BOLD fMRI:
Mechanisms & Sensitivity
(How Acquisition Choices Matter)

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MR Physics for SPM – May 2026

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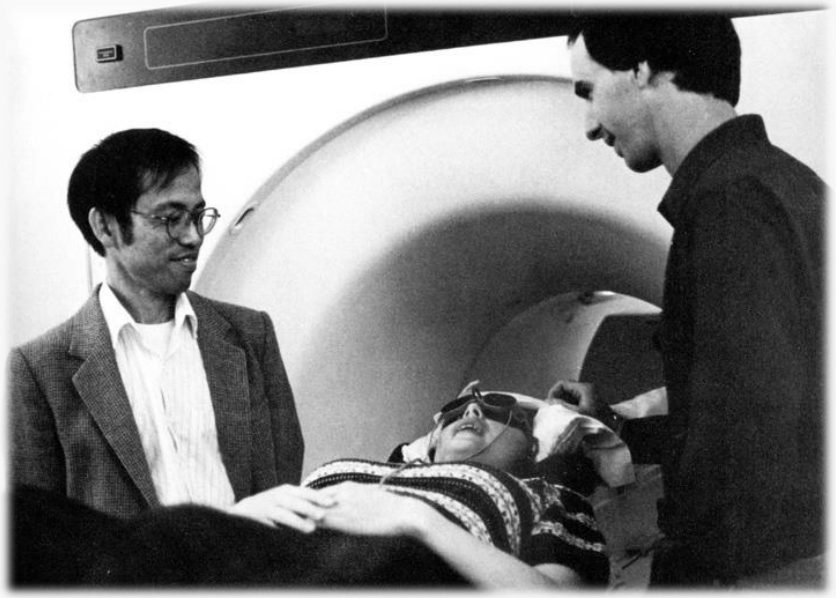
Learning Objectives

- Explain the principle of BOLD contrast in fMRI
- Understand physiological and MR-related factors influencing the BOLD signal
- Identify key acquisition parameters
- Make informed decisions to optimise BOLD sensitivity

BOLD Mechanisms

Functional MRI

- A non-invasive imaging technique measuring brain activity **indirectly via haemodynamic changes**
- Introduced in the early 1990s
- Widely used in:
  - Cognitive neuroscience
  - Clinical research
  - Brain mapping

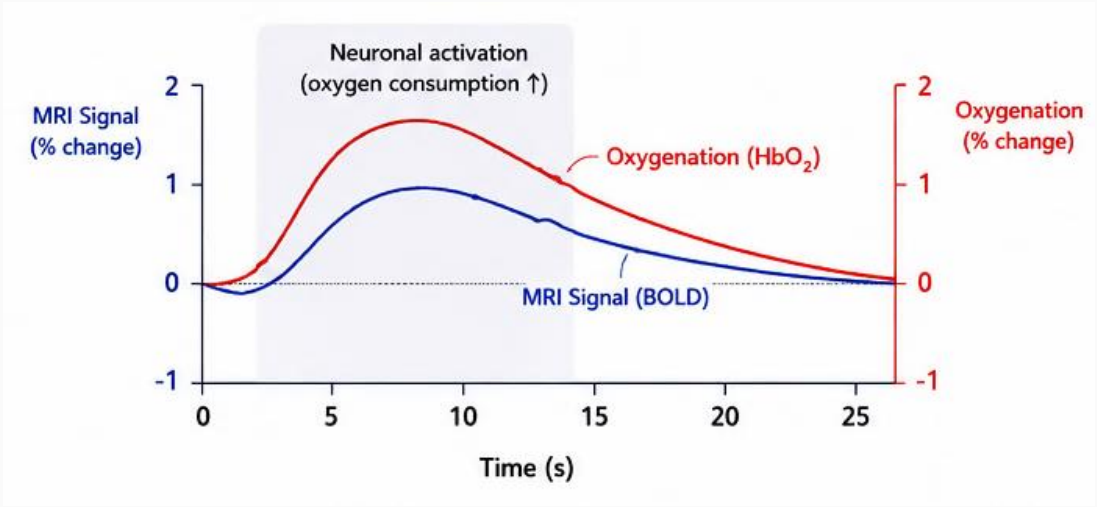


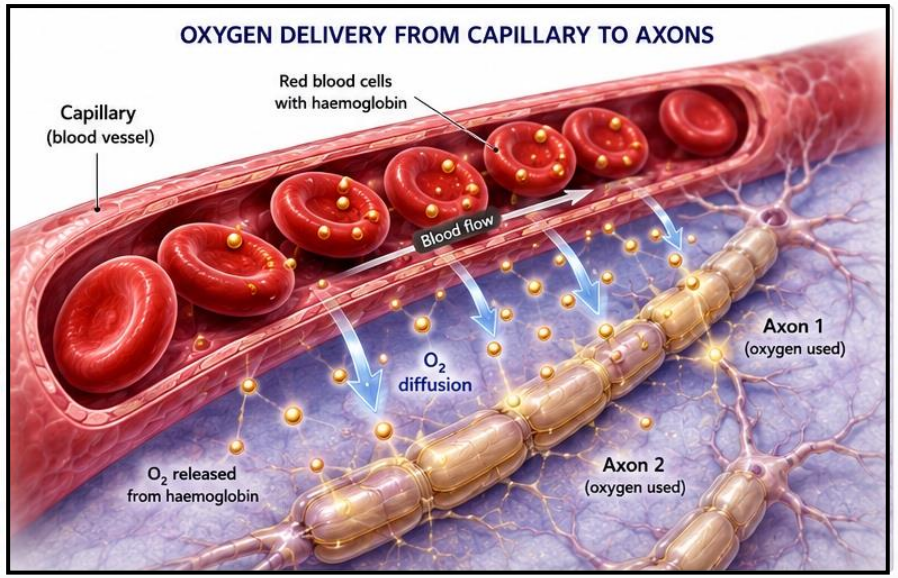
Ken Kwong et al. at early days of fMRI (MGH-Harvard)

Lv H, et al. *Am. J. Neuroradiol.* 2018;39(8):1390-139.

What is BOLD?

- Blood Oxygenation Level Dependent signal
- Uses [de]oxy-haemoglobin as an endogenous contrast agent
- Relies on magnetic susceptibility differences → MRI is sensitive to
- Reflects changes in blood oxygenation

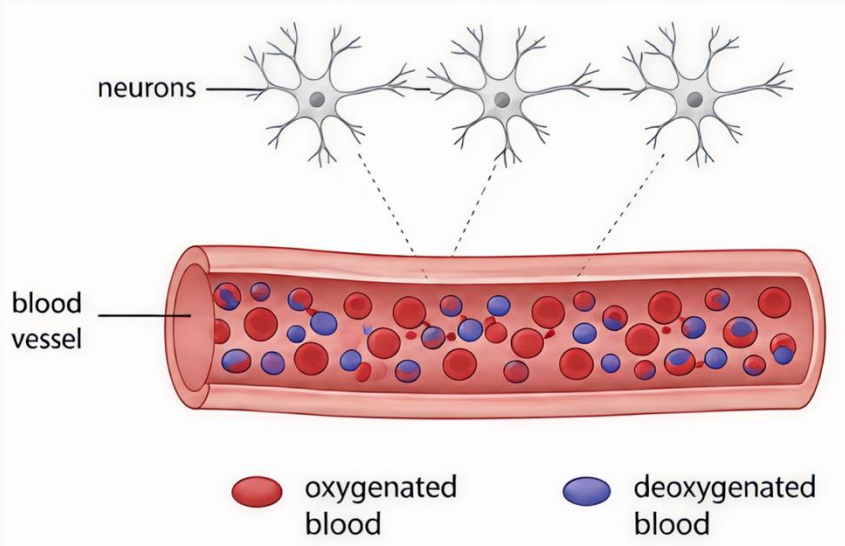




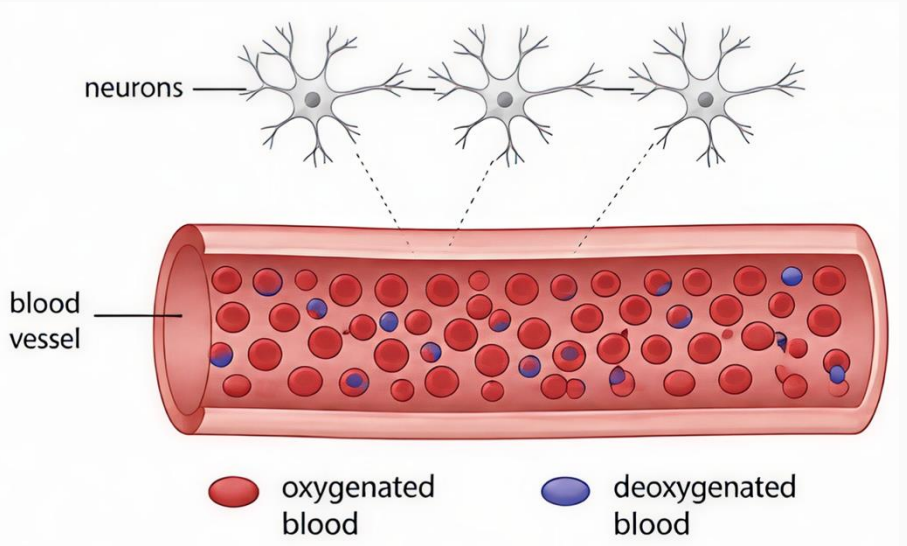
Neural Activation → BOLD

- Physiological effects leading to a change of blood oxygenation, and thus a BOLD signal change:

AT REST
Higher deoxyhaemoglobin concentration



NEURAL ACTIVATION
Increased blood flow, reduced deoxyhaemoglobin

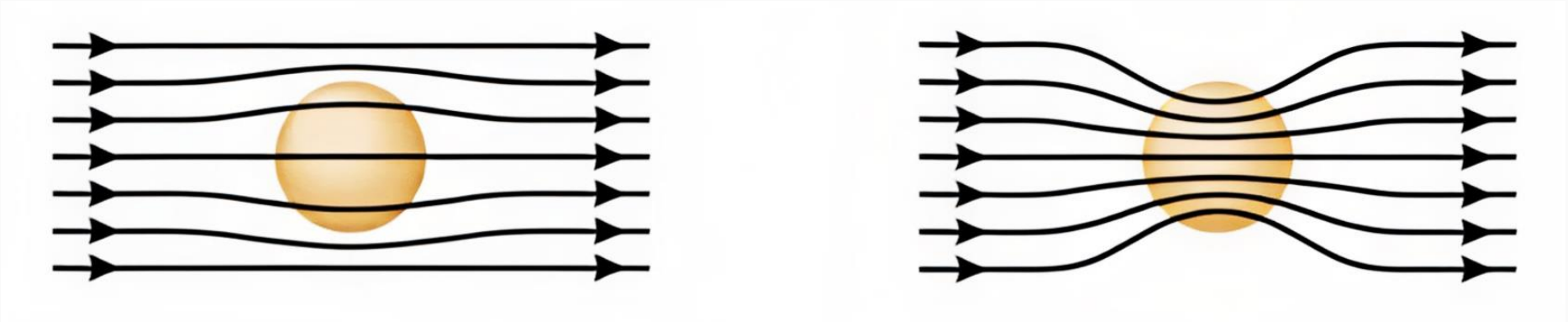


High *deoxy:oxygenated* blood ratio → Higher T_2*

Low *deoxy:oxygenated* blood ratio → Lower T_2*

Magnetic susceptibility

- A measure of how easily a material becomes magnetized when placed in an external magnetic field
  - Diamagnetic $(\chi < 0)$: weakly repelled by the external magnetic field
  - Paramagnetic $(\chi > 0)$: attracted to the external magnetic field

