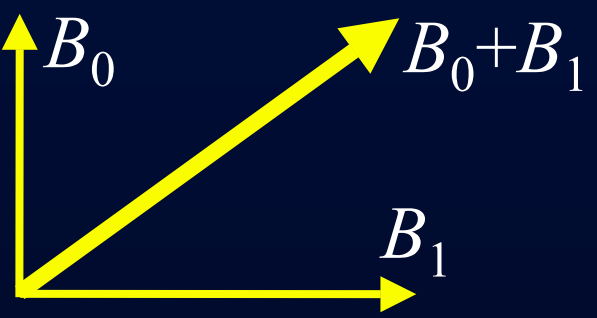
A Mechanical Analogy

- A gyroscope in the Earth's gravitational field is like magnetization in an externally applied magnetic field



How to Make *M* not be Parallel to *B*?

- A way that does *not* work:
  - Turn on a second big magnetic field B_1 perpendicular to main B_0 (for a few seconds)
  - *M* would drift over to be aligned with sum of B_0 and B_1



  - Then turn B_1 off; *M* is now not parallel to magnetic field B_0
- This fails because cannot turn huge (Tesla) magnetic fields on and off quickly
  - But it contains the kernel of the necessary idea:

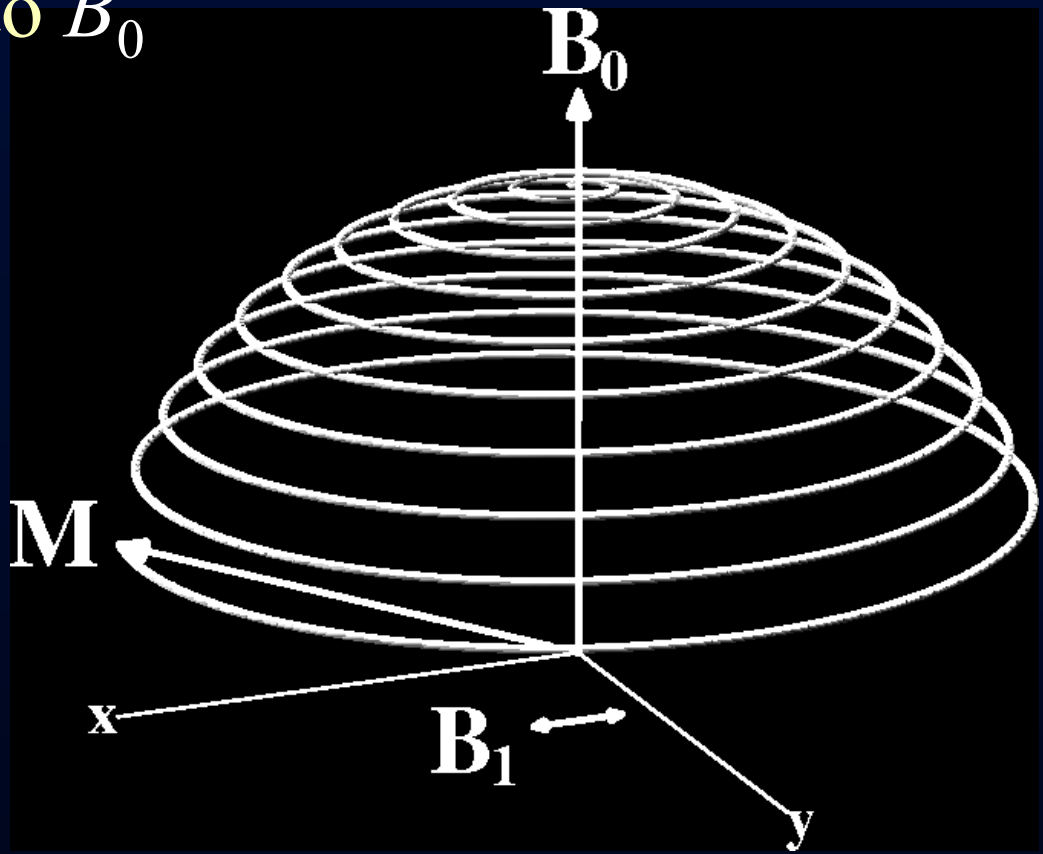
A magnetic field B_1 perpendicular to B_0

B_1 = Excitation (Transmitted) RF Field

- Left alone, M will align itself with B in about 2–3 s
- So don't leave it alone: apply (transmit) a magnetic field B_1 that fluctuates at the precession frequency and points perpendicular to B_0

- The effect of the tiny B_1 is to cause M to spiral away from the direction of the static B field
- $B_1 \approx 10^{-4}$ Tesla
- This is called *resonance*
- If B_1 frequency is not close to resonance, B_1 has no effect

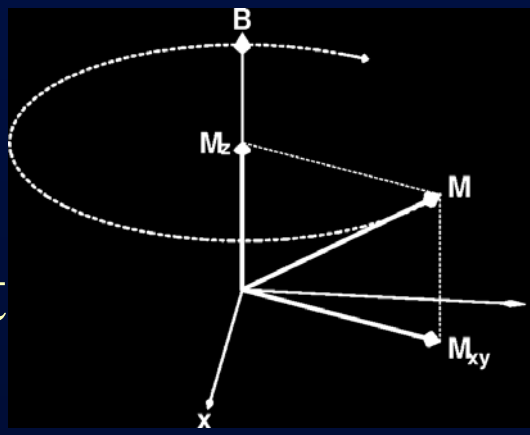
Time = 2–4 ms



Another Mechanical Analogy: A Swingset

- Person sitting on swing at rest is "aligned" with externally imposed force field (gravity)
- To get the person up high, you could simply supply enough force to overcome gravity and lift him (and the swing) up
  - Analogous to forcing M over by turning on a huge static B_1
- The other way is to push back and forth with a tiny force, synchronously with the natural oscillations of the swing
  - Analogous to using the tiny RF B_1 to slowly flip M over

Readout RF



- When excitation RF is turned off, *M* is left pointed off at some angle to B_0 [*flip angle*]
- Precessing part of *M* [M_{xy}] is like having a magnet rotating around at very high speed (at RF frequencies)
- Will generate an oscillating voltage in a coil of wires placed around the subject — this is magnetic *induction*
- This voltage is the *RF signal* whose measurements form the raw data for MRI
  - At each instant in time, can measure one voltage $V(t)$, which is proportional to the sum of all transverse M_{xy} inside the coil

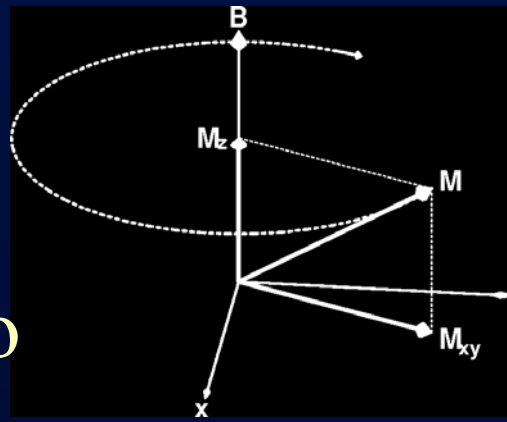
➔ Must find a way to separate signals from different regions

But before I talk about localization (imaging):

Part the Second

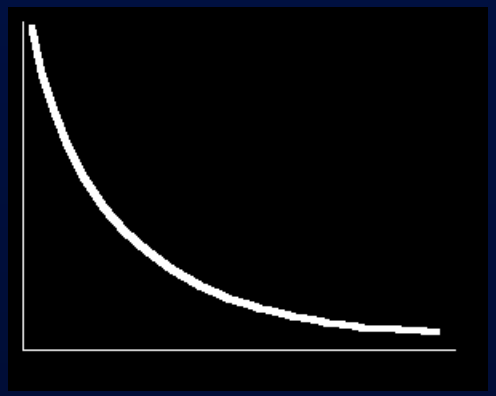
Fundamental Ideas
about
the NMR RF Signal

Relaxation: Nothing Lasts Forever



- In absence of external B_1, M will go back to being aligned with static field B_0 — this is called *relaxation*
- Part of M perpendicular to B_0 shrinks [M_{xy}]
  - This part of M is called *transverse magnetization*
  - It provides the detectable RF signal
- Part of M parallel to B_0 grows back [M_z]
  - This part of M is called *longitudinal magnetization*
  - Not directly detectable, but is converted into transverse magnetization by externally applied B_1

Relaxation Times and Rates



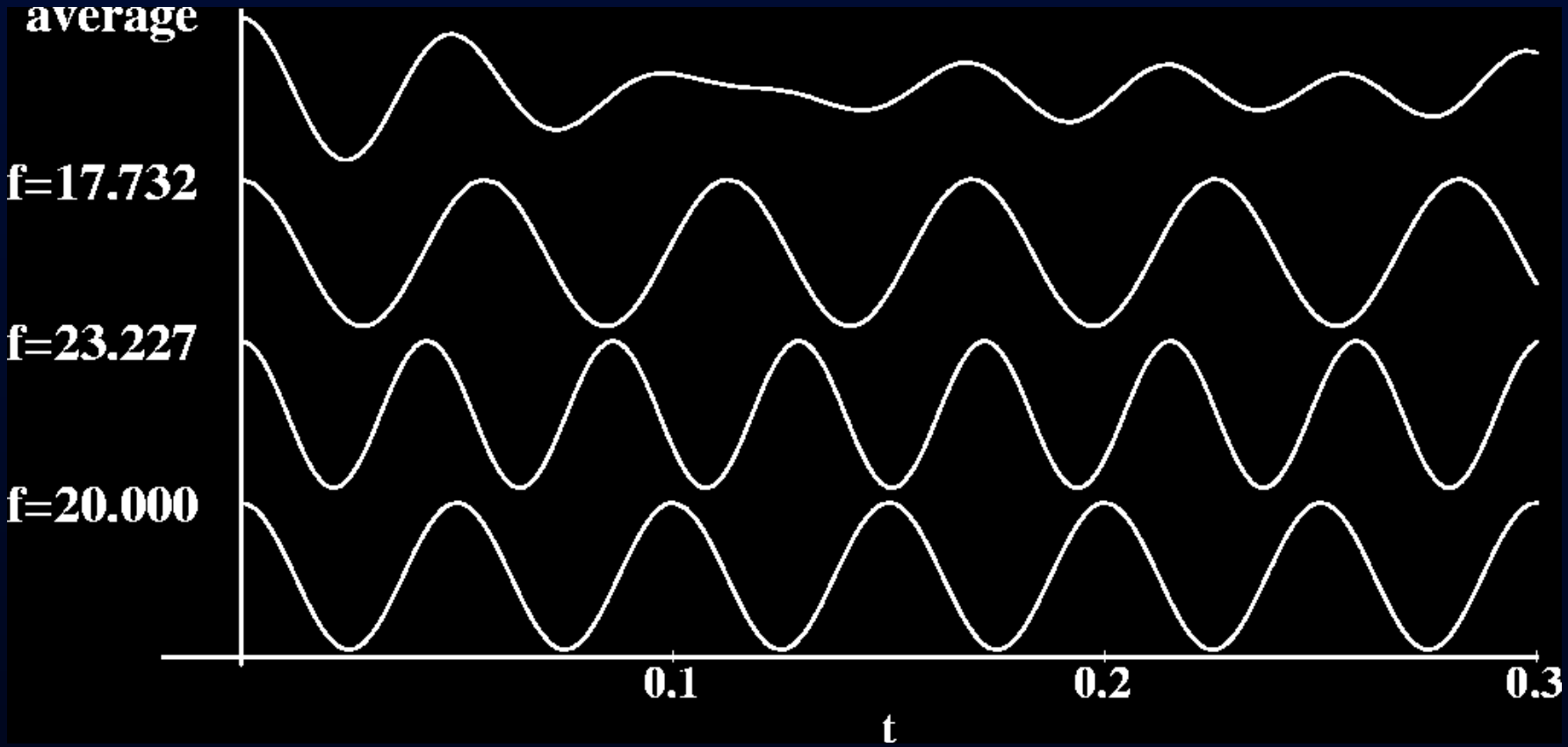
- Times: ‘T’ in exponential laws like $e^{-t/T}$
  - Rates: R = 1/T [so have relaxation like e^{-Rt}]
- T1: Relaxation of M back to alignment with B_0
  - Usually 500-1000 ms in the brain [lengthens with bigger B_0]
- T2: Intrinsic decay of the transverse magnetization over a microscopic region (≈ 5-10 micron size)
  - Usually 50-100 ms in the brain [shortens with bigger B_0]
- T2*: Overall decay of the observable RF signal over a macroscopic region (millimeter size)
  - Usually about half of T2 in the brain [i.e., faster relaxation]

