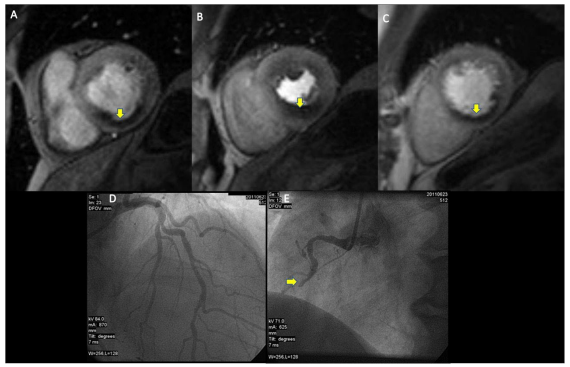
Quantitative MRI: Diffusion, Perfusion, BOLD

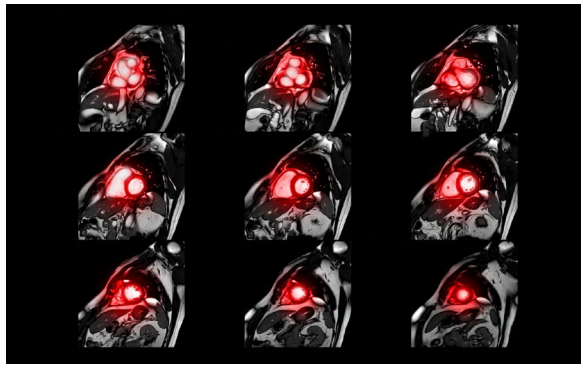
With Emphasis on Cardiac Perfusion MRI (CMR)

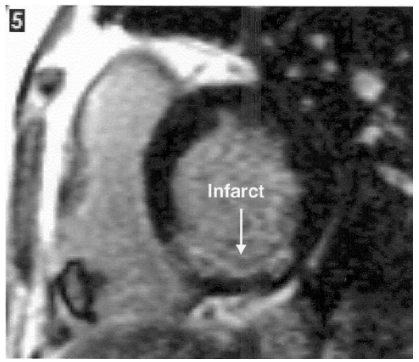
Dipl. Phys. Dr. Bernd Müller-Bierl

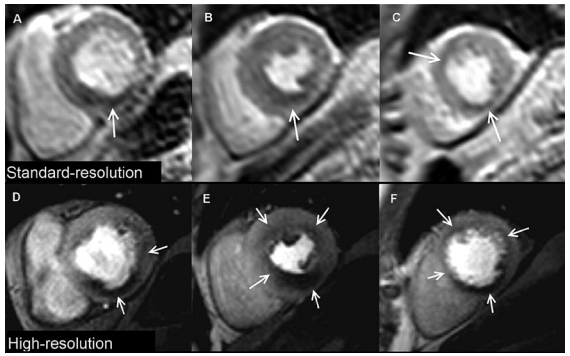
- Quantitative interpretation of MRI signals
- Mathematical models linking signal and physiology
- Reliable clinical parameters (diffusion, perfusion, brain activation)

Clinical Motivation: Why Cardiac Perfusion MRI?









Clinical Objective

Detection of myocardial ischemia

Current Clinical Practice

- Stress perfusion imaging
- Visual interpretation
- Semi-quantitative metrics

Limitation

Visual assessment is:

- Observer-dependent
- Nonlinear
- Poorly reproducible

Need

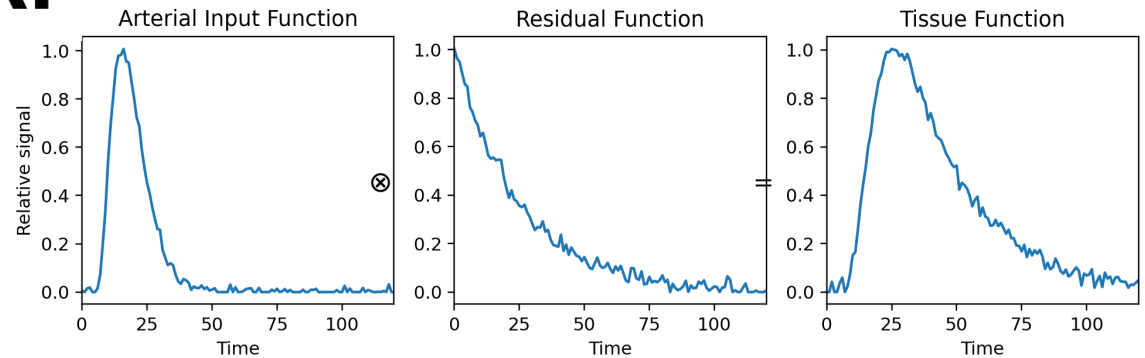
Robust quantitative myocardial blood flow (MBF) estimation