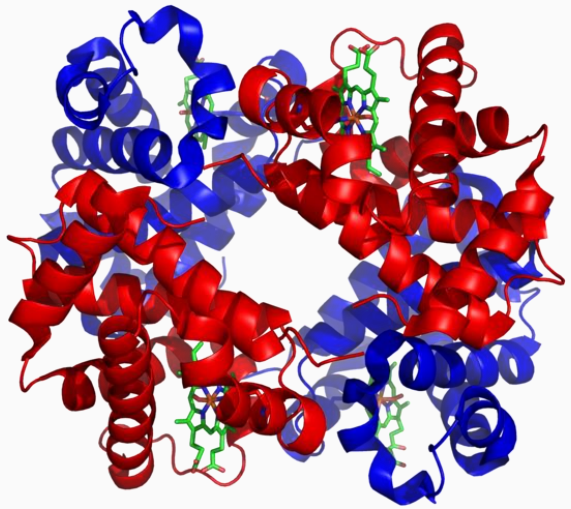


Field bends slightly away from the material

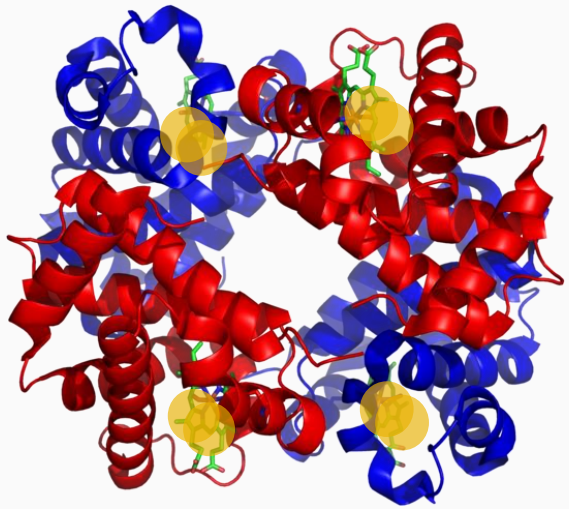
Field bends toward the material

Susceptibility → Signal Change

- Deoxyhaemoglobin creates local field gradients
- Act like microscopic dipoles affecting background magnetic field



Heme groups containing ***Iron***
→ making Hb **paramagnetic**

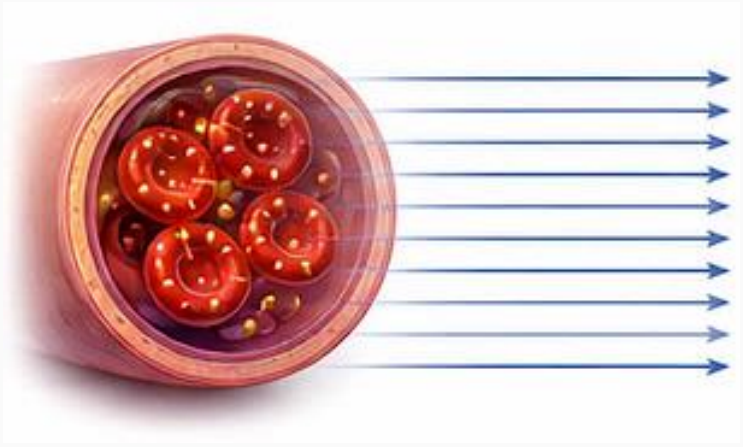


Bound ***oxygen*** shields Heme groups
→ making HBO_2 **diamagnetic**

Susceptibility → Signal Change

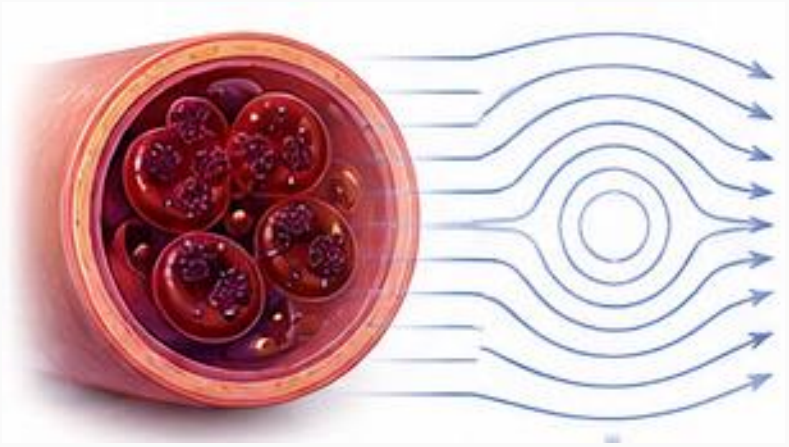
- Deoxyhaemoglobin creates local field gradients
- Act like microscopic dipoles affecting background magnetic field

Acting like the tissue



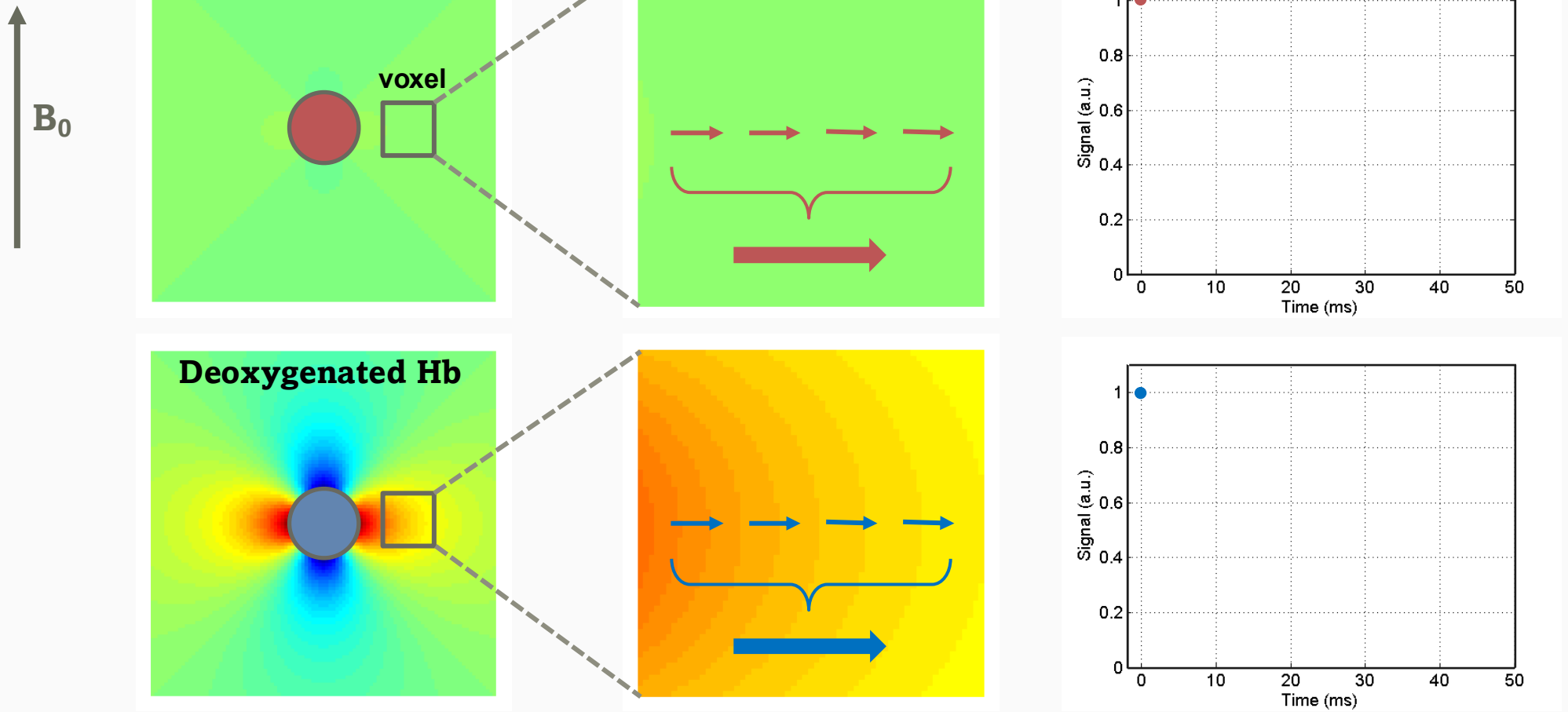
Heme groups containing ***Iron***
→ making Hb **paramagnetic**