Material Induced Inhomogeneities in B

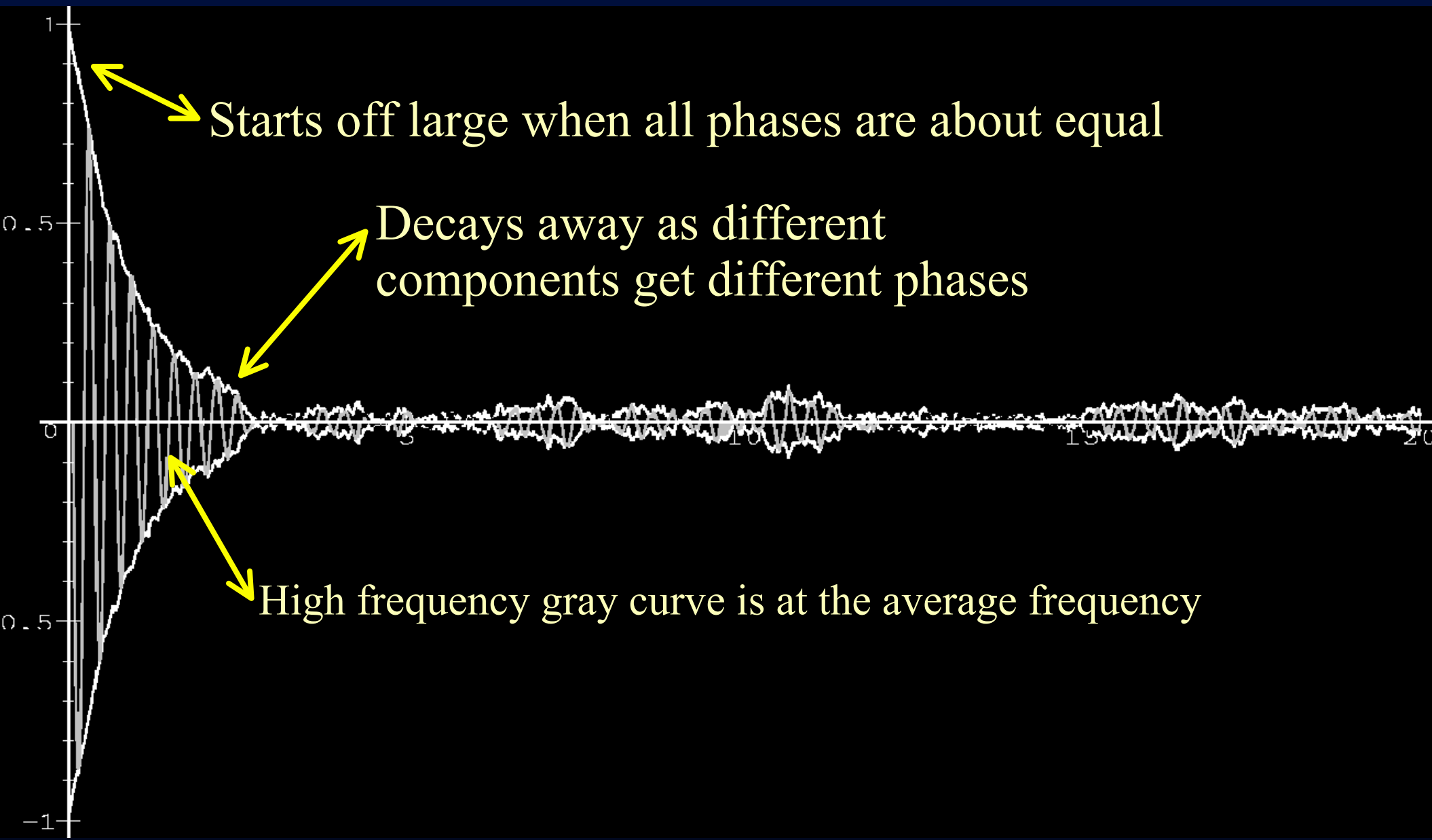
- Adding a nonuniform object (like a person) to B_0 will make the total magnetic field B nonuniform
  - This is due to *susceptibility*: generation of extra magnetic fields in materials that are immersed in an external field
  - *Diamagnetic* materials produce negative B fields
  - *Paramagnetic* materials produce positive B fields
  - Size about $10^{-7} \cdot B_0$ = 1–10 Hz change in precession f
- Makes the precession frequency nonuniform, which affects the image intensity and quality
- For large scale (10+ cm) inhomogeneities, scanner-supplied nonuniform magnetic fields can be adjusted to "even out" the ripples in B — this is called *shimming*
  - Nonuniformities in B bigger than voxel size affect whole image
  - Nonuniformities in B smaller than voxel size affect voxel "brightness"

Frequency and Phase

- RF signals from different regions that are at different frequencies will get *out of phase* and thus tend to cancel out
  - Phase = the ωt in $\cos(\omega t)$ [frequency f $= \omega/2\pi$]



Sum of 500 Cosines with Random Frequencies

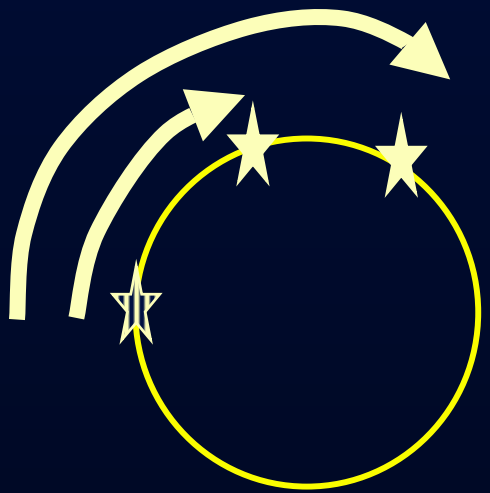


Transverse Relaxation and NMR Signal

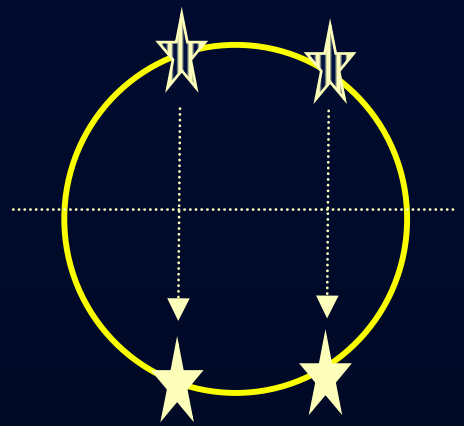
- Random frequency differences inside intricate tissue environment cause RF signals (from M_{xy}) to *dephase*
  - Measurement = sum of RF signals from many places
  - ➔ Measured signal decays away over time [T2*≈40 ms at 1.5 T]
  - At a microscopic level (microns), M_{xy} signals still exist; they just add up to zero when observed from outside (at the RF coil)
- Contents of tissue can affect local magnetic field
  - ➔ Signal decay rate depends on tissue structure and material
  - ➔ Measured signal strength will depend on tissue details
  - ➔ If tissue contents change, NMR signal will change
  - e.g., oxygen level in blood affects signal strength

Hahn Spin Echo: Retrieving Lost Signal

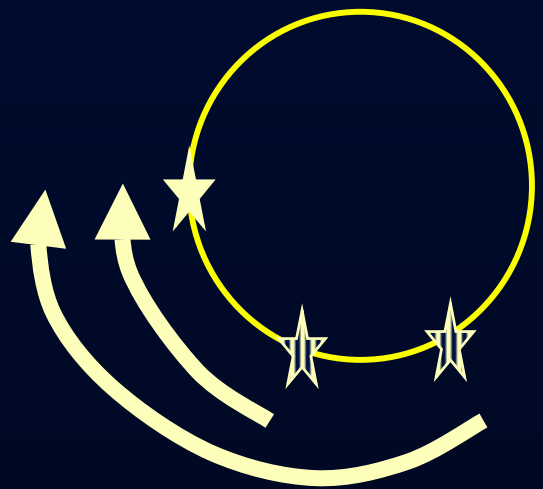
- Problem: M_{xy} rotates at different rates in different spots
- Solution: take all the M_{xy}'s that are ahead and make them get behind (in phase) the slow ones
  - After a while, fast ones catch up to slow ones ⇒ re-phased!



