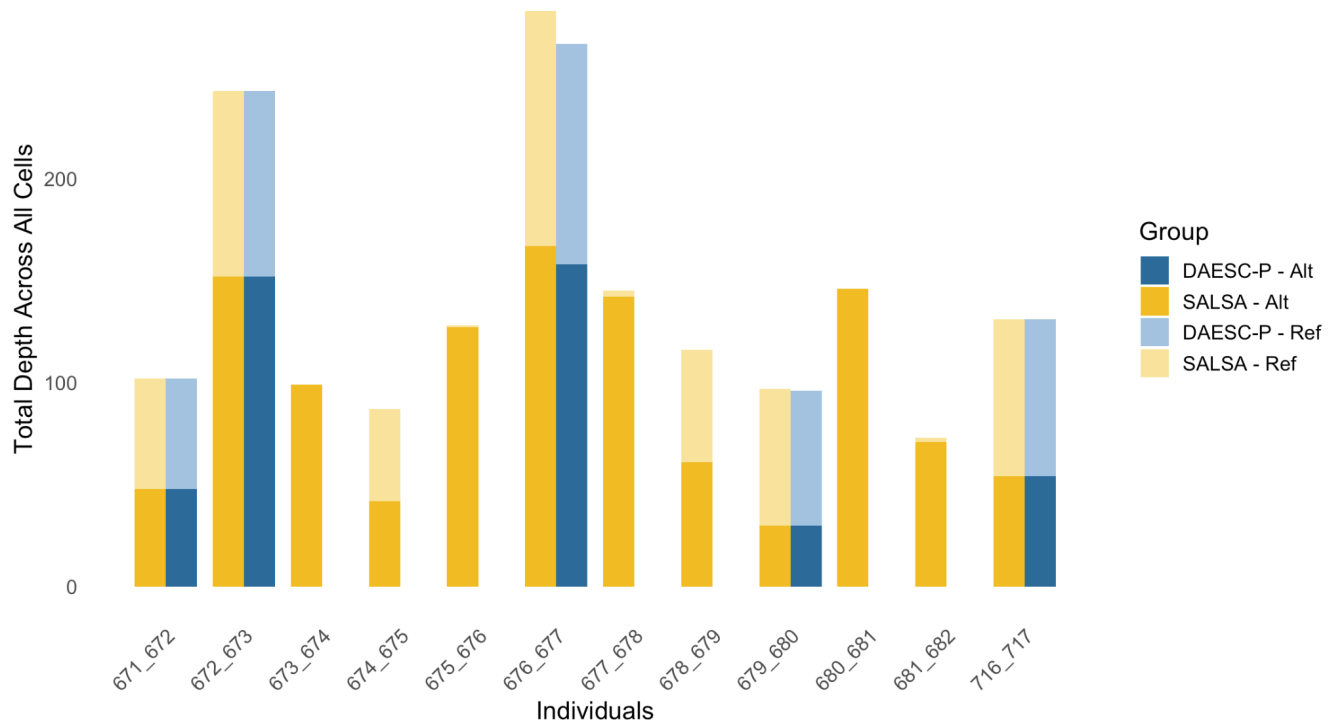
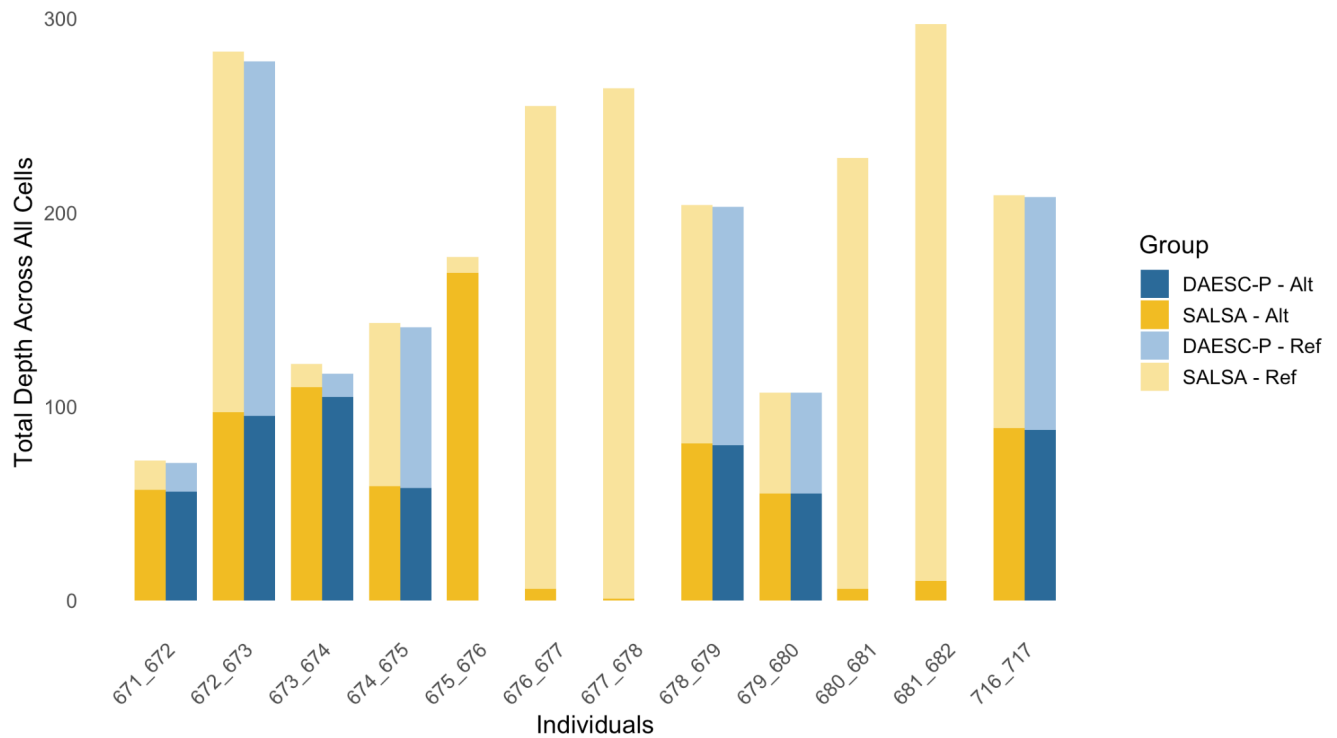