Acting different from the tissue

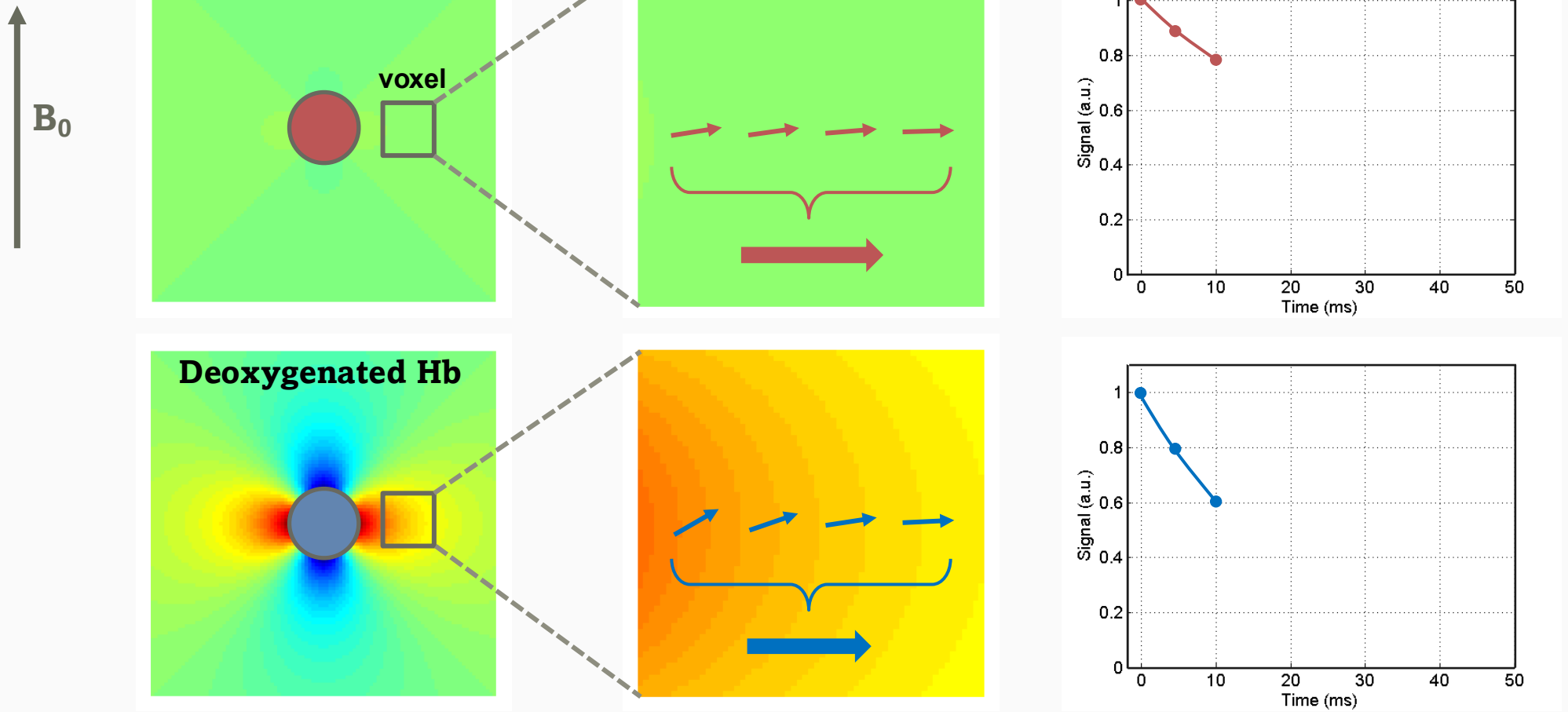


Bound ***oxygen*** shields Heme groups
→ making HBO_2 **diamagnetic**

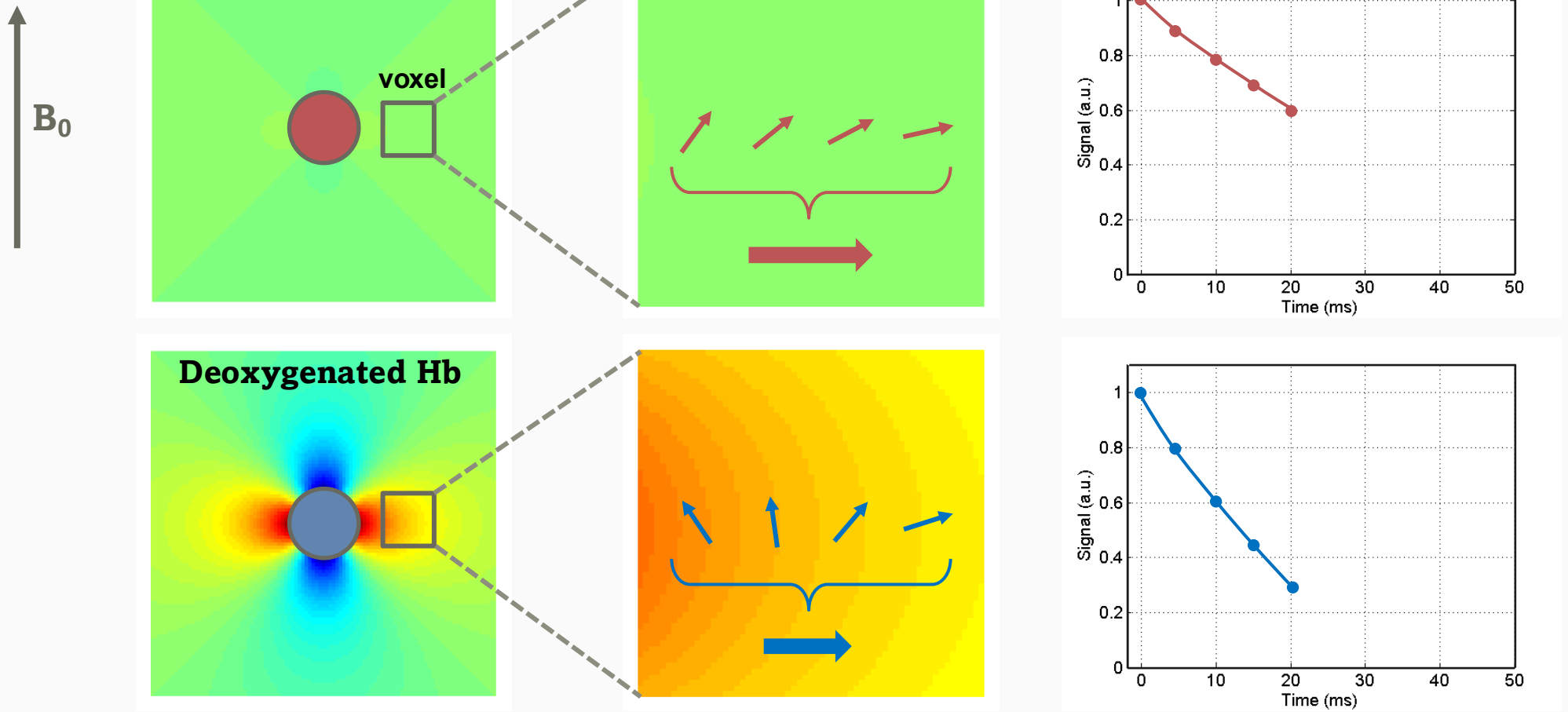
Susceptibility → Signal Change



Susceptibility → Signal Change



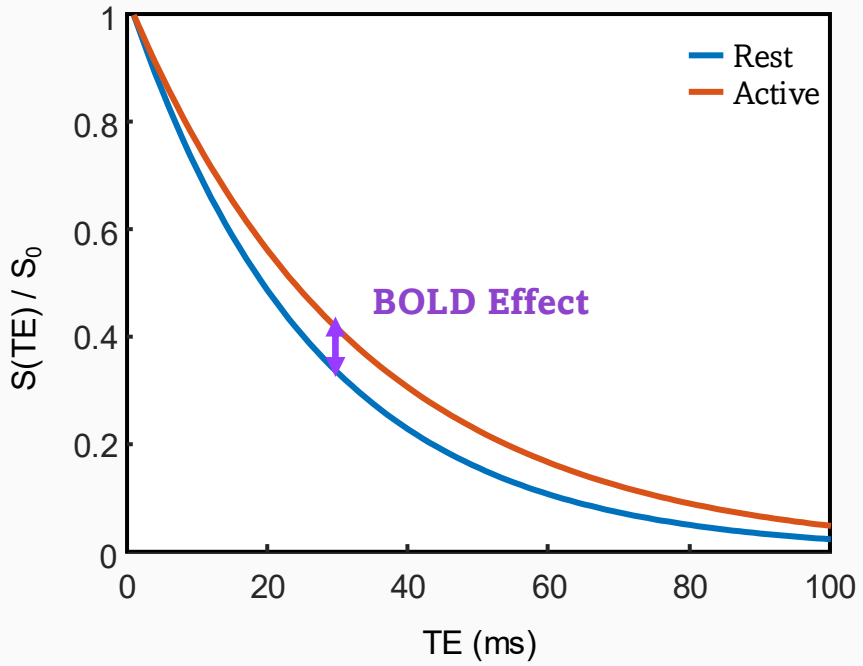
Susceptibility → Signal Change



BOLD Signal

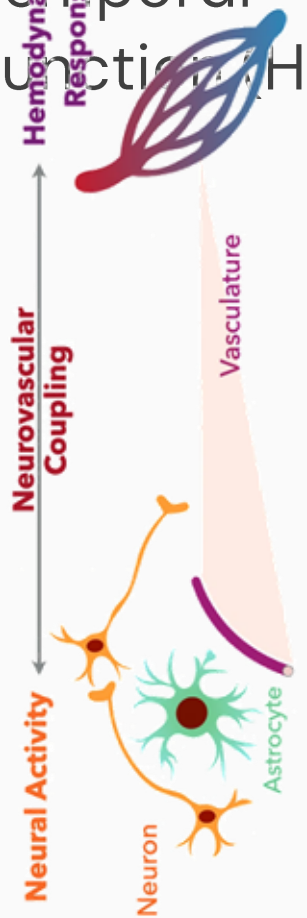
- Small effect (1–5%)
- Spatially variable
- Competes with:
  - Thermal noise
  - Physiological noise

