Results

2020-07-09

Contents

Criteria for drug/placebo performance measurement

We consider the criteria to measure the performance of the drug or placebo through the score v.s. time trajectory. Take the curve of subject 12 for example. We can calculate the:

- Change score: $Y(t = 8) - Y(t = 0) = 5 - 18 = -13$
- Integral: continuous/discrete
- Weighted intergal: continuous/discrete

The red curve is estimated by fit the LME (without the predictors)

$$Y_k = X\beta_k + Xb_k + \epsilon$$

And the curve has a function $y = f(t) = 16.7 - 5.1t + 0.45t^2$. The area under the curve can be calculated through the integral,

$$\int_0^8 f(t)dt = 16.7 \times 8 - 5.1/2 \times 8^2 + 0.45/3 \times 8^3 \approx 47.6$$

However, the quadratic curve is estimated, which is not the true trajectory for this subject. The area under the curve may be not accurate.

I then tried to calculate the area through the discrete approach (the area of the bars), which is just the summation of the scores

$$\text{discrete area: } 15 \times 1 + 4 \times 1 + 1 \times 4 + 5 \times 2 = 33$$

In we consider the weighted intergral, we may just use the value of time as the weight to calculate the integral, i.e.
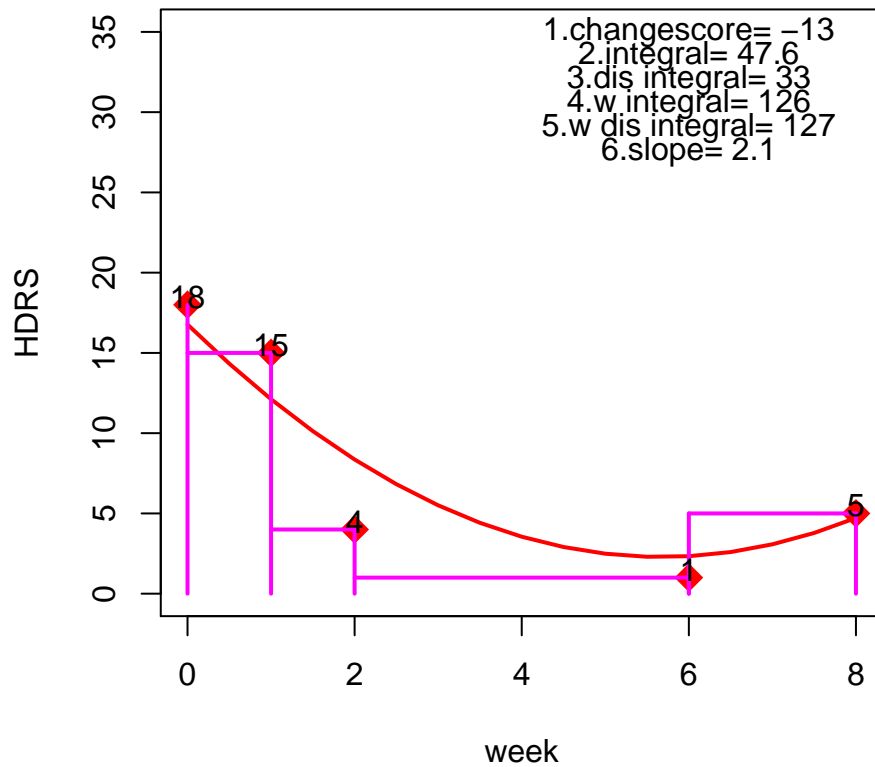
$$\int_0^8 tf(t)dt = \int_0^8 16.7t - 5.1t^2 + 0.45t^3 \approx 126$$

The discrete weigthed area under the curve is just the previous area times the value of each time points, i.e.

$$\text{weighted discrete area: } 15 \times 1 \times 1 + 4 \times 1 \times 2 + 1 \times 4 \times 6 + 5 \times 2 \times 8 = 126$$
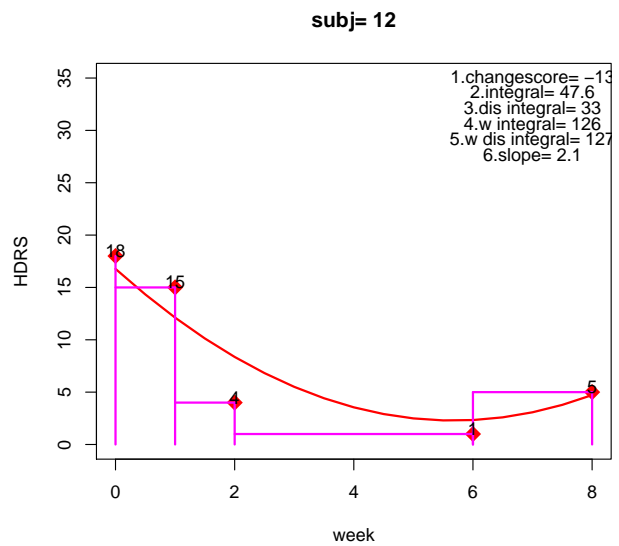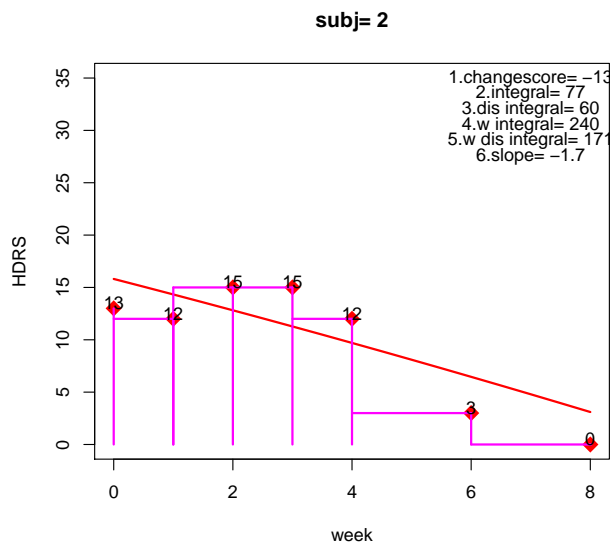
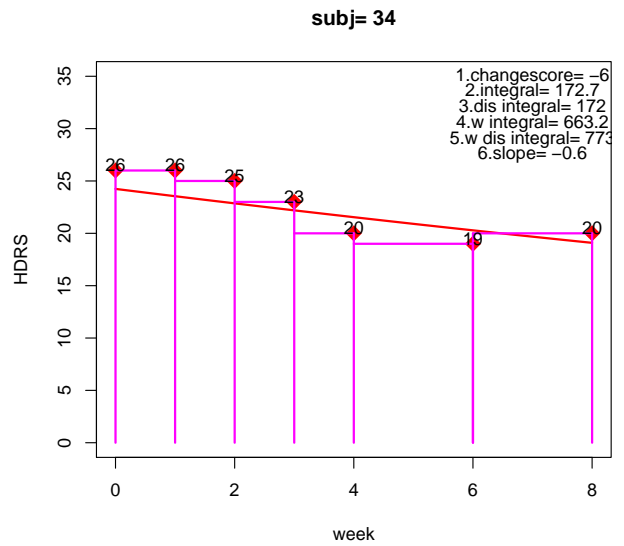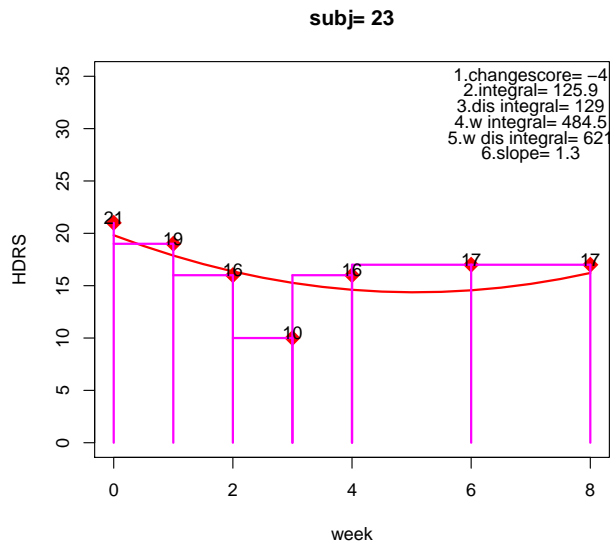The different criteria values are shown in the following plot.

