DVX - Differential Variation and eXpression analysis

This file was created on January 24, 2018 at 04:30:47.

Note: the report was generated automatically by DVX. Text in blue font and yellow marker highlights were added manually to the report, and some plots were resized.

ExpressionSet metadata

|	
name	N/A
lab	N/A
contact	N/A
title	Age effect on normal adult brain: frontal cortical region
url	N/A
pubMedIds	24670762
samples	41
features	54675
abstract	Analysis of postmortem neuropathologically normal brain samples from the frontal cortical regions of young, middle aged, normal aged and extremely aged adults. Results provide insight into molecular mechanisms of aging in frontal cortical regions of the brain.

Dataset Summary - Gene Expression Statistics

| min	Q1	Median	Q3	max	Mean	Missing
2.27	4.08	4.85	5.92	14.04	5.15	0

Phenotype data - Factors

Variable	Content (counts)
age	extremely aged (95-106yr) (4), middle aged (40-70yr) (9), normal aged (70-94yr) (16), young (<40yr) (12)
gender	female (21), male (20)

We are interested in testing for differences in gene expression between age groups. We will perform three comparisons – Young vs. Middle aged, Middle aged vs. Normal aged, and Normal aged vs. Extremely aged.

Plots
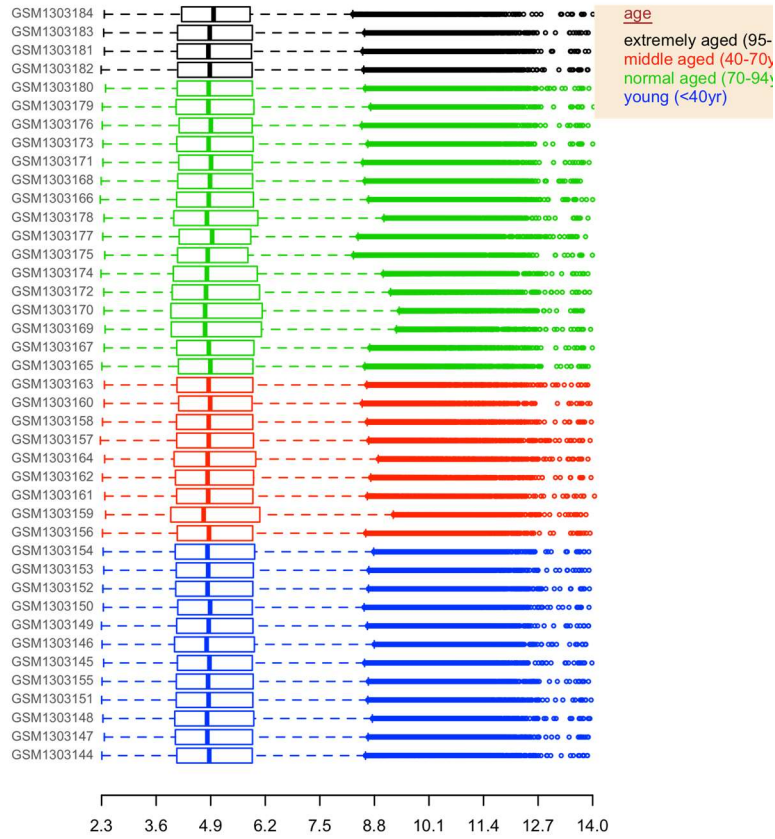
The boxplots seem a bit skewed. Also, the mean vs. log-variance plots on the next page suggest that there is a relationship between the means and the variances. A transformation may have to be considered.
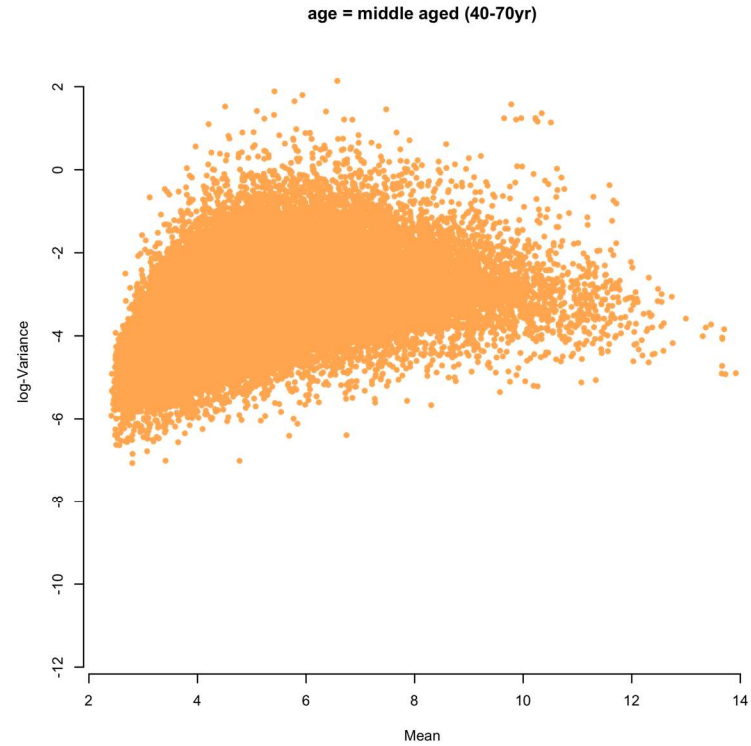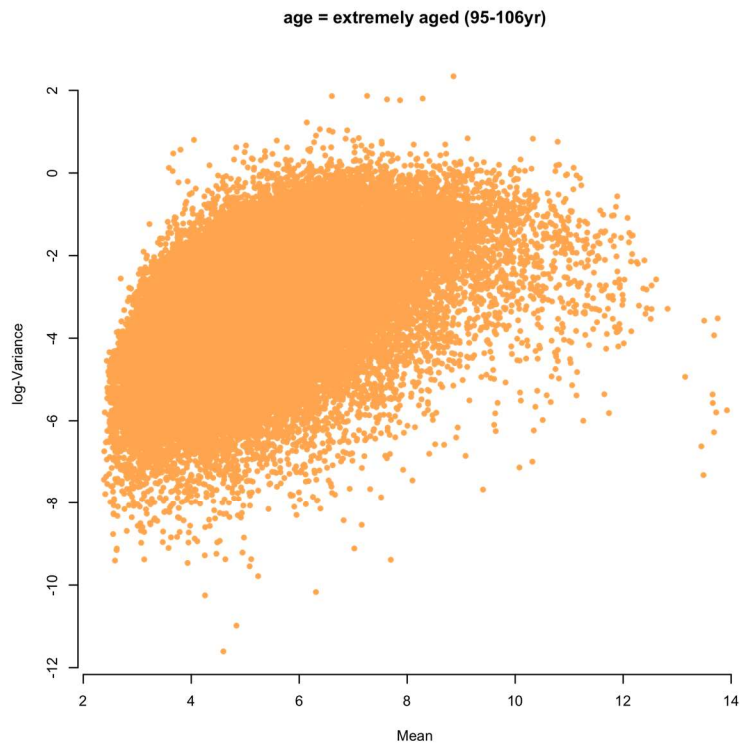
The data in the NCBI dataset was already log-transformed. Patterns such as these may also be due to a large number of low-abundance/low-variance genes. The next plots show that indeed, there is a large number of genes with low mean expression levels across all samples
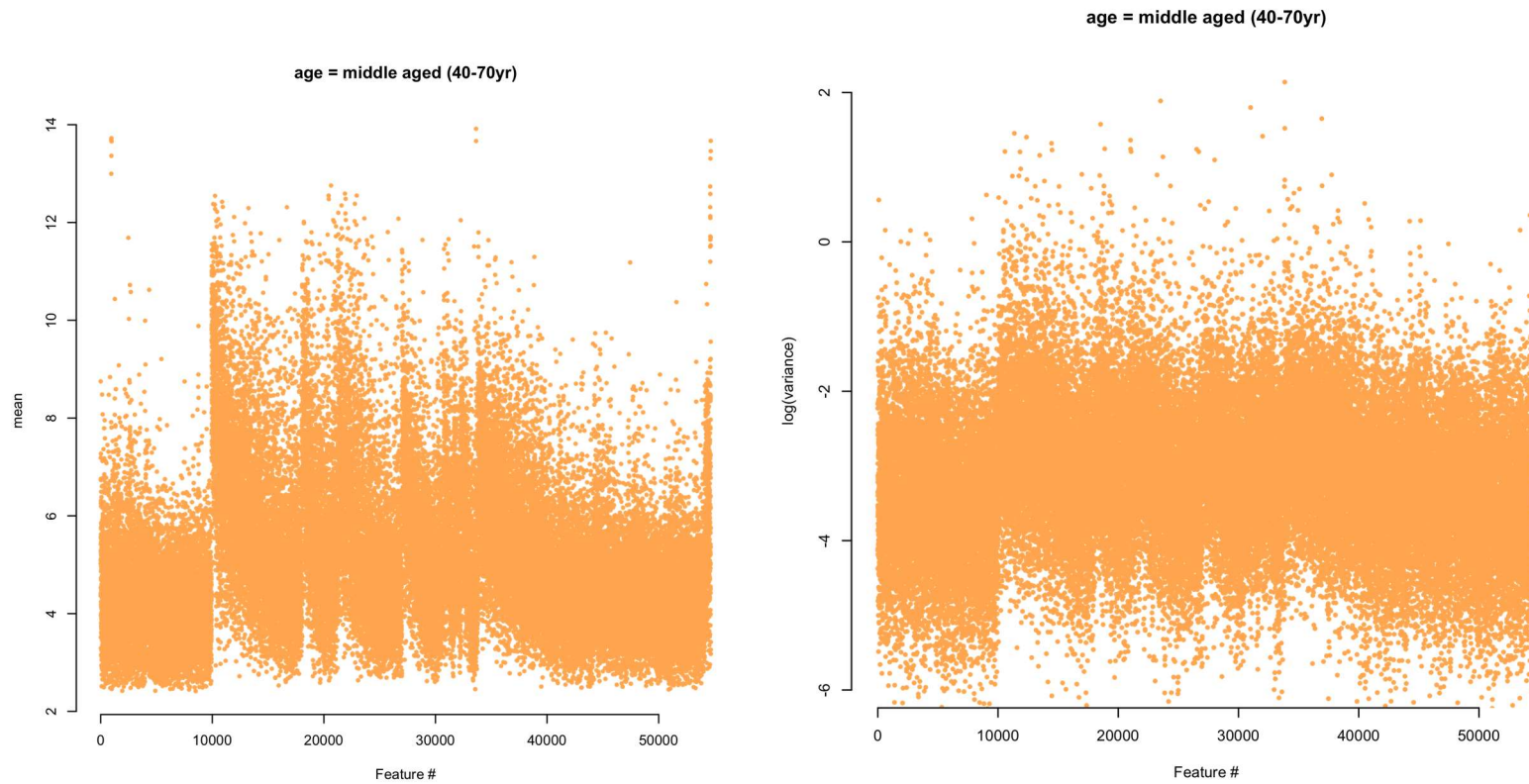
The plot on the left shows the mean expression levels for all features, in the middle-aged group. The plot on the right shows the logarithm of the variances for all features in the same age group. We will consider filtering out low-abundance genes.

