

SUPPLEMENTARY MATERIAL FOR:

Estimation of intravoxel incoherent motion (IVIM) parameters in vertebral bone

marrow: a comparative study of five algorithms

Table S1. The values of the signal of an ROI drawn in each lumbar vertebra (L1, L2, etc.) in two repeated acquisitions (mean 1 and mean 2), the standard deviation of the difference and the signal-to-noise ratio calculated the using the dual acquisition, subtraction method. V1 = volunteer 1, V2 = volunteer 2, etc.

		MEAN 1	MEAN 2	STD of DIFF	SNR	SNR_M
V1	L1	569	576	50	16	16
	L2	500	496	37	19	
	L3	366	397	31	17	
	L4	322	326	36	13	
	L5	328	313	34	14	
V3	L1	507	490	38	19	19
	L2	495	483	36	19	
	L3	390	387	23	24	
	L4	344	331	32	15	
	L5	310	317	25	18	
V4	L1	497	481	31	23	17
	L2	402	392	31	18	
	L3	320	324	31	15	
	L4	342	327	43	11	
	L5	371	370	31	17	
V5	L1	328	316	38	12	14
	L2	269	262	27	14	
	L3	272	274	24	16	
	L4	235	244	25	13	
	L5	219	221	24	13	
V6	L1	434	422	37	17	17
	L2	411	410	35	17	
	L3	400	402	31	18	
	L4	359	360	34	15	
	L5	320	323	26	17	

Table S2. The statistical analysis results of the IVIM parameters estimated from the data acquired *in vivo*, in each lumbar vertebra (L1, L2, L3, L4, L5) and for each volunteer (V1, V2, V3, V4, V5, V6). The table can be read in the following way: for the diffusion coefficient D , for instance, in 22 out of 30 cases (i.e., in most cases) the ANOVA test with Bonferroni's post-test did not show a statistically significant difference between the values estimated by the One-Step and those estimated by Bayesian algorithm. On the contrary, for all other paired comparisons only in a small number of cases no significant difference was observed (One-Step vs Two-Step: $n = 4$; One-Step vs Three-Step: $n = 4$; Bayesian vs Two-Step: $n = 5$; Bayesian vs Three-Step: $n = 5$). It should be noted that D is the same in the Two-Step and Three-Step, so no statistical test is necessary for comparison.

Diffusion coefficient D

One-Step				
Two-Step	4			
Three-Step	4			
Bayesian	22	5	5	
	One-Step	Two-Step	Three-Step	Bayesian

Perfusion fraction f

One-Step				
Two-Step	0			
Three-Step	0	2		
Bayesian	27	2	0	
	One-Step	Two-Step	Three-Step	Bayesian

Pseudo-diffusion coefficient D^*

One-Step				
Two-Step	3			
Three-Step	2	29		
Bayesian	18	28	28	
	One-Step	Two-Step	Three-Step	Bayesian

Figure S1. Signal-vs- b plot along with the fitting curves. Left: ROI average of Volunteer-1 L1; Right: a single voxel (picked from center region of Volunteer-1 L1).

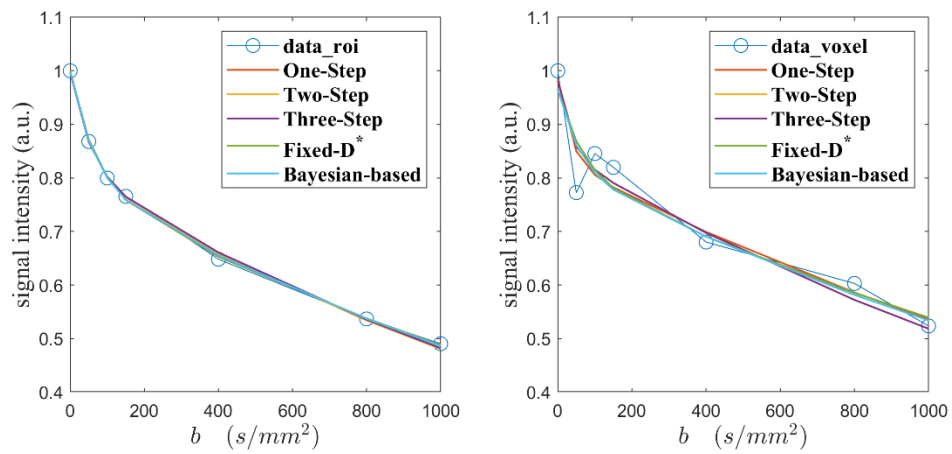


Figure S2. The relative error of D , f and D^* obtained by the deterministic algorithms plotted vs the relative error of the Bayesian approach, for different values of SNR (10, 20, 50, 100). The data above the unity line indicates the superiority of the Bayesian approach over the deterministic algorithms.