subj= 12

1.changescore= −13
2.integral= 47.6
3.dis integral= 33
4.w integral= 126
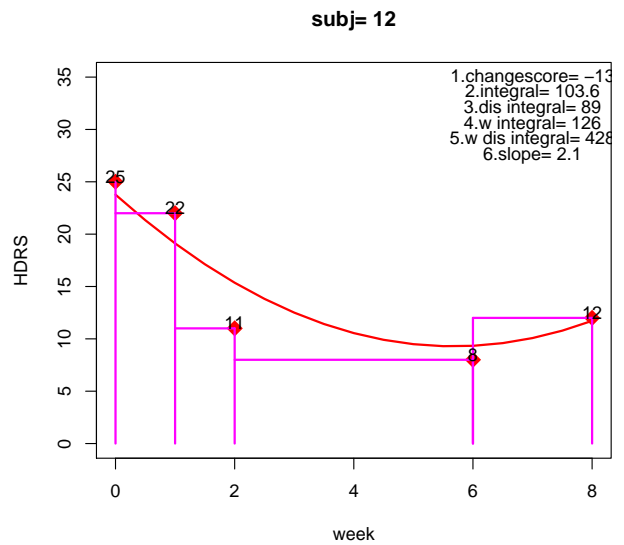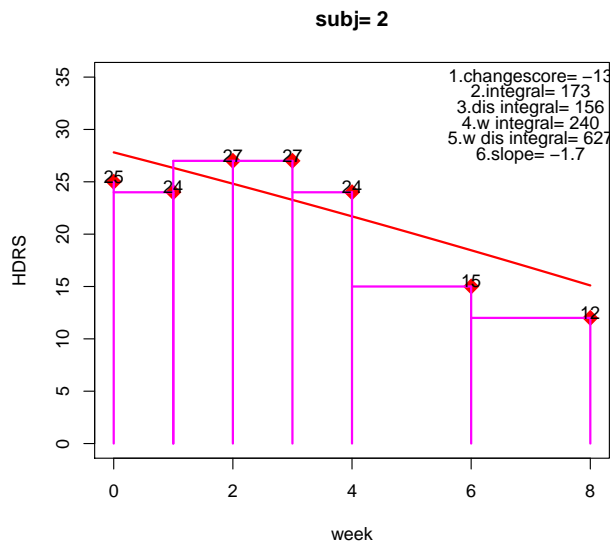5.w dis integral= 127
6.slope= 2.1

EMBARC: example trajectories

We may draw more subjects' trajectories to study their features.

subj= 2

1.changescore= −13
2.integral= 77
3.dis integral= 60
4.w integral= 240
5.w dis integral= 171
6.slope= −1.7

subj= 12

1.changescore= −13
2.integral= 47.6
3.dis integral= 33
4.w integral= 126
5.w dis integral= 127
6.slope= 2.1

2

subj= 23

1.changescore= −4
2.integral= 125.9
3.dis integral= 129
4.w integral= 484.5
5.w dis integral= 621
6.slope= 1.3

subj= 34

1.changescore= −6
2.integral= 172.7
3.dis integral= 172
4.w integral= 663.2
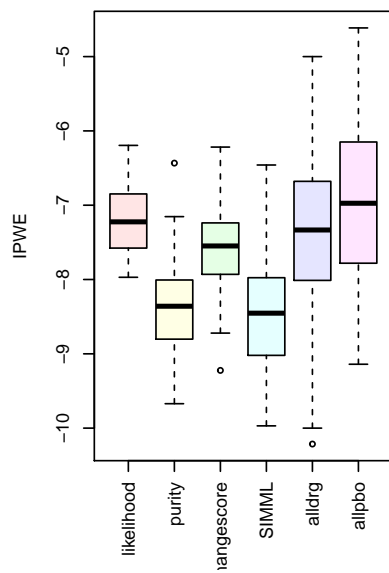5.w dis integral= 773
6.slope= −0.6

However, there may have some problem in terms of the integral area, since they have different intercept. Let's move the curves parallelly to have a common intercept and then calculate the integrals.
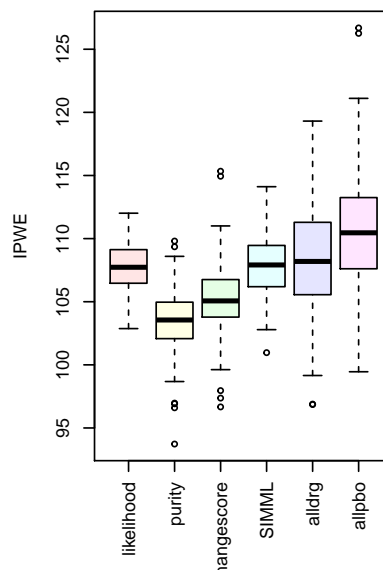
subj= 2

1.changescore= −13
2.integral= 173
3.dis integral= 156
4.w integral= 240
5.w dis integral= 627
6.slope= −1.7

subj= 12

1.changescore= −13
2.integral= 103.6
3.dis integral= 89
4.w integral= 126
5.w dis integral= 428
6.slope= 2.1