Fast & slow runners

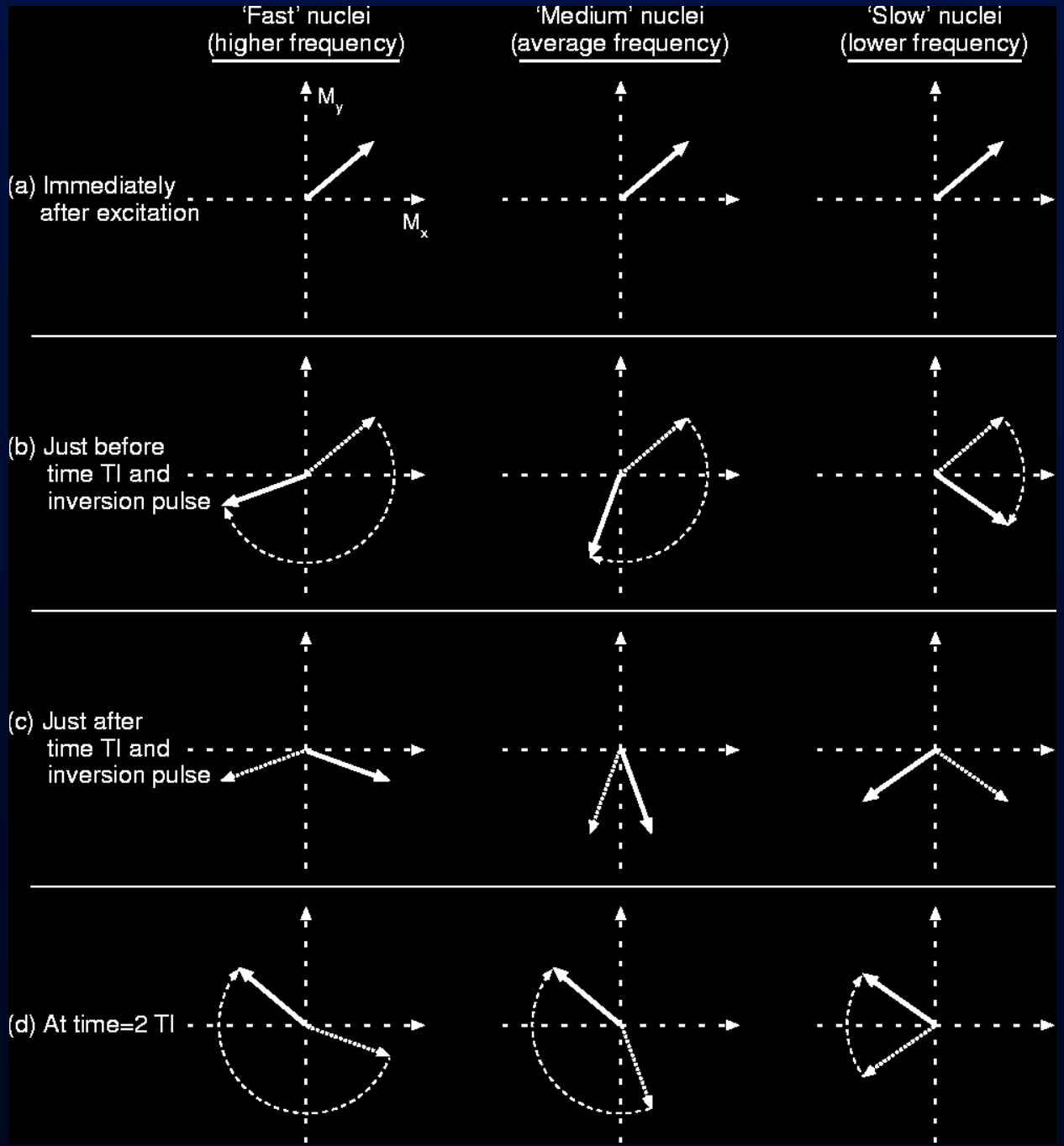


Magically "beam" runners across track



Let them run the same time as before

- The "magic" trick: *inversion* of the magnetization M
- Apply a second B_1 pulse to produce a flip angle of 180° about the y-axis (say)
- Time between first and second B_1 pulses is called TI
- "Echo" occurs at time TE = 2·TI



Relaxation: My Last Word

- Spin echo doesn't work forever (TI can't be too big)
  - Main reason: water molecules diffuse around randomly
    - About 5-10 microns during 10-100 ms readout window

  ➔ They "see" different magnetic fields and so their precession frequency changes from fast to slow to fast to .....

  - This process cannot be reversed by the inversion RF pulse
    - Time scale for irreversible decay of M_{xy} is called T2
- Longitudinal relaxation of M_z back to "normal" (T1)
  - Caused by internal RF magnetic fields in matter
  - Thermal agitation of H_2O molecules
  - Can be enhanced by magnetic impurities in tissue

  ➔ Drugs containing such impurities can alter T1, T2, and T2* — contrast agents (e.g., Gd-DTPA, MION)

Part the Third

Localization
of the
NMR Signal,
or,
How to Make Images

Steps in 3D Localization

- Can only detect total RF signal from entire 3D volume inside the "RF coil" (the detecting antenna)

❶ Excite M_{xy} in only a thin (2D) slice of the subject

- ➔ The RF signal we detect must come from this slice
- ➔ Have localized from 3D down to 2D

❷ Deliberately make magnetic field strength *B* depend on location within slice

- ➔ Frequency of RF signal will depend on where it comes from
- ➔ Breaking total signal into frequency components will provide more localization information

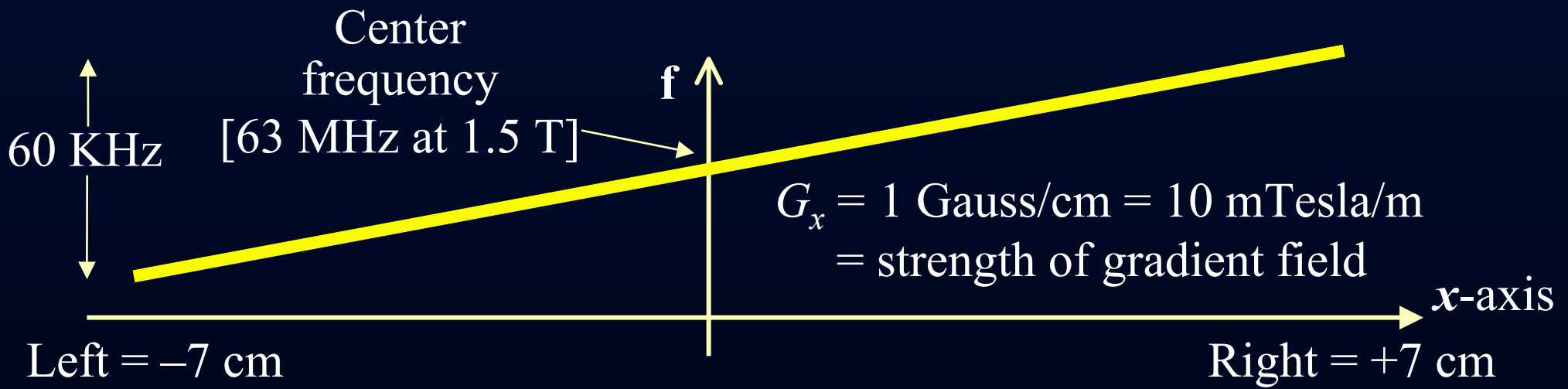
❸ Make RF signal phase depend on location within slice

Spatially Nonuniform *B*: Gradient Fields

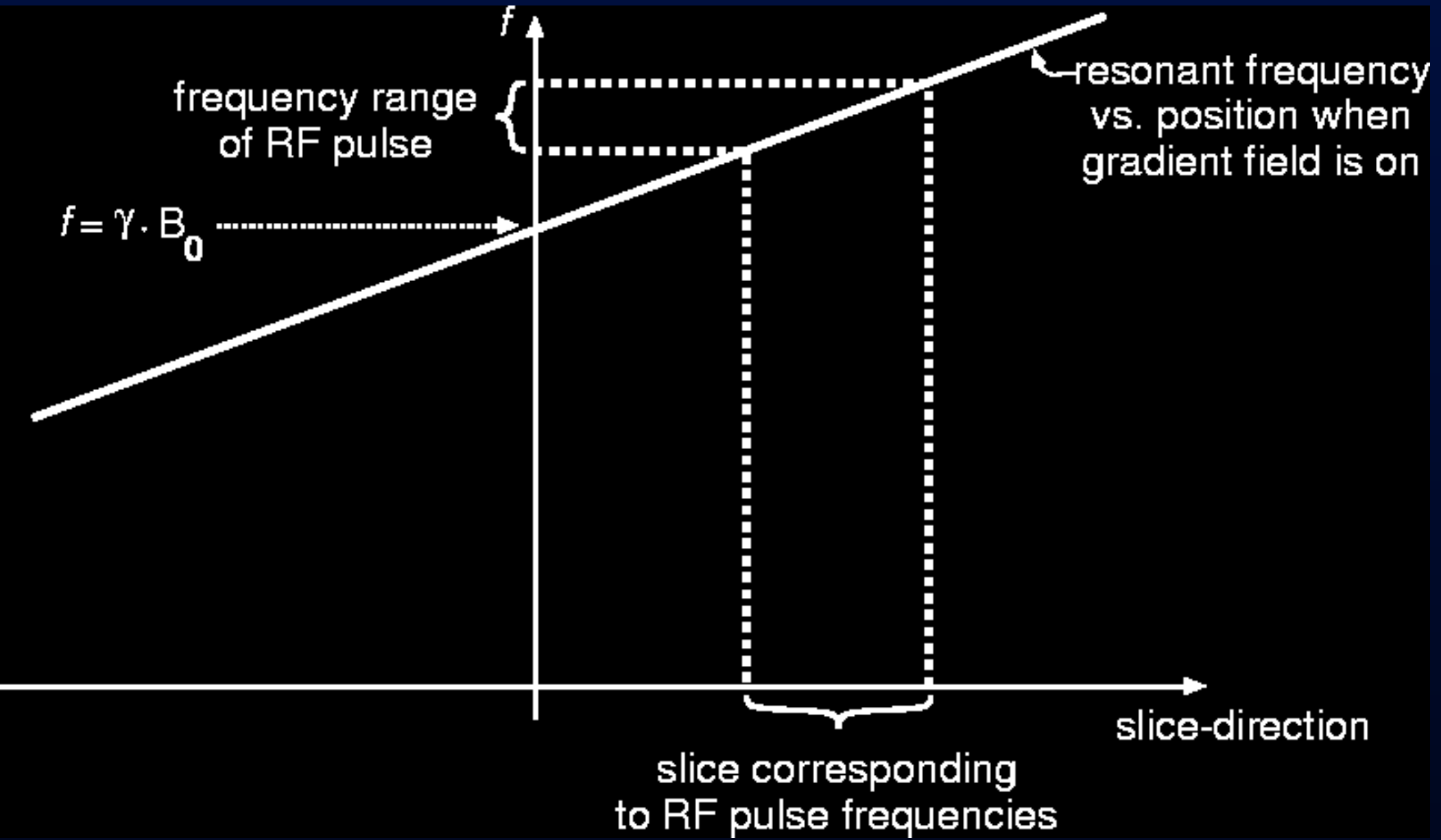
- Extra static magnetic fields (in addition to B_0) that vary their intensity in a linear way across the subject

