# Appendix

Details of the algorithm used to estimate hyper-parameters $c$ and $\pi$:
To maximize the likelihood

$$L(\pi, c; \mathbf{a}, \hat{s}_1^2, ..., \hat{s}_J^2) = p(\hat{s}_1, ..., \hat{s}_J|\pi, \mathbf{a}, c) \tag{1}$$

$$= \prod_{j=1}^{J} \sum_{k} \pi_k p(\hat{s}_j; a_k, c) \tag{2}$$

we iteratively update $c$ and $\pi$ using the following steps until they converge:

$$c^{new} = \arg\max_c \log L(c, a_1^{old}, ...a_K^{old}, \pi_1^{old}, ..., \pi_K^{old}) \tag{3}$$

$$(\pi_1^{new}, ..., \pi_K^{new}) = \left( \frac{\sum_j \tilde{\pi}_{j1}^{old}}{\sum_{j'} \sum_{k'} \tilde{\pi}_{j'k'}^{old}}, ..., \frac{\sum_j \tilde{\pi}_{jK}^{old}}{\sum_{j'} \sum_{k'} \tilde{\pi}_{j'k'}^{old}} \right). \tag{4}$$

Because there is no analytic solution to the optimization problem (3) we approximate the optimum via the quasi-Newton method using the function `optim` in R. The updating procedure (3)-(4) is a fixed point mapping function, hence we can accelerate the overall optimization procedure by the R package `SQUAREM`, which is computationally efficient in solving fixed point problems.

# Supplementary tables and figures

| | A | B | C | D | E | F | G | H |
|---|---|---|---|---|---|---|---|---|
| baseline | 70.79 | 131.30 | 57.67 | 49.51 | 47.19 | 60.65 | 56.88 | 40.85 |
| limma | 38.55 | 108.23 | 29.02 | 20.06 | 25.70 | 43.54 | 52.97 | 14.58 |
| limmaR | 38.86 | 103.50 | 29.88 | 20.60 | 25.90 | 41.85 | 39.00 | 14.58 |
| vash.opt | 38.54 | 91.39 | 28.56 | 19.86 | 25.69 | 38.60 | 47.34 | 14.31 |

(a) $\text{RMSE}_{var}$ in the cases where df=3.

| | A | B | C | D | E | F | G | H |
|---|---|---|---|---|---|---|---|---|
| baseline | 38.73 | 66.01 | 31.50 | 26.98 | 25.82 | 31.25 | 40.43 | 22.36 |
| limma | 29.80 | 73.09 | 23.57 | 17.27 | 19.87 | 30.56 | 44.14 | 12.82 |
| limmaR | 29.88 | 59.13 | 23.19 | 17.18 | 19.92 | 26.33 | 35.47 | 12.78 |
| vash.opt | 29.80 | 60.18 | 22.73 | 16.72 | 19.87 | 26.87 | 39.37 | 12.37 |

(b) $\text{RMSE}_{var}$ in the cases where df=10.

| | A | B | C | D | E | F | G | H |
|---|---|---|---|---|---|---|---|---|
| baseline | 17.28 | 37.07 | 14.13 | 12.08 | 11.52 | 16.56 | 14.74 | 10.00 |
| limma | 16.27 | 38.46 | 13.34 | 10.78 | 10.85 | 16.61 | 18.80 | 8.42 |
| limmaR | 16.28 | 36.49 | 12.95 | 10.33 | 10.86 | 16.08 | 14.05 | 8.31 |
| vash.opt | 16.27 | 36.89 | 12.85 | 10.19 | 10.85 | 16.27 | 15.68 | 7.80 |

(c) $\text{RMSE}_{var}$ in the cases where df=50.

Table S1: Table of average $\text{RMSE}_{var}$ of *limma*, *limmaR* and *vash* in the 8 simulation scenarios A-H.

| | A | B | C | D | E | F | G | H |
|---|---|---|---|---|---|---|---|---|
| baseline | 803.49 | 801.65 | 961.77 | 768.21 | 1205.23 | 1276.52 | 1223.56 | 1356.00 |
| limma | 16.67 | 17.03 | 13.48 | 12.92 | 25.00 | 32.81 | 30.56 | 28.63 |
| limmaR | 16.67 | 17.02 | 13.46 | 12.91 | 25.00 | 32.82 | 30.58 | 28.64 |
| vash.opt | 16.67 | 17.06 | 13.45 | 12.90 | 25.00 | 32.81 | 30.38 | 28.76 |

(a) $\text{RMSE}_{prec}$ in the cases where df=3.

| | A | B | C | D | E | F | G | H |
|---|---|---|---|---|---|---|---|---|
| baseline | 35.23 | 34.47 | 35.97 | 38.21 | 52.85 | 57.59 | 52.96 | 50.26 |
| limma | 13.76 | 13.87 | 11.81 | 11.72 | 20.64 | 27.04 | 26.68 | 26.28 |
| limmaR | 13.76 | 13.85 | 11.75 | 11.69 | 20.64 | 27.08 | 26.90 | 26.41 |
| vash.opt | 13.76 | 13.85 | 11.72 | 11.70 | 20.64 | 26.48 | 24.85 | 24.74 |