3

subj= 23

1.changescore= −4
2.integral= 157.9
3.dis integral= 161
4.w integral= 484.5
5.w dis integral= 773
6.slope= 1.3

subj= 34

1.changescore= −6
2.integral= 164.7
3.dis integral= 164
4.w integral= 663.2
5.w dis integral= 735
6.slope= −0.6
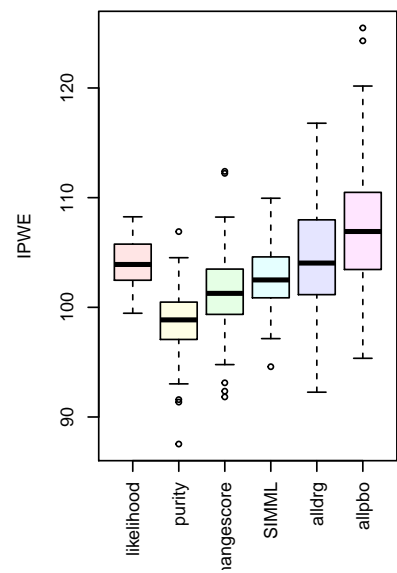
EMBARC: boxplots based on criteria

EMBARC with 13 covariances, change score

integral

discrete integral

4

weighted integral

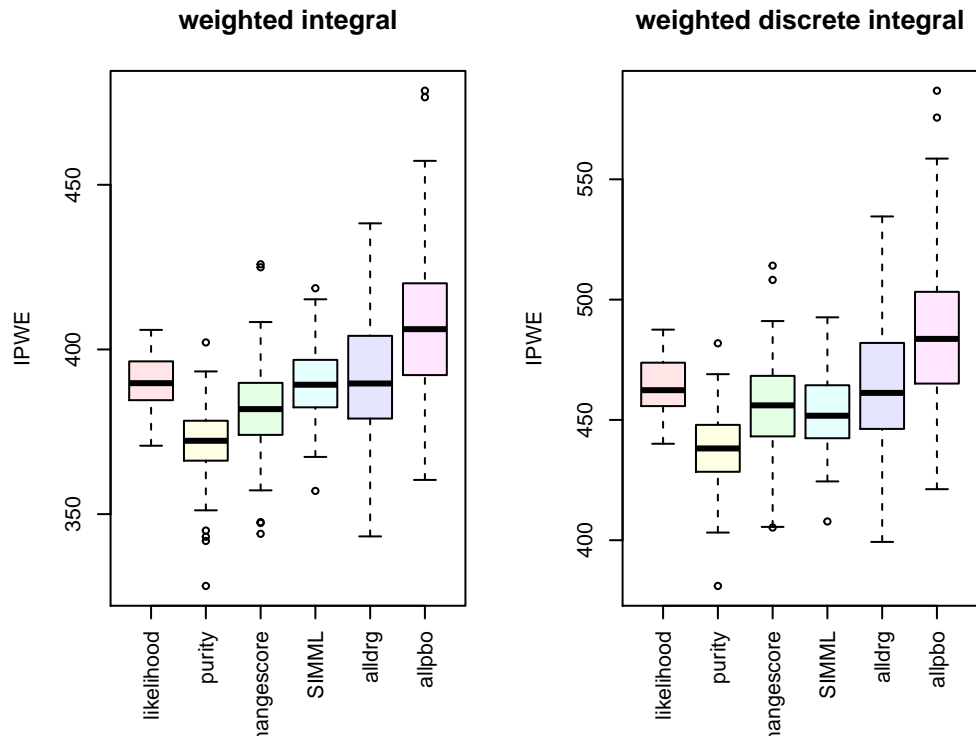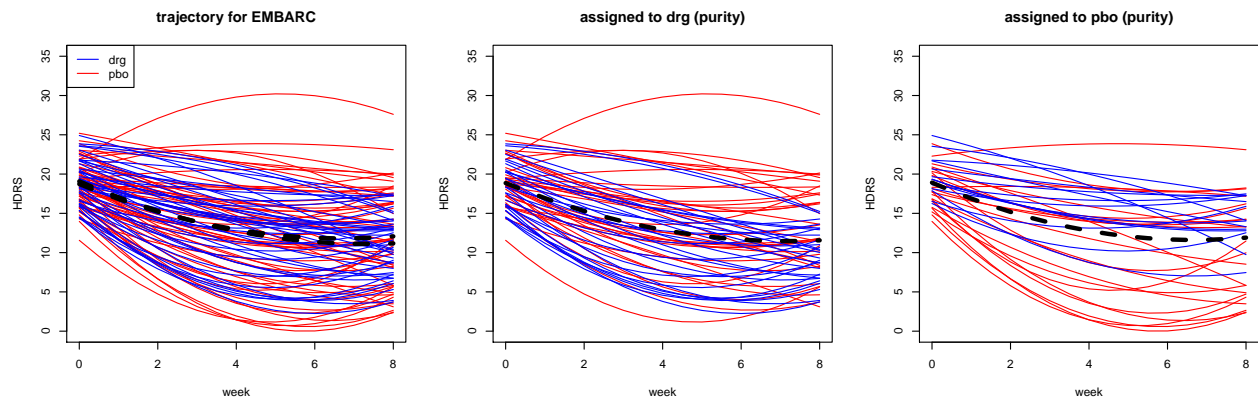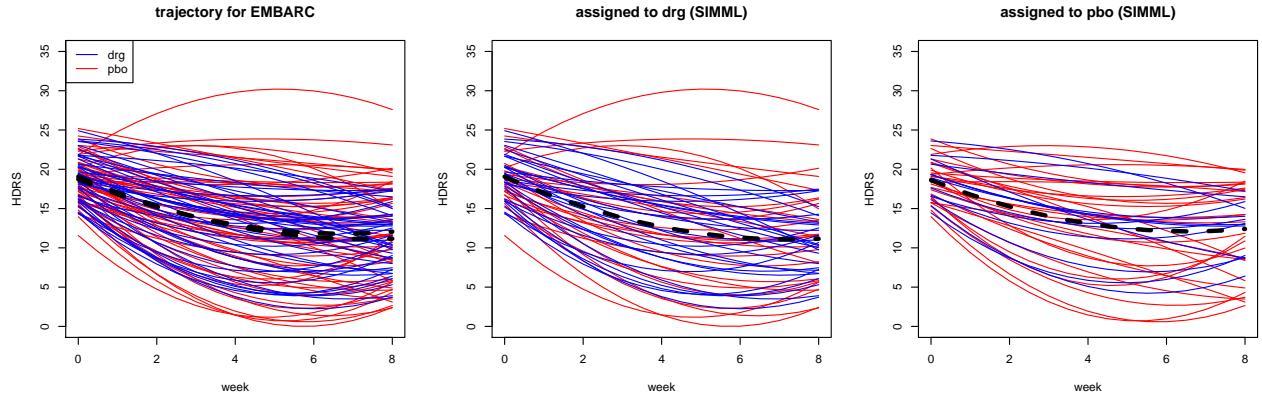**weighted discrete integral**