The next analysis is preformed after we remove genes with median expression levels less than or equal to 5.5, across all samples. We also equalize the medians across all samples, to mitigate any subject-specific effects.

DVX - Differential Variation and eXpression analysis
This file was created on January 26, 2018 at 11:44:41.

ExpressionSet metadata

name	N/A
lab	N/A
contact	N/A
title	Age effect on normal adult brain: frontal cortical region
url	N/A
pubMedIds	24670762
samples	41
features	17833
abstract	Analysis of postmortem neuropathologically normal brain samples from the frontal cortical regions of young, middle aged, normal aged and extremely aged adults. Results provide insight into molecular mechanisms of aging in frontal cortical regions of the brain.

Dataset Summary - Gene Expression Statistics

min	Q1	Median	Q3	max	Mean	Missing
2.23	5.90	6.52	7.46	14.25	6.83	0

Phenotype data - Factors

Variable	Content (counts)
age	extremely aged (95-106yr) (4), middle aged (40-70yr) (9), normal aged (70-94yr) (16), young (<40yr) (12)
gender	female (21), male (20)

Plots
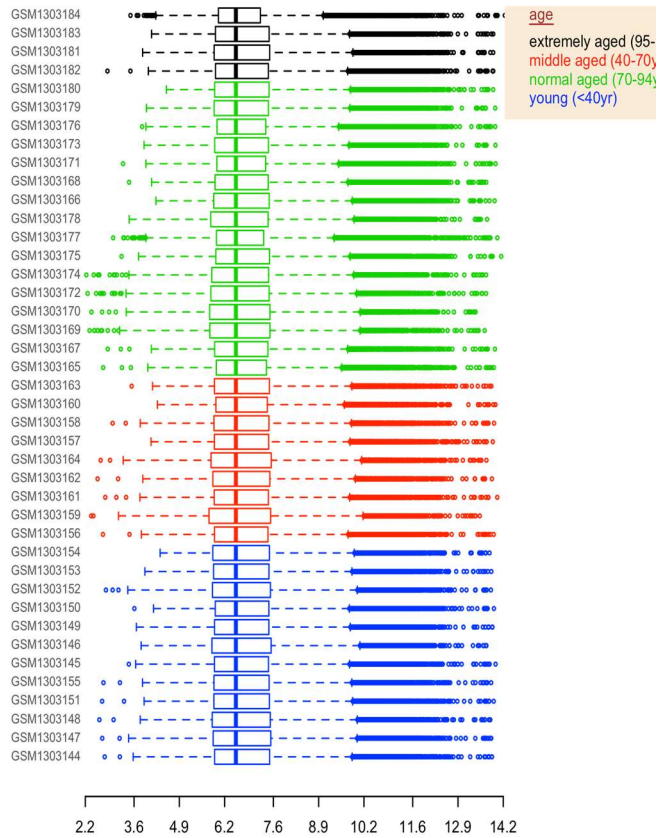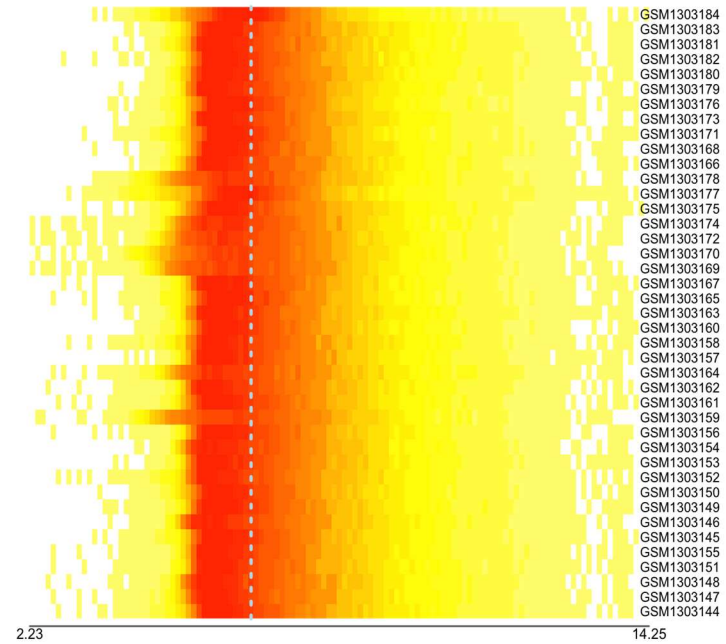
The boxplots and the flat-histogram plot show the distribution of the remaining 17,833 genes, after we filtered out genes with median expression ≤ 5.5. All the medians have been centered.
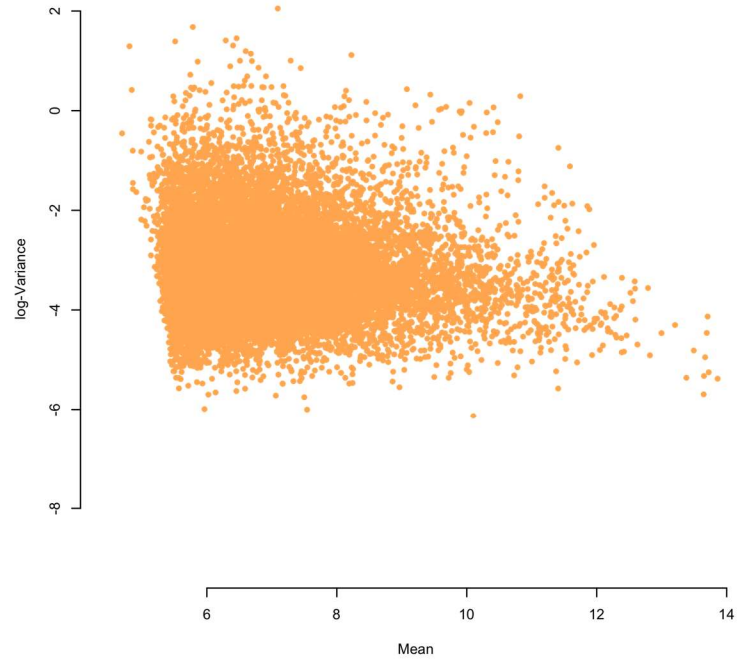
The following plots depict the log-variance vs. the mean expression of each gene, for each age group separately. Overall, there is no obvious pattern (recall that before the filtering, the variance seemed to be increasing with the mean, for small means)
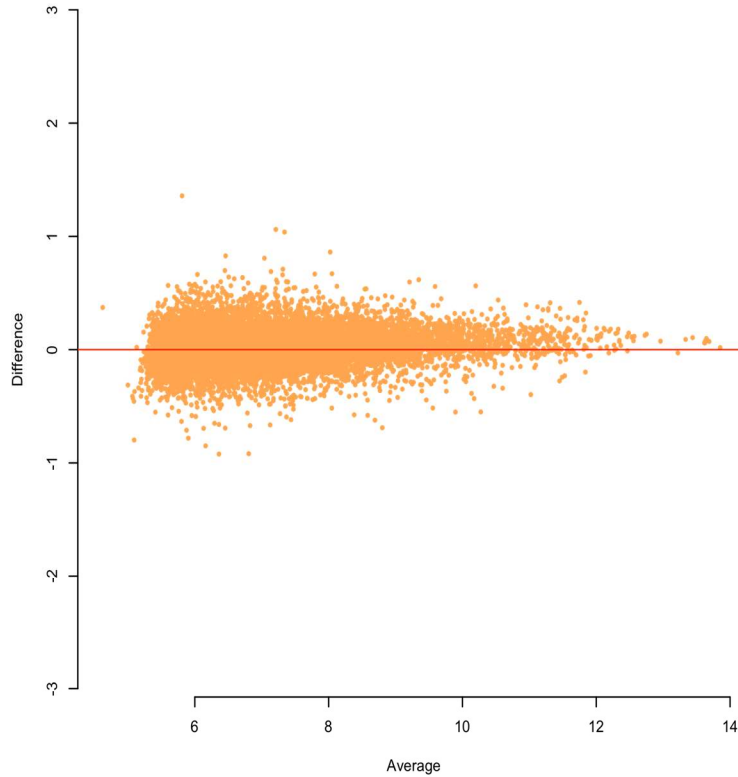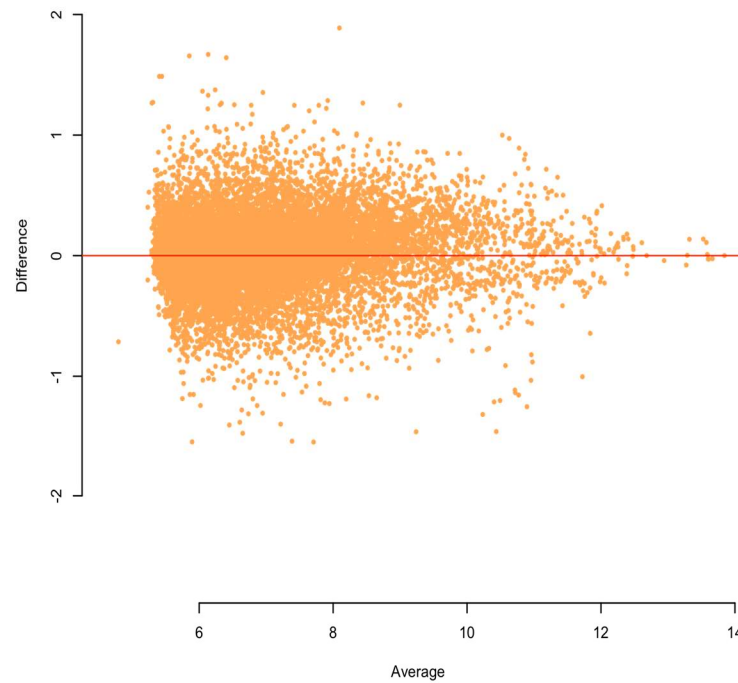
age = extremely aged (95-106yr)

age = middle aged (40-70yr)
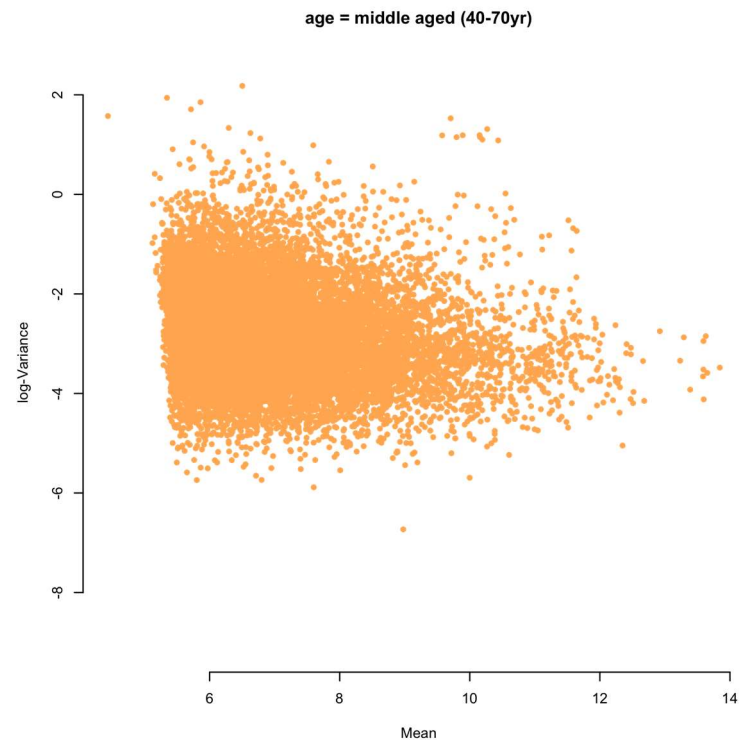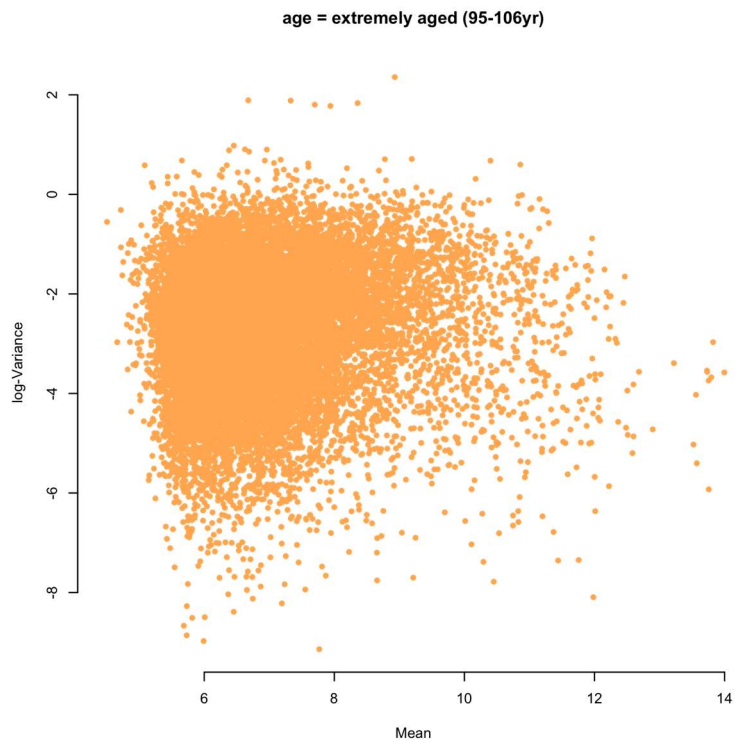
age = normal aged (70-94yr)
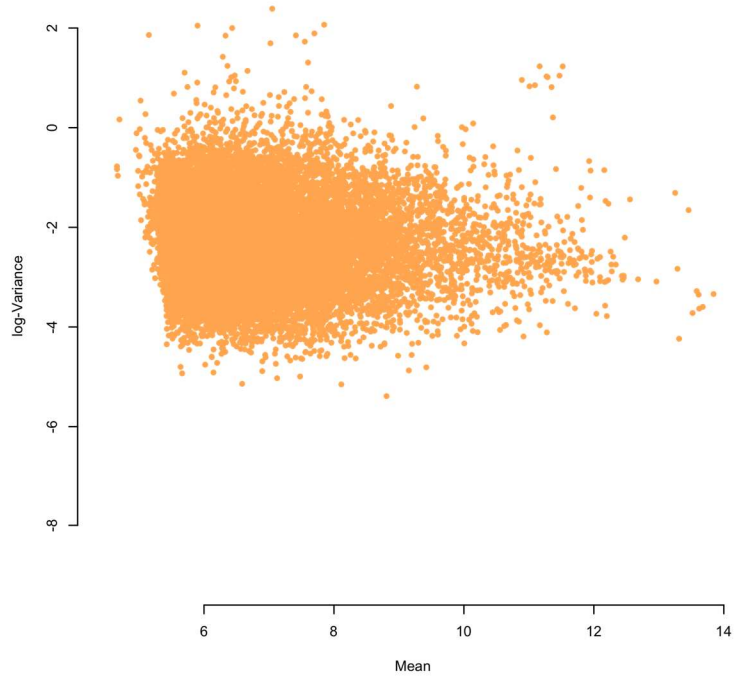
age = young (<40yr)

