

## Supplementary Materials for the paper

### *A Clustering Approach to Improve IntraVoxel Incoherent Motion Maps from DW-MRI using Conditional Auto-Regressive Bayesian Model*

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#### Abstract

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    - (b) Likelihood function for the first step
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## 1. Details on the Bayesian CAR approach

### 1.1. Likelihood function for the first step

The coefficients to be estimated are included in set  $\Theta_I = \mathbf{D} \cup \tilde{\mathbf{f}}$ , with  $\mathbf{D} = \{D(i, j), (i, j) \in \mathcal{I}\}$  and  $\tilde{\mathbf{f}} = \{\tilde{f}(i, j), (i, j) \in \mathcal{I}\}$ .

Each coefficient in  $\Theta_I$  and the signal intensity at  $b = 0$  are assumed to be random variables. Therefore, the decay equation becomes a random process, in which the probability density function of each  $SI(i, j, b)$  is expressed as conditioned to  $D(i, j)$ ,  $f(i, j)$  and  $SI(i, j, 0)$ :

$$SI(i, j, b) \sim \mathcal{L}_{simp} \left( SI(i, j, b) | D(i, j), \tilde{f}(i, j), SI(i, j, 0) \right) \\ \forall (i, j) \in \mathcal{I}, b \in B : b \geq \hat{b} \quad (1)$$

where  $\mathcal{L}_{simp}$  denotes the probability law based on the simplified IVIM model.

Values  $SI(i, j, 0)$  are assumed to follow a Gaussian distribution with mean value  $SI_{ij0}^{obs}$  and standard deviation  $\sigma_{lik}$  [12]:

$$SI(i, j, 0) \sim \mathcal{N}(SI_{ij0}^{obs}, \sigma_{lik}^2) \quad \forall (i, j) \in \mathcal{I} \quad (2)$$

Observations  $SI_{ijb}^{obs}$  with  $b \geq \hat{b}$  are assumed to be subject to an error (e.g., a measurement error) and modeled as stochastic variables. Other Gaussian distributions  $\mathcal{N}$  with mean value  $SI(i, j, b)$  computed by (1) and standard deviation  $\sigma_{lik}$  are considered:

$$SI_{ijb}^{obs} \sim \mathcal{N}(SI(i, j, b), \sigma_{lik}^2) \quad \forall (i, j) \in \mathcal{I}, b \geq \hat{b} \quad (3)$$

A Rician distribution should be theoretically employed at low  $SNR$ , while the Rician distribution is well approximated by the Gaussian one for high  $SNR$ . Nevertheless, Gaussian and Rician likelihood functions give similar results for a large range of  $SNR$  [20].

Parameter  $\sigma_{lik}$  is another parameter to be estimated together with  $\Theta_I$ . The conditional law of each observation  $SI_{i,j,b}^{obs}$  is given by the combination of (1) and (3), and their product over  $(i, j) \in \mathcal{I}$  and  $b \geq \hat{b}$  gives the likelihood function, which depends on  $\Theta_I$  and  $\sigma_{lik}$ .

### 1.2. Likelihood function for the second step

The coefficients to be estimated in the second step are included in set  $\Theta_{II} = \mathbf{D}^* \cup \mathbf{f}$ , with  $\mathbf{D}^* = \{D^*(i, j), (i, j) \in \mathcal{I}\}$  and  $\mathbf{f} = \{f(i, j), (i, j) \in \mathcal{I}\}$ .

All observations are considered, and the parameters  $D(i, j)$  assume the expected value of the respective marginal posterior density from the first step. Again, each coefficient in  $\Theta_{II}$  and the signal intensity at  $b = 0$  are assumed to be random variables. Therefore:

$$\begin{aligned} SI(i, j, b) &\sim \mathcal{L}(SI(i, j, b) | D^*(i, j), f(i, j), SI(i, j, 0)) \\ \forall (i, j) \in \mathcal{I}, b &\in B \setminus \{0\} \end{aligned} \quad (4)$$

where  $\mathcal{L}$  with no subscript denotes the conditional probability law based on the original IVIM model.

The same Gaussian distributions with standard deviation equal to  $\sigma_{lik}$  are assumed for  $SI(i, j, 0)$  and the observations  $SI_{ijb}^{obs}$  with  $b \in B \setminus \{0\}$ , as in the first step.