EMBARC: assigned trajectories

How do the subjects' trajectories look like when they are assigned to drug group or placebo group based on purity method, loglikelihood method or SIMML?
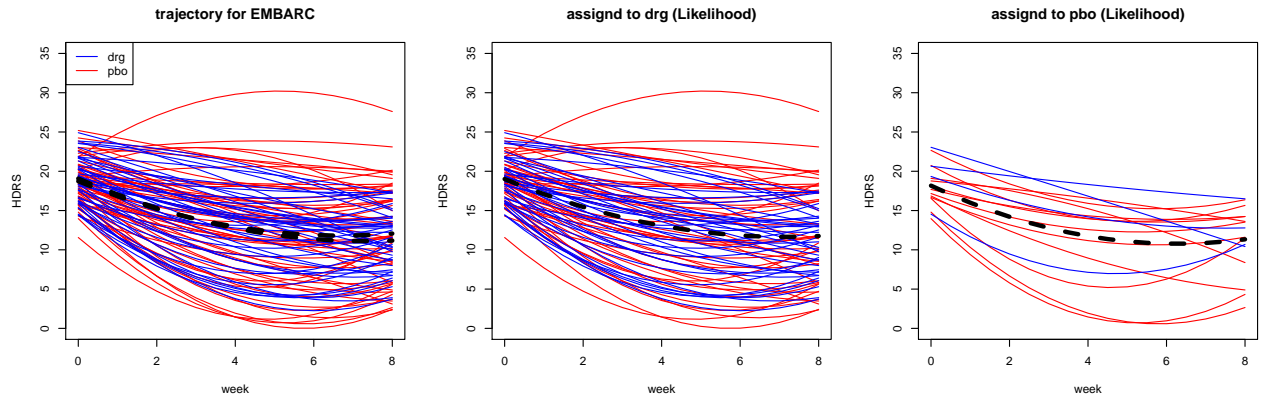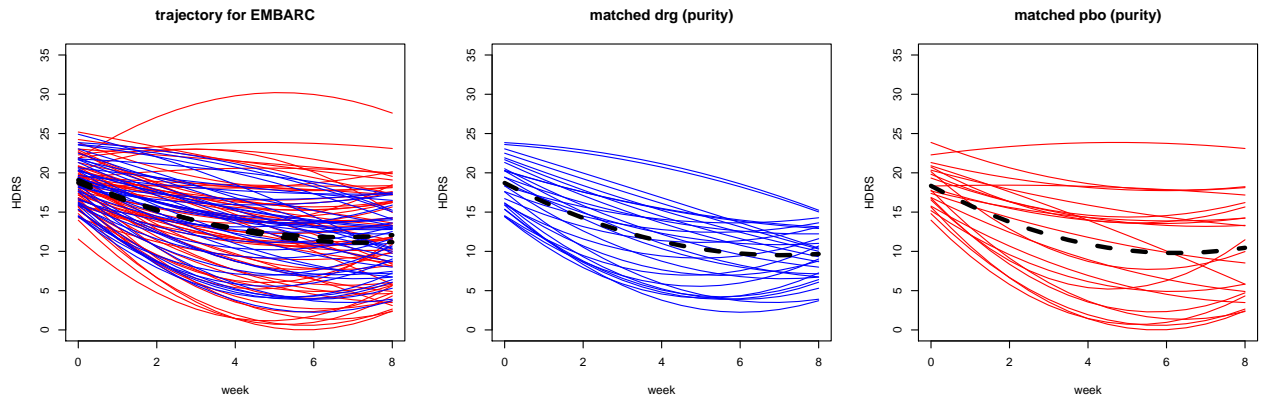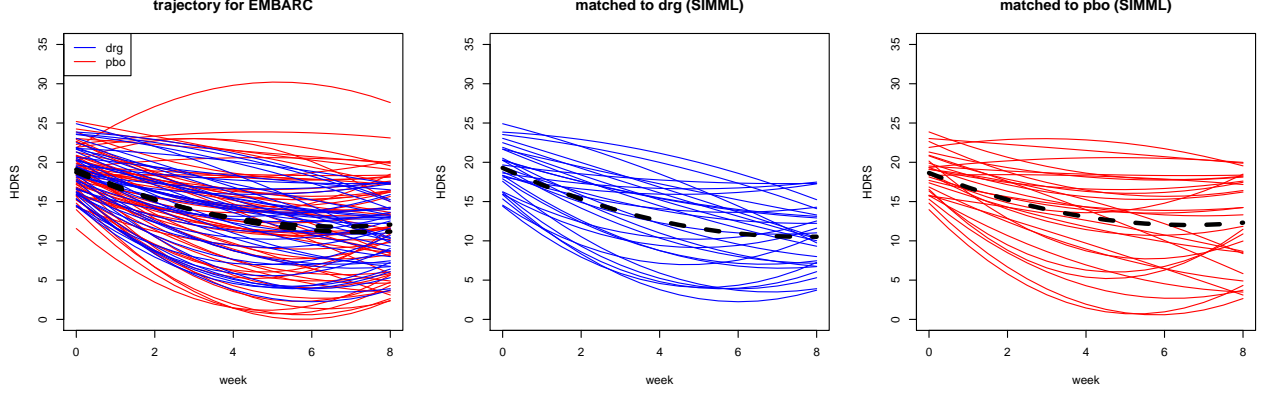
by Purity

by SIMML

by Likelihood

If we only keep the trajectory that observed assignment matchs the predicted assignment, i.e. the subject who should get drug and are assigned to drug group in the trial and the subject who should get placebo and are assigned to placebo group in the trial.
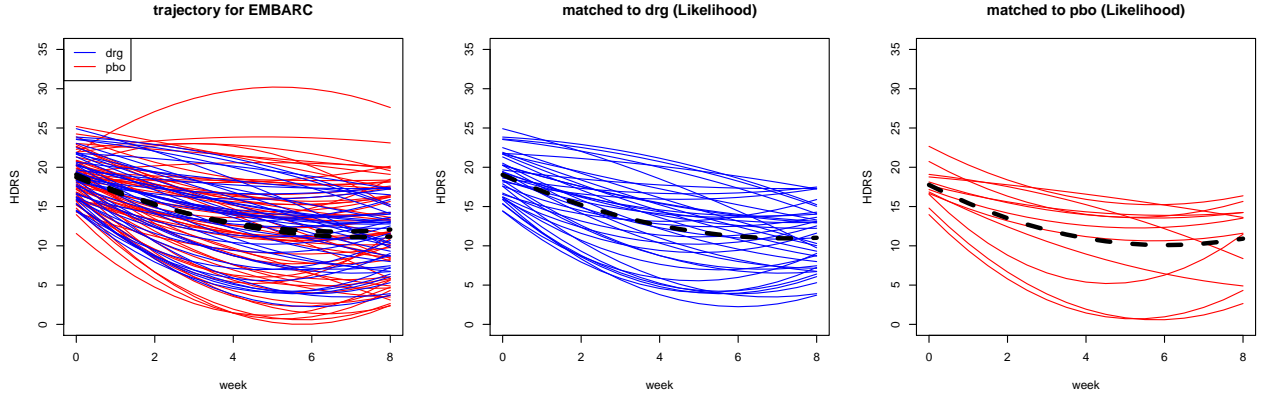
by Purity