➔ Precession frequency of *M* varies across subject

- This is called *frequency encoding* — using a deliberately applied nonuniform field to make the precession frequency depend on location



❶ Exciting M_{xy} in a Thin Slice of Tissue

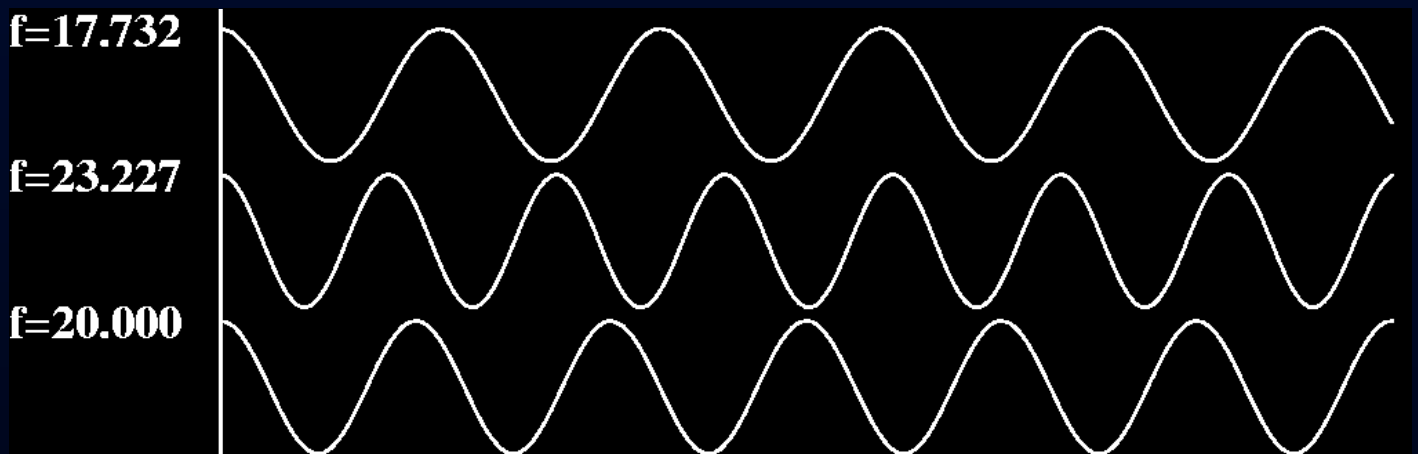


❷ Readout Localization

- After RF pulse (B_1) ends, acquisition (readout) of NMR RF signal begins
  - During readout, gradient field perpendicular to slice selection gradient is turned on
  - Signal is sampled about once every microsecond, digitized, and stored in a computer
    - Readout *window* ranges from 5–100 milliseconds (can't be longer than about 2·T2*, since signal dies away after that)
  - Computer breaks measured signal $V(t)$ into frequency components $v(\mathrm{f})$ — using the Fourier transform
  - Since frequency f varies across subject in a known way, we can assign each component $v(\mathrm{f})$ to the place it comes from

Image Resolution (in Plane)

- Spatial resolution depends on how well we can separate frequencies in the data $V(t)$
  - Resolution is proportional to Δf = frequency accuracy
  - Stronger gradients $\Rightarrow$ nearby positions are better separated in frequencies $\Rightarrow$ resolution can be higher for fixed Δf
  - Longer readout times $\Rightarrow$ can separate nearby frequencies better in $V(t)$ because phases of $\cos(f \cdot t)$ and $\cos([f+\Delta f] \cdot t)$ will have longer to separate: $\Delta f = 1/(\text{readout time})$



❸ The Last Dimension: Phase Encoding

- Slice excitation provides one localization dimension
- Frequency encoding provides second dimension
- The third dimension is provided by *phase encoding*:
  - We make the phase of M_{xy} (its angle in the *xy*-plane) signal depend on location in the third direction
  - This is done by applying a gradient field in the third direction ($\perp$ to both slice select and frequency encode)
  - Fourier transform measures phase ϕ of each $v(f)$ component of $V(t)$, as well as the frequency f
  - By collecting data with many different amounts of phase encoding strength, can break each $v(f)$ into phase components, and so assign them to spatial locations in 3D

Part the Fourth

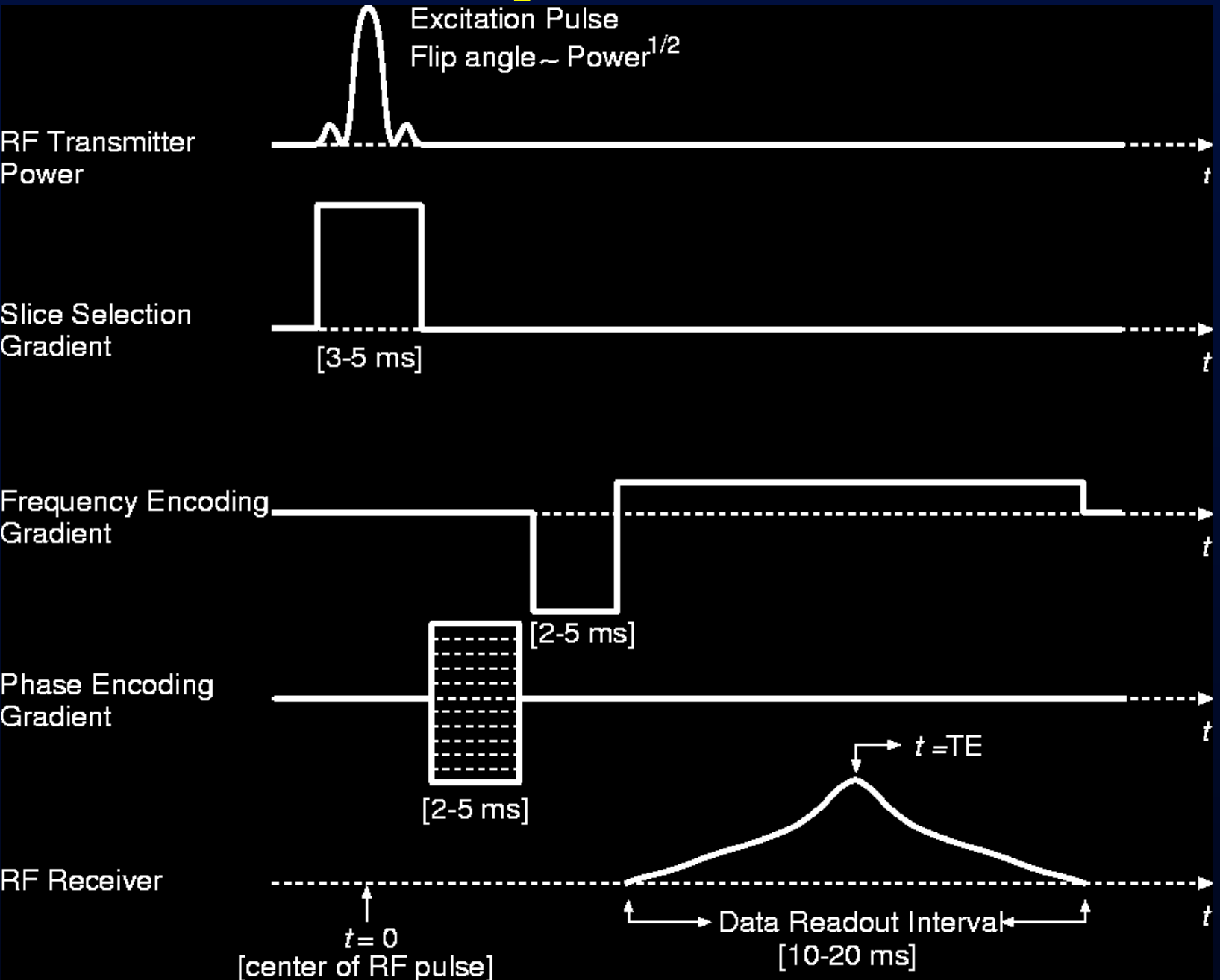
Some Imaging Methods

The Gradient Echo

- Spin echo: when "fast" regions get ahead in phase, make them go to the back and catch up
- Gradient echo: make "fast" regions become "slow" and vice-versa
  - Only works when different precession rates are due to scanner-supplied gradient fields, so we can control them
  - Turn gradient field on with negative slope for a while, then switch it to have positive slope
  - What was fast becomes slow (and vice-versa) and after a time, the RF signal phases all come back together

  ➔ The total RF signal becomes large at that time (called TE)