The conditional law of each observation  $SI_{ijb}^{obs}$  is given by the combination of (4) and (3), and their product over  $(i, j) \in \mathcal{I}$  and  $b \in B \setminus \{0\}$  gives the likelihood function, which depends on  $\Theta_{II}$  and  $\sigma_{lik}$ .

### 1.3. Hyperparameters of the mixture prior densities

The hyperparameters of the Gaussian component are set as follows:  $\mu_{\tilde{f}} = \sigma_{0\tilde{f}} = 0.1$  and  $\mu_D = \sigma_{0D} = 0.001mm^2/s$  for the first step;  $\mu_f = \sigma_{0f} = 0.1$  and  $\mu_{D^*} = \sigma_{0D^*} = 0.01mm^2/s$  for the second step. Mean values are chosen to center the priors on values with the same order of magnitude than those reported in the literature, while  $\sigma_{0\lambda} = \mu_\lambda$  defines large densities. In addition, the priors of  $D$  and  $D^*$  are truncated in the interval  $(0, +\infty)$ , to ensure positivity [12], while that of  $f$  in the interval  $(0, 0.5)$ , which largely covers its range of variability and avoid symmetries.

The hyperparameters of the CAR specification are set as follows:  $\sigma_{\tilde{f}} \sim \text{Gamma}(0.25, 1)$  and  $\sigma_D \sim \text{Gamma}(0.001mm^2/s, 1)$  for the first step;  $\sigma_f \sim \text{Gamma}(0.25, 1)$  and  $\sigma_{D^*} \sim \text{Gamma}(0.01mm^2/s, 1)$  for the second step. In the absence of information about the variability associated with the CAR specification, the imposed  $\sigma_\lambda$  gives large densities.

They reflect the values adopted in Lanzarone *et al.* [15].

## 2. Supplementary tables

Median error		SNR10			SNR25			SNR50		
		D	f	D*	D	f	D*	D	f	D*
HN1	Bayes	0.086	0.022	0.142	0.023	0.020	0.056	0.003	0.024	0.025
	CAR-orig	-0.036	0.345	0.229	-0.034	0.238	-0.125	-0.019	0.071	0.031
	CAR-cluster	-0.023	0.346	-0.249	-0.025	0.206	-0.110	-0.001	0.025	0.002
HN2	Bayes	0.104	0.013	0.530	0.054	-0.025	0.442	0.009	0.017	0.156
	CAR-orig	-0.062	0.162	-1.137	-0.022	0.049	-0.282	0.013	-0.018	0.009
	CAR-cluster	-0.059	0.120	-1.252	-0.011	0.006	-0.217	0.005	-0.011	0.059
HN3	Bayes	0.111	-0.150	0.475	0.060	-0.079	0.303	0.009	0.008	0.059
	CAR-orig	-0.110	0.033	-0.010	-0.065	0.079	-0.098	-0.007	0.018	0.078
	CAR-cluster	-0.105	0.069	-0.479	-0.051	0.054	0.026	-0.006	0.012	0.078
HN4	Bayes	0.025	-0.002	0.298	0.037	0.010	0.128	0.007	0.027	0.039
	CAR-orig	-0.371	0.252	-0.140	-0.205	0.099	0.215	-0.075	0.048	0.183
	CAR-cluster	-0.285	0.216	0.066	-0.157	0.013	0.238	-0.057	0.042	0.157
HN5	Bayes	0.138	-0.243	0.405	0.062	-0.116	0.262	0.012	0.020	0.050
	CAR-orig	0.026	-0.366	0.214	0.087	-0.233	0.502	0.000	-0.018	0.143
	CAR-cluster	0.063	-0.355	0.273	0.081	-0.199	0.503	0.003	0.006	0.069
P1	Bayes	0.016	0.018	0.163	0.053	-0.033	0.294	0.015	0.018	0.183
	CAR-orig	0.021	-0.059	0.012	0.041	-0.139	-0.135	0.021	-0.059	0.012
	CAR-cluster	0.016	-0.035	0.080	0.034	-0.094	-0.052	0.016	-0.036	0.083
P2	Bayes	0.022	0.015	-0.060	0.049	-0.014	-0.167	0.023	0.008	-0.100
	CAR-orig	-0.027	0.094	-0.295	0.000	0.171	-0.898	-0.027	0.094	-0.295
	CAR-cluster	-0.031	0.062	-0.178	0.026	0.143	-0.533	-0.035	0.055	-0.151
P3	Bayes	0.027	0.004	0.170	0.071	0.011	0.302	0.031	0.000	0.169
	CAR-orig	0.013	0.029	-0.020	0.008	0.058	-0.097	0.013	0.029	-0.020
	CAR-cluster	0.010	0.014	-0.058	0.017	0.035	-0.094	-0.003	0.013	-0.055
P4	Bayes	0.019	0.025	0.008	0.014	0.045	-0.005	0.019	0.024	0.010
	CAR-orig	0.012	0.021	-0.087	-0.018	0.016	-0.143	0.012	0.021	-0.087
	CAR-cluster	0.007	0.014	-0.049	-0.007	0.001	-0.086	0.009	0.015	-0.051
P5	Bayes	0.032	-0.026	0.171	0.033	0.030	0.280	0.033	-0.027	0.165
	CAR-orig	-0.015	-0.026	-0.117	-0.080	0.020	-0.780	-0.015	-0.026	-0.117
	CAR-cluster	-0.004	-0.007	-0.094	-0.025	-0.004	-0.493	-0.002	-0.005	-0.114