by SIMML

by Likelihood

Simulation

Parameter settings

Scenario 1

- dimension of the predictors $p = 3, 10$
- $\beta_{drg} = \beta_{pbo} = 1, -0.05, -0.02$
- $\Gamma_{drg} = (0, -\sin(\frac{\pi}{3}/10, -\cos(\frac{\pi}{3})/10)$
- $\Gamma_{pbo} = (0, \cos(\frac{\pi}{3}/10, -\sin(\frac{\pi}{3})/10)$
- $S = [1, t, t^2]$, $t = [0, 1, 2, 3, 4, 6, 8]$ is the design matrix for fixed effect and random effect
- $x \sim MVN(\mu_x, \Sigma_x)$, $\mu_x = \mathbf{0}_p$, Σ_x has diagonal equals to 1 and 0.5 everywhere else.
- $D_{drg} = D_{pbo} = \begin{pmatrix} 1 & 0.3 & 0.1 \\ 0.3 & 1 & 0.5 \\ 0.1 & 0.5 & 1 \end{pmatrix}$
- $\epsilon_{drg}, \epsilon_{pbo} \sim N(0, 1^2)$
- $\alpha = \alpha_1 + \delta\alpha_{2k}, k = 1, 2, \delta = 0, 1, 10, 100\ldots$
  - $\alpha_1 = (1, 1, 1)$
  - drg: $\alpha_{21} = (1, ..., p)$
  - pbo: $\alpha_{22} = (p, ..., 1)$

If $\delta = 0$, $\alpha_1 = \alpha_2 = (\frac{1}{\sqrt{3}}, \frac{1}{\sqrt{3}}, \frac{1}{\sqrt{3}})$. The cosine similarity is 1.

If $\delta = 10$,

- $\alpha_1 = (0.2818660, 0.5381079, 0.7943497)$
- $\alpha_2 = (0.7943497, 0.5381079, 0.2818660)$

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- cosine similarity is 0.737

If $\delta = 100$,

- $\alpha_1 = (0.2687815, 0.5349018, 0.8010222)$
- $\alpha_2 = (0.8010222, 0.5349018, 0.2687815)$
- cosine similarity is 0.717

Scenario 2

- dimension of the predictors $p = 3, 10$
- $\beta_{drg} = \beta_{pbo} = 1, -0.05, -0.02$
- $\Gamma_{drg} = (0, -\sin(\frac{\pi}{3}/10, -\cos(\frac{\pi}{3})/10)$
- $\Gamma_{pbo} = (0, \cos(\frac{\pi}{3}/10, -\sin(\frac{\pi}{3})/10)$
- $S = [1, t, t^2]$, $t = [0, 1, 2, 3, 4, 6, 8]$ is the design matrix for fixed effect and random effect
- $x \sim MVN(\mu_x, \Sigma_x)$, $\mu_x = \mathbf{0}_p$, Σ_x has diagonal equals to 1 and 0.5 everywhere else.
- $D_{drg} = D_{pbo} = \begin{pmatrix} 0.1 & 0.01 & 0.01 \\ 0.01 & 0.1 & 0.01 \\ 0.01 & 0.01 & 0.05 \end{pmatrix}$
- $\epsilon_{drg}, \epsilon_{pbo} \sim N(0, 1^2)$
- $\alpha = \alpha_1 + \delta\alpha_{2k}, k = 1, 2, \delta = 0, 1, 10, 100\dots$
  - $\alpha_1 = (1, 1, 1)$
  - drg: $\alpha_{21} = (1, ..., p)$
  - pbo: $\alpha_{22} = (-p, ..., -1)$

If $\delta = 0$, $\alpha_1 = \alpha_2 = (\frac{1}{\sqrt{3}}, \frac{1}{\sqrt{3}}, \frac{1}{\sqrt{3}})$. The cosine similarity is 1.
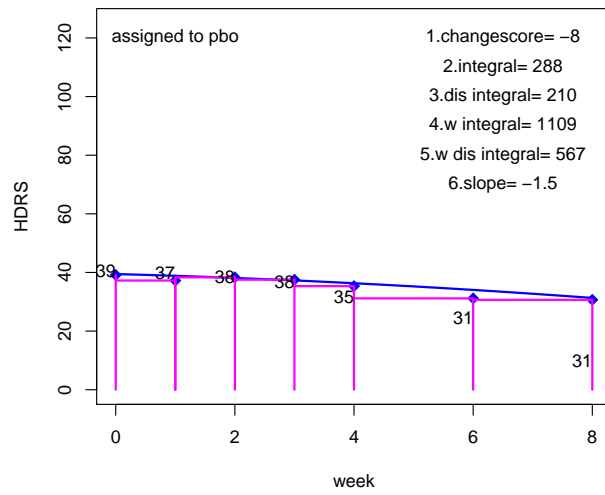
If $\delta = 10$,

- $\alpha_1 = (0.2818660, 0.5381079, 0.7943497)$
- $\alpha_2 = (-0.8096264, -0.5304449, -0.2512634)$
- cosine similarity is -0.713

If $\delta = 100$,

- $\alpha_1 = (0.2687815, 0.5349018, 0.8010222)$
- $\alpha_2 = (-0.8025494, -0.5341382, -0.2657271)$
- cosine similarity is -0.714

If $\delta = 0$, $\alpha_1 = \alpha_2 = (\frac{1}{\sqrt{3}}, \frac{1}{\sqrt{3}}, \frac{1}{\sqrt{3}})$. The cosine similarity is 1.