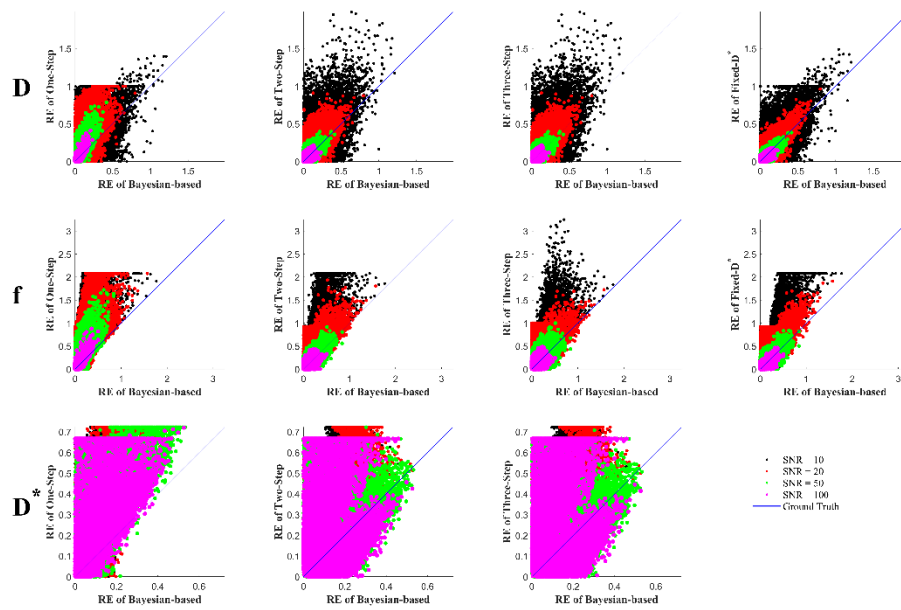


Table S3: Quantification results of bone marrow IVIM – 1 Volunteers 1 – 3

	Algorithm	Volunteer 1						Volunteer 2						Volunteer 3					
		D		f (%)		D^*		D		f (%)		D^*		D		f (%)		D^*	
L1	One-Step	(0.42 0.14) ¹		14.4	11.4	14.0	10.6	0.53	0.20	13.5	11.1	12.3	10.2	0.41	0.14	10.4	10.6	12.7	10.3
	Two-Step	0.49	0.13	11.7	10.1	16.3	10.6	0.60	0.21	10.0	8.5	15.2	10.6	0.47	0.12	8.6	8.3	14.5	10.8
	Three-Step	0.49	0.13	10.1	10.4	16.5	9.1	0.60	0.21	8.5	9.0	15.7	9.4	0.47	0.12	7.3	9.0	15.3	9.2
	Fixed- D^*	0.46	0.13	11.6	10.6	15.0	0.0	0.59	0.20	9.3	8.8	15.0	0.0	0.44	0.11	8.3	8.9	15.0	0.0
	Bayesian-based	0.43	0.14	14.6	4.3	15.4	2.6	0.54	0.19	13.0	4.3	14.6	2.4	0.39	0.12	13.2	3.7	14.9	2.2
L2	One-Step	0.43	0.16	15.5	12.7	13.4	10.4	0.55	0.25	12.8	10.2	12.9	10.0	0.42	0.16	10.4	10.4	13.9	10.8
	Two-Step	0.49	0.16	12.5	10.9	15.9	10.6	0.61	0.23	10.0	8.7	15.8	10.2	0.46	0.14	8.9	9.0	14.9	10.9
	Three-Step	0.49	0.16	10.7	11.6	15.6	9.0	0.61	0.23	9.0	10.2	15.8	8.8	0.46	0.14	7.7	9.8	15.8	9.3
	Fixed- D^*	0.47	0.16	11.9	11.4	15.0	0.0	0.59	0.26	9.7	8.9	15.0	0.0	0.44	0.14	8.6	9.5	15.0	0.0
	Bayesian-based	0.45	0.16	14.6	4.5	15.4	2.3	0.55	0.23	13.2	4.0	14.9	2.2	0.39	0.14	13.4	3.9	15.1	2.3
L3	One-Step	0.44	0.16	14.3	11.8	13.9	10.9	0.51	0.22	12.6	10.8	12.1	10.3	0.42	0.19	10.5	10.1	12.8	10.3