The following are Bland-Altman plots for all three comparison. Let m1 be the mean expression level in the treatment group, and let m0 be the mean expression level in the baseline group. The plot shows m1-m0 vs. (m1+m0)/2. Histograms corresponding to these plots will be depicted below, in the analysis section. These plots show that, overall, the mean difference between each two groups is approximately 0, and the differences, m1-m0, do no exhibit any pattern.

age: young (<40yr) vs. middle aged (40-70yr

age: middle aged (40-70yr vs. normal aged (70-94yr

age: normal aged (70-94yr vs. extremely aged (95-1
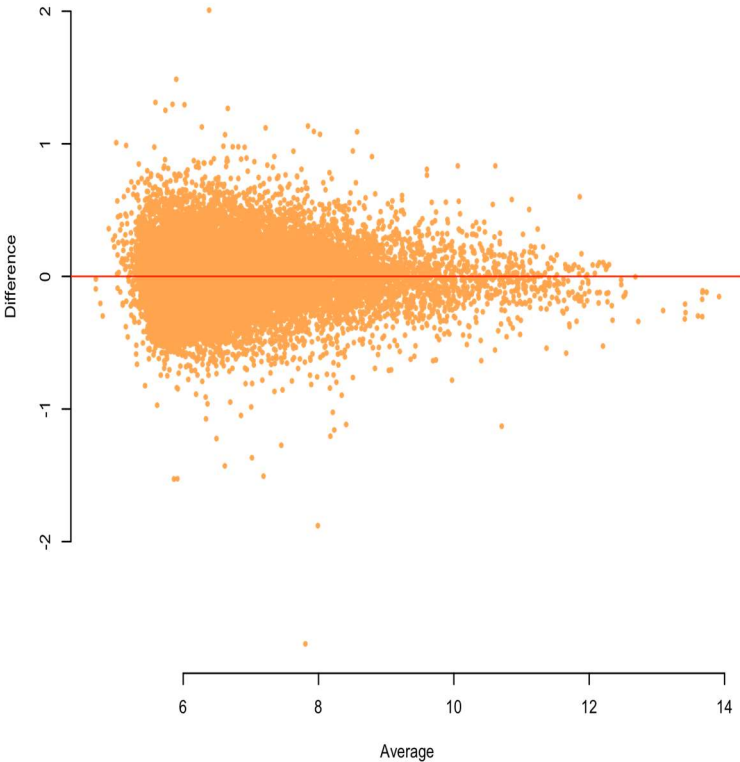
The following plots show the second principal component versus the first. The points are labeled by the age group (left) and the gender (right). There is some overall difference between male and female (the males tend to be positioned lower along the PC2 axis) so we may want to account for this difference by including gender as a predictor in the fitted models.
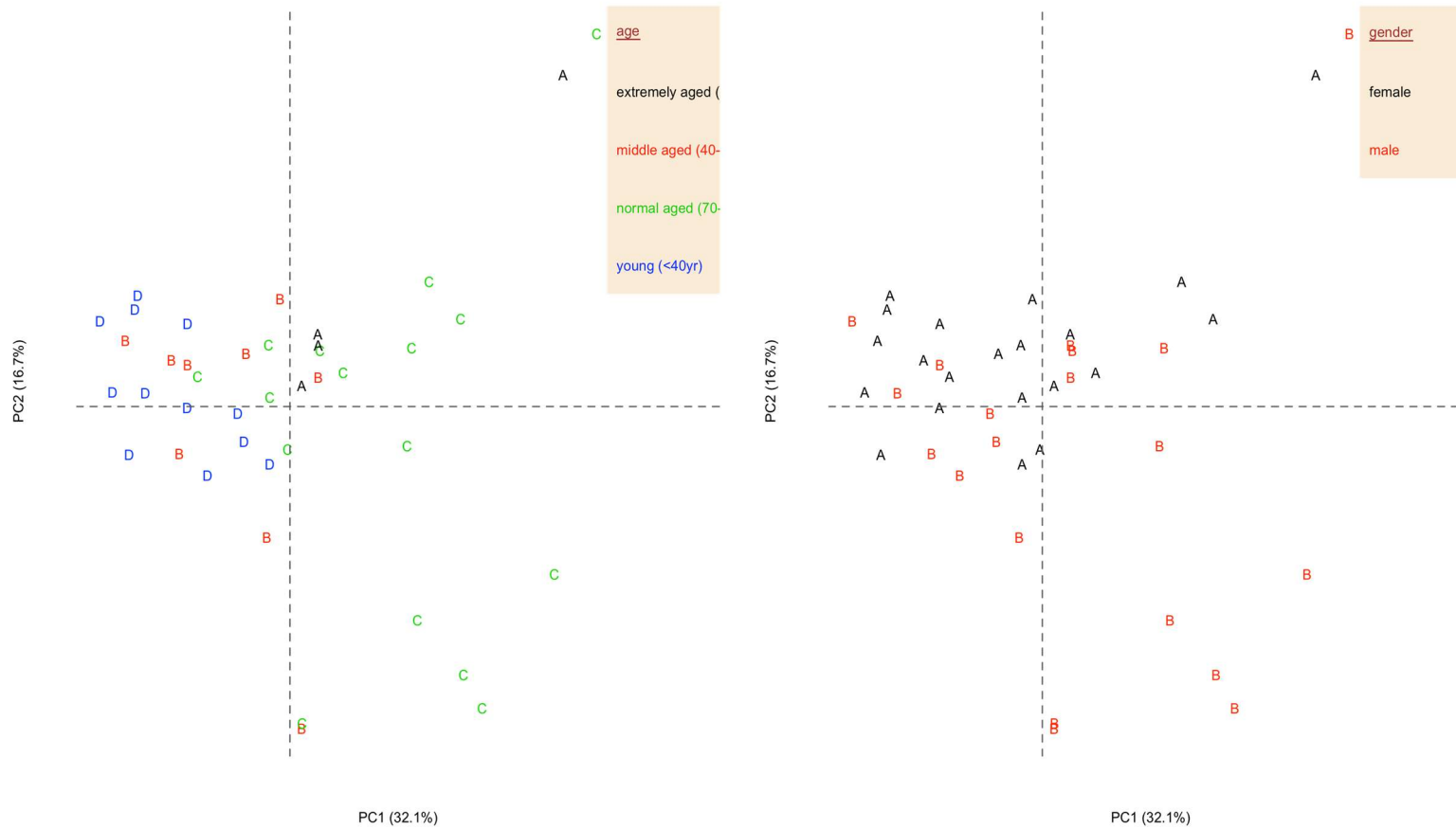