MRI Pulse Sequence for Gradient Echo Imaging



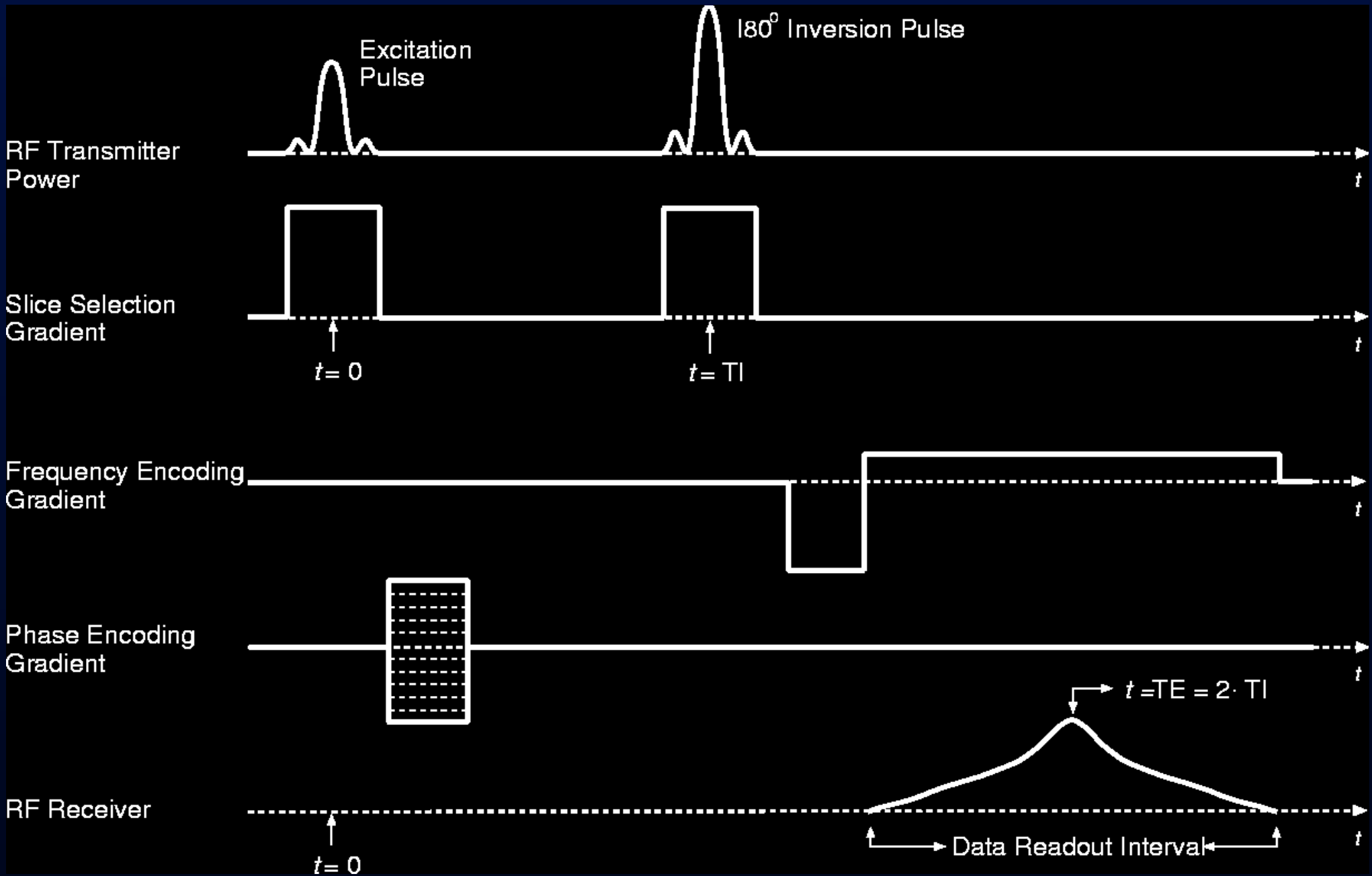
Illustrates sequence of events during scanning

As shown, this method (FLASH) takes 35 ms per RF shot, so would take 2.25 s for a 64×64 image

Why Use the Gradient Echo?

- Why not readout without negative frequency encoding?
- Purpose: delay the time of maximum RF signal
  - Occurs at t = TE after the RF pulse
  - During this time, magnetization M will evolve not only due to externally imposed gradients, but also due to microscopic (sub-voxel) structure of magnetic field inside tissue
  - Delaying readout makes signal more sensitive to these internal details
- Resulting image intensity $I(x,y)$ depends strongly on T2* at each location (x,y)
  - Most sensitive if we pick TE ≈ average T2*

MRI Pulse Sequence for Spin Echo Imaging



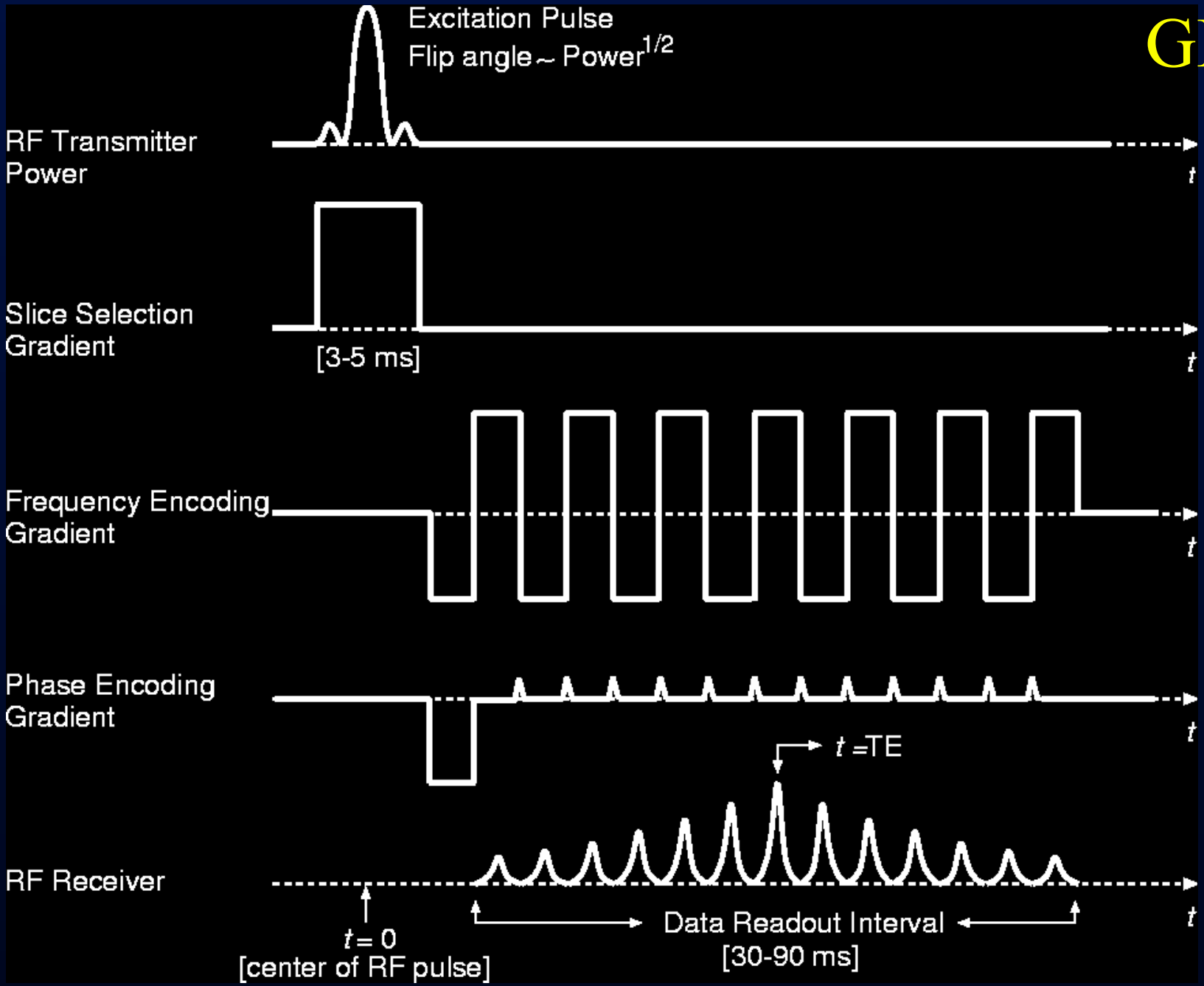
Why Use the Spin Echo?

- Purpose: re-phase the NMR signals that are lost due to sub-voxel magnetic field spatial variations
- Resulting image intensity $I(x,y)$ depends strongly on T2 at each location (x,y)
  - Most sensitive if we pick TE ≈ average T2
- SE images depend mostly on tissue properties at the 5 micron and smaller level (molecular to cellular sizes) = diffusion scale of H_2O in tissue during readout
- GE images depend on tissue properties over all scales up to voxel dimensions (molecular to cellular to structural)

Echo Planar Imaging (EPI)

- Methods shown earlier take multiple RF shots to readout enough data to reconstruct a single image
  - Each RF shot gets data with one value of phase encoding
- If gradient system (power supplies and gradient coil) are good enough, can read out all data required for one image after one RF shot
  - Total time signal is available is about $2 \cdot T2^*$ [80 ms]
- Must make gradients sweep back and forth, doing all frequency and phase encoding steps in quick succession
- Can acquire 10-20 low resolution 2D images per second

GE-EPI Pulse Sequence



Actually have 64 (or more) freq. encodes in one readout (each one < 1 ms)

[only 13 freq. encodes shown here]

What Makes the Beeping Noise in EPI?

- Gradients are created by currents through wires in the gradient coil — up to 100 Amperes
- Currents immersed in a magnetic field have a force on them — the Lorentz force — pushing them sideways
- Switching currents back and forth rapidly causes force to push back and forth rapidly
- Force on wires causes coil assembly to vibrate rapidly
- Frequency of vibration is audio frequency
  - about 1000 Hz = switching rate of frequency encode gradients
  - scanner is acting like a (low-fidelity) loudspeaker

Other Imaging Methods

- Can "prepare" magnetization to make readout signal sensitive to different physical properties of tissue
  - Diffusion weighting (scalar or tensor)
  - Magnetization transfer (sensitive to proteins in voxel)
  - Flow weighting (bulk movement of blood)
  - Perfusion weighting (blood flow into capillaries)
  - Temperature; T1, T2, T2*; other molecules than H_2O
- Can readout signal in many other ways
  - Must program gradients to sweep out some region in *k*-space = coordinates of phase/frequency

$$k(t) = \int_0^t G(\tau)\, d\tau$$

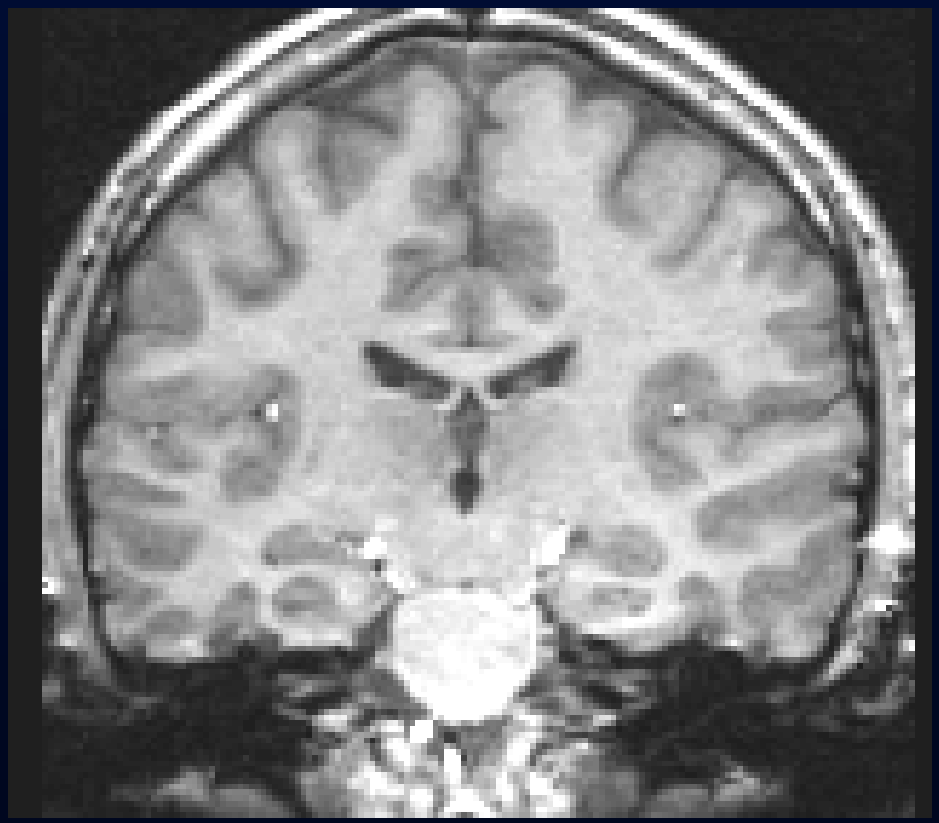
  - Example: spiral imaging (from Stanford)