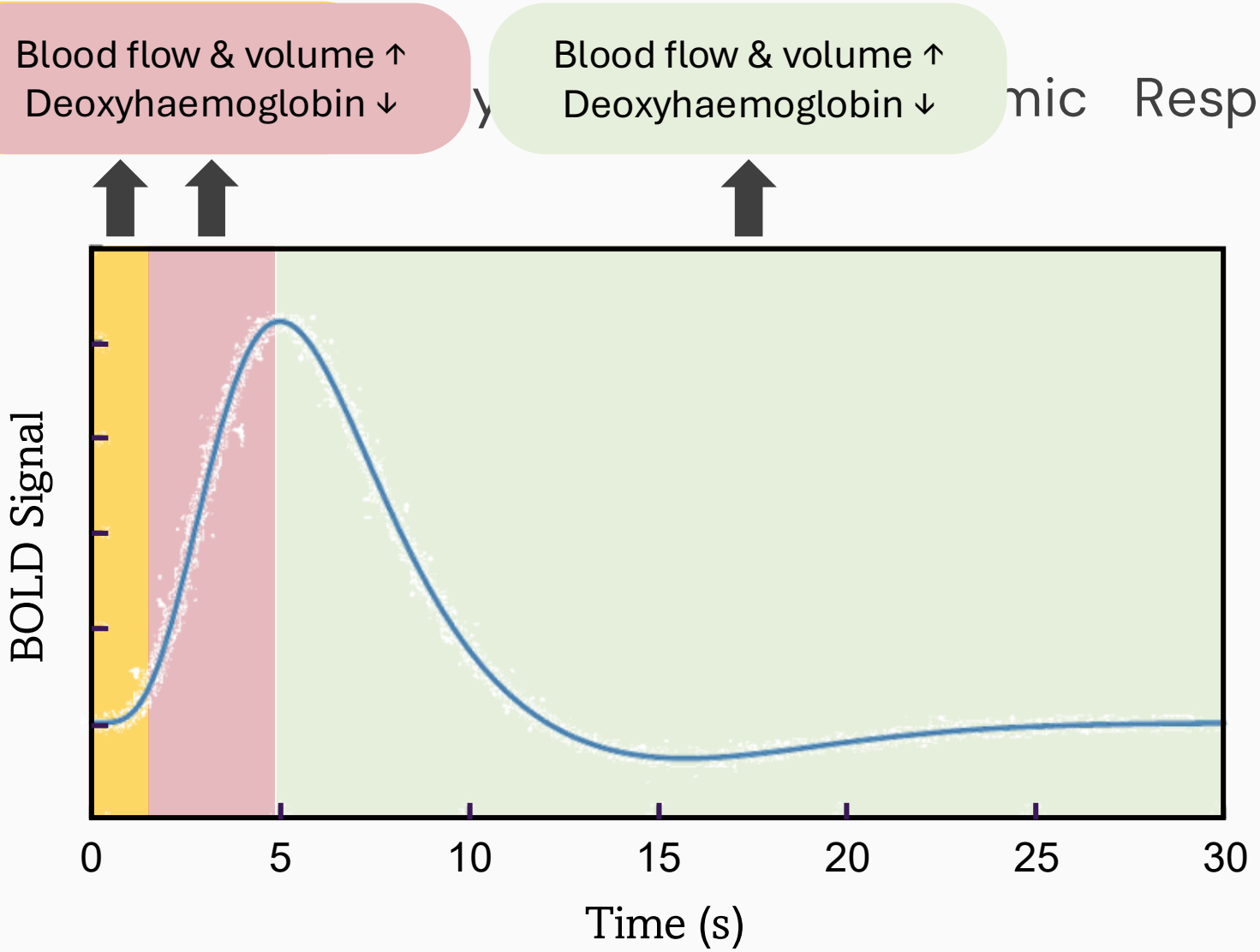
$$S(TE) = S_0 e^{-TE/T_2^*}$$



BOLD Signal Time Course

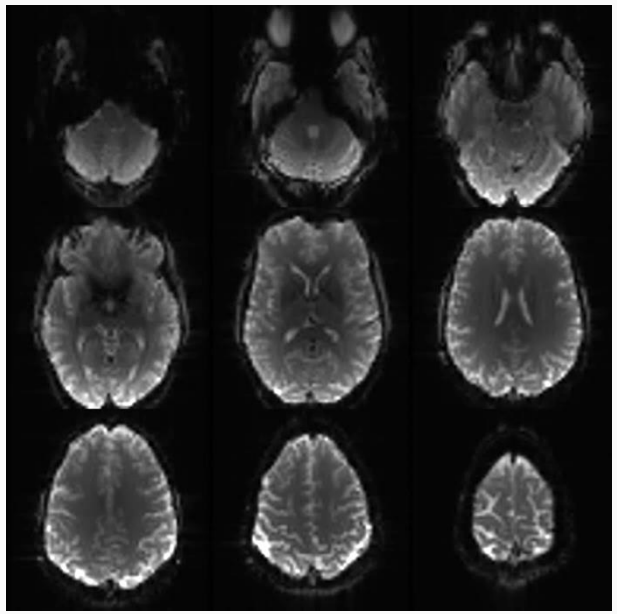
- Temporal beh… …mic Response Functi… (HRF)



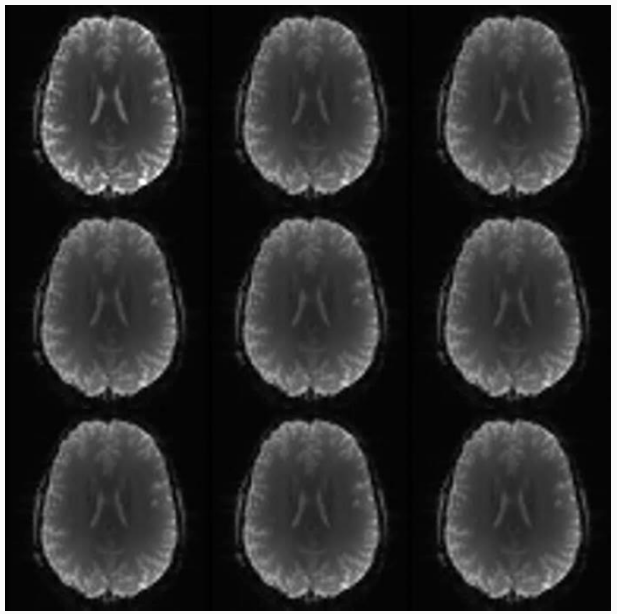


Sampling Requirements

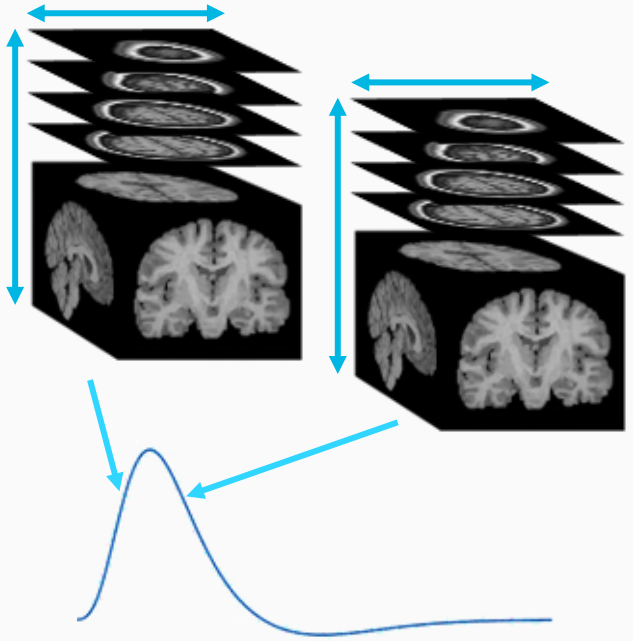
Cover spatial extent



Capture dynamics

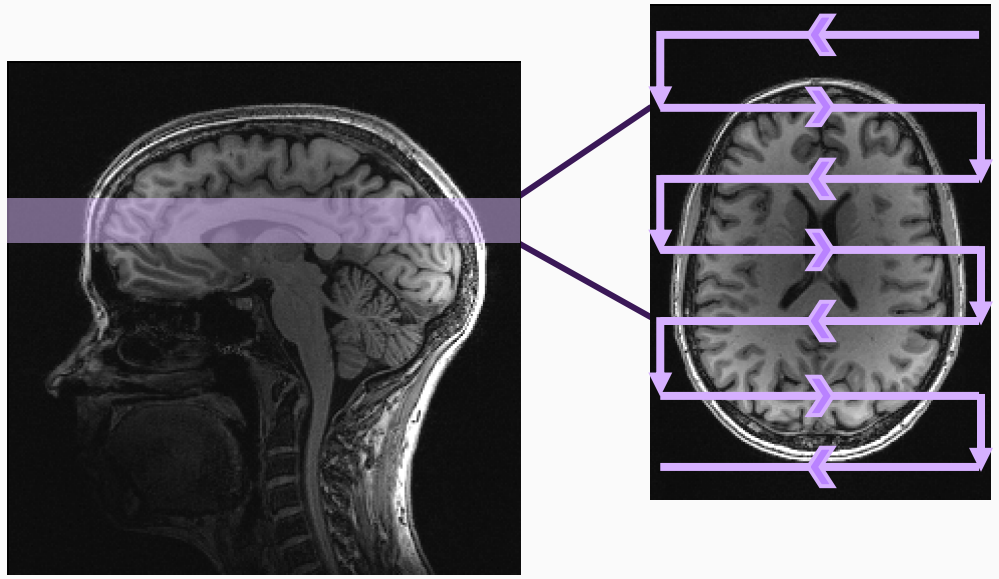


Be sufficiently fast



How To Measure BOLD?

- Gradient-Echo Echo Planar Imaging (GRE-EPI)
  - ✓ Provides T2* contrast
  - ✓ Acquires whole slice in one shot
  - ✓ Very fast → captures dynamics



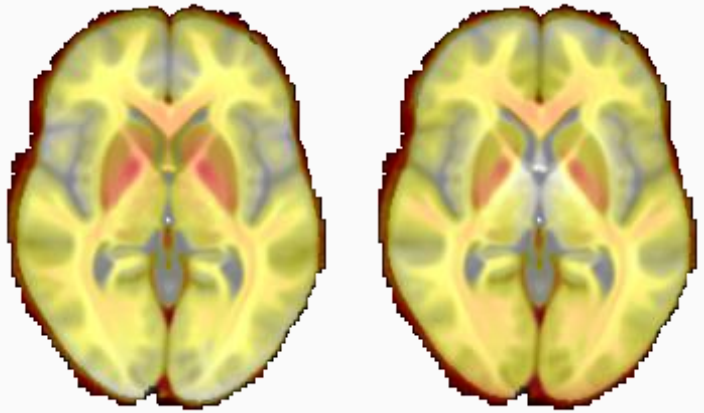
👉 Key benefit:
Enables whole-brain imaging every ~ 2–3 seconds

BOLD Sensitivity

BOLD Sensitivity

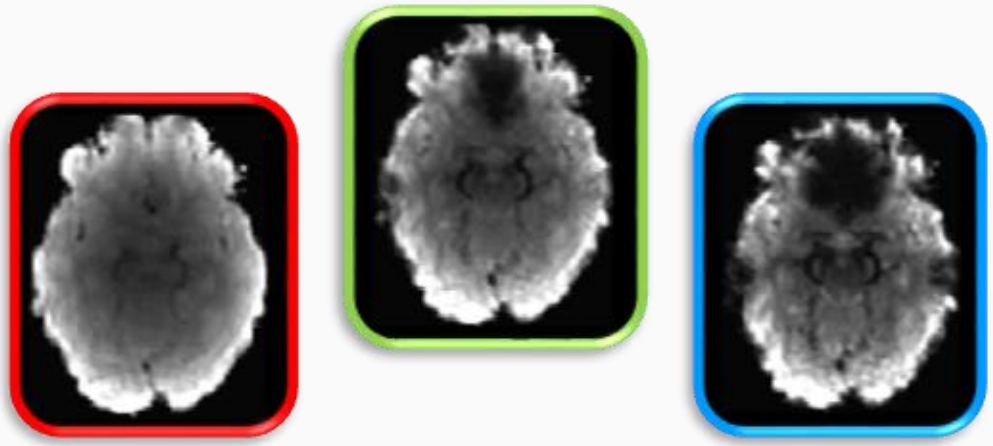
- Ability to detect small neural changes reliably
- Simplified Model:
- Depends on:
  - ✓ TE (Contrast)
  - ✓ Signal strength
  - ✓ Sampling (acquisition strategy)