The following pages contain diagnostics plots for each of the three comparisons, using all three models. In all cases, the L2N model gives the best fit in terms of providing the lowest rMSE.
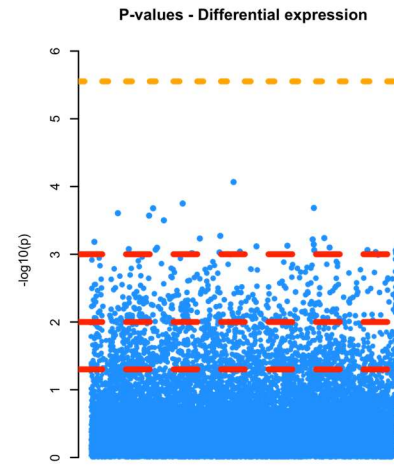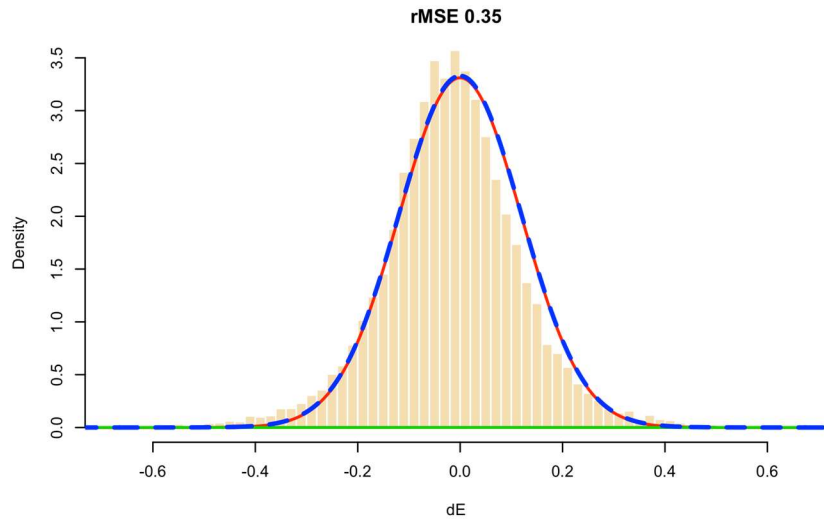
Differential factor: age, **Baseline level:** young (<40yr)   **Treatment level:** middle aged (40-70yr), **Model:** L2N, **Predictors:** gender
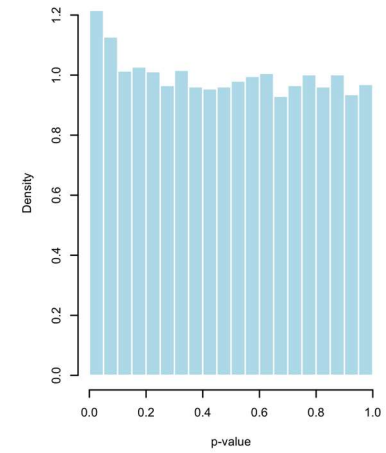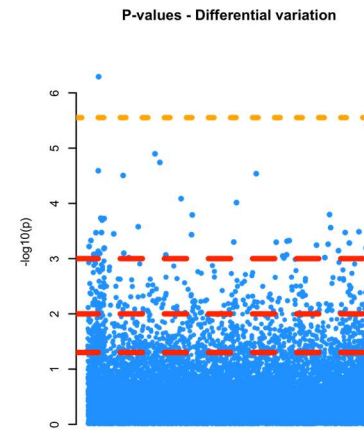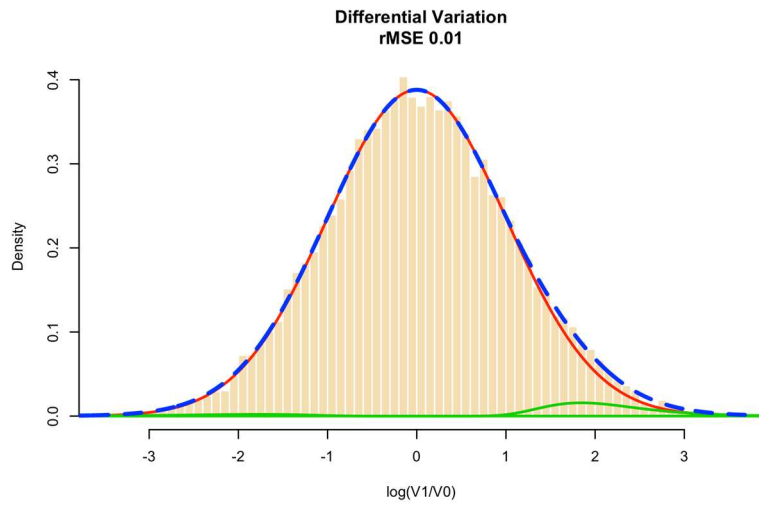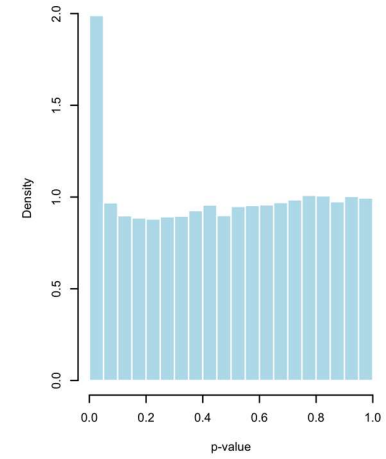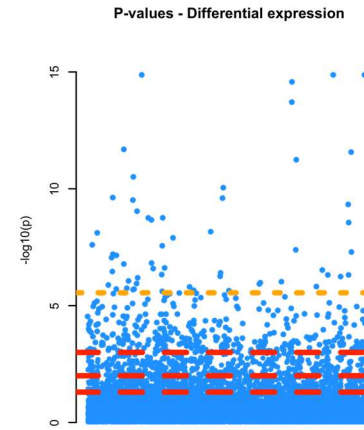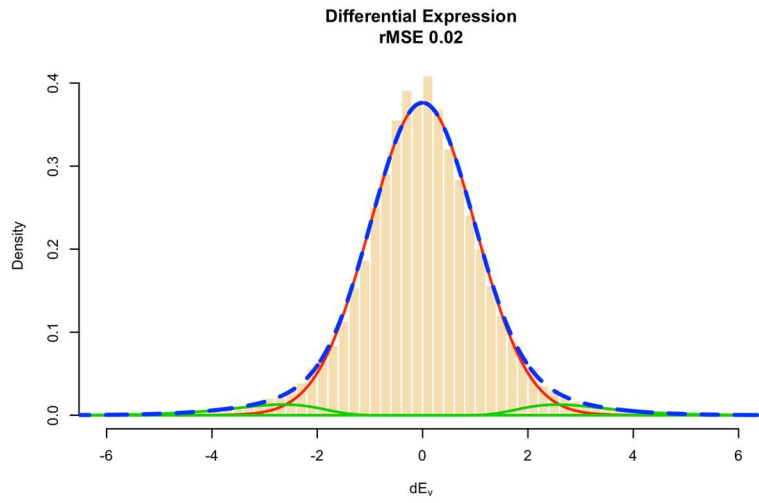