Table S1. Median error  $\varepsilon$  for each simulated image at SNR10, SNR25 and SNR50 using the three different methods. HN: Head-and-Neck simulations; P: pelvis simulations.

Median error		SNR100			SNR150			SNR200		
		D	f	D*	D	f	D*	D	f	D*
HN1	Bayes	0.006	0.024	0.025	0.005	0.006	0.026	0.005	0.004	0.030
	CAR-orig	-0.019	0.071	0.031	0.003	0.016	0.029	0.003	0.002	0.022
	CAR-cluster	-0.001	0.023	0.003	0.003	0.010	0.011	0.001	-0.005	0.007
HN2	Bayes	0.009	0.020	0.160	0.006	0.019	0.067	0.003	0.013	0.043
	CAR-orig	0.013	-0.018	0.009	0.005	-0.018	-0.006	0.002	-0.025	-0.012
	CAR-cluster	0.006	-0.011	0.072	0.001	0.000	0.006	0.002	0.000	-0.006
HN3	Bayes	0.009	0.011	0.064	0.007	0.009	0.028	0.008	0.005	0.024
	CAR-orig	-0.007	0.018	0.078	-0.014	0.014	0.062	-0.004	0.011	0.048
	CAR-cluster	-0.008	0.015	0.076	-0.017	0.007	0.053	-0.001	0.004	0.029
HN4	Bayes	0.008	0.028	0.043	0.006	0.006	0.011	0.008	0.007	0.022
	CAR-orig	-0.075	0.048	0.183	-0.027	0.002	0.114	-0.006	0.004	0.103
	CAR-cluster	-0.051	0.041	0.161	-0.011	0.001	0.116	-0.002	0.002	0.110
HN5	Bayes	0.012	0.019	0.040	0.005	0.011	0.059	0.006	0.011	0.101
	CAR-orig	0.000	-0.018	0.143	-0.005	0.012	0.045	-0.004	-0.003	0.023
	CAR-cluster	0.002	0.006	0.054	-0.001	0.006	-0.007	-0.003	0.010	-0.014
P1	Bayes	0.010	0.005	0.050	0.005	0.007	0.030	0.002	0.005	0.046
	CAR-orig	0.000	-0.011	0.025	0.004	-0.005	0.017	-0.002	0.001	0.007
	CAR-cluster	0.003	-0.015	0.035	0.008	-0.007	0.018	0.000	-0.001	0.009
P2	Bayes	0.010	0.011	0.021	0.002	0.012	0.016	0.005	0.008	0.027
	CAR-orig	-0.030	0.048	-0.158	-0.028	0.044	-0.109	-0.026	0.047	-0.095
	CAR-cluster	-0.017	0.036	-0.102	-0.018	0.033	-0.075	-0.006	0.008	-0.030
P3	Bayes	0.008	0.015	0.031	0.000	0.015	0.021	0.003	0.008	0.021
	CAR-orig	-0.010	0.016	-0.038	-0.007	0.006	0.009	-0.003	0.001	0.008
	CAR-cluster	-0.002	0.007	-0.017	0.000	0.001	0.021	0.002	-0.003	0.017
P4	Bayes	0.008	0.001	0.020	0.001	0.008	0.012	0.002	0.005	0.014
	CAR-orig	-0.004	0.012	-0.016	-0.005	0.007	0.006	-0.001	0.001	0.002
	CAR-cluster	-0.001	0.004	-0.005	-0.002	0.002	0.003	0.000	-0.001	0.000
P5	Bayes	0.010	0.015	0.030	0.004	0.015	0.014	0.003	0.012	0.027
	CAR-orig	-0.004	-0.015	-0.043	-0.001	-0.011	-0.031	-0.003	-0.004	-0.013
	CAR-cluster	0.000	0.002	-0.058	0.003	-0.004	-0.031	0.000	-0.001	-0.016