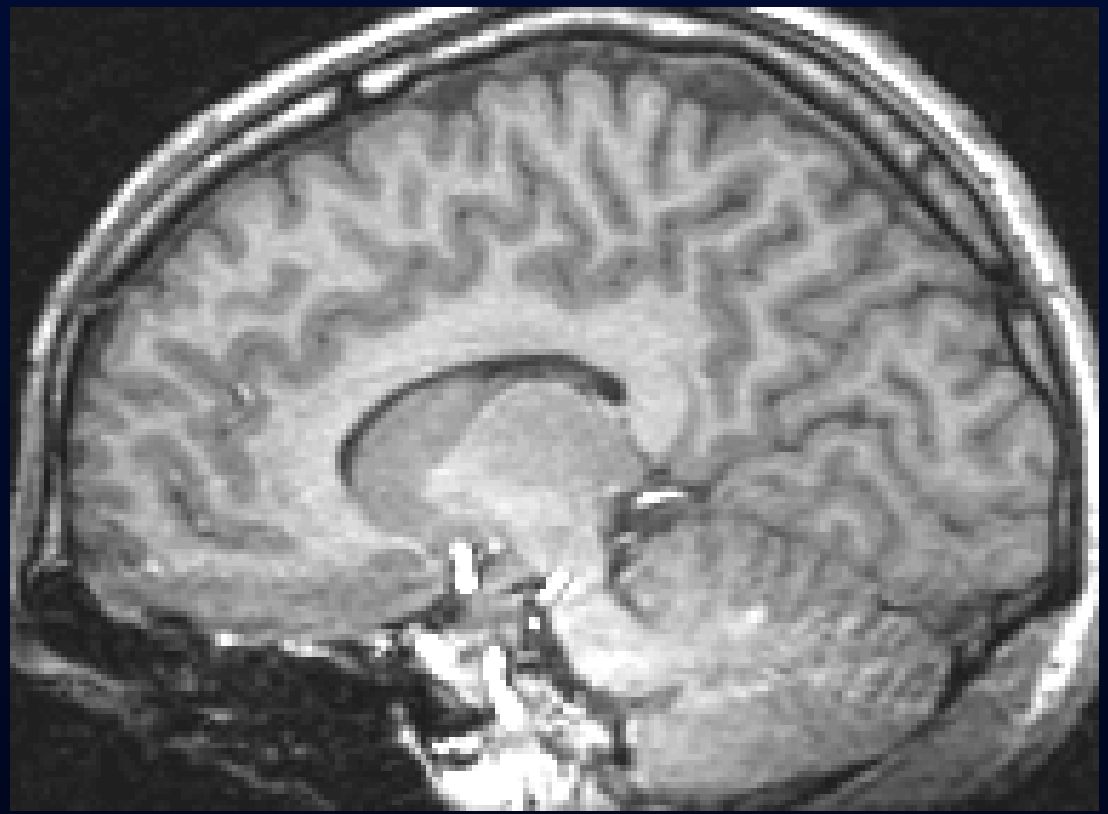
Part the Fifth

Image Contrast
and
Imaging Artifacts

The Concept of Contrast (or Weighting)

- *Contrast* = difference in RF signals — emitted by water protons — between different tissues
- Example: gray-white contrast is possible because T1 is different between these two types of tissue





Types of Contrast Used in Brain FMRI

- T1 contrast at high spatial resolution
  - Technique: use very short timing between RF shots (small TR) and use large flip angles
  - Useful for anatomical reference scans
  - 3 - 10 minutes to acquire 256×256×128 volume
  - 1 mm resolution
- T2 (spin-echo) and T2* (gradient-echo) contrast
  - Useful for functional activation studies
  - 2-4 seconds to acquire 64×64×20 volume
  - 4 mm resolution [better is possible with better gradient system, and a little longer time per volume]

Other Interesting Types of Contrast

- Perfusion weighting: sensitive to capillary flow
- Diffusion weighting: sensitive to diffusivity of H_2O
  - Very useful in detecting stroke damage
  - Directional sensitivity can be used to map white matter tracts
- Flow weighting: used to image blood vessels (MR angiography)
- Brain is mostly WM, GM, and CSF
  - Each has different value of T1
  - Can use this to classify voxels by tissue type
- Magnetization transfer: provides indirect information about H nuclei that aren't in H_2O (mostly proteins)

Imaging Artifacts

- MR images are computed from raw data $V(t)$
  - Assumptions about data are built into reconstruction methods
  - ☒ Magnetic fields vary as we command them to
  - ☒ The subject's protons aren't moving during readout or between RF excitations
  - ☒ All RF signal actually comes from the subject
- Assumptions aren't perfect
  - ➔ Images won't be reconstructed perfectly
  - Resulting imperfections are called *artifacts*:
    - Image distortion; bleed-through of data from other slices; contrast depends on things you didn't allow for; weird "zippers" across the image; et cetera .....

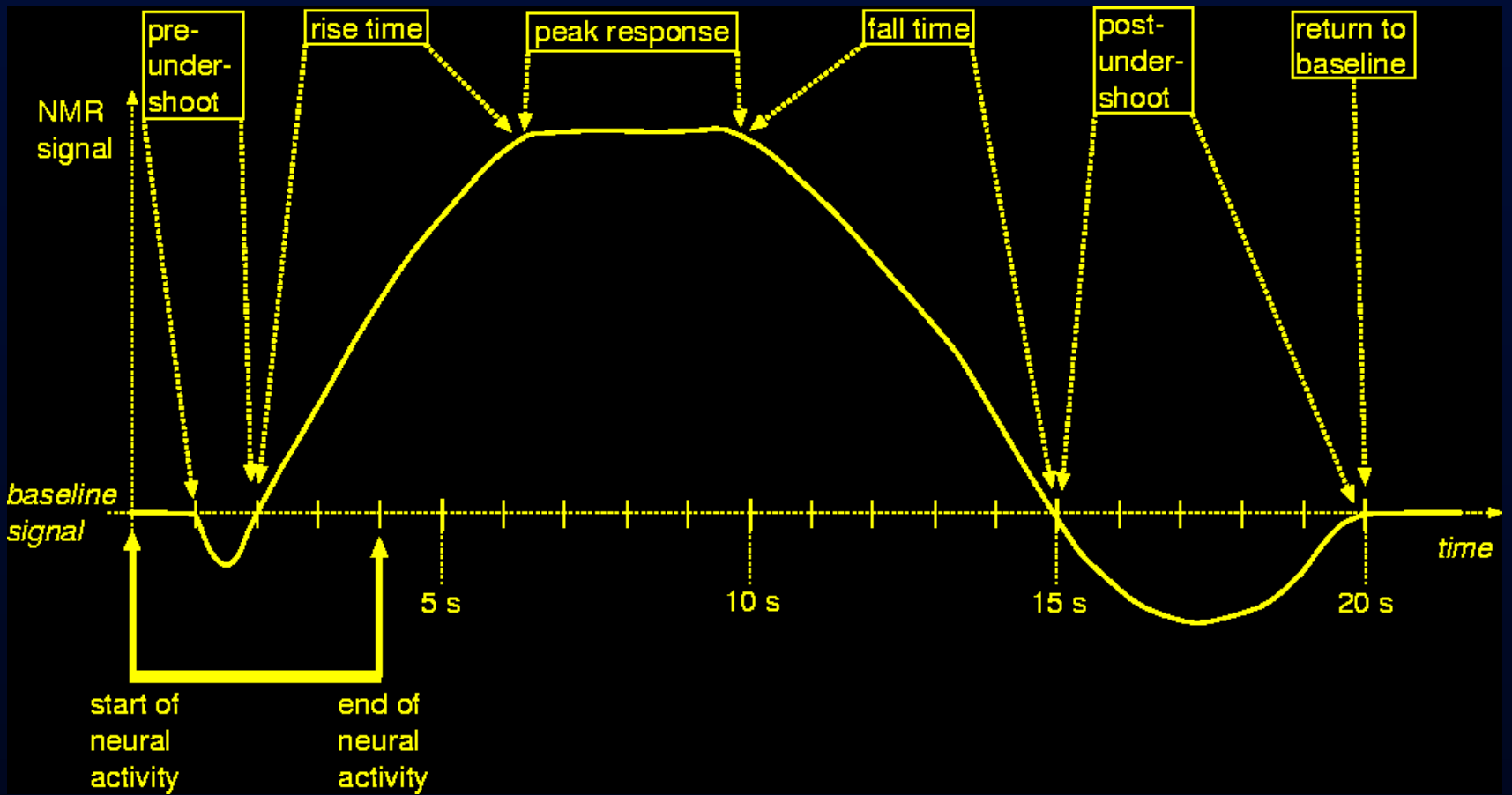
Part the Sixth

Functional Neuroimaging

What is Functional MRI?

- 1991: Discovery that MRI-measurable signal increases a few % *locally* in the brain subsequent to increases in neuronal activity (Kwong, *et al*.)