If $\delta = 10$,

- $\alpha_1 = (0.2818660, 0.5381079, 0.7943497)$
- $\alpha_2 = (-0.8096264, -0.5304449, -0.2512634)$
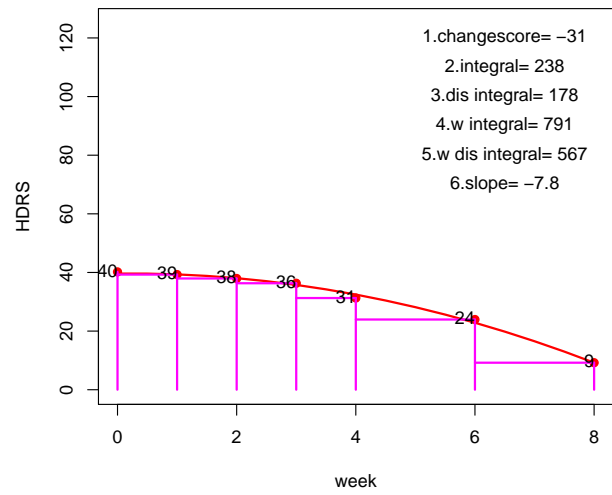- cosine similarity is -0.71
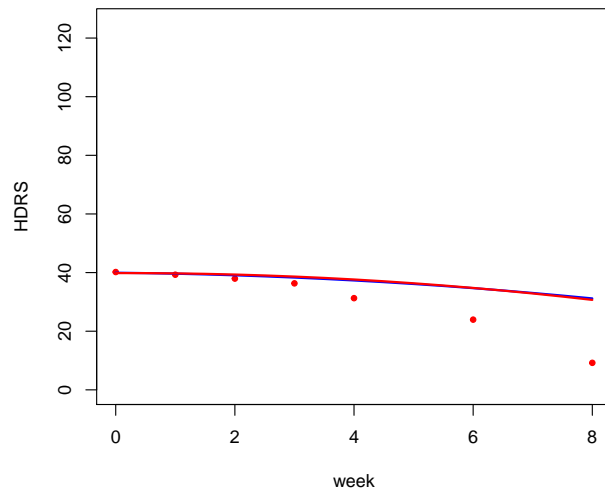
Assignment trajectory plots

delta = 0

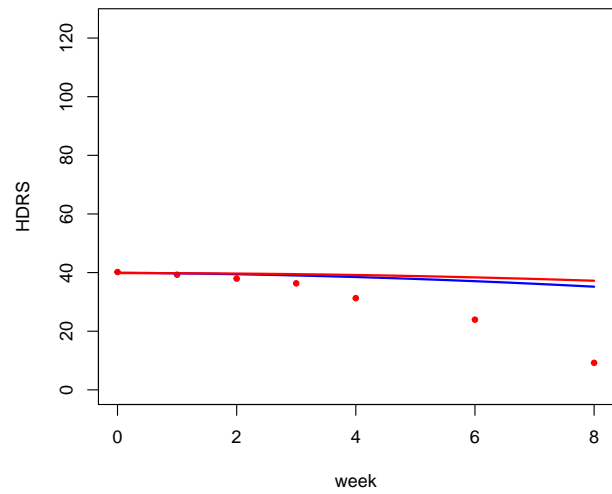**true trajectory (drg); subj= 10**

assigned to pbo

1.changescore= −8
2.integral= 288
3.dis integral= 210
4.w integral= 1109
5.w dis integral= 567
6.slope= −1.5

true trajectory (pbo); subj= 10

1.changescore= −31
2.integral= 238
3.dis integral= 178
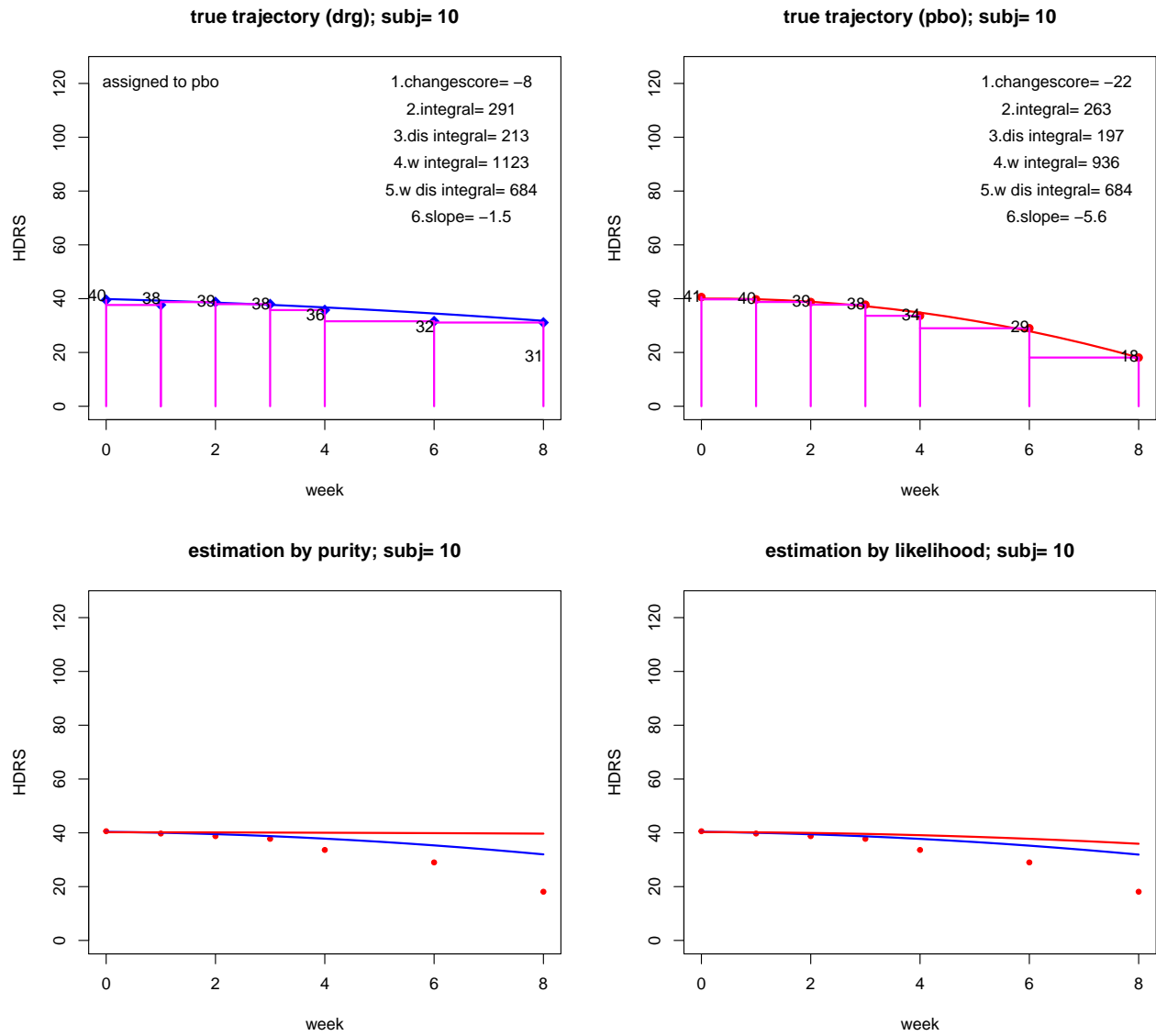4.w integral= 791
5.w dis integral= 567
6.slope= −7.8

estimation by purity; subj= 10

estimation by likelihood; subj= 10

delta = 10

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true trajectory (drg); subj= 10

assigned to pbo

1.changescore= −8
2.integral= 291
3.dis integral= 213
4.w integral= 1123
5.w dis integral= 684
6.slope= −1.5