Supplementary Information

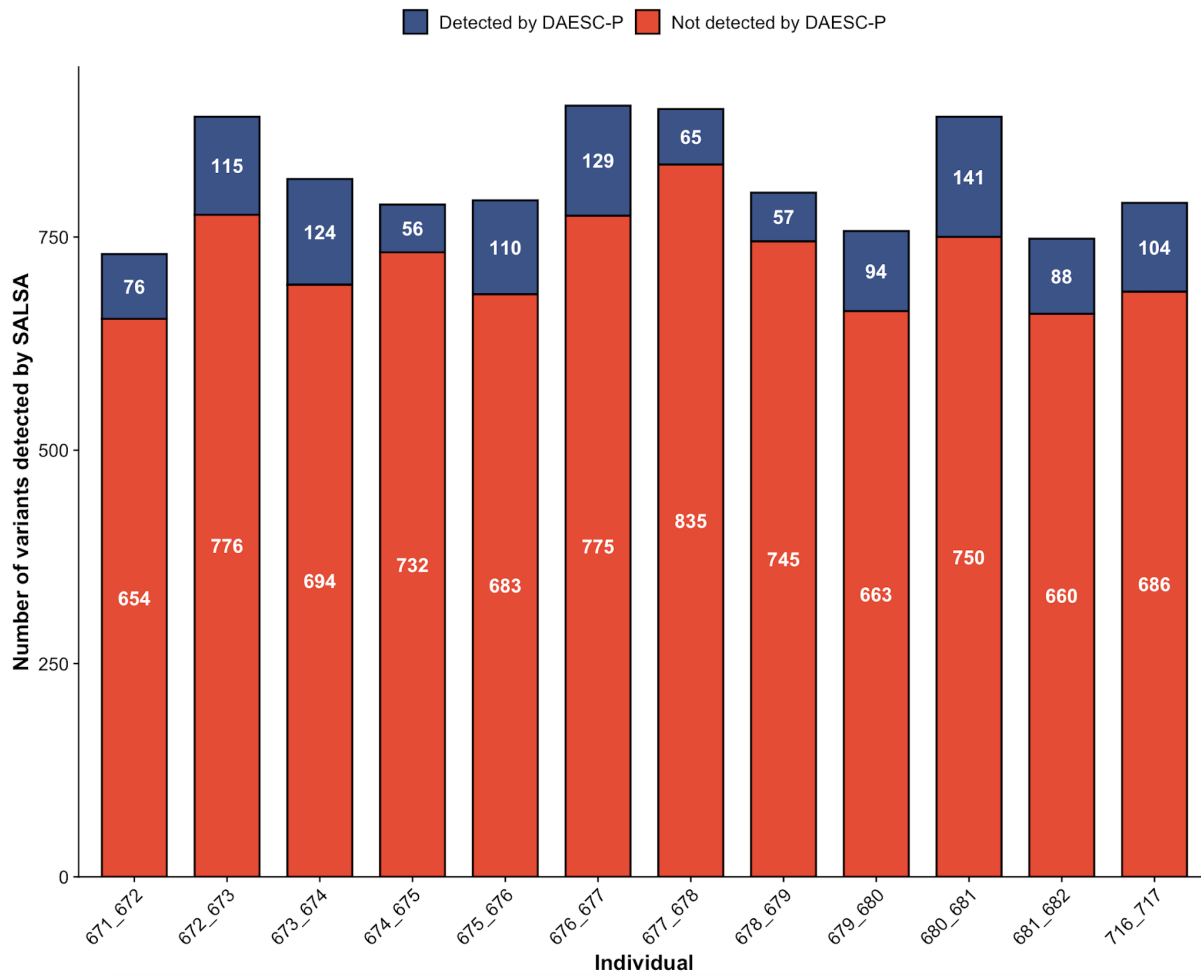
Compare SALSA and DAESC-P on the variant chr3_196654965_A_G