Cartoon of MRI signal in an "activated" brain voxel



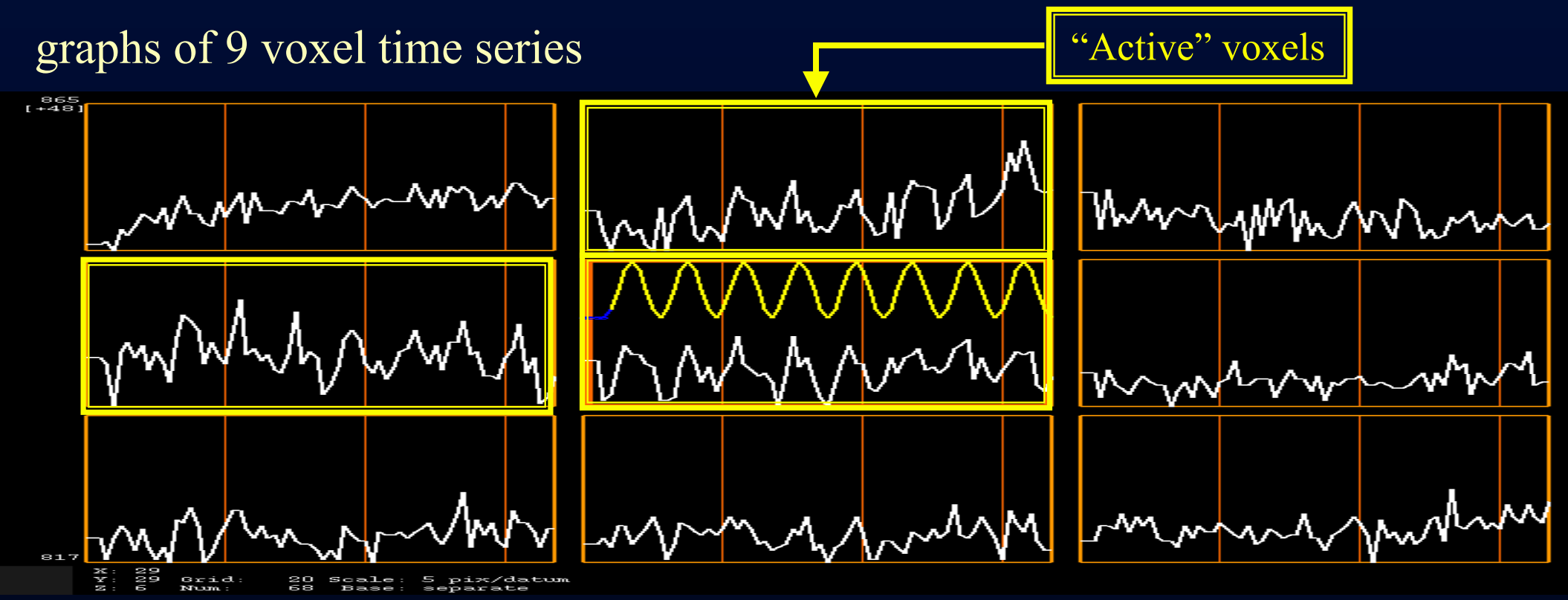
How FMRI Experiments Are Done

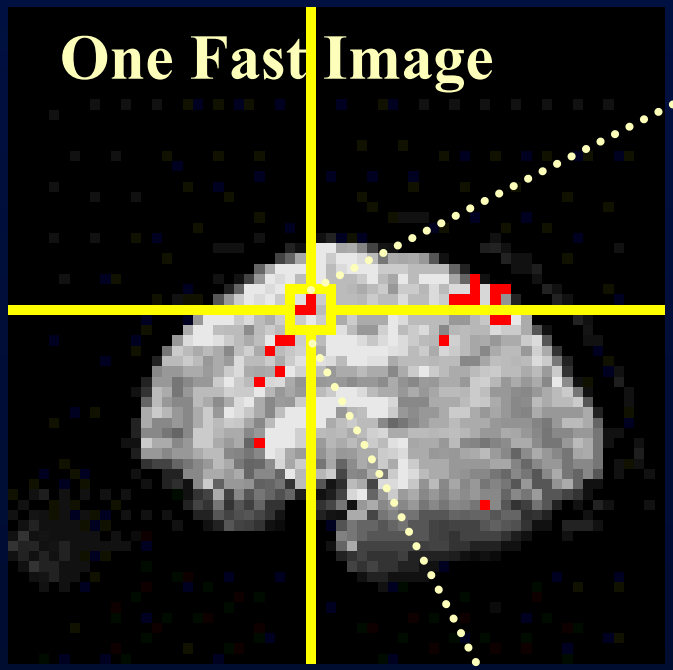
- Alternate subject's neural state between 2 (or more) conditions using sensory stimuli, tasks to perform, ...
  - Can only measure relative signals, so must look for changes
- Acquire MR images repeatedly during this process
- Search for voxels whose NMR signal time series matches the stimulus time series pattern
- Signal changes due to neural activity are small
  - → Need 50+ images in time series (each slice) ⇒ takes minutes
  - → Other small effects can corrupt the results ⇒ postprocess
- Lengthy computations for image recon and temporal pattern matching ⇒ data analysis usually done offline

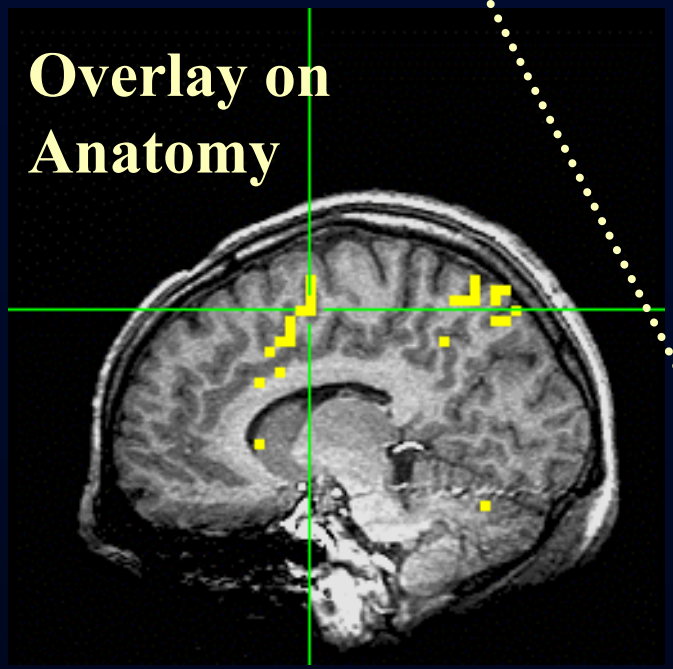
Some Sample Data Time Series

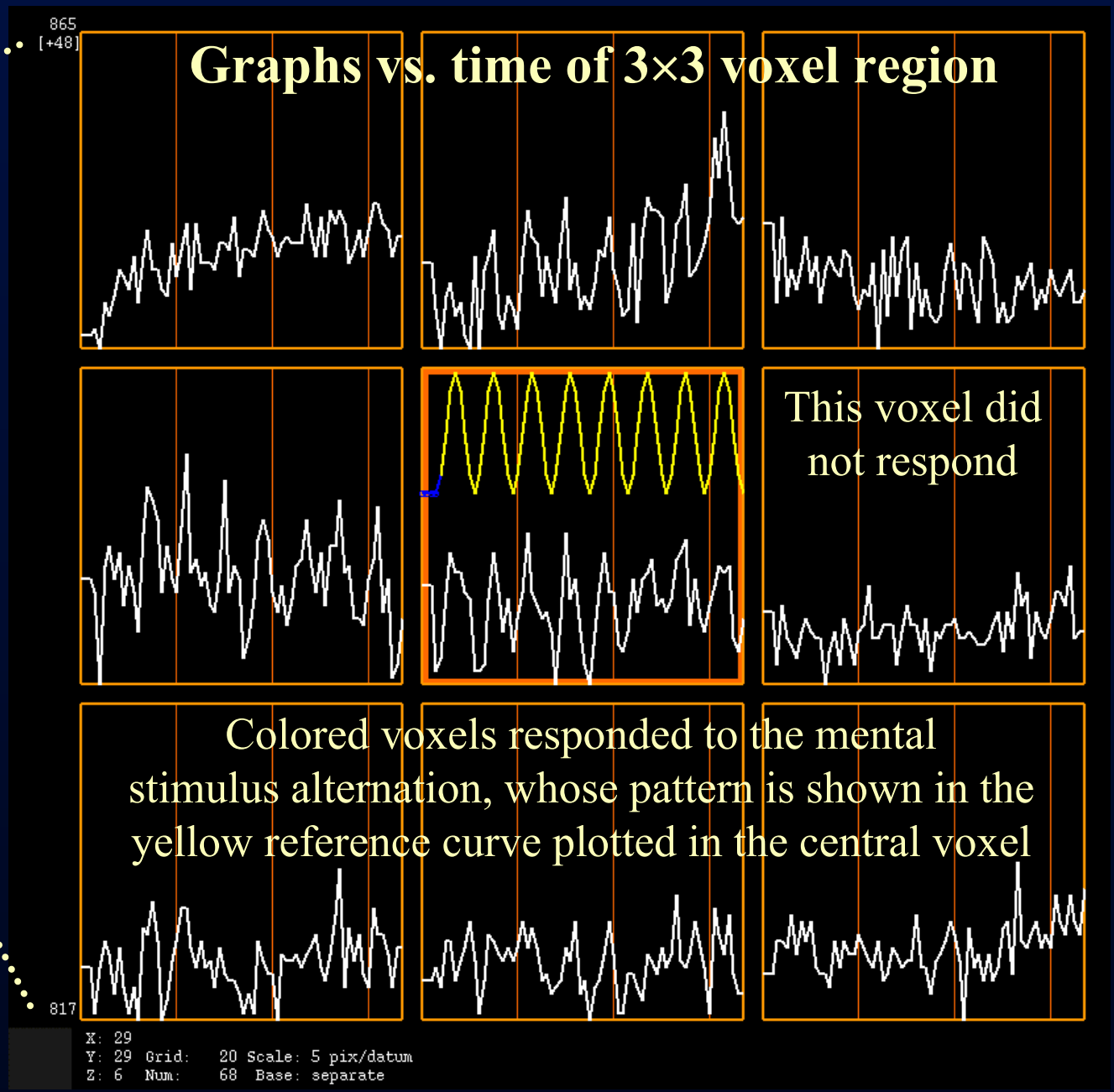
- 16 slices, 64×64 matrix, 68 repetitions (TR=5 s)
- Task: phoneme discrimination: 20 s “on”, 20 s “rest”

graphs of 9 voxel time series









68 points in time 5 s apart; 16 slices of 64×64 images

Why (and How) Does NMR Signal Change With Neuronal Activity?