Differential Expression
rMSE 0.02

P-values - Differential expression

Differential Variation
rMSE 0.01

P-values - Differential variation

Differential factor: age, **Baseline level:** young (<40yr), **Treatment level:** middle aged (40-70yr), **Model:** N3, **Predictors:** gender
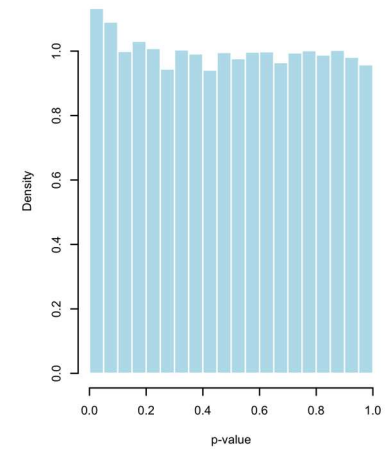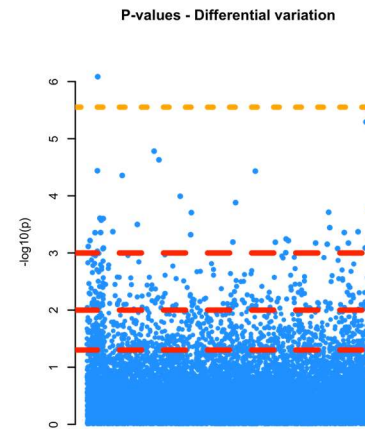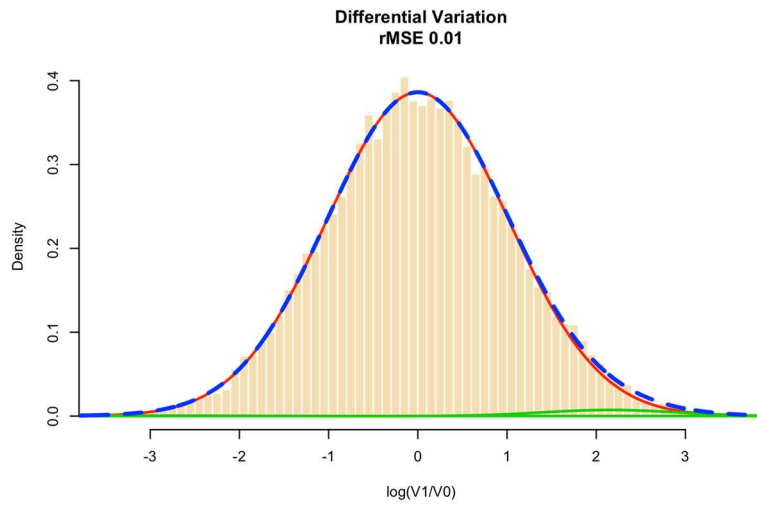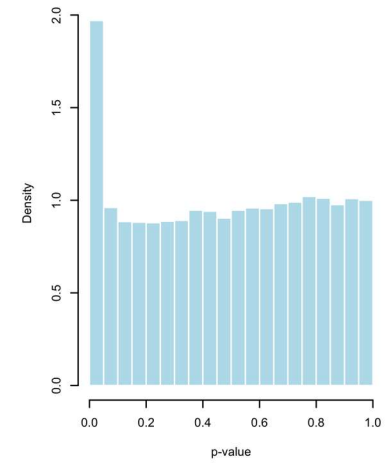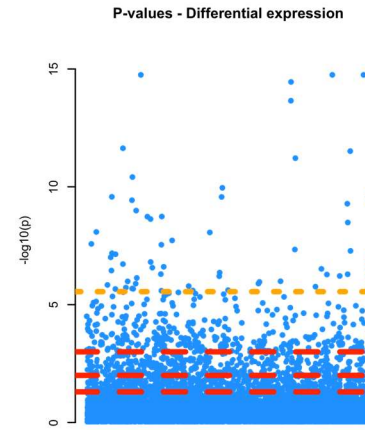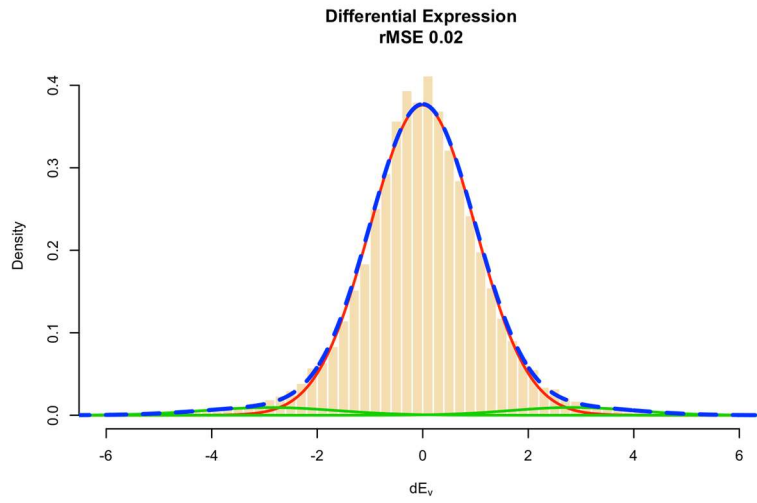
Differential factor: age, **Baseline level:** young (<40yr), **Treatment level:** middle aged (40-70yr), **Model:** limma, **Predictors:** gender
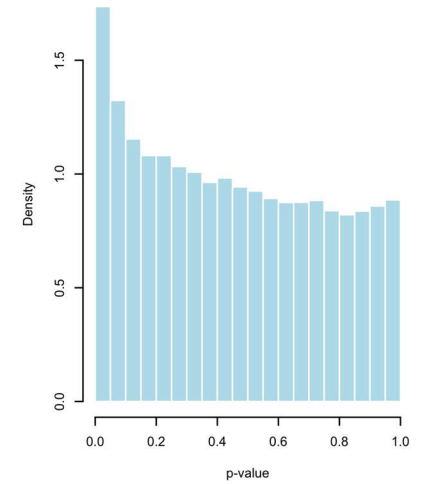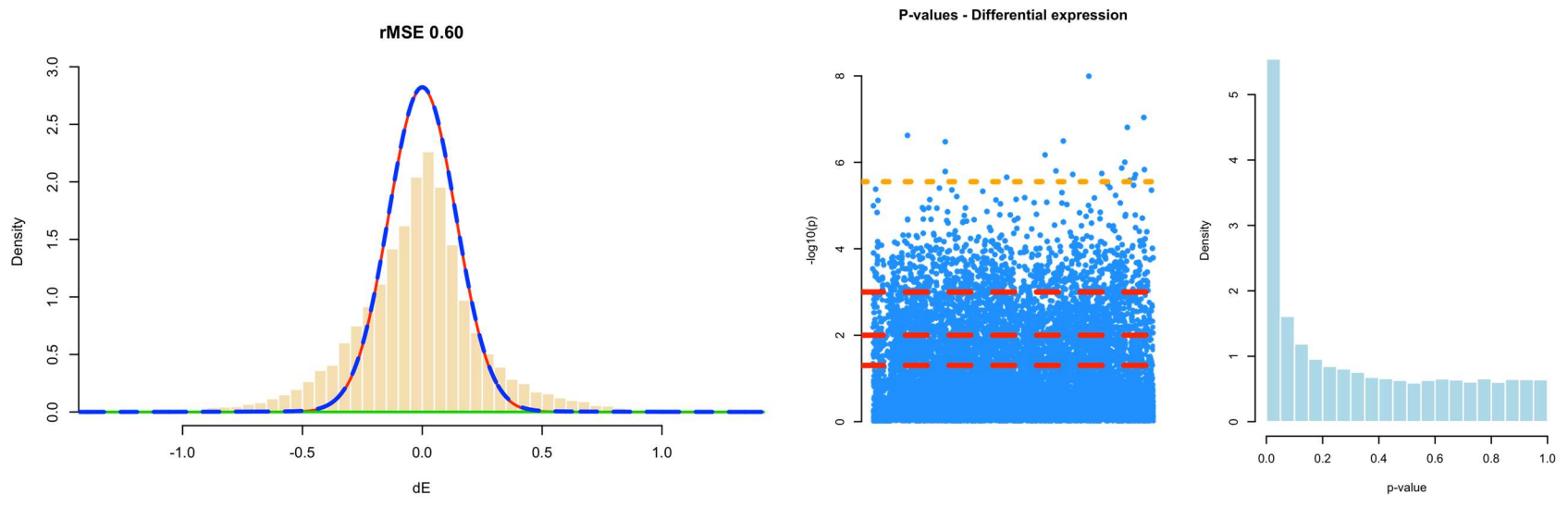