Compare SALSA and DAESC-P on the variant chr3_30631239_G_A

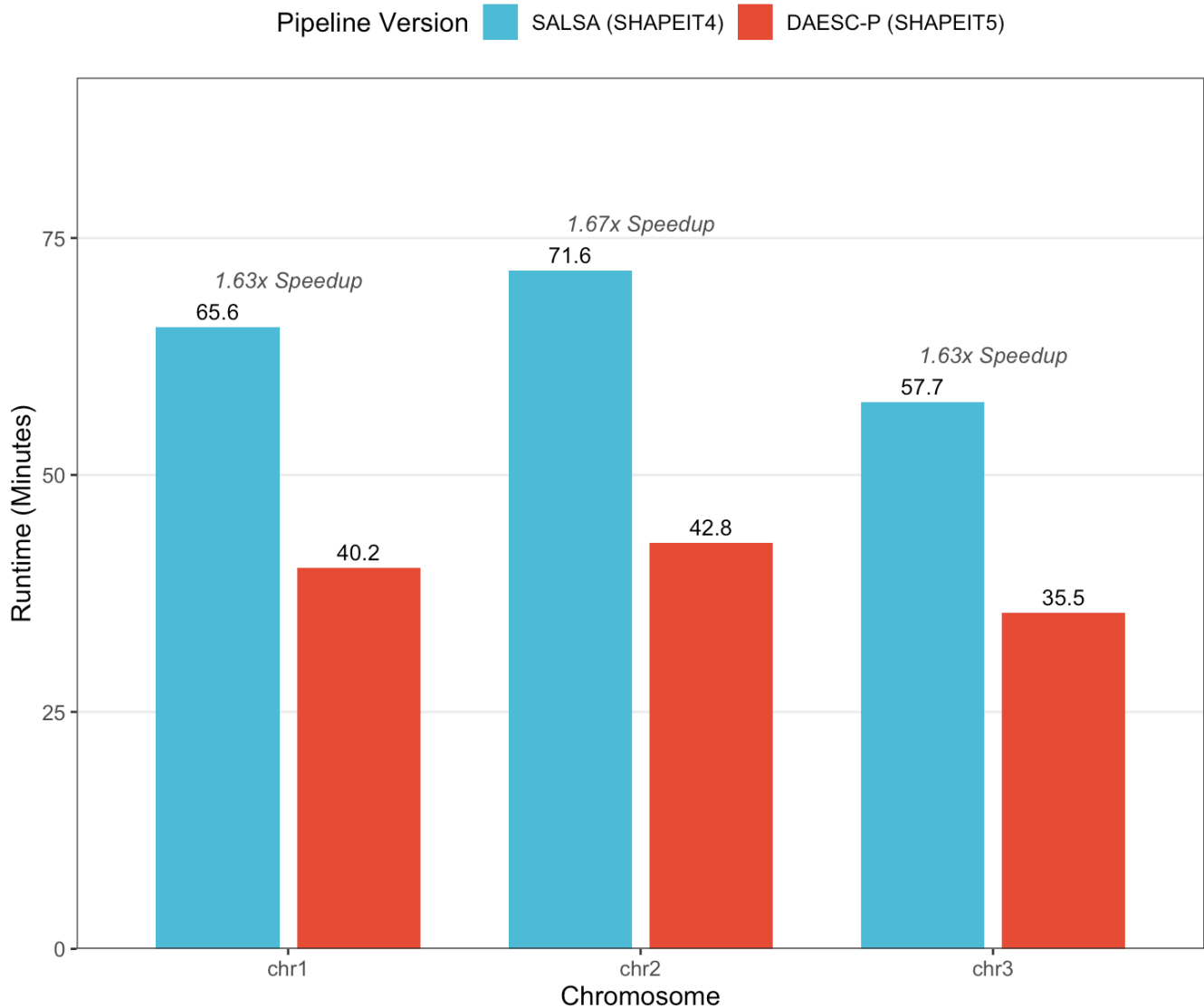


Supplementary Figure 1. Comparison the scASE counts from SALSA and DAESC-P on two variants. X-axis indicates the individuals, Y-axis indicates the sum of counts across all cells for specific individuals and variants