- There must be something that affects the water molecules *and/or* the magnetic field inside voxels that are "active"
  - neural activity changes blood flow
  - blood flow changes which H_2O molecules are present and *also* changes the magnetic field
- FMRI is thus *doubly* indirect from physiology of interest (synaptic activity)
  - also is much slower: 4-6 seconds after neurons
  - also "smears out" neural activity: cannot resolve 10-100 ms timing of neural sequence of events

Neurophysiological Changes & FMRI

- There are 4 changes currently used in FMRI:

1. Increased Blood Flow
   - New protons flow into slice
   - More protons are aligned with B_0
   - Equivalent to a shorter T1 (protons are realigned faster)
   - NMR signal goes up [mostly in arteries]
2. Increased Blood Volume (due to increased flow)
   - Total deoxyhemoglobin increases
   - Magnetic field randomness increases
   - NMR signal goes down [near veins and capillaries]

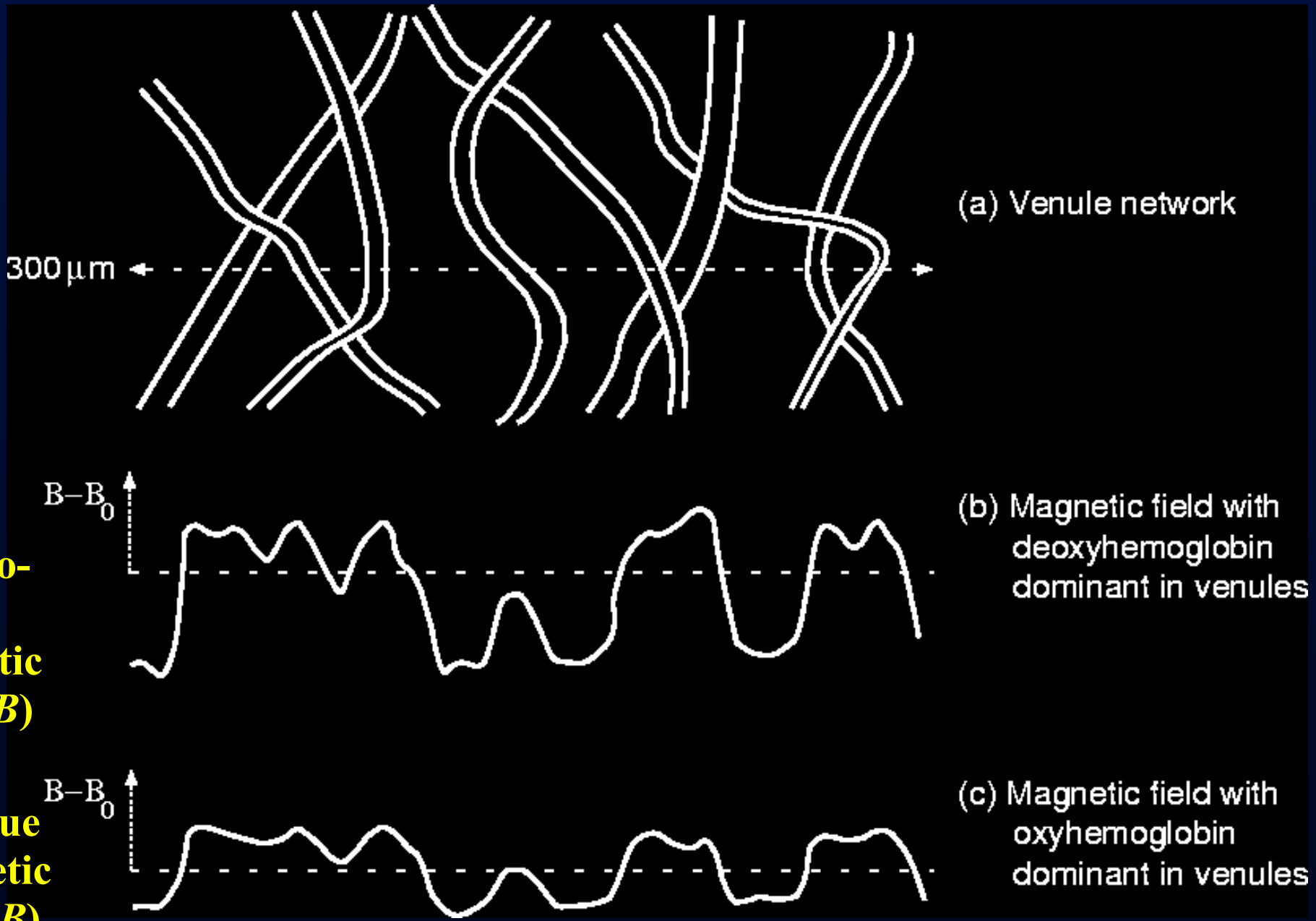
❸ "Oversupply" of oxyhemoglobin after activation

- Total deoxyhemoglobin decreases
- Magnetic field randomness decreases
- NMR signal goes up [near veins and capillaries]

❹ Increased capillary perfusion

- Inflowing spins exchange to parenchyma at capillaries
- Can be detected with perfusion-weighted imaging methods
- This is also the basis for ^{15}O water-based PET

Cartoon of Veins inside a Voxel



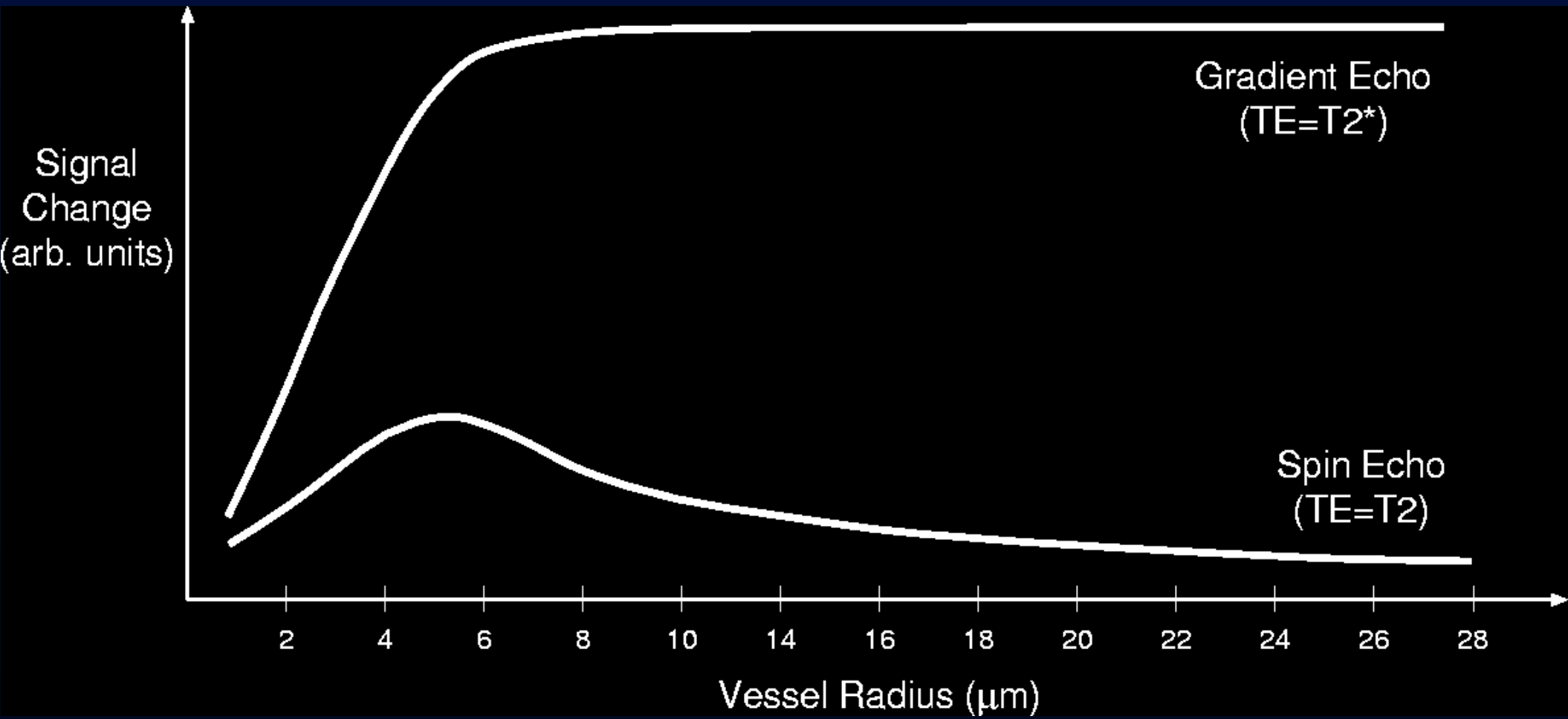
Deoxyhemo-globin is paramagnetic (increases *B*)

Rest of tissue is diamagnetic (decreases *B*)

BOLD Contrast

- **BOLD** = **B**lood **O**xygenation **L**evel **D**ependent
- Amount of deoxyhemoglobin in a voxel determines how inhomogeneous that voxel's magnetic field is at the scale of the blood vessels (and red blood cells)
- Increase in oxyhemoglobin in veins after neural activation means magnetic field becomes more uniform inside voxel
  - So NMR signal goes up (T2 and T2* are larger)
  - Gradient echo: depends on vessels of all sizes
  - Spin echo: depends only on smaller vessels

BOLD Sensitivity to Blood Vessel Sizes



Spatial Localization of Activity

- Tradeoff : detectability (or scan time) vs. accuracy
- Gradient echo
  - Largest signal changes, but veins draining active area will show "activity", perhaps 10 mm away
  - Due to very short T2*, very hard to use at ultra-high B_0
- Spin echo
  - Smaller signal changes, but more localized to small vessels
- Perfusion weighted imaging
  - Even smaller signal changes, but potentially best localization
  - "Difference of differences"

Physiological Artifacts

- Blood flow cycles up and down with cardiac cycle
  - Imaging rate slower than heartbeat means this looks like noise
  - Brainstem also moves about 0.5 mm with cardiac cycle
- Respiration causes periodic changes in blood oxygenation and magnetic field (due to movement of chest tissue)
- Subject movements inside gradient coil cause signal changes
  - Movements of imaged tissue are major practical problem
  - Movements of tissue outside image (e.g., swallowing, speaking) can change magnetic field inside image
- Vasculature is different in each voxel, so BOLD response will be different even if neural activity is same
  - ➔ Hard to compare response magnitude and timing between locations and subjects

Structural Artifacts

- Un-shimmable distortions in *B* field cause protons to precess in ways not allowed for
  - Field is perturbed by interfaces between regions with different susceptibilities, especially air-tissue boundaries
  - Worst areas: above the nasal sinuses; near the ear canals
- EP images will be warped in phase-encoding direction
  - Can be partly corrected by measuring *B* field and using that in reconstruction (the "VTE" method)
- 2D images will have signal dropout if through-slice field is not uniform
  - Palliatives: shorten TE; use thinner slices