Differential factor: age, **Baseline level:** middle aged (40-70yr), **Treatment level:** normal aged (70-94yr), **Model:** L2N, **Predictors:** gender
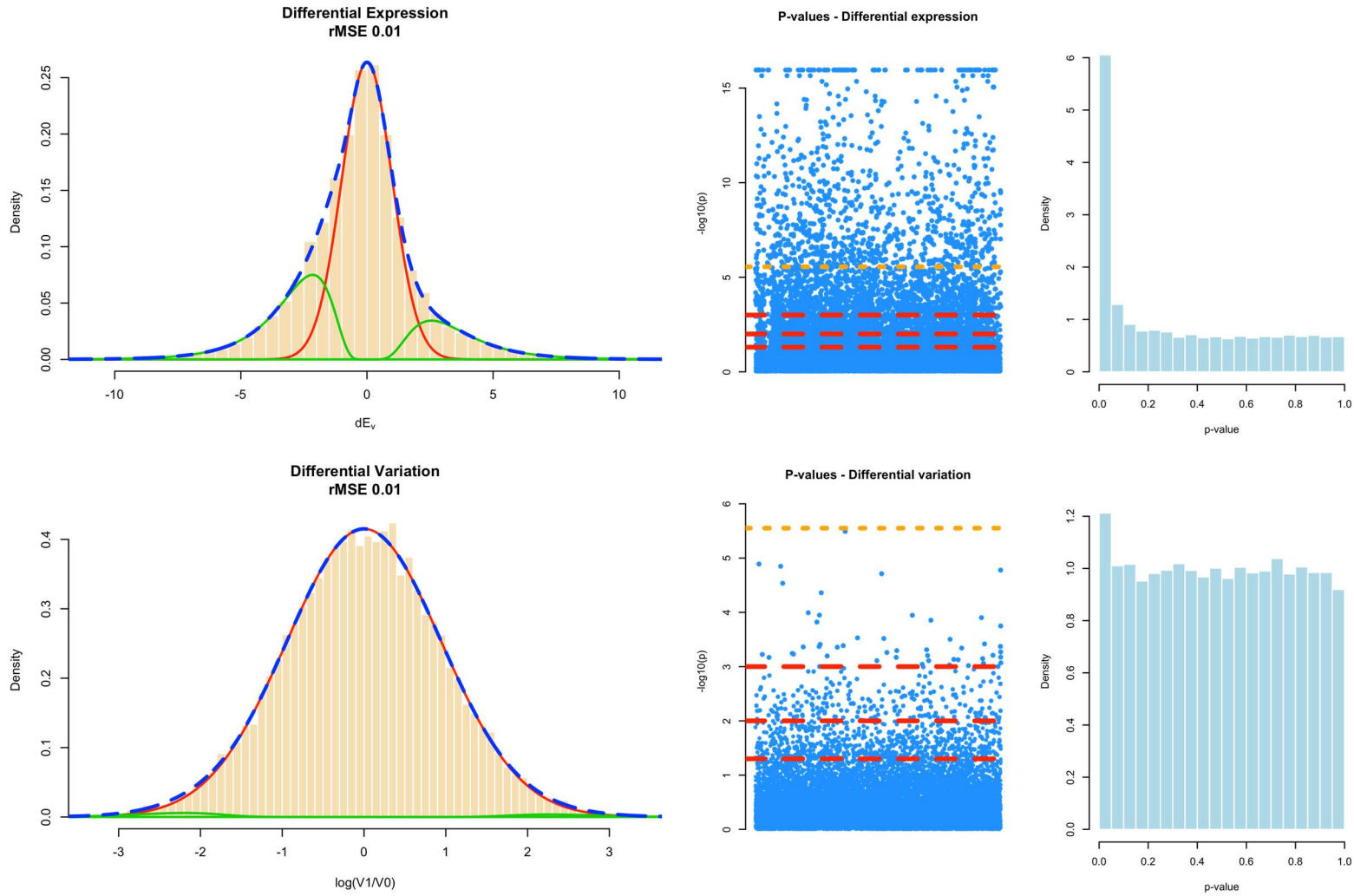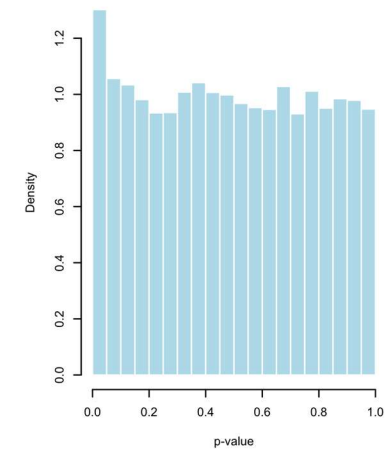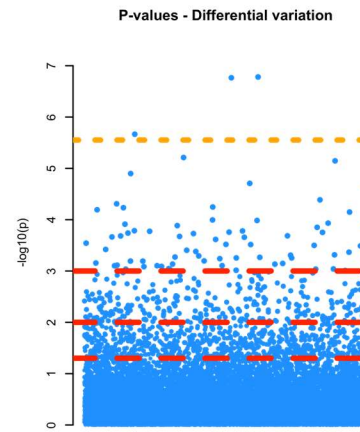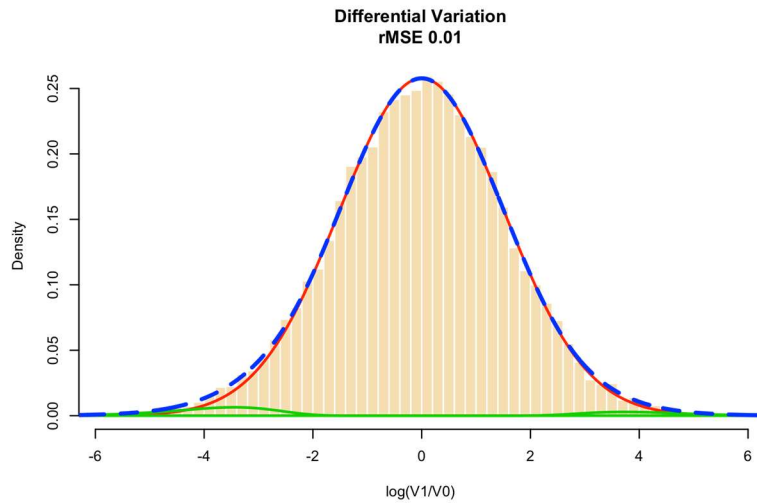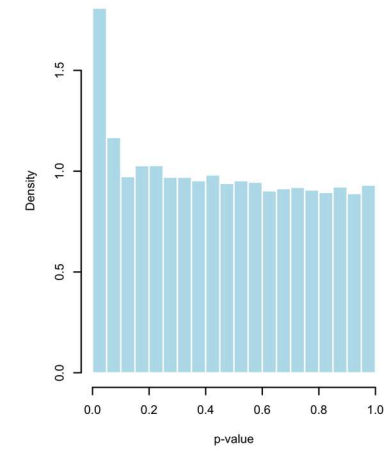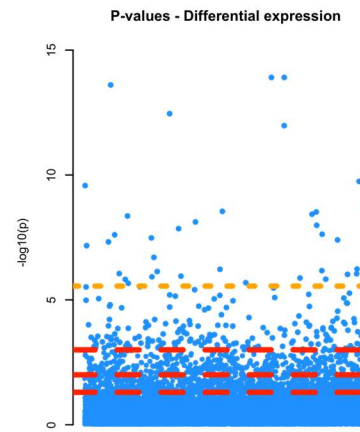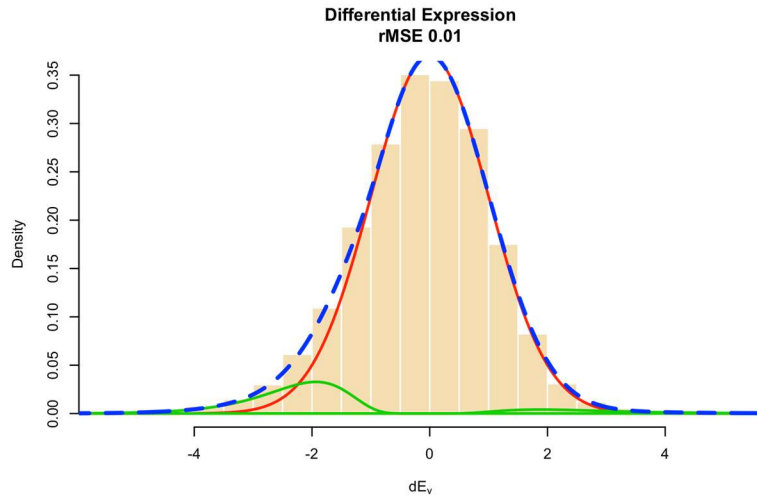
Differential factor: age, **Baseline level:** middle aged (40-70yr), **Treatment level:** normal aged (70-94yr), **Model:** N3, **Predictors:** gender
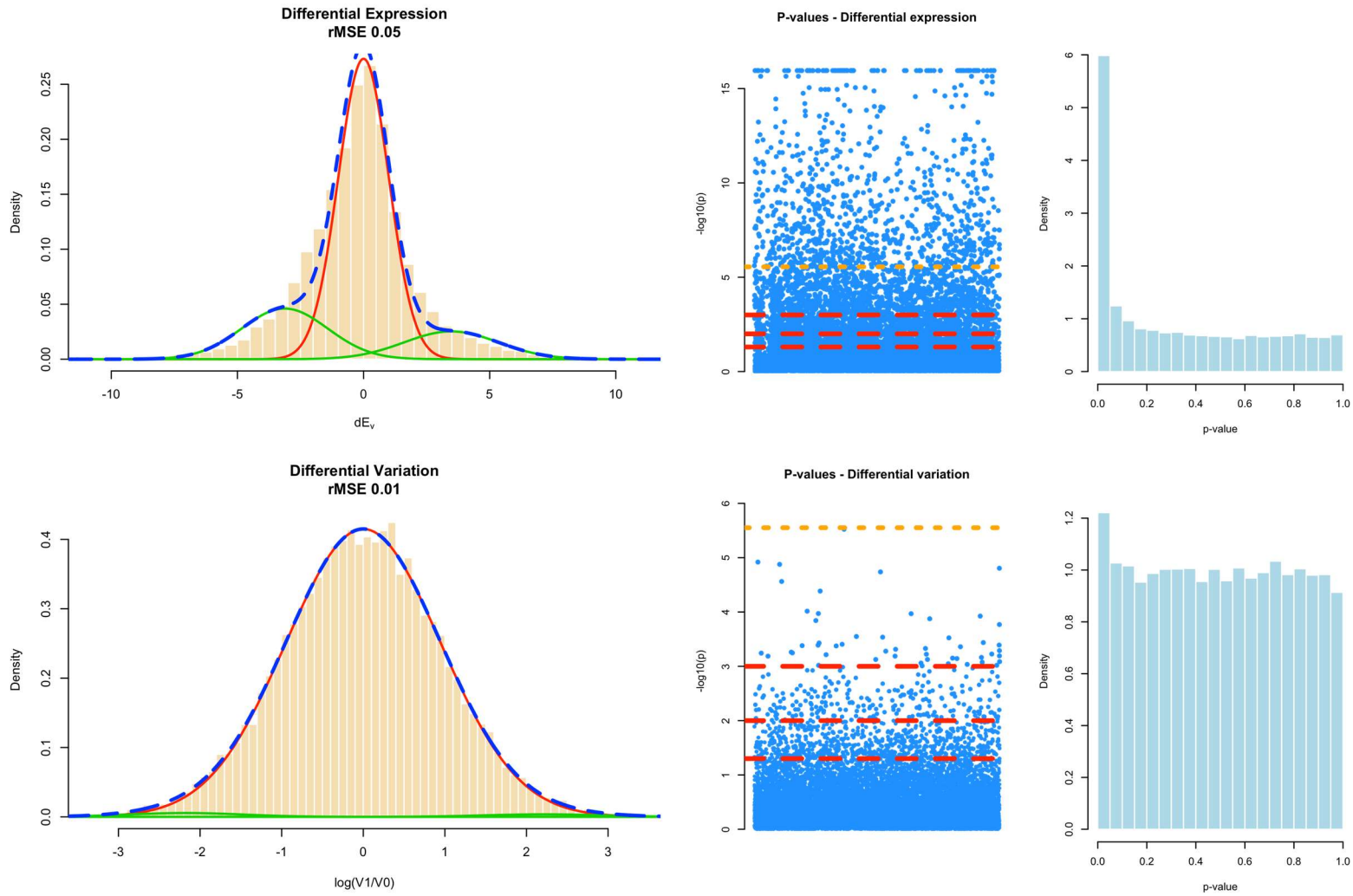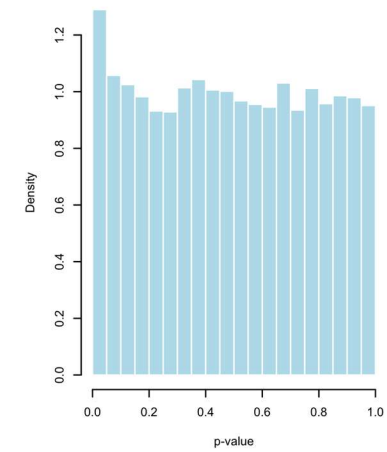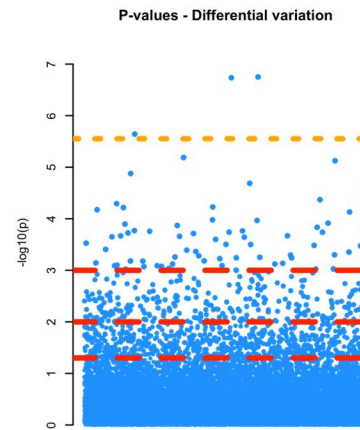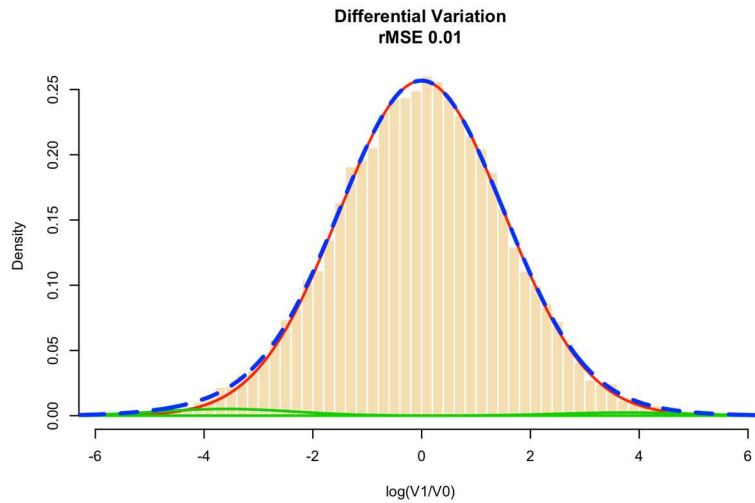