	Two-Step	0.51	0.17	11.3	10.3	16.4	11.0	0.56	0.22	9.8	8.7	13.7	10.1	0.46	0.19	8.9	9.0	14.9	11.0
	Three-Step	0.51	0.17	9.4	10.6	16.1	9.5	0.56	0.22	8.7	11.1	14.4	8.7	0.46	0.19	7.6	9.8	14.8	9.3
	Fixed- D^*	0.48	0.17	10.8	10.7	15.0	0.0	0.55	0.24	9.2	9.5	15.0	0.0	0.45	0.18	8.1	9.2	15.0	0.0
	Bayesian-based	0.45	0.16	14.3	4.6	15.3	2.4	0.50	0.22	13.4	4.1	14.8	2.6	0.40	0.19	12.9	3.9	14.9	2.2
L4	One-Step	0.46	0.18	13.6	11.1	13.0	10.2	0.50	0.22	12.2	11.1	13.6	10.5	0.43	0.23	12.6	10.7	16.7	11.2
	Two-Step	0.52	0.17	10.7	8.7	15.7	10.5	0.54	0.14	9.5	9.0	15.5	10.3	0.49	0.24	10.3	9.0	19.0	10.6
	Three-Step	0.52	0.17	8.9	9.0	16.0	9.2	0.54	0.14	8.7	11.3	15.9	8.9	0.49	0.24	9.3	10.2	18.7	9.4
	Fixed- D^*	0.50	0.16	10.4	9.3	15.0	0.0	0.54	0.20	9.4	9.5	15.0	0.0	0.45	0.22	11.0	10.1	15.0	0.0
	Bayesian-based	0.46	0.16	14.6	4.0	15.2	2.2	0.49	0.18	13.0	4.3	14.7	2.2	0.44	0.22	14.2	4.0	15.9	2.2
L5	One-Step	0.41	0.30	13.5	11.6	15.2	11.1	0.60	0.30	10.9	10.7	13.3	10.2	0.36	0.21	11.7	11.8	13.5	10.9
	Two-Step	0.47	0.29	11.3	10.0	17.3	10.8	0.64	0.30	8.9	8.9	14.5	10.1	0.42	0.22	9.6	9.8	15.5	10.9
	Three-Step	0.47	0.29	10.0	11.1	17.4	9.4	0.64	0.30	8.0	10.8	15.1	8.6	0.42	0.22	8.6	10.4	15.4	9.0
	Fixed- D^*	0.43	0.30	11.3	10.9	15.0	0.0	0.63	0.30	8.4	8.9	15.0	0.0	0.38	0.21	9.5	10.0	15.0	0.0
	Bayesian-based	0.43	0.26	14.4	4.6	15.8	2.3	0.58	0.28	12.2	4.3	14.7	2.3	0.36	0.19	13.9	4.9	15.7	2.6

¹ Form of the data is "(MEAN STD)"