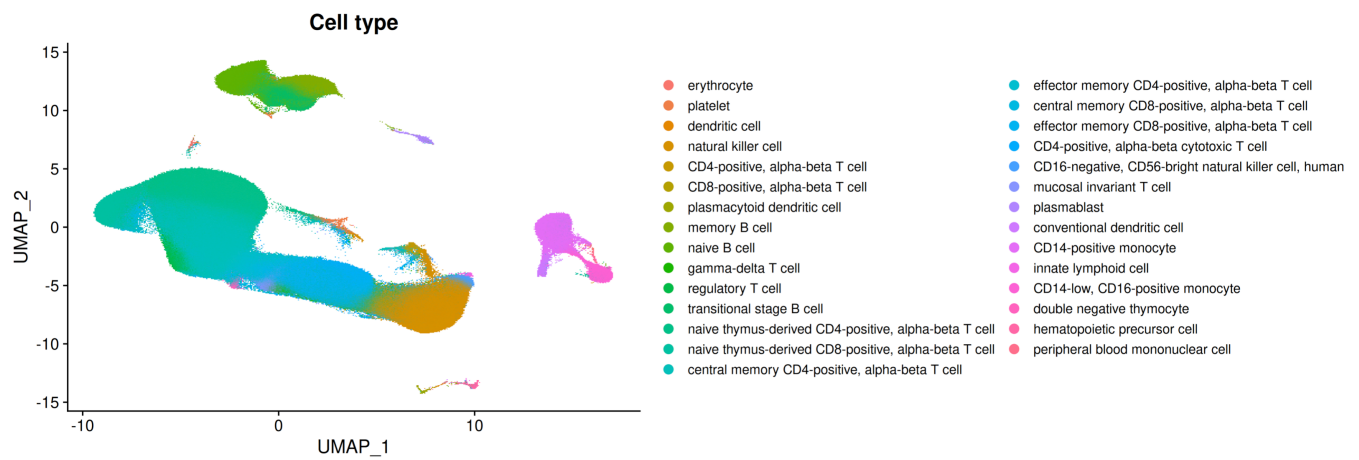


Supplementary Figure 2. Comparison of the number of variants detected by SALSA and DAESC-P. X-axis indicates the individuals, Y-axis indicates the number of variants detected by SALSA and DAESC-P.

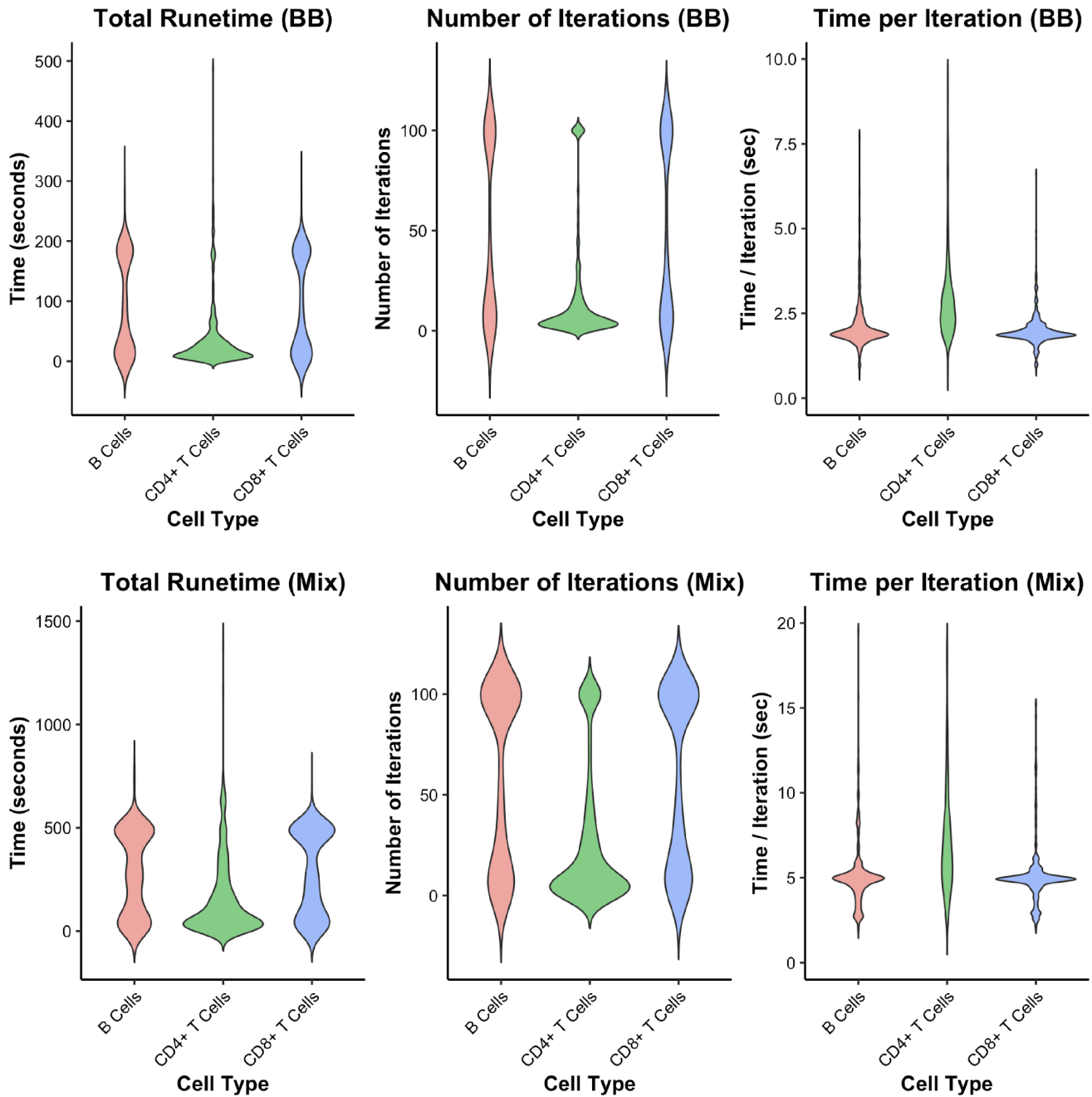
Bioinformatics Pipeline Performance Optimization