40 38 39 38 36 32 31

true trajectory (pbo); subj= 10

1.changescore= −22
2.integral= 263
3.dis integral= 197
4.w integral= 936
5.w dis integral= 684
6.slope= −5.6

41 40 39 38 34 29 18

estimation by purity; subj= 10

estimation by likelihood; subj= 10

Boxplots of criteria

Scenario 1, $\delta = 0$

ChangeScore_p= 3 ; delta = 0

−0.51 −0.86 −1.53 −0.77 −13.18

integral p= 3 ; delta = 0

514.6 513.38 512.62 514.37 481.6

weighted integral p= 3 ; delta = 0

1284.58 1280.34 1277.48 1283.63 1168.89

10
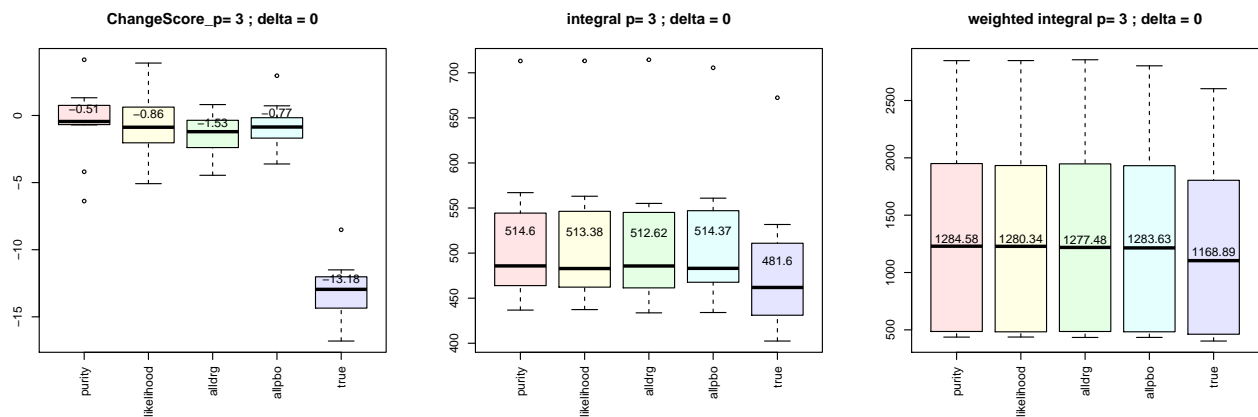
Scenario 1, $\delta = 0$, coefficient estimation

estimation of beta_drg2 | estimation of beta_drg3 | estimation of beta_pbo2 | estimation of beta_pbo3

estimation of gamma_drg2 | estimation of gamma_drg3 | estimation of gamma_pbo2 | estimation of gamma_pbo3
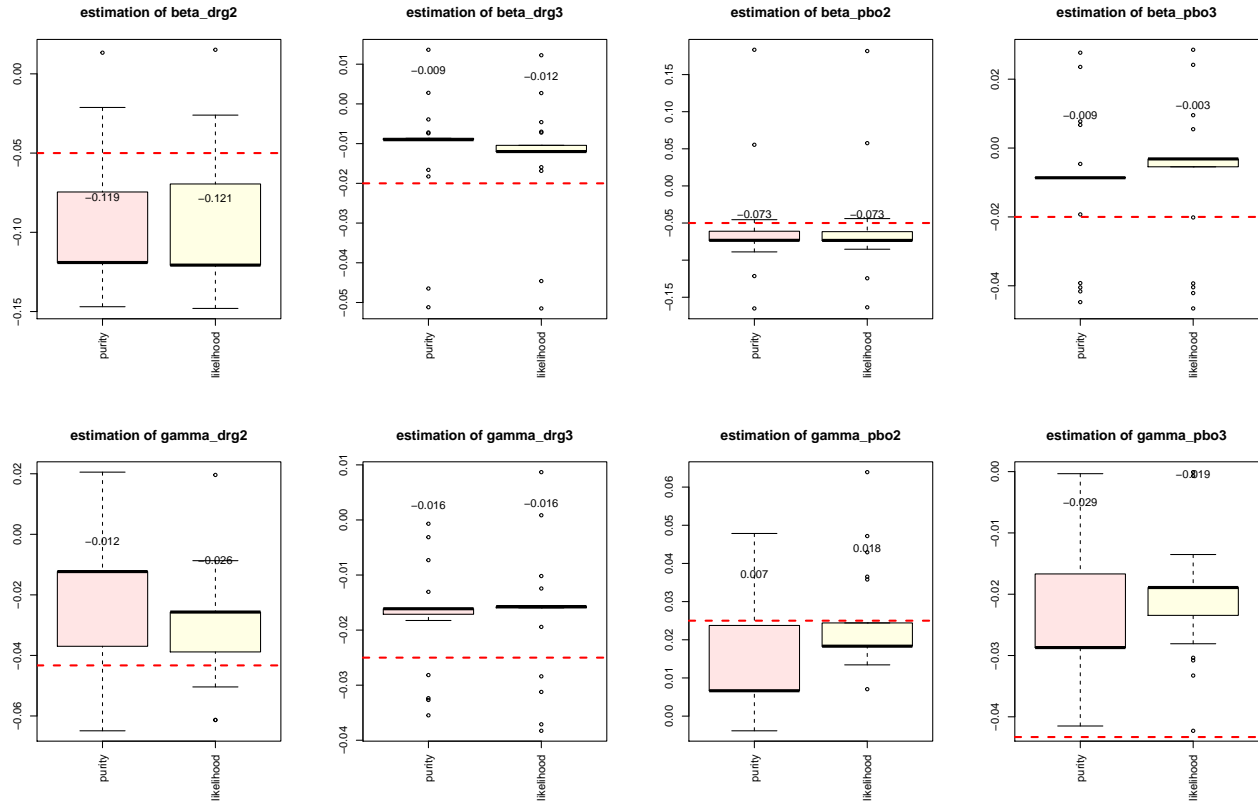
sine similarity between alpha from likelihood and