The units for D and D^* are the same, $\times 10^{-3} \text{ mm}^2/\text{s}$

Table S4: Quantification results of bone marrow IVIM – 2 Volunteers 4 – 6

	Algorithm	Volunteer 4						Volunteer 5						Volunteer 6					
		D		f (%)		D^*		D		f (%)		D^*		D		f (%)		D^*	
L1	One-Step	(0.50 0.35) ¹		11.0	10.6	13.1	10.1	0.31	0.21	17.4	13.5	14.0	10.3	0.46	0.29	12.8	11.2	14.4	10.2
	Two-Step	0.54	0.34	9.2	9.3	15.4	10.3	0.40	0.21	14.4	11.6	15.7	10.6	0.48	0.26	11.2	10.2	16.0	10.2
	Three-Step	0.54	0.34	8.0	10.4	15.1	8.7	0.40	0.21	12.6	11.6	16.2	9.1	0.48	0.26	10.4	12.7	15.9	8.9
	Fixed- D^*	0.53	0.35	8.5	9.6	15.0	0.0	0.36	0.18	14.3	12.0	15.0	0.0	0.48	0.28	10.6	10.7	15.0	0.0
	Bayesian-based	0.50	0.34	12.3	4.5	14.7	2.5	0.36	0.15	16.2	4.6	15.8	2.3	0.45	0.28	13.5	4.5	15.2	2.3
L2	One-Step	0.47	0.24	12.2	10.6	13.7	10.4	0.31	0.26	15.9	13.3	12.6	10.0	0.40	0.24	14.4	12.2	13.3	10.2
	Two-Step	0.52	0.24	10.3	9.0	15.7	10.5	0.39	0.28	13.0	11.2	15.1	10.7	0.45	0.25	12.1	11.1	14.8	10.2
	Three-Step	0.52	0.24	9.0	10.0	15.1	8.8	0.39	0.28	10.6	11.5	14.9	9.1	0.45	0.25	10.9	12.5	15.4	8.9
	Fixed- D^*	0.50	0.24	10.0	9.8	15.0	0.0	0.36	0.28	11.8	11.7	15.0	0.0	0.43	0.24	11.8	11.8	15.0	0.0
	Bayesian-based	0.47	0.24	13.8	4.4	15.2	2.2	0.37	0.26	15.6	4.3	15.5	2.2	0.41	0.23	14.8	4.8	15.4	2.4
L3	One-Step	0.36	0.19	16.4	12.5	13.1	10.7	0.27	0.22	17.2	13.2	14.0	10.6	0.44	0.23	11.7	11.0	14.3	10.9
	Two-Step	0.44	0.20	12.8	10.2	15.4	10.8	0.37	0.25	12.9	10.7	16.8	10.7	0.49	0.23	9.8	9.2	15.6	11.0
	Three-Step	0.44	0.20	10.8	10.6	15.8	9.5	0.37	0.25	11.1	11.2	16.9	9.5	0.49	0.23	8.2	9.3	15.7	9.4
	Fixed- D^*	0.42	0.17	11.9	10.8	15.0	0.0	0.33	0.25	13.0	11.3	15.0	0.0	0.46	0.22	9.5	10.0	15.0	0.0
	Bayesian-based	0.40	0.16	15.1	3.9	15.4	2.1	0.37	0.23	15.6	4.7	15.8	2.2	0.42	0.21	13.8	4.2	15.3	2.3
L4	One-Step	0.38	0.17	13.4	12.6	13.6	10.8	0.34	0.32	13.6	12.8	15.8	11.0	0.38	0.16	13.9	11.6	13.5	10.4
	Two-Step	0.45	0.17	11.4	11.1	15.5	11.2	0.38	0.36	11.5	11.2	18.7	10.8	0.45	0.16	11.0	9.4	15.4	10.4
	Three-Step	0.45	0.17	9.6	11.2	15.5	9.4	0.38	0.36	10.3	12.6	16.9	8.9	0.45	0.16	9.2	9.3	15.4	8.9
	Fixed- D^*	0.41	0.15	10.7	11.5	15.0	0.0	0.36	0.34	11.8	12.0	15.0	0.0	0.42	0.15	10.8	10.1	15.0	0.0
	Bayesian-based	0.38	0.14	15.0	4.2	15.4	2.2	0.42	0.28	15.2	4.8	16.2	2.3	0.40	0.15	14.4	4.1	15.3	2.1
L5	One-Step	0.40	0.21	14.5	12.0	14.5	10.8	0.31	0.31	15.7	12.8	18.2	11.1	0.39	0.21	12.3	11.3	12.8	9.7
	Two-Step	0.47	0.20	11.8	10.1	16.7	10.8	0.25	0.48	14.6	11.9	18.7	10.5	0.44	0.23	10.3	9.1	14.9	10.2
	Three-Step	0.47	0.20	10.4	10.7	16.4	9.4	0.25	0.48	13.0	13.0	17.7	9.2	0.44	0.23	8.5	8.8	14.5	8.6
	Fixed- D^*	0.44	0.19	11.5	10.8	15.0	0.0	0.33	0.32	13.3	12.6	15.0	0.0	0.43	0.22	9.2	8.9	15.0	0.0
	Bayesian-based	0.43	0.19	14.5	4.2	15.4	2.2	0.43	0.28	16.5	5.2	16.4	2.6	0.41	0.21	13.4	3.9	15.0	2.0

¹ Form of the data is "(MEAN STD)"

The units for D and D^* are the same, $\times 10^{-3} \text{ mm}^2/\text{s}$

Table S5. The coefficient of variation of D , f and D^* , calculated from two repeated measurements (denoted as x_1 and x_2) on 5 volunteers, for each vertebra. The CV (coefficient of variation) was calculated as $\frac{|x_1-x_2|}{x_1+x_2} \times 100\%$.