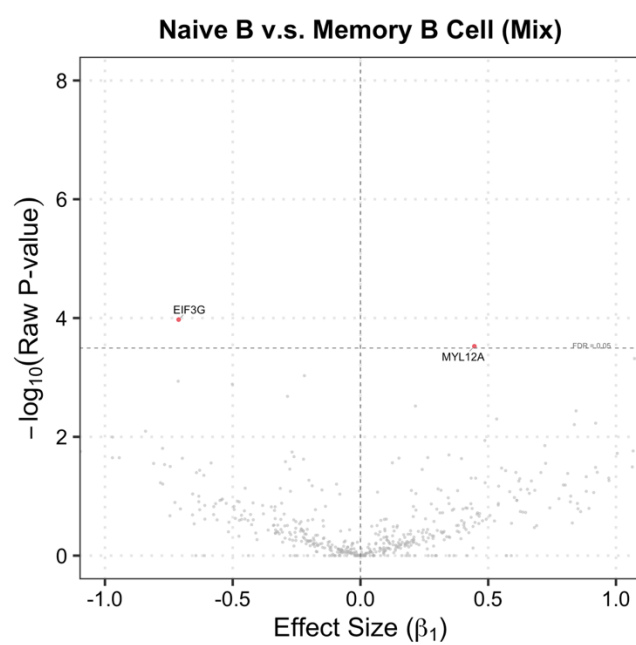
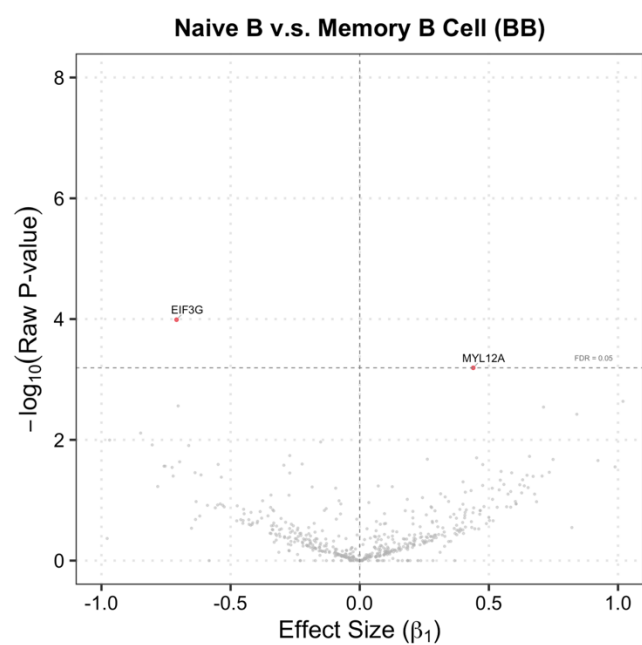
Supplementary Figure 3. Computational performance of DAESC-P and SALSA. We use both pipelines to process chromosomes 1–3 of a representative individual (ID: 847848) from the OneK1K cohort (Pool 11). The optimization of DAESC-P significantly reduces the computational burden required for full-scale analysis across all 22 autosomes. All benchmarking tests were conducted on an Intel Xeon Gold 6248R processor (3.0 GHz) using 8 parallel threads.