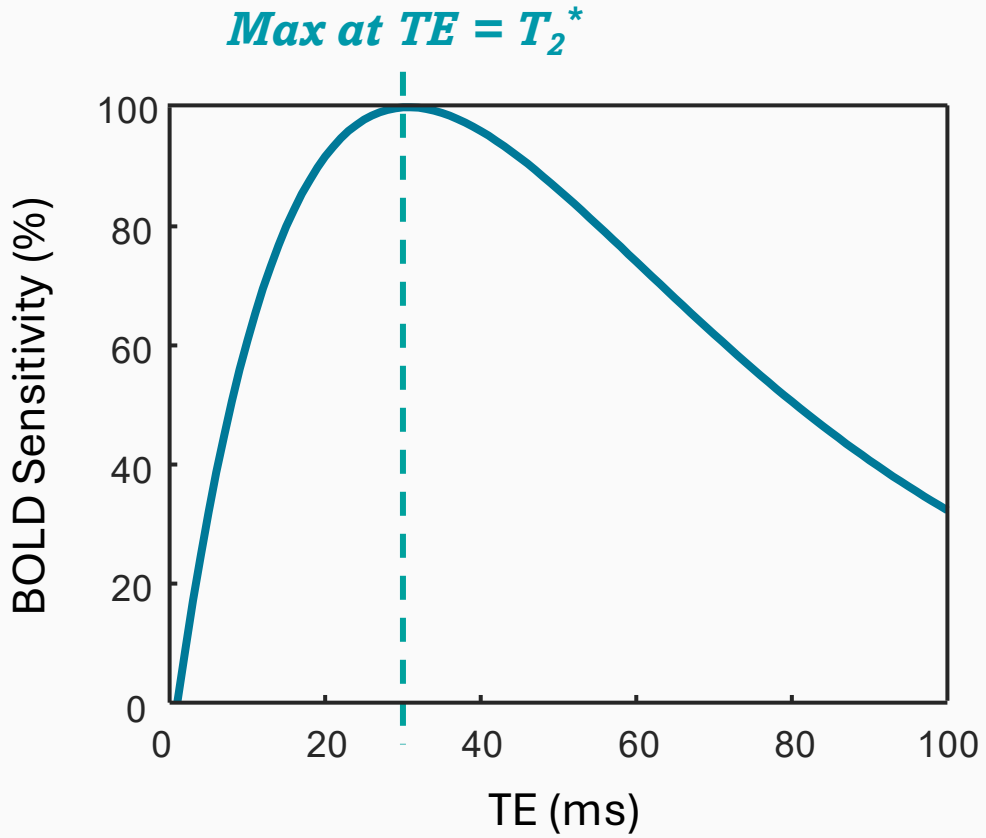
Sensitivity ≈ TE × Signal



BOLD Sensitivity – Echo Time (TE)

- TE must be sufficiently long for the BOLD signal to evolve
  - Short TE → weak BOLD contrast
  - Long TE → signal already gone
  - Optimal TE ≈ T2*



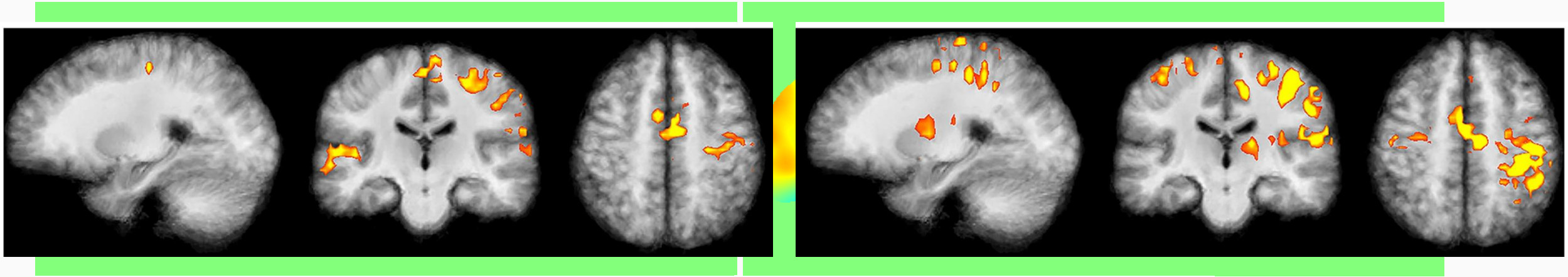


→ *matching tissue property*

Kundu P, et al. *NeuroImage*. 2017;154:59-80.

BOLD Sensitivity – Signal

- Field strength
- Field inhomogeneities



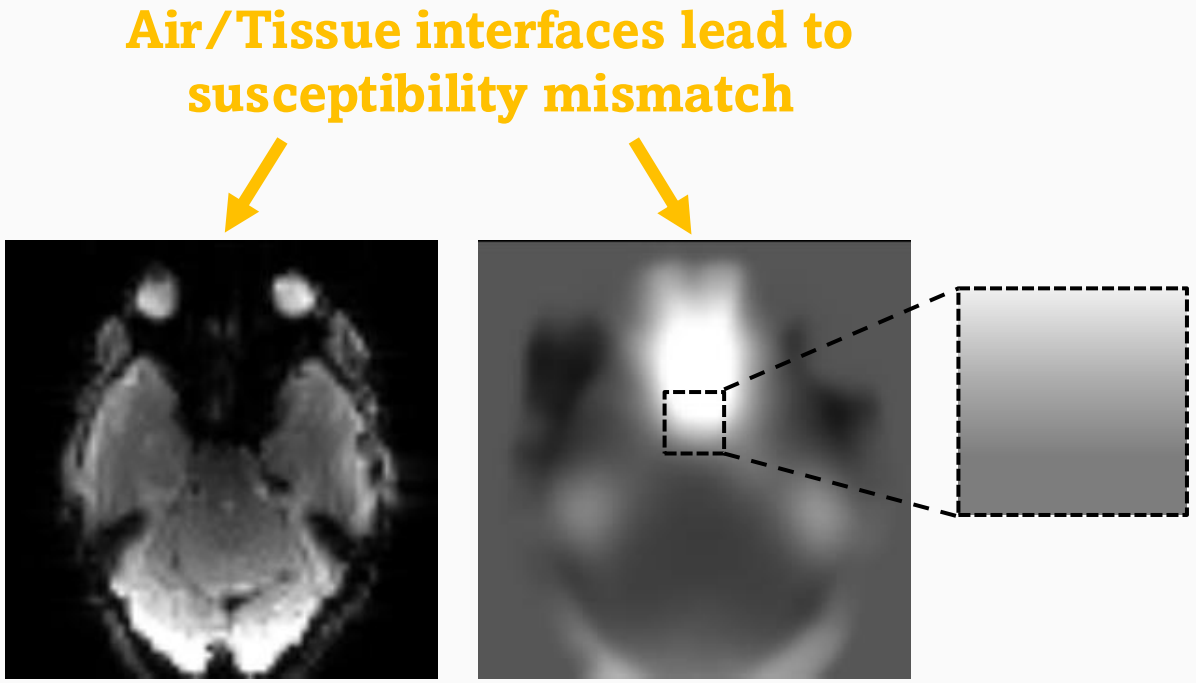
3T 7T

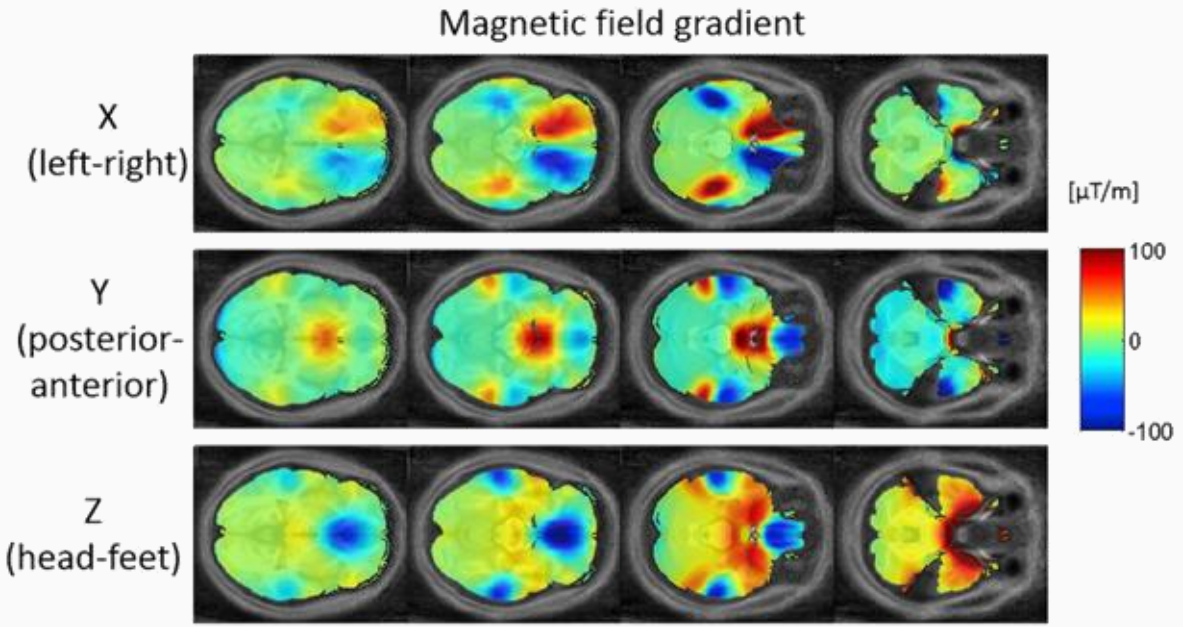
Frequency offset: $\Delta\omega_0 = \gamma\Delta B_0$

Baecke S, et al. *Sci Rep*. 2015;5:8413.

BOLD Sensitivity – Field Inhomogeneities

- Occur at interfaces with large susceptibility differences
  - ✓ air–tissue interfaces (e.g., sinuses, ear canals in the head)

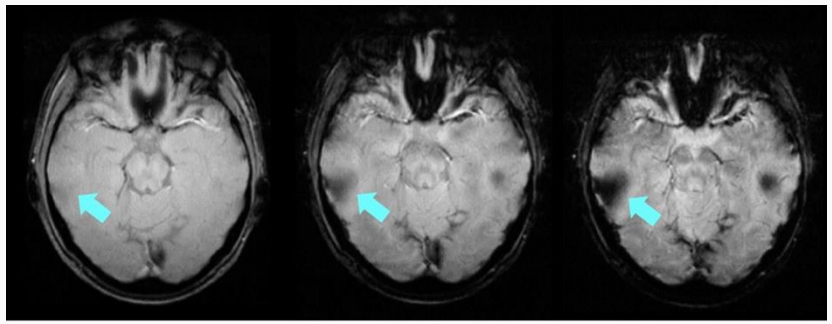


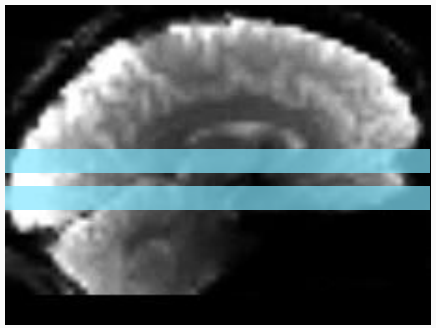


Volz S, et al. *NeuroImage*. 2019;189:159-170.