	Algorithm	Volunteer 1			Volunteer 3			Volunteer 4			Volunteer 5			Volunteer 6		
		CV of D	CV of f	CV of D*	CV of D	CV of f	CV of D*	CV of D	CV of f	CV of D*	CV of D	CV of f	CV of D*	CV of D	CV of f	CV of D*
L1	One-Step	0.3%	4.7%	8.2%	1.5%	13.8%	3.9%	2.4%	11.8%	0.8%	2.2%	4.3%	3.6%	3.6%	7.8%	3.1%
	Two-Step	2.3%	1.6%	4.9%	0.8%	18.2%	3.7%	0.3%	9.2%	0.5%	3.1%	7.9%	6.7%	0.2%	2.9%	6.2%
	Three-Step	2.3%	2.8%	5.5%	0.8%	17.7%	0.5%	0.3%	18.8%	1.5%	3.1%	9.4%	3.5%	0.2%	1.4%	4.2%
	Fixed-Dstar	2.0%	0.1%	0.0%	1.1%	16.5%	0.0%	3.2%	10.7%	0.0%	1.5%	5.6%	0.0%	2.4%	5.5%	0.0%
	Bayesian-based	0.5%	3.3%	0.3%	0.3%	7.0%	1.8%	1.6%	2.7%	0.1%	0.7%	2.8%	0.2%	0.5%	0.8%	1.1%
L2	One-Step	4.9%	20.9%	3.1%	0.3%	12.8%	17.5%	3.6%	2.8%	1.5%	8.5%	3.0%	8.8%	2.2%	4.5%	4.0%
	Two-Step	2.9%	20.2%	3.8%	2.3%	22.8%	7.6%	1.5%	2.4%	0.5%	9.6%	6.6%	5.3%	1.9%	6.4%	3.8%
	Three-Step	2.9%	20.6%	4.4%	2.3%	28.6%	8.2%	1.5%	4.7%	1.6%	9.6%	10.1%	5.5%	1.9%	6.0%	2.9%
	Fixed-Dstar	2.0%	17.6%	0.0%	2.2%	24.2%	0.0%	1.4%	3.0%	0.0%	10.4%	7.9%	0.0%	3.0%	7.8%	0.0%
	Bayesian-based	1.1%	6.4%	0.8%	0.6%	7.6%	4.0%	2.8%	1.7%	1.1%	5.3%	0.6%	1.6%	0.4%	3.0%	1.8%
L3	One-Step	0.9%	13.6%	5.5%	2.2%	8.3%	2.5%	5.8%	5.7%	4.2%	4.1%	2.3%	5.2%	1.6%	12.4%	5.6%
	Two-Step	0.8%	14.0%	3.2%	0.8%	1.6%	2.6%	6.0%	7.8%	4.2%	0.6%	7.6%	3.0%	2.3%	16.3%	1.5%
	Three-Step	0.8%	13.1%	2.0%	0.8%	0.0%	2.5%	6.0%	7.7%	5.0%	0.6%	9.5%	0.8%	2.3%	19.6%	1.2%
	Fixed-Dstar	0.3%	11.8%	0.0%	0.7%	6.5%	0.0%	6.0%	9.8%	0.0%	1.0%	7.0%	0.0%	1.4%	15.1%	0.0%
	Bayesian-based	3.1%	2.8%	0.9%	1.1%	2.2%	0.0%	2.5%	1.4%	1.5%	1.3%	0.6%	1.1%	2.1%	2.7%	1.8%
L4	One-Step	3.6%	12.5%	4.2%	1.4%	12.6%	8.9%	1.6%	2.5%	16.4%	9.0%	2.9%	2.3%	2.9%	3.4%	6.5%
	Two-Step	1.8%	6.7%	2.0%	0.7%	16.2%	2.0%	3.3%	2.9%	14.7%	3.7%	0.3%	4.3%	1.9%	2.8%	5.0%
	Three-Step	1.8%	9.1%	0.7%	0.7%	20.9%	6.4%	3.3%	0.4%	15.7%	3.7%	1.5%	2.8%	1.9%	2.7%	0.9%
	Fixed-Dstar	0.8%	7.9%	0.0%	0.4%	17.0%	0.0%	5.0%	4.1%	0.0%	4.6%	3.5%	0.0%	2.4%	2.8%	0.0%
	Bayesian-based	1.2%	1.5%	0.4%	4.8%	6.2%	2.4%	3.0%	1.2%	2.5%	9.1%	3.0%	1.8%	0.4%	0.1%	1.1%
L5	One-Step	3.5%	25.1%	0.5%	2.8%	1.1%	11.9%	0.4%	10.4%	4.8%	12.4%	10.8%	3.8%	1.9%	31.2%	5.5%
	Two-Step	2.4%	27.9%	1.0%	7.0%	6.6%	7.4%	1.9%	7.7%	5.6%	0.3%	16.6%	4.7%	1.0%	32.3%	2.6%
	Three-Step	2.4%	33.9%	1.6%	7.0%	12.2%	3.0%	1.9%	6.9%	6.4%	0.3%	18.6%	7.3%	1.0%	36.0%	1.1%
	Fixed-Dstar	1.8%	24.0%	0.0%	5.9%	8.0%	0.0%	1.4%	10.3%	0.0%	8.2%	16.8%	0.0%	1.6%	29.3%	0.0%
	Bayesian-based	3.2%	8.3%	2.2%	3.3%	1.3%	2.8%	3.2%	2.8%	1.0%	15.6%	9.1%	2.4%	7.1%	7.9%	1.9%