Signal Formation in Perfusion MRI

Contrast Mechanism

Gadolinium-based contrast agent:

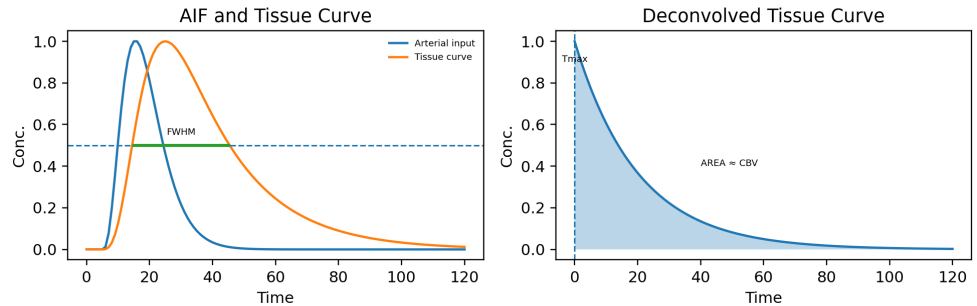
- Shortens T1
- Increases signal in T1-weighted gradient echo sequences



Important Nonlinearity

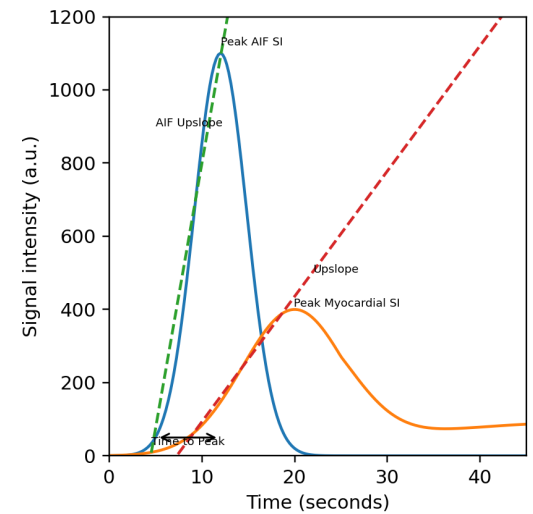
MRI signal ≠ linear concentration

$$S(t) \propto \frac{1 - e^{-TR/T_1(t)}}{1 - \cos(\alpha)\, e^{-TR/T_1(t)}}$$



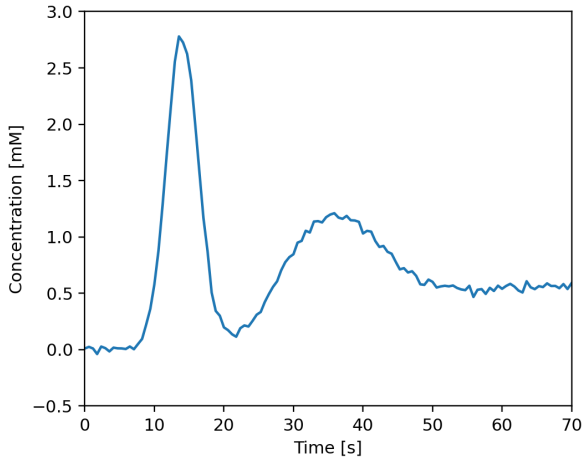
Consequence

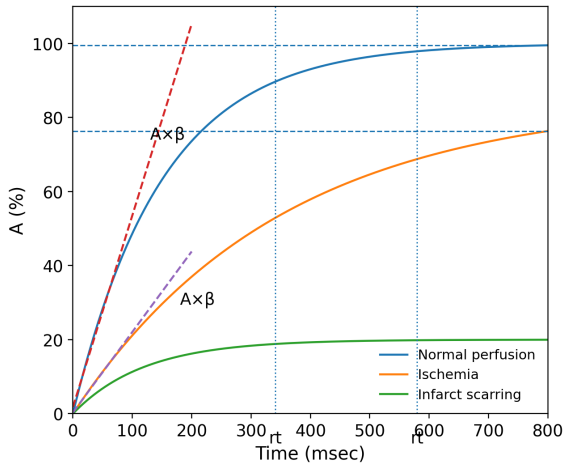
Signal must be converted to contrast concentration before modeling.