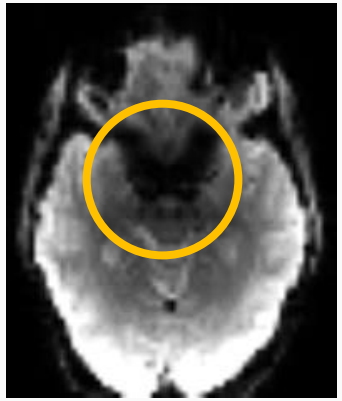
BOLD Sensitivity – Field Inhomogeneities

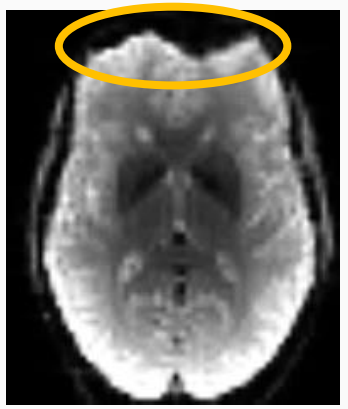
- Through-slice dephasing:
  - Signal loss (dropouts)





- In-plane dephasing:
  - Signal stretch/compress in PE direction
  - Signal loss (dropouts or void)

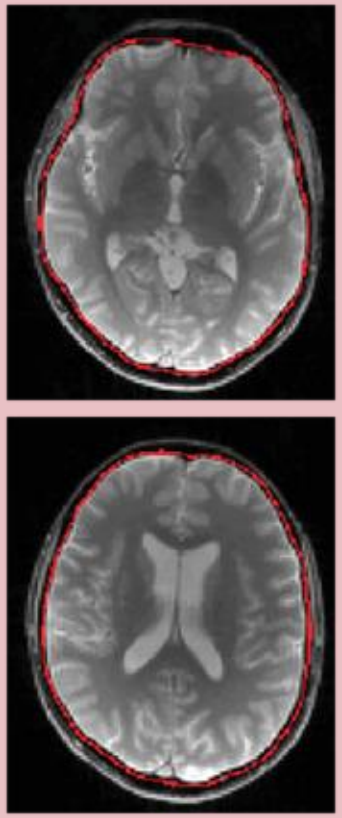




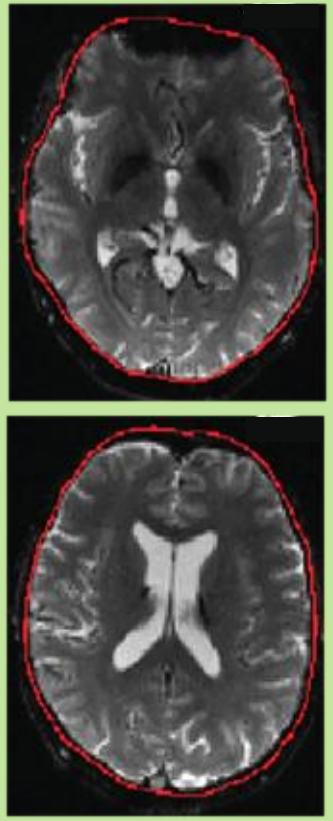
Haskell MW, et al. *NMR in Biomedicine*. 2023;36(5):e4867.

BOLD Sensitivity – Field Inhomogeneities

Conventional GRE



GRE EPI



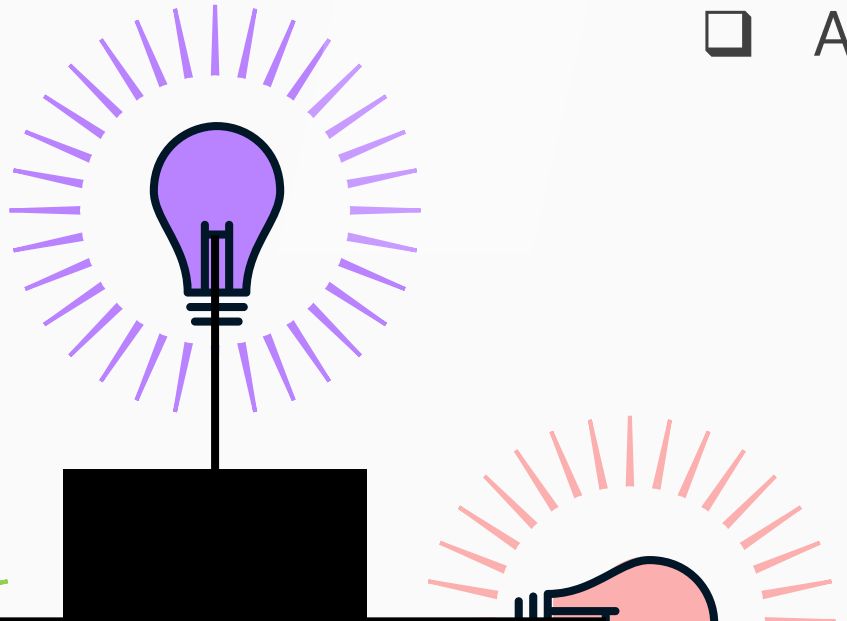
Yang Q, et al. *Magn Reson Med*. 2023;89:2157-2170.

How to Improve BOLD Sensitivity?

Improving Sensitivity

1 Slice Angulation

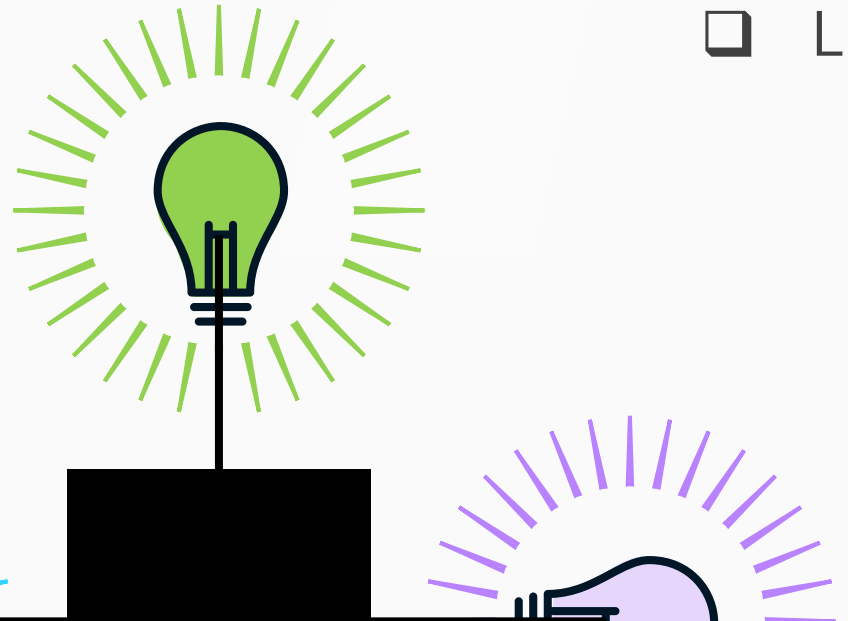
- Susceptibility gradients depend on orientation
- Adjust slice orientation to:
  - Redistribute gradients



Improving Sensitivity

2 Compensation Gradients

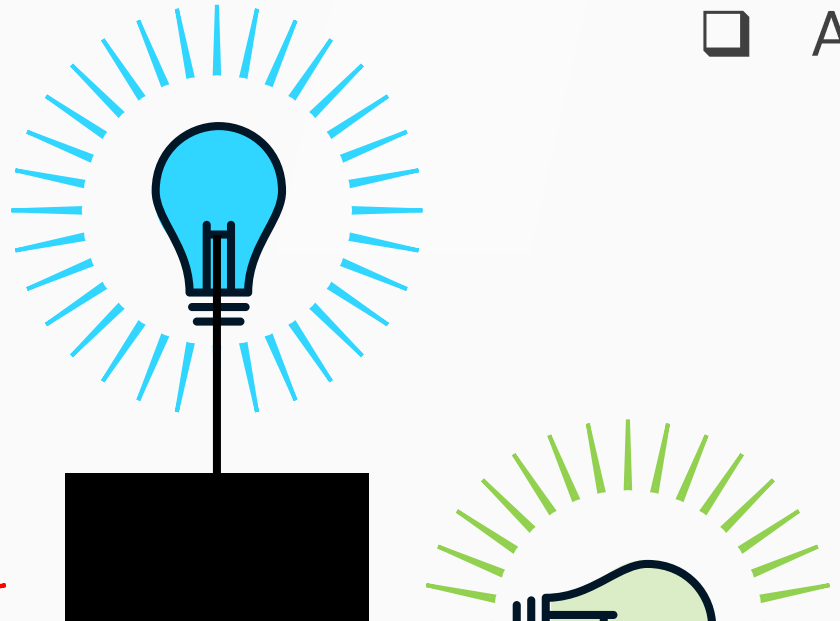
- Refocus signal → reduce through-slice signal loss
- Limitations:
  - Not always available (e.g. in multiband)
  - Dephasing other regions



Improving Sensitivity

3 Phase Encoding Direction

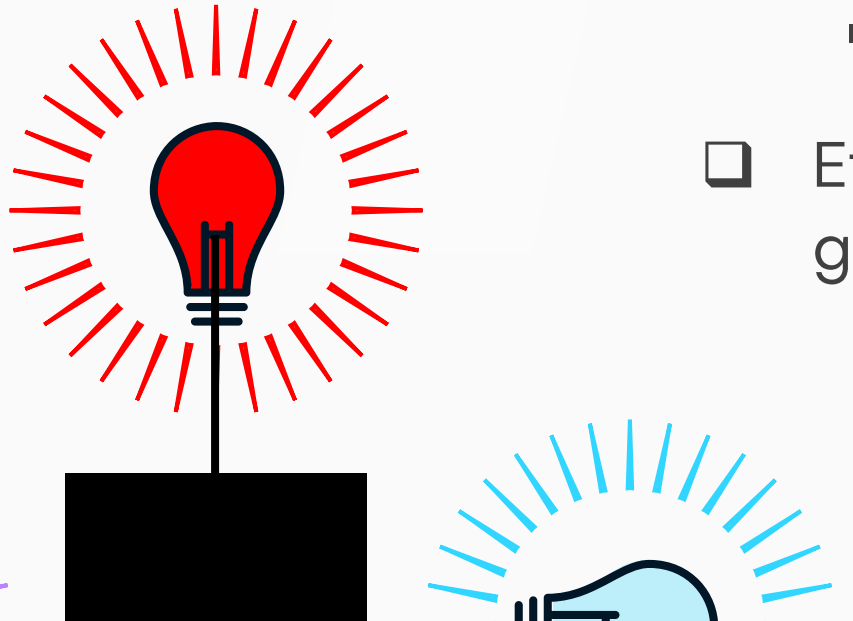
- Determines the direction of distortion
- AP vs PA encoding:
  - Not changing *whether* distortion happens
  - But changing *where* signal is misplaced