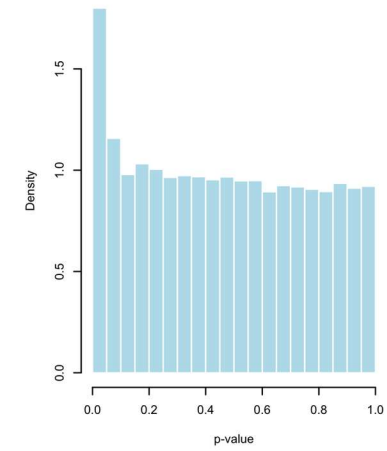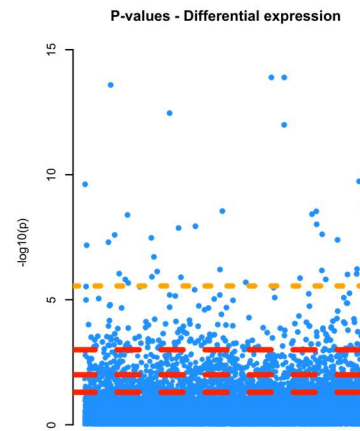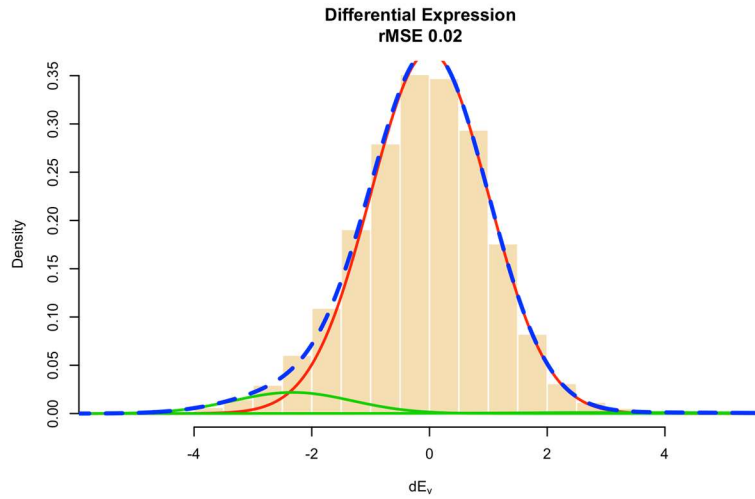
Differential factor: age, **Baseline level:** middle aged (40-70yr), **Treatment level:** normal aged (70-94yr), **Model:** limma, **Predictors:** gender

Differential factor: age, **Baseline level:** normal aged (70-94yr), **Treatment level:** extremely aged (95-106yr), **Model:** L2N, **Predictors:** gender

Differential factor: age, **Baseline level:** normal aged (70-94yr), **Treatment level:** extremely aged (95-106yr), **Model:** N3, **Predictors:** gender

Differential factor: age, **Baseline level:** normal aged (70-94yr), **Treatment level:** extremely aged (95-106yr), **Model:** limma, **Predictors:** gender