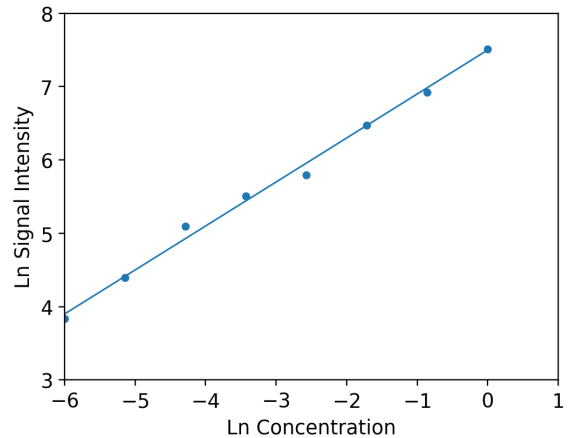


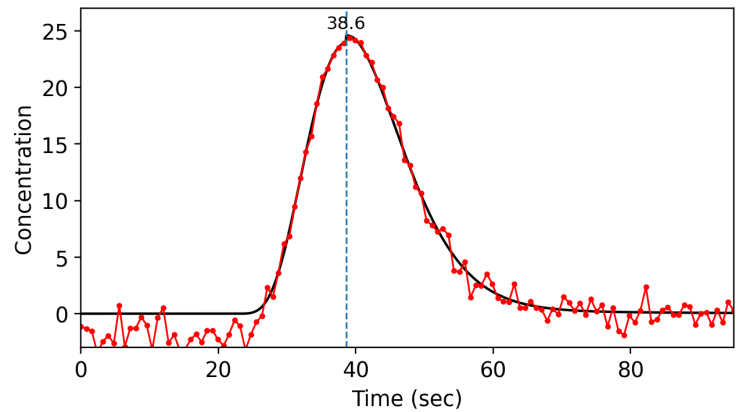
Signal-to-Concentration Conversion

We first undo the scanner physics before we can interpret physiology









Two Required Curves

- Arterial Input Function (AIF)
- Myocardial tissue curve

Steps

1. Baseline T1 estimation
2. Convert signal → ΔR1
3. Convert ΔR1 → concentration

Dynamic Contrast Enhanced T1w Sequences

Key Risk

Incorrect linearization → systematic perfusion bias

The Central Convolution Model

Indicator-Dilution Theory

Fredholm integral equation of the first kind

$$C_t(t) = F \cdot (AIF \otimes R(t))$$

Where:

- Ct(t) = tissue concentration
- F = perfusion (flow)
- R(t) = residue function
- ⊗ = convolution

Interpretation

Perfusion MRI is an inverse problem:

We observe Ct and AIF → estimate F and R(t)

This is mathematically ill-posed.

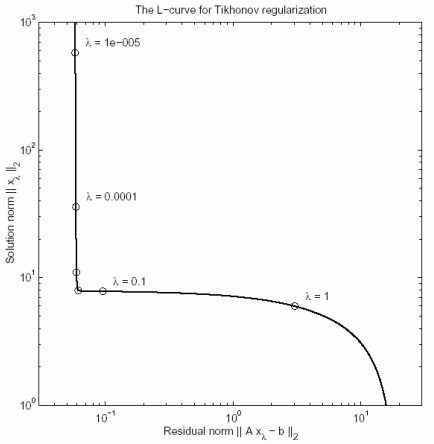
This simply says: tissue signal is a blurred and delayed version of the arterial input.

Modeling Strategies in Cardiac Perfusion

Method	Core Equation	Main Parameters	Typical Use
Indicator Dilution / Convolution	$C_t(t) = F \int_0^t C_a(\tau) R(t-\tau) d\tau$	F (flow), $R(t)$ residue function	General perfusion framework
Deconvolution (SVD)	$R(t) = \mathcal{D}[C_t(t), C_a(t)]$	$F = R(0)$	DSC perfusion MRI
Patlak Model	$\frac{C_t(t)}{C_a(t)} = K^{trans} \frac{\int_0^t C_a(\tau) d\tau}{C_a(t)} + v_p$	K^{trans}, v_p	BBB leakage / oncology
Tofts Model	$C_t(t) = K^{trans} \int_0^t C_a(\tau) e^{-k_{ep}(t-\tau)} d\tau$	K^{trans}, k_{ep}	DCE MRI
Extended Tofts (mTofts)	$C_t(t) = v_p C_a(t) + K^{trans} \int_0^t C_a(\tau) e^{-k_{ep}(t-\tau)} d\tau$	K^{trans}, k_{ep}, v_p	Tumor perfusion
2-Compartment Exchange Model (2CXM)	$C_t(t) = F_p \int_0^t C_a(\tau) [a_1 e^{-m_1(t-\tau)} + a_2 e^{-m_2(t-\tau)}] d\tau$	F_p, PS, v_p, v_e	Quantitative perfusion
Steepest Descent / Gradient Fit	$\theta_{n+1} = \theta_n - \alpha \nabla E(\theta_n)$	iterative parameter estimation	numerical fitting

The Inverse Problem & Regularization

Without regularization, small noise leads to completely wrong blood flow values.