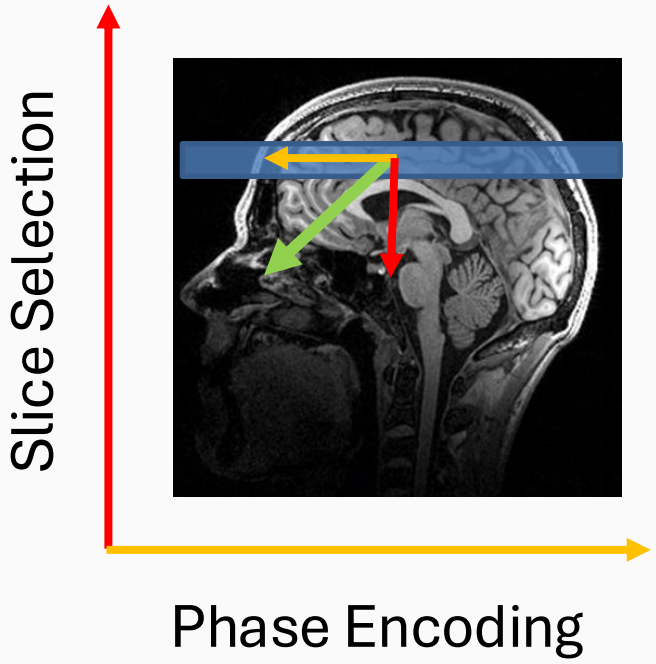
Improving Sensitivity

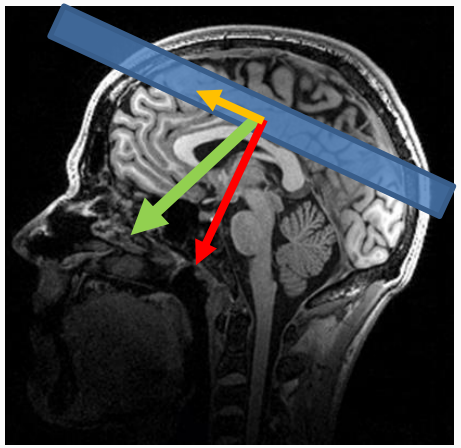
4 Match TE

- TE should reflect regional T_2*
  - Not always feasible from signal perspective
- Effective local TE is influenced by the susceptibility gradients in the PE direction



Improving Sensitivity





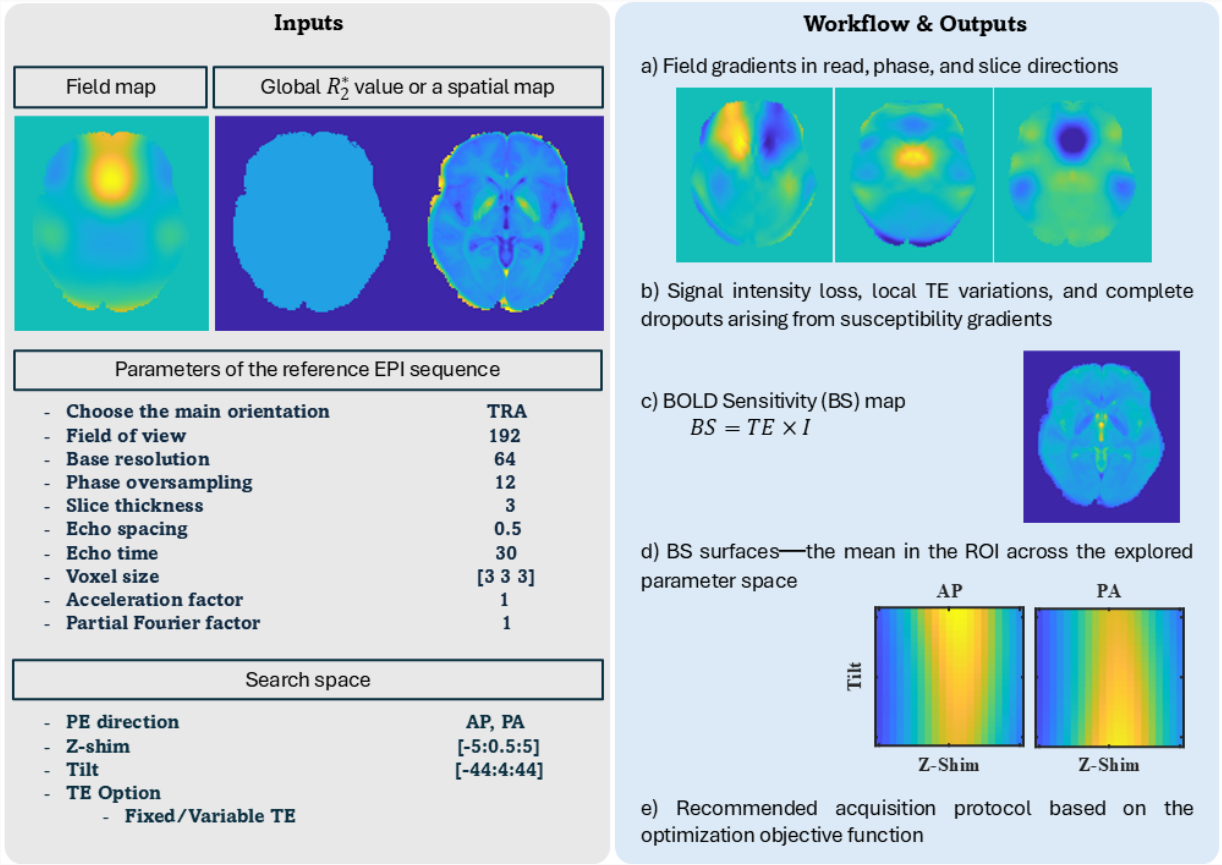
Combined angulation, z-shimming and optimal PE direction

→ moves the sources of trouble away from the region of interest…

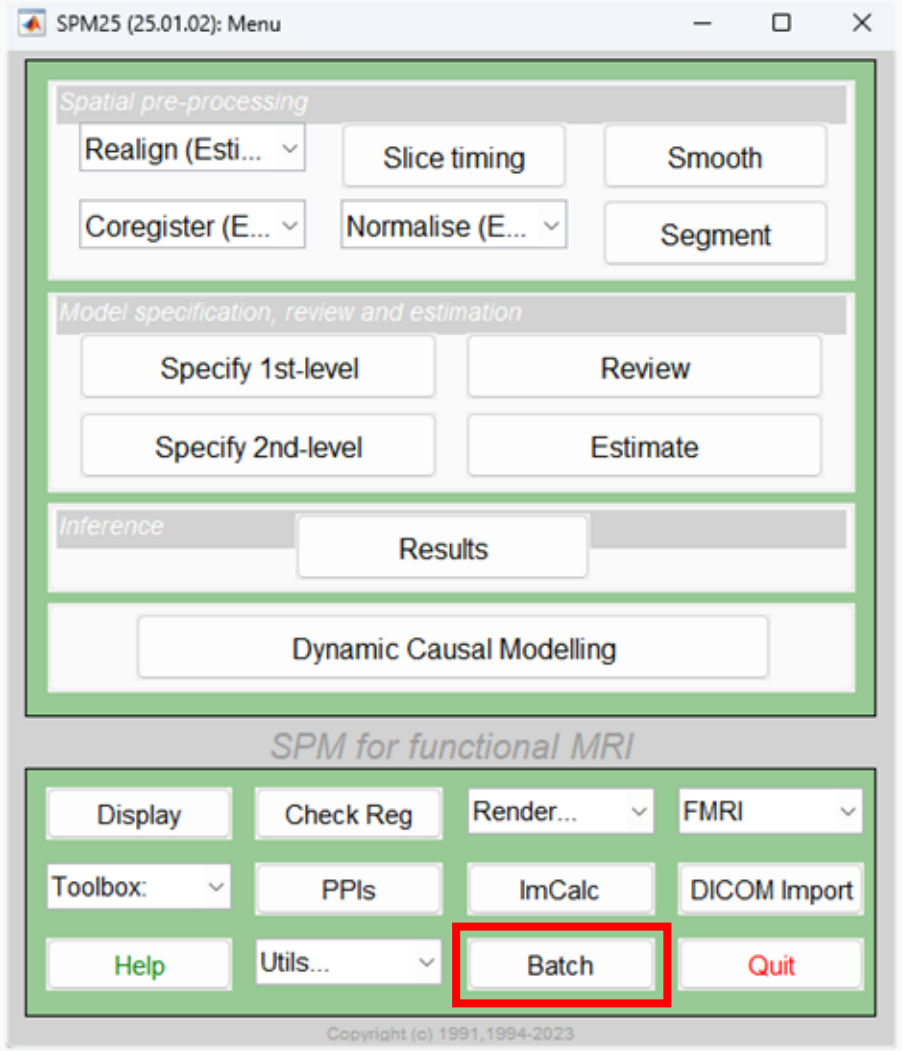
How to make Informed decision to improve BOLD Sensitivity?