Scenario 1, $\delta = 100$
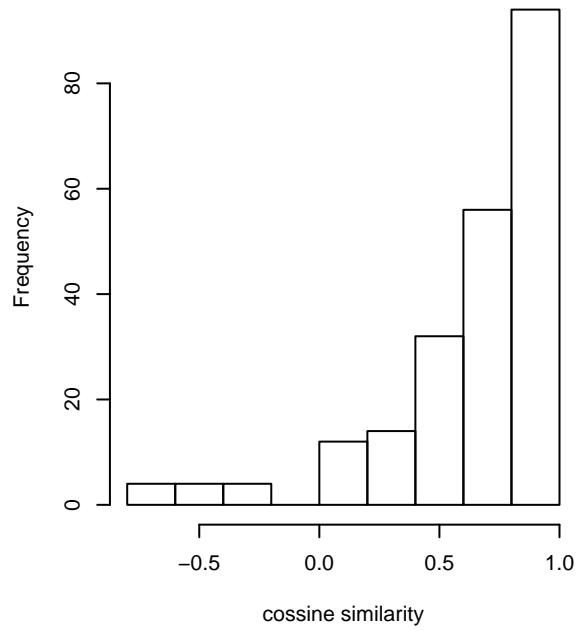
ChangeScore_p = 3 ; delta = 100   **integral p = 3 ; delta = 100**   **weighted integral p = 3 ; delta = 100**
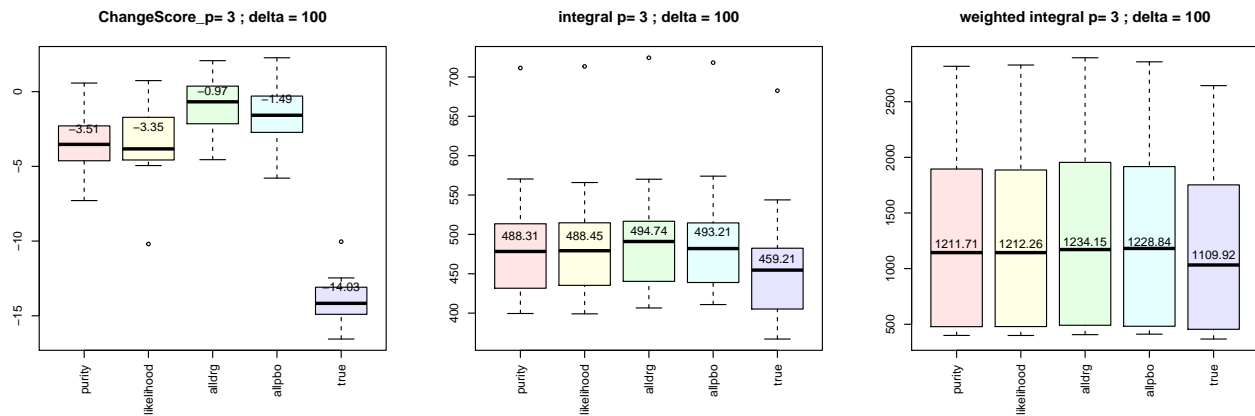
Scenario 1, $\delta = 100$, coefficient estimation

estimation of beta_drg2   **estimation of beta_drg3**   **estimation of beta_pbo2**   **estimation of beta_pbo3**

estimation of gamma_drg2   **estimation of gamma_drg3**   **estimation of gamma_pbo2**   **estimation of gamma_pbo3**

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Histogram of cossim
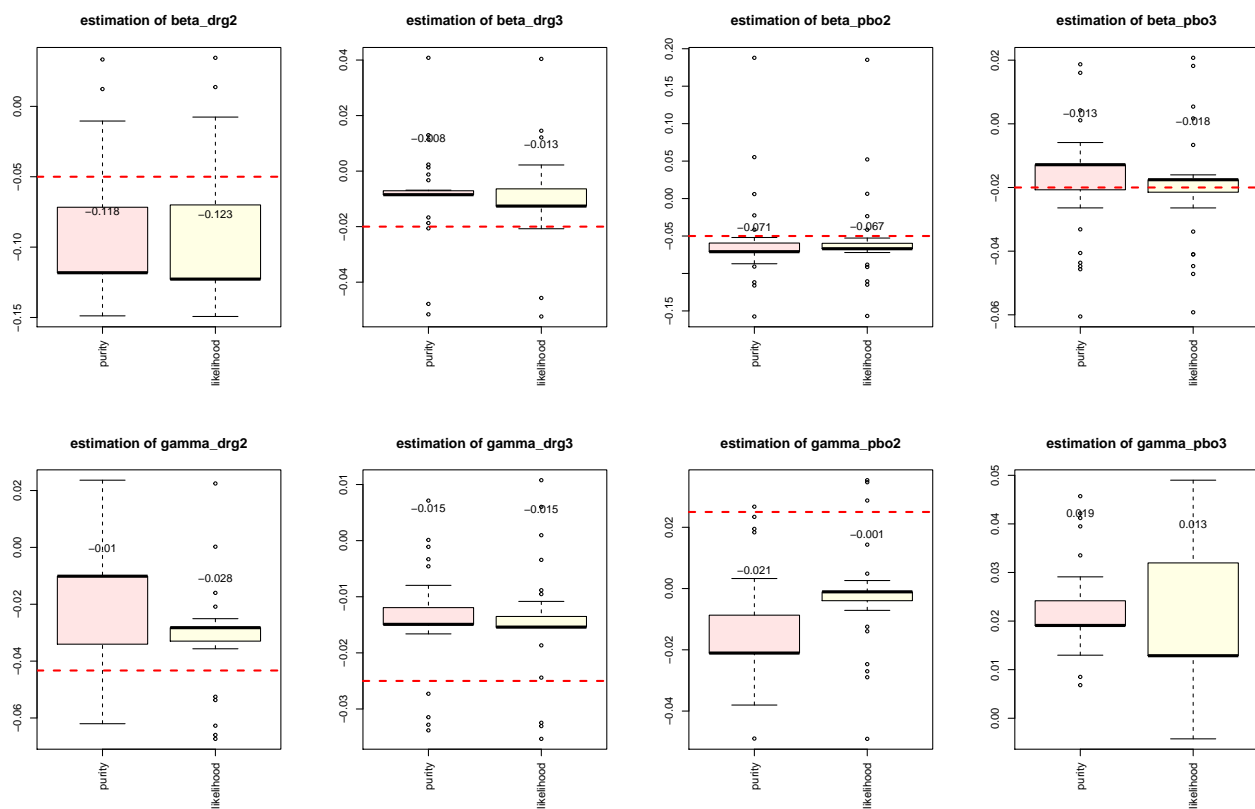