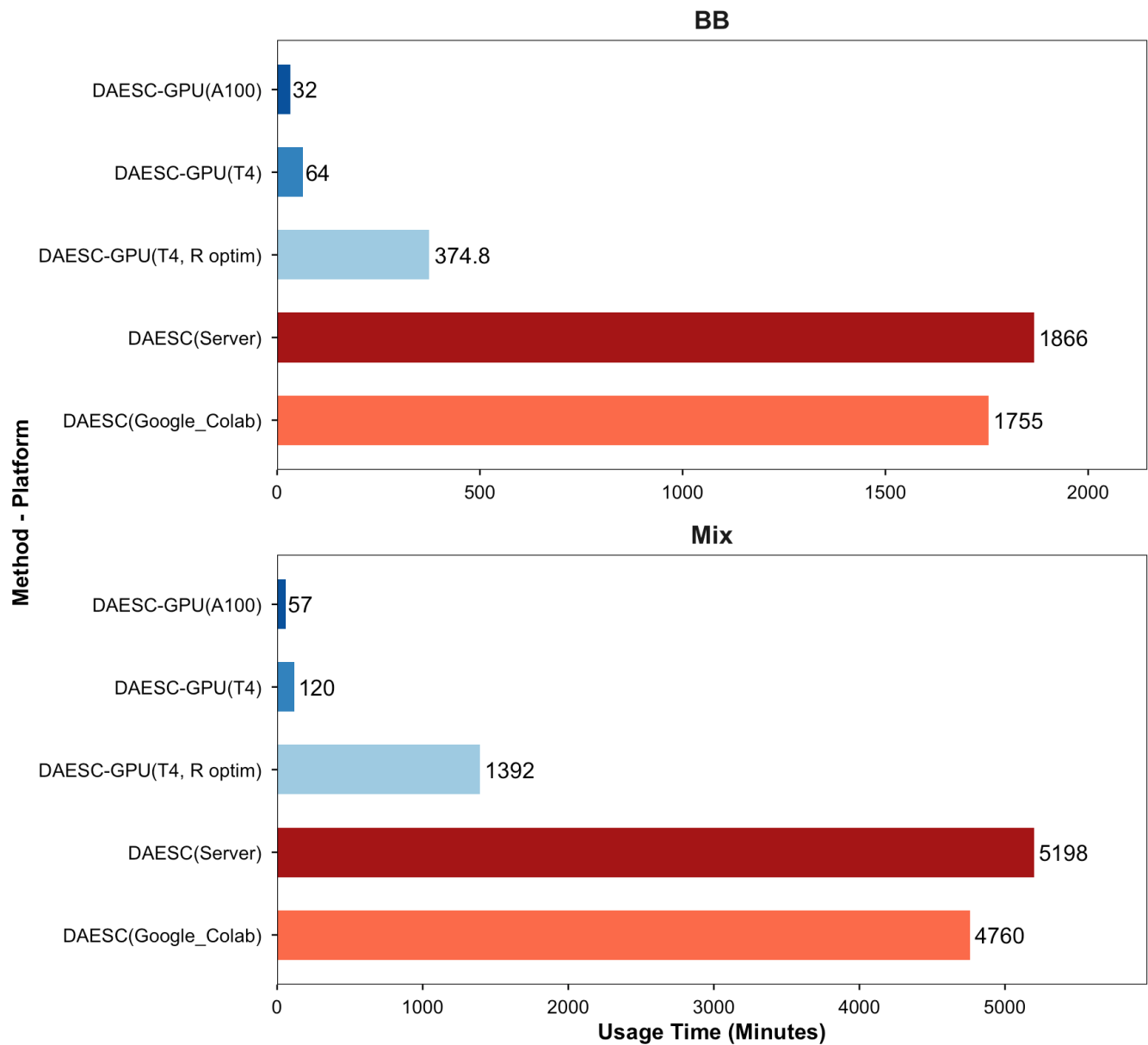
Supplementary Figure 4. UMAP of OneK1K Data. We used DAESC-P to process the first ten pools of the OneK1K cohort (118 individuals).