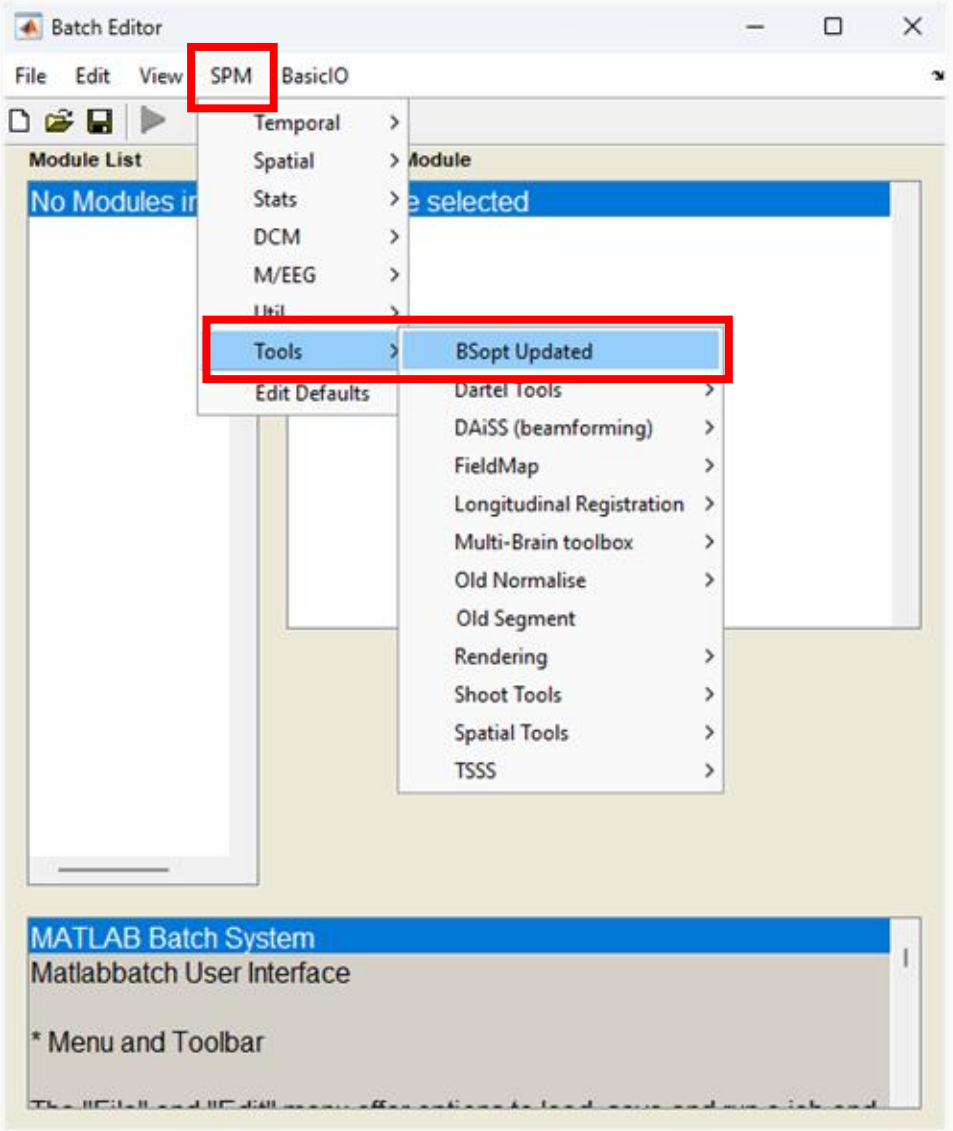
Optimisation Toolbox

- ❑ Available in SPM
- ❑ Predicts signal loss & Sensitivity across brain
- ❑ Enables data-driven protocol design
- ❑ Supports ROI-based optimisation
- ❑ Upcoming→ Global optimisation across multiple ROIs

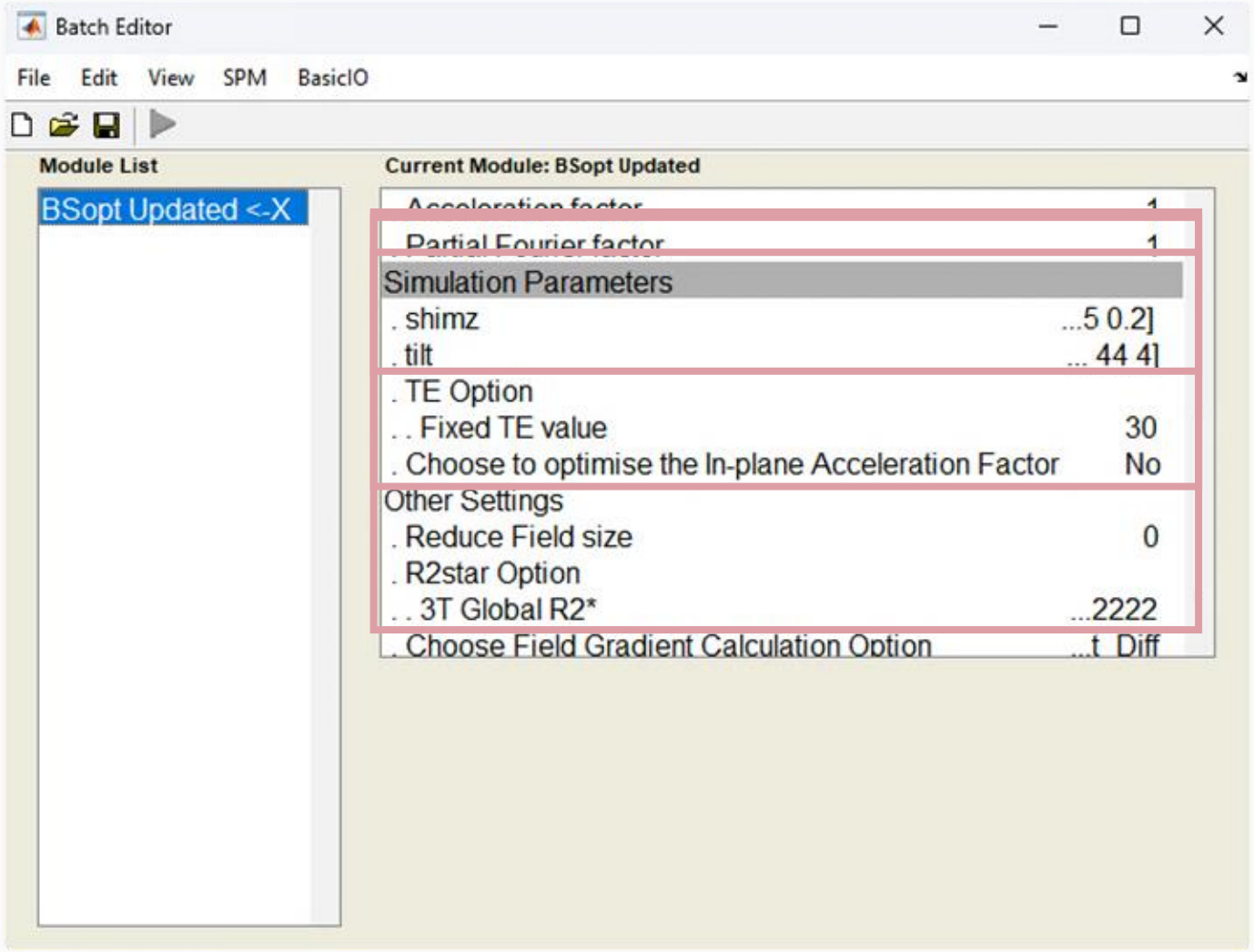


Optimisation Toolbox



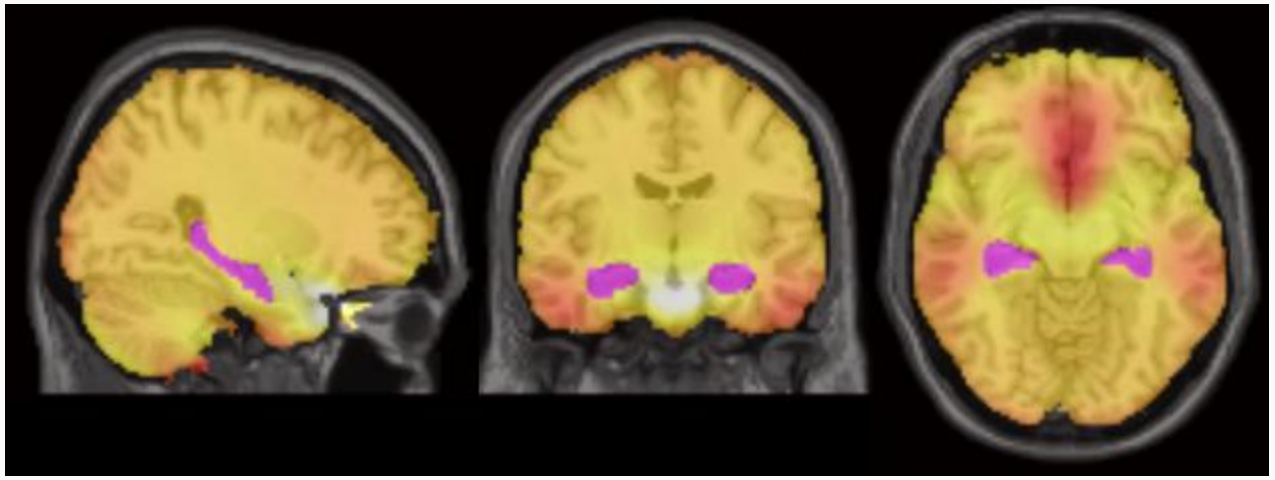


Optimisation Toolbox

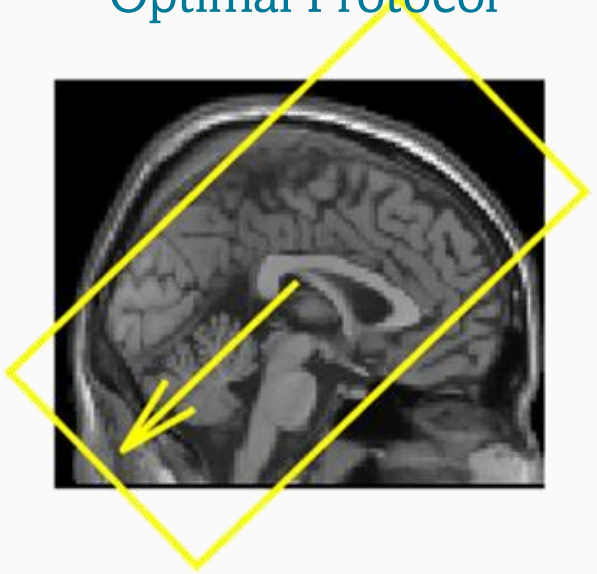


Optimisation Toolbox

BOLD Sensitivity map of the optimised protocol



Optimal Protocol



Optimization summary for echotime = 30.00 and in-plane acceleration factor = 1

ROI_Nr	ROI	BS_gain (%)	z-shim	tilt	PE
1	{'Hippocampus'}	15.08	0.4	-44	"AP"

Summary & Take-Home Messages

1. BOLD signal is small, indirect, and physically constrained
2. Sensitivity depends on: TE, geometry, and acquisition strategy
3. Trade-offs are unavoidable → design must match research question
4. Optimisation = managing trade-offs, not eliminating them

Good fMRI 👉 informed compromise

Acknowledgement & Questions

- SPM Course Organisation Team & FIL Physics Team
- Some images generated using *OpenAI* tools.