Why Ill-Posed?

- Convolution smoothing
- High temporal noise
- Limited sampling rate

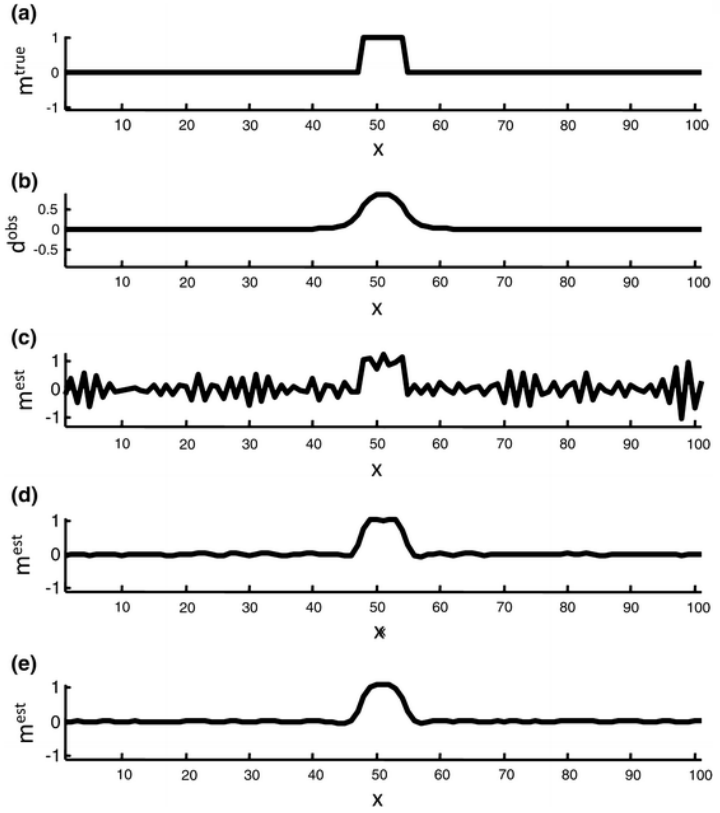
Small noise → large parameter error

Solution: Regularization

$$\min\|Ax - b\|^2 + \lambda\|Lx\|^2$$

Regularization stabilizes but introduces bias.

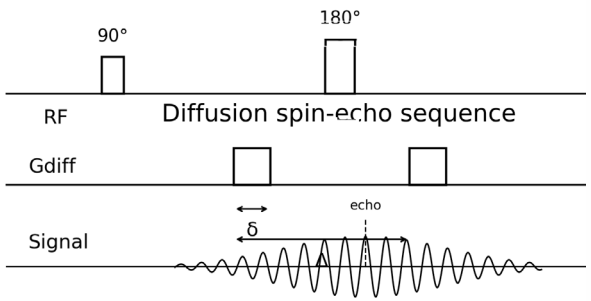
Clinical quantification requires balancing both.

