Information Criteria weighted Parameter Estimates in DCE-MRI

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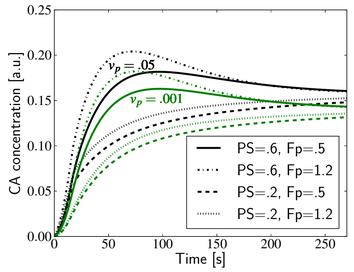
Motivation – Accurate and Precise Parameter Estimates

- The choice of a suitable pharmacokinetic model for the analysis of DCE-MRI is crucial for the reliability, i.e. the accuracy and precision, of the consequent parameter estimates.
- Models may overfit or underfit the data even within the same dataset. Thus data driven model selection has been proposed. A lack of a systematic benefit from AIC weighted estimates has been reported [Luypaert, 2012].
- We aim to reveal the performance of AIC weighted parameter estimates within the scope of a typical DCE-MRI experiment for non-nested models.

Procedure – Simulating the Tissue Uptake

- Simulations are based on a typical arterial input function (AIF) in a mousetail [Moroz et. al., 2012] and a typical human AIF in the cephalic vein [Parker et. al., 2006].
- the Multiple Path, Multiple tracer, Indicator Dilution, 4 region (MMID4) model provides the ground truth tissue response [Kroll et. al.,1996], accounting for tissue heterogeneity and flow dispersion.



- We simulate parameter combinations: plasma flow [ml/g/min] $= 0.5, 1.2$; permeability surface area [ml/g/min] $= 0.2, 0.6$; fract. plasma volume $= 0.001, 0.05$; fract. interstitial volume $= 0.4$.

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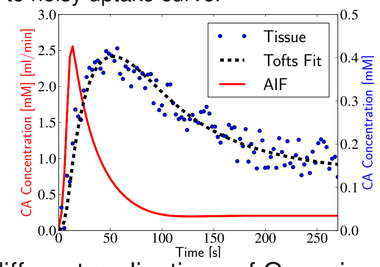
Procedure - Resampling Bootstrap

1. Generate tissue uptake curves $C(t)$ for given AIFs using MMID4 with fixed tissue parameters.
2. Add Gaussian noise to $C(t)$.
   - Convert uptake curve to MR signal using the FLASH signal equation.
   - Add Gaussian noise (SNR = 30).
   - Transform noisy signal back to noisy uptake curve.
3. Fit pharmacokinetic model to the (known) AIF and the noisy uptake curve. Initial guesses are derived from brute force fits of the noise free data.



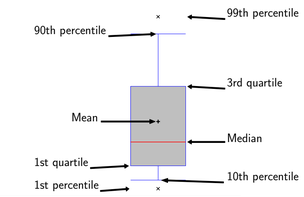
4. Iterate steps 2 and 3 for different realizations of Gaussian noise (10^3 iterations) to derive a K^{trans} parameter distribution.
   - This distribution reflects the sampling statistic of the parameter within the respective model.

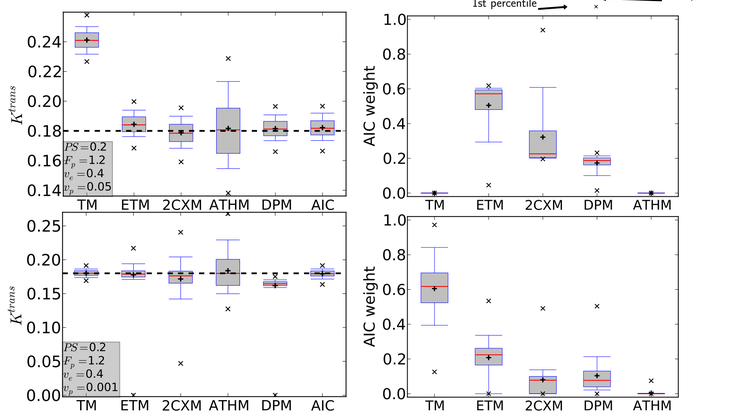
Procedure – Models and Model Weighting

- The uptake curves are modelled by convolution of the AIF with the tissue response function. Each model is defined by it's response function.
  - **Tofts Model (TM)**: Assumes a high plasma flow (or weak vascularization and well mixed EES) and a negligible plasma volume. 2 free parameters.
  - **Extended Tofts Model (ETM)**: Same assumptions as TM with finite plasma volume. 3 free parameters.
  - **Two-compartment exchange model (2CXM)**: Assumes well mixed compartments. 4 free parameters.
  - **Adiabatic approximation to the tissue homogeneity model (ATHM)**: Assumes plug-flow plasma compartment, well mixed EES, and tracer exchange at outlet. 4 free parameters.
  - **Distributed Parameter Model (DPM)**: Assumes a plug-flow plasma compartment and a distributed EES. 4 free parameters.
- Model weights are based on Akaike's information criterion:
  - $AIC = N \ln\left(\frac{RSS}{N}\right) + 2K$
- Based on Kullback-Leibler divergence, they measure the probability for each model to be best of the set of evaluated models [Burnham, 2004].
- The models are only partially nested. Not only the model complexity is weighted, but also the different model assumptions.

Results - Detecting the Adequacy of a Parsimonious Model

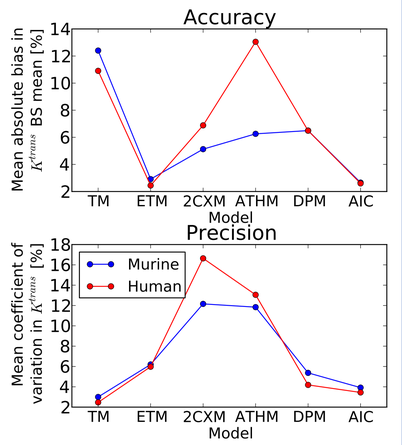
For tissue setups that differ by a significant (5%, top row) and a negligible (.1%, bottom row) plasma volume the AIC facilitates the automatic choice of model:





Results - Average Improvements in Accuracy and Precision

The precision and accuracy, averaged over eight sets of tissue parameters is shown on the right. The AIC weighted K^{trans} estimates are on average as precise and as accurate as the most precise and the most accurate model, respectively. No considerably exemption for any of the eight single tissue types and two different AIFs has been observed.



Conclusion - AIC Improves K^{trans} Estimates

AIC weighted K^{trans} estimates are almost always more accurate and precise than the best model. They are distinctly better than any fixed choice of model.

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