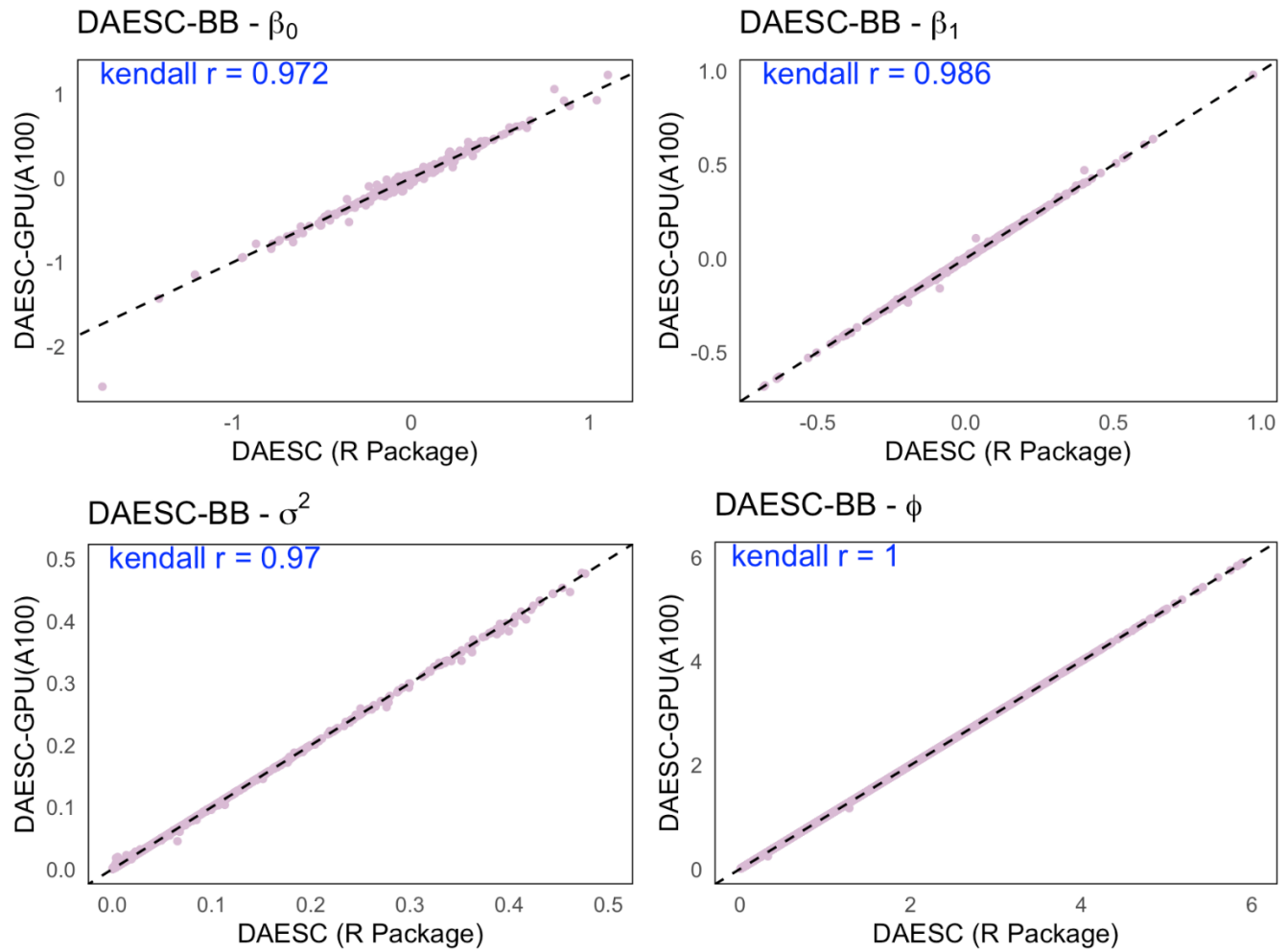
Supplementary Figure 5. Total runtime, number of iterations and time per iteration for DAESC applied to OneK1K. The DAESC R package was run on UW Server. (a) DAESC-BB (b) DAESC-Mix.



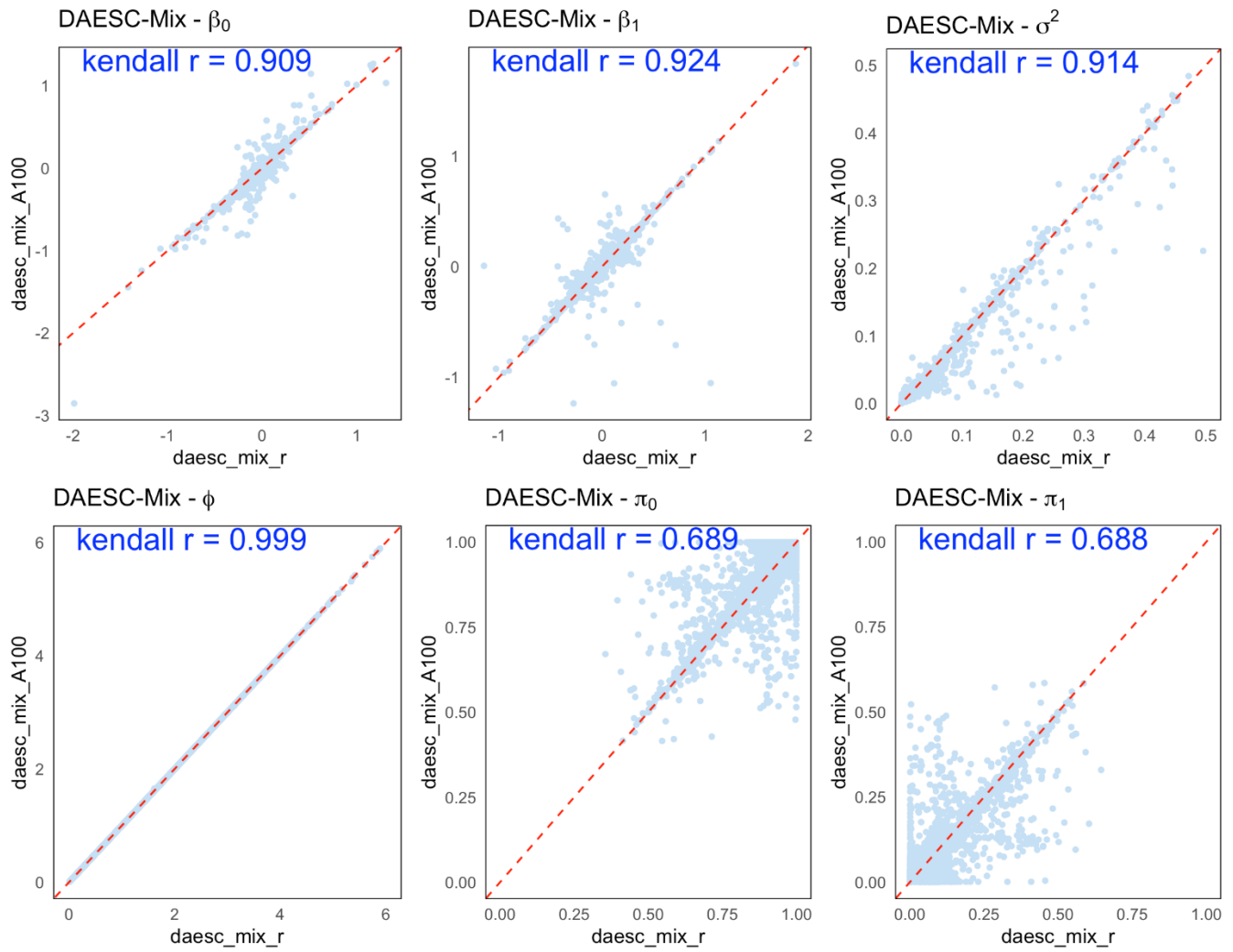
Supplementary Figure 6. Volcano plot of differential ASE analysis for B cells.