(b) $\text{RMSE}_{prec}$ in the cases where df=10.

| | A | B | C | D | E | F | G | H |
|---|---|---|---|---|---|---|---|---|
| baseline | 10.08 | 9.96 | 10.52 | 11.05 | 15.12 | 16.66 | 15.38 | 14.62 |
| limma | 8.20 | 8.18 | 7.97 | 8.40 | 12.29 | 15.46 | 16.27 | 18.10 |
| limmaR | 8.20 | 8.16 | 7.90 | 8.46 | 12.30 | 15.59 | 17.23 | 19.39 |
| vash.opt | 8.20 | 8.16 | 7.83 | 8.10 | 12.30 | 14.29 | 13.07 | 13.42 |

(c) $\text{RMSE}_{prec}$ in the cases where df=50.

Table S2: Table of average $\text{RMSE}_{prec}$ of *limma*, *limmaR* and *vash* in the 8 simulation scenarios A-H.

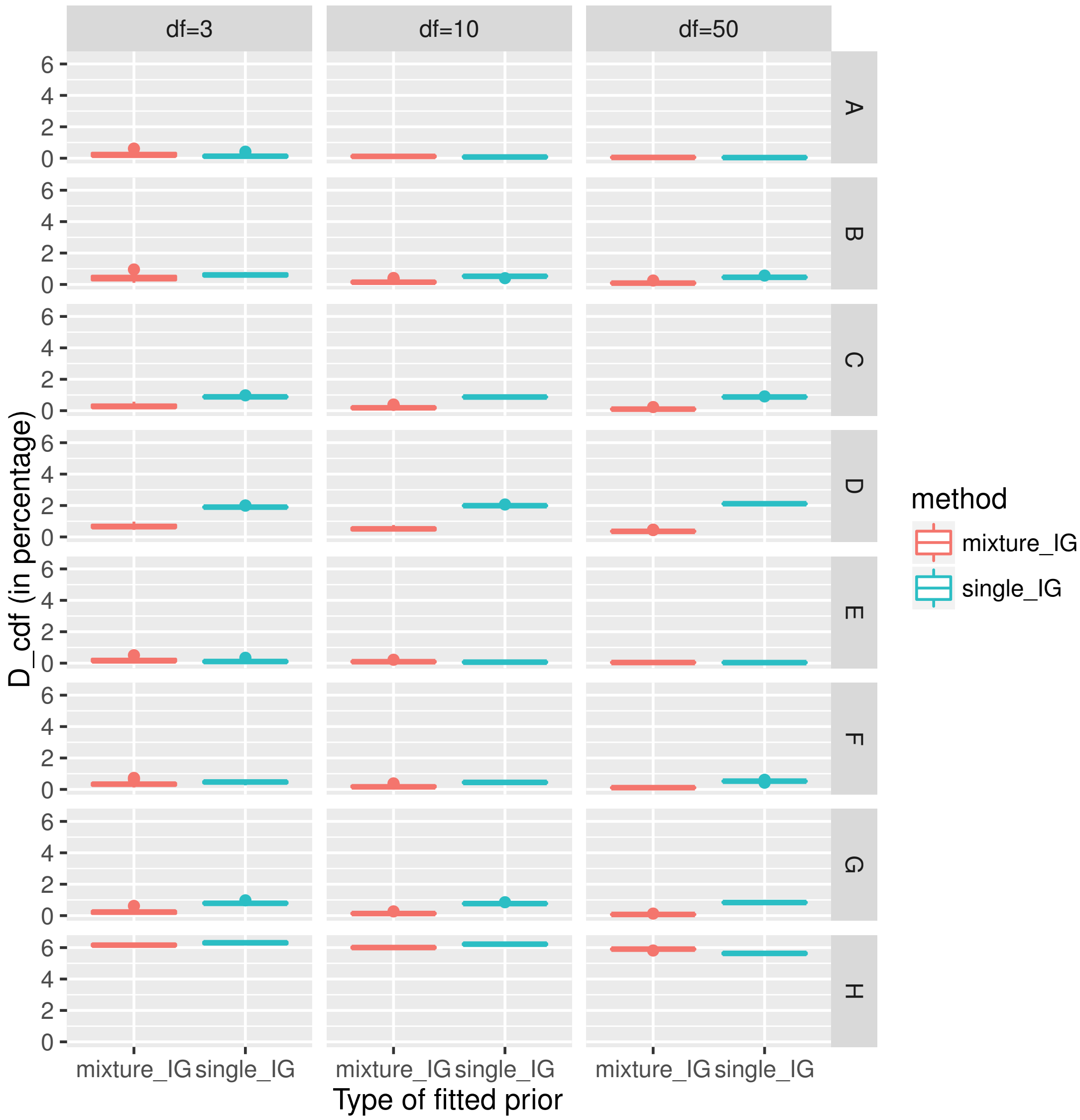


Figure S1: $D_{\text{cdf}}$, the average distance between the cdfs of true variance prior and estimated prior by mixture prior model or single component prior model.


Figure S2: AUC (area under ROC curve) of *limma*, *limmaR* and *vash* and baseline method (original t-test) in the 8 simulation scenarios A-H.