Table S2. Median error  $\varepsilon$  for each simulated image at SNR100, SNR150 and SNR200 using the three different methods. HN: Head-and-Neck simulations; P: pelvis simulations.

CV		SNR10			SNR25			SNR50		
		D	f	D*	D	f	D*	D	f	D*
HN1	Bayes	0.229	0.335	0.352	0.133	0.245	0.353	0.055	0.079	0.160
	CAR-orig	0.085	0.096	0.087	0.057	0.065	0.148	0.040	0.057	0.118
	CAR-cluster	0.067	0.086	0.195	0.040	0.048	0.115	0.048	0.025	0.068
HN2	Bayes	0.203	0.320	0.289	0.117	0.253	0.261	0.031	0.135	0.195
	CAR-orig	0.085	0.104	0.398	0.070	0.111	0.201	0.057	0.114	0.224
	CAR-cluster	0.076	0.090	0.303	0.046	0.064	0.149	0.029	0.061	0.130
HN3	Bayes	0.193	0.310	0.276	0.132	0.272	0.293	0.041	0.216	0.228
	CAR-orig	0.068	0.112	0.321	0.049	0.128	0.256	0.032	0.134	0.174
	CAR-cluster	0.056	0.092	0.375	0.032	0.105	0.223	0.021	0.064	0.112
HN4	Bayes	0.204	0.285	0.256	0.156	0.204	0.326	0.065	0.195	0.176
	CAR-orig	0.098	0.120	0.152	0.091	0.135	0.165	0.062	0.140	0.137
	CAR-cluster	0.078	0.076	0.169	0.054	0.108	0.141	0.027	0.060	0.101
HN5	Bayes	0.213	0.318	0.248	0.126	0.273	0.256	0.047	0.232	0.271
	CAR-orig	0.123	0.125	0.204	0.096	0.156	0.160	0.057	0.115	0.150
	CAR-cluster	0.102	0.085	0.190	0.075	0.129	0.138	0.039	0.090	0.090
P1	Bayes	0.074	0.140	0.215	0.142	0.195	0.285	0.072	0.114	0.208
	CAR-orig	0.101	0.097	0.195	0.133	0.119	0.281	0.101	0.097	0.195
	CAR-cluster	0.051	0.065	0.114	0.067	0.104	0.171	0.053	0.085	0.127
P2	Bayes	0.104	0.243	0.323	0.163	0.287	0.342	0.105	0.246	0.315
	CAR-orig	0.075	0.096	0.206	0.108	0.115	0.216	0.075	0.096	0.206
	CAR-cluster	0.056	0.061	0.131	0.078	0.075	0.194	0.074	0.066	0.141
P3	Bayes	0.075	0.162	0.240	0.127	0.217	0.315	0.074	0.160	0.238
	CAR-orig	0.082	0.101	0.204	0.124	0.105	0.271	0.082	0.101	0.204
	CAR-cluster	0.067	0.059	0.109	0.099	0.069	0.175	0.069	0.058	0.106
P4	Bayes	0.080	0.125	0.251	0.143	0.189	0.297	0.082	0.121	0.240
	CAR-orig	0.077	0.064	0.127	0.103	0.081	0.151	0.077	0.064	0.127
	CAR-cluster	0.061	0.059	0.095	0.072	0.069	0.108	0.060	0.055	0.095
P5	Bayes	0.075	0.107	0.277	0.116	0.206	0.258	0.075	0.109	0.276
	CAR-orig	0.073	0.081	0.195	0.094	0.089	0.201	0.073	0.081	0.195
	CAR-cluster	0.046	0.056	0.128	0.060	0.066	0.158	0.050	0.052	0.140

Table S3. CV for each simulated image at SNR10, SNR25 and SNR50 using the three different methods. HN: Head-and-Neck simulations; P: pelvis simulations.