Supplementary Figure 7. Runtime of DAESC-GPU, simplified version DAESC-GPU (DAESC-GPU (T4, R optim)), and DAESC R package. DAESC-GPU (T4, R optim) utilizes R built-in optimizer (BFGS) during the M-step.



Supplementary Figure 8. Consistency of parameter estimates between DAESC and DAESC-GPU for the BB model. See Methods for the definition of the parameters. Kendall's τ is marked in each panel to quantify the consistency. Red dashed line is $y = x$.



Supplementary Figure 9. Consistency of parameter estimates between DAESC and DAESC-GPU for the Mix model. See Methods for the definition of the parameters. Kendall's τ is marked in each panel to quantify the consistency. Red dashed line is $y = x$.

Supplementary Table 1. Significant differential ASE genes (FDR<0.05) in the OneK1K analysis.

Variant ID	P-value	FDR adjusted p-value	Gene name	Validated among eGenes	Cell type and statistical model
chr18_3256114_A_G	6.42E-04	4.86E-02	MYL12A	FALSE	B cell - BB Model
chr19_10115580_A_G	1.02E-04	9.05E-03	EIF3G	TRUE	B cell - BB Model
chr18_3256114_A_G	2.99E-04	4.24E-02	MYL12A	FALSE	B cell - Mix Model
chr19_10115580_A_G	1.06E-04	2.81E-02	EIF3G	TRUE	B cell - Mix Model
chr10_69104641_G_T	2.09E-05	1.43E-03	SRGN	TRUE	CD4 - BB Model
chr12_124911942_T_C	7.55E-29	8.27E-27	UBC	FALSE	CD4 - BB Model
chr14_22575102_T_G	7.02E-06	6.41E-04	DAD1	TRUE	CD4 - BB Model
chr15_82538982_A_G	9.59E-04	4.78E-02	ENSG00000284803	FALSE	CD4 - BB Model
chr17_82314997_C_T	1.36E-04	7.43E-03	CD7	TRUE	CD4 - BB Model
chr1_26320235_A_G	1.27E-04	7.43E-03	CD52	TRUE	CD4 - BB Model
chr10_69104641_G_T	3.77E-06	3.44E-04	SRGN	TRUE	CD4 - Mix Model
chr11_62852157_G_A	6.55E-04	2.39E-02	SNHG1	FALSE	CD4 - Mix Model
chr11_840363_C_T	5.21E-04	2.20E-02	POLR2L	TRUE	CD4 - Mix Model
chr14_22575102_T_G	2.14E-06	2.93E-04	DAD1	TRUE	CD4 - Mix Model
chr14_49618853_G_A	1.21E-03	3.67E-02	RPL36AL	TRUE	CD4 - Mix Model
chr15_69452821_C_T	1.28E-03	3.68E-02	RPLP1	FALSE	CD4 - Mix Model
chr15_82538982_A_G	4.63E-04	2.11E-02	ENSG00000284803	FALSE	CD4 - Mix Model
chr17_82314997_C_T	2.21E-04	1.34E-02	CD7	TRUE	CD4 - Mix Model
chr1_26320235_A_G	3.15E-04	1.72E-02	CD52	TRUE	CD4 - Mix Model
chr1_39034514_G_A	6.12E-04	2.39E-02	NDUFS5	TRUE	CD4 - Mix Model
chr1_86862842_C_T	1.86E-06	2.93E-04	SELENOF	FALSE	CD4 - Mix Model
chr20_3805990_G_C	9.68E-04	3.32E-02	CDC25B	TRUE	CD4 - Mix Model
chr20_63738996_T_C	7.48E-06	5.85E-04	ENSG00000273154	TRUE	CD4 - Mix Model
chr4_6642546_C_G	1.43E-03	3.71E-02	MRFAP1	FALSE	CD4 - Mix Model
chr5_35871088_G_A	1.14E-03	3.67E-02	IL7R	TRUE	CD4 - Mix Model