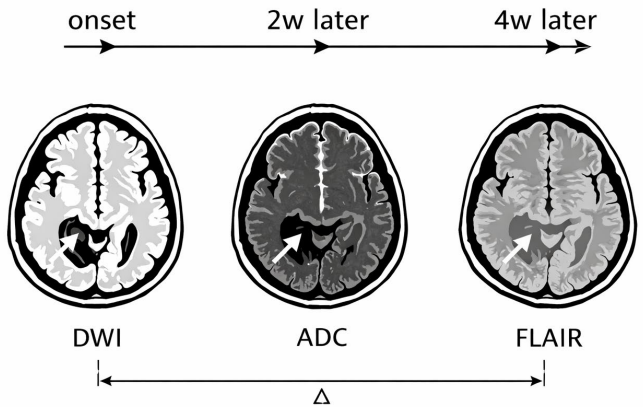


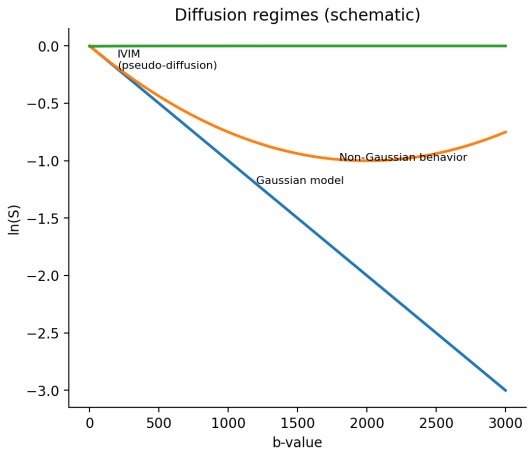
Diffusion MRI: Basic Model

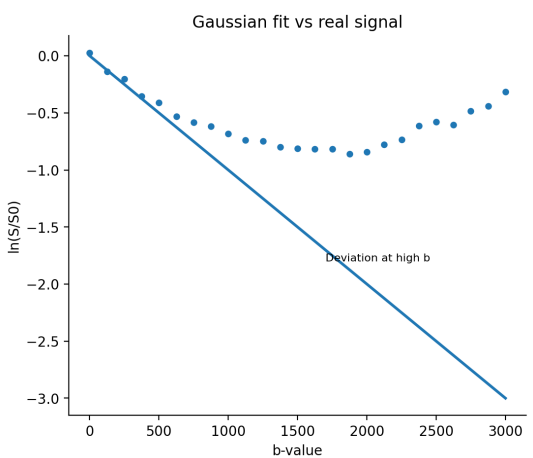
Unlike perfusion, diffusion does not require deconvolution—but still requires model fitting under noise.

Log-linearization hides the inverse problem.









Mono-Exponential Model

Where:

- b = diffusion weighting
- D = apparent diffusion coefficient (ADC)

Stejskal–Tanner relation

$$S(b) = S_0 e^{-bD}$$

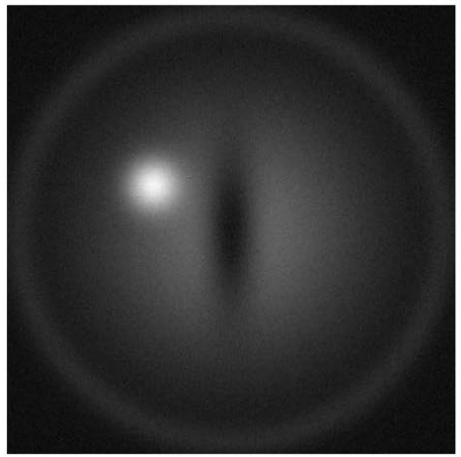
Clinical Use

- Stroke detection
- Tumor cellularity

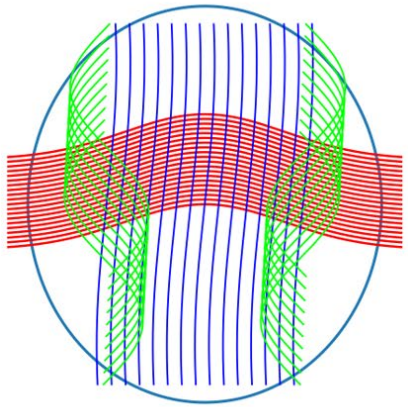
Also an inverse estimation problem.

Diffusion Tensor Imaging (DTI)

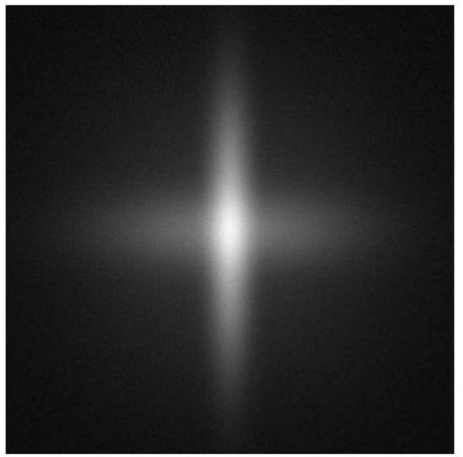
Diffusion weighted Image



DTI Fiber Tractography



Fractional Anisotropy Map



Tensor Model

$$S(b, g) = S_0 e^{-bg^T Dg}$$

Where:

- D = symmetric 3×3 tensor
- 3 eigenvalues (λ1, λ2, λ3)

Derived Metric

Fractional Anisotropy (FA)

FA ≈ 0 → isotropic

High FA → organized white matter

Again: nonlinear fitting + noise sensitivity.