Table S6. The mean value (MEAN) and standard deviation (STD) of the coefficient of variation of D , f and D^* for each volunteer (calculated as the average over the five lumbar vertebrae). Overall, the Bayesian approach display a lower coefficient of variation with respect to the LSQ-based algorithms.

	Algorithm	Volunteer 1			Volunteer 3			Volunteer 4			Volunteer 5			Volunteer 6		
		CV of D	CV of f	CV of D*	CV of D	CV of f	CV of D*	CV of D	CV of f	CV of D*	CV of D	CV of f	CV of D*	CV of D	CV of f	CV of D*
MEAN	One-Step	2.6%	15.4%	4.3%	1.6%	9.7%	9.0%	2.8%	6.6%	5.6%	7.2%	4.7%	4.8%	2.5%	11.9%	4.9%
	Two-Step	2.1%	14.1%	3.0%	2.3%	13.1%	4.7%	2.6%	6.0%	5.1%	3.4%	7.8%	4.8%	1.5%	12.1%	3.8%
	Three-Step	2.1%	15.9%	2.8%	2.3%	15.9%	4.1%	2.6%	7.7%	6.0%	3.4%	9.8%	4.0%	1.5%	13.1%	2.0%
	Fixed-Dstar	1.4%	12.3%	0.0%	2.1%	14.4%	0.0%	3.4%	7.6%	0.0%	5.2%	8.2%	0.0%	2.2%	12.1%	0.0%
	Bayesian-based	1.8%	4.5%	0.9%	2.0%	4.9%	2.2%	2.6%	2.0%	1.2%	6.4%	3.2%	1.4%	2.1%	2.9%	1.5%
STD	One-Step	1.9%	7.9%	2.8%	0.9%	5.3%	6.1%	2.0%	4.3%	6.3%	4.1%	3.5%	2.5%	0.8%	11.4%	1.4%
	Two-Step	0.8%	10.5%	1.5%	2.7%	8.7%	2.6%	2.2%	3.1%	5.8%	3.8%	5.8%	1.4%	0.8%	12.6%	1.8%
	Three-Step	0.8%	12.0%	2.0%	2.7%	10.7%	3.1%	2.2%	6.8%	5.8%	3.8%	6.1%	2.5%	0.8%	14.7%	1.5%
	Fixed-Dstar	0.8%	9.1%	0.0%	2.2%	7.3%	0.0%	2.1%	3.7%	0.0%	4.1%	5.1%	0.0%	0.7%	10.7%	0.0%
	Bayesian-based	1.2%	2.8%	0.8%	1.9%	2.9%	1.5%	0.6%	0.7%	0.9%	6.2%	3.5%	0.8%	2.9%	3.0%	0.4%