CV		SNR100			SNR150			SNR200		
		D	f	D*	D	f	D*	D	f	D*
HN1	Bayes	0.055	0.079	0.155	0.037	0.059	0.101	0.028	0.048	0.084
	CAR-orig	0.040	0.057	0.118	0.039	0.055	0.104	0.031	0.056	0.126
	CAR-cluster	0.040	0.027	0.068	0.022	0.019	0.064	0.025	0.019	0.068
HN2	Bayes	0.032	0.208	0.222	0.019	0.112	0.179	0.018	0.057	0.128
	CAR-orig	0.057	0.114	0.224	0.047	0.110	0.196	0.039	0.092	0.139
	CAR-cluster	0.028	0.064	0.113	0.024	0.055	0.077	0.019	0.059	0.089
HN3	Bayes	0.042	0.219	0.228	0.028	0.117	0.175	0.021	0.092	0.142
	CAR-orig	0.032	0.134	0.174	0.030	0.098	0.179	0.032	0.086	0.165
	CAR-cluster	0.021	0.064	0.113	0.021	0.054	0.095	0.018	0.041	0.066
HN4	Bayes	0.066	0.174	0.174	0.047	0.119	0.129	0.036	0.117	0.104
	CAR-orig	0.062	0.140	0.137	0.054	0.122	0.124	0.052	0.114	0.101
	CAR-cluster	0.027	0.061	0.107	0.023	0.051	0.112	0.024	0.046	0.100
HN5	Bayes	0.062	0.360	0.261	0.027	0.152	0.196	0.025	0.163	0.122
	CAR-orig	0.057	0.115	0.150	0.045	0.111	0.130	0.047	0.089	0.145
	CAR-cluster	0.048	0.086	0.085	0.033	0.067	0.060	0.026	0.047	0.064
P1	Bayes	0.039	0.069	0.141	0.028	0.053	0.105	0.019	0.043	0.080
	CAR-orig	0.072	0.059	0.171	0.061	0.050	0.114	0.042	0.045	0.080
	CAR-cluster	0.044	0.073	0.094	0.028	0.048	0.048	0.032	0.062	0.059
P2	Bayes	0.052	0.121	0.216	0.045	0.115	0.166	0.035	0.080	0.133
	CAR-orig	0.054	0.081	0.168	0.045	0.073	0.141	0.047	0.089	0.145
	CAR-cluster	0.045	0.041	0.108	0.031	0.036	0.067	0.030	0.053	0.080
P3	Bayes	0.034	0.088	0.156	0.025	0.059	0.134	0.020	0.044	0.123
	CAR-orig	0.055	0.087	0.147	0.052	0.080	0.130	0.031	0.071	0.113
	CAR-cluster	0.033	0.043	0.071	0.029	0.037	0.063	0.023	0.037	0.052
P4	Bayes	0.046	0.084	0.150	0.031	0.054	0.125	0.021	0.042	0.089
	CAR-orig	0.055	0.057	0.111	0.038	0.047	0.095	0.032	0.045	0.072
	CAR-cluster	0.064	0.087	0.099	0.055	0.087	0.109	0.029	0.058	0.079
P5	Bayes	0.037	0.069	0.156	0.020	0.031	0.113	0.018	0.026	0.081
	CAR-orig	0.049	0.064	0.127	0.050	0.055	0.110	0.046	0.061	0.145
	CAR-cluster	0.035	0.042	0.085	0.024	0.036	0.059	0.032	0.037	0.081

Table S4. CV for each simulated image at SNR100, SNR150 and SNR 200 using the three different methods. HN: Head-and-Neck simulations; P: pelvis simulations.