Diffusion Tensor Imaging (DTI)

Step 1 — Basic Diffusion Model

Monoexponential model:

$$S(b) = S_0 e^{-bD}$$

Here, diffusion coefficient D is assumed isotropic (same in all directions).

That works in CSF.

Not in white matter.

Step 2 — Tensor Model (DTI)

Instead of a single scalar D, use a **3×3 symmetric tensor**:

$$S(b, \mathbf{g}) = S_0 \exp(-b\, \mathbf{g}^T D \mathbf{g})$$

Now diffusion depends on gradient direction $\mathbf{g}$.

The tensor has 3 eigenvalues:

$$\lambda_1, \lambda_2, \lambda_3$$

These represent diffusivities along principal axes.

Step 3 — Fractional Anisotropy (FA)

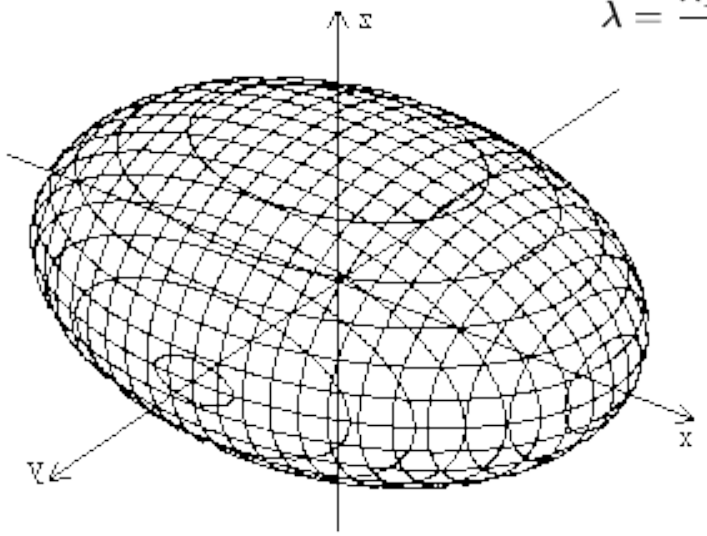
FA measures how unequal the eigenvalues are.

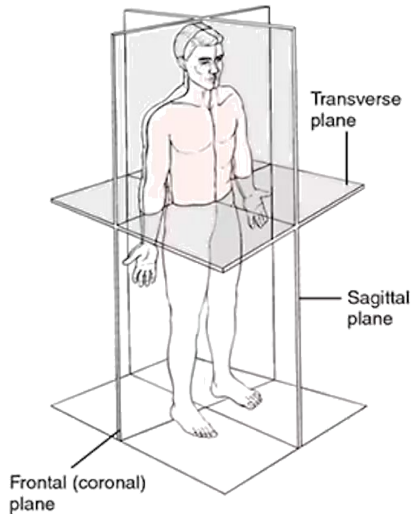
Formula:

$$FA = \sqrt{\frac{3}{2}} \frac{\sqrt{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

where

$$\bar{\lambda} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$





Structural Parallels: Perfusion vs Diffusion

Feature	Perfusion MRI	Diffusion MRI
Core Model	Convolution	Exponential
Unknowns	Flow, residue	ADC, tensor
Instability Source	Deconvolution	Log-linear fit noise
Regularization	Essential	Implicit/explicit
Parameter Coupling	Strong	Moderate–Strong

Unifying Insight

Both are:

Model-based inverse estimation problems under noise.

Clinical meaning depends on statistical stability.

Clinical Applications of Quantitive MRI

Signal mechanism	Measured signal change	Mathematical model	Physiological parameter	Clinical applications
Water diffusion	Diffusion-weighted signal attenuation	Exponential decay	Diffusion coefficient, anisotropy	Acute stroke detection, white-matter tractography, tumor characterization
Contrast bolus passage	Signal change during contrast transit	Tracer-kinetic / transport models	Blood flow, blood volume, permeability	Tumor grading, ischemia assessment, oncology perfusion imaging
Blood oxygenation changes	Susceptibility-dependent signal fluctuation	Hemodynamic response model	Neuronal activation (indirect)	Functional brain mapping, presurgical planning

Functional MRI (fMRI)

Another delayed nonlinear system with memory

The Buxton model is the nonlinear ODE system

$$\dot{s} = u - \kappa s - \gamma(f - 1)$$

$$\dot{f} = s$$

$$\tau_0 \dot{v} = f - v^{1/\alpha}$$

$$\tau_0 \dot{q} = f \frac{E(f)}{E_0} - v^{1/\alpha - 1} q$$

with output

$$y(t) = V_0 \Big[k_1(1 - q) + k_2(1 - q/v) + k_3(1 - v) \Big].$$

Because the system contains **two slow processes**

- venous balloon expansion
- deoxyhemoglobin washout

the response becomes

- delayed
- nonlinear
- with possible undershoot or initial dip.

$s(t)$ vasodilatory signal

$f(t)$ normalized cerebral blood inflow

$v(t)$ normalized venous blood volume

$q(t)$ normalized deoxyhemoglobin content

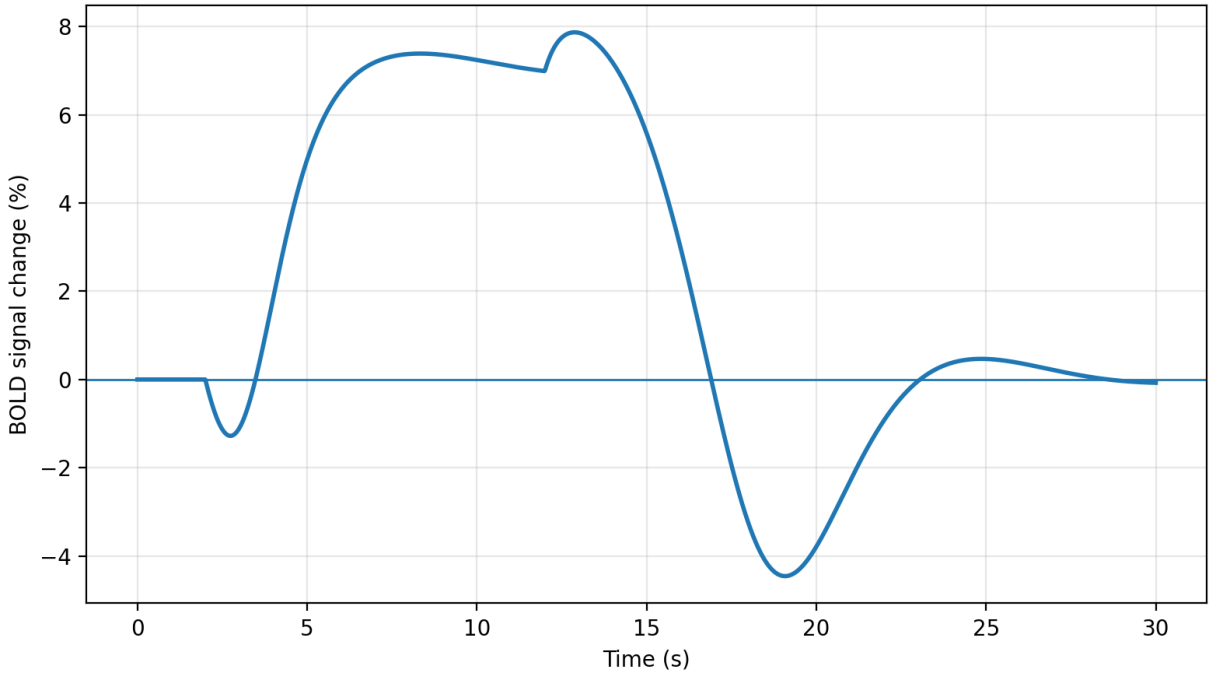
At rest:

$$f = v = q = 1, \qquad s = 0$$

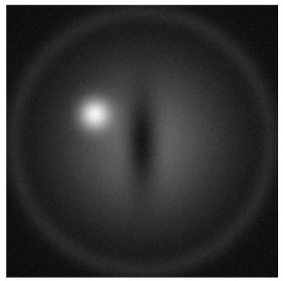
Neural input:

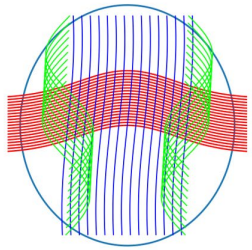
$$u(t)$$

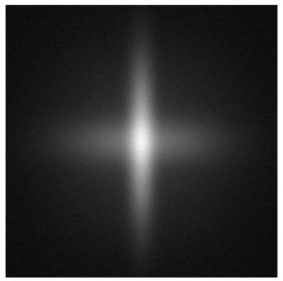
Numerically integrated Buxton-type BOLD response with initial dip

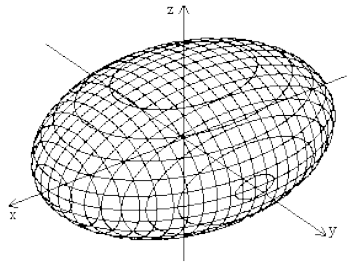


Summary: Quantitative MRI Methods (model-based approaches)





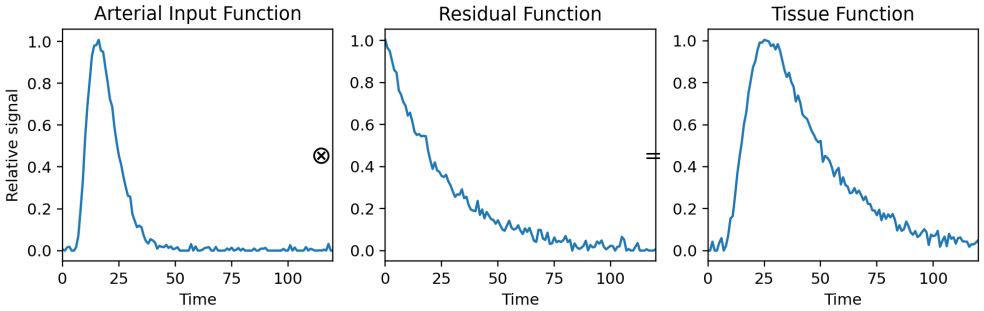


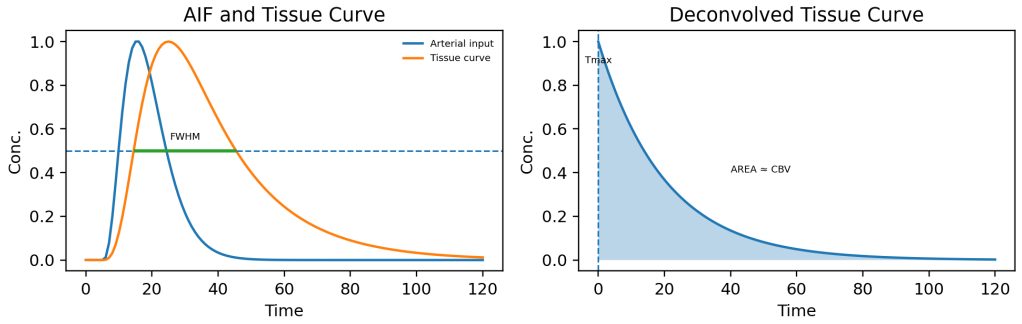


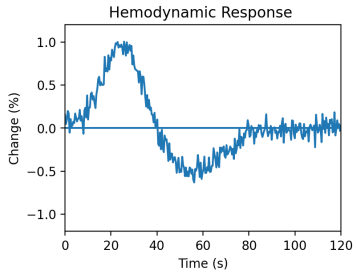
DICOM = data standard

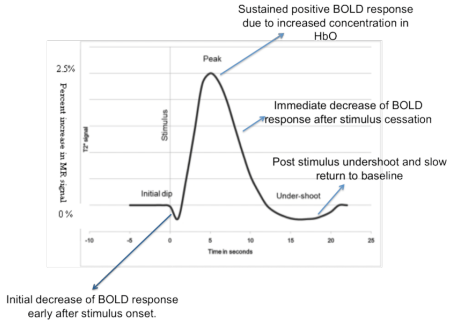
NIfTI = neuroimaging data format

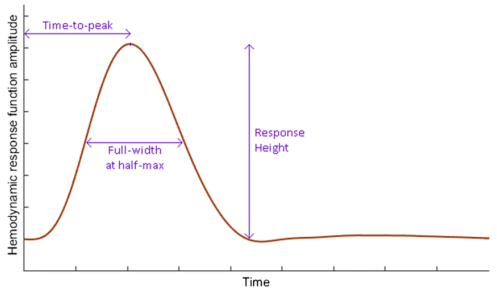
PACS = image storage and archive system

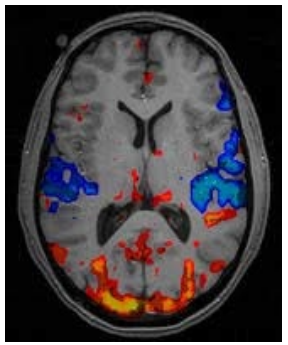












Conclusion

qMRI is Model-Based Inference under Noise

Central Thesis

Quantitative MRI is not merely imaging.

It is:

- A physical signal model
- An inverse mathematical problem
- A statistical estimation task

In Cardiac Perfusion MRI:

Reliable myocardial blood flow requires:

- Correct signal linearization
- Robust modeling
- Controlled regularization
- Statistical awareness

The same structural principles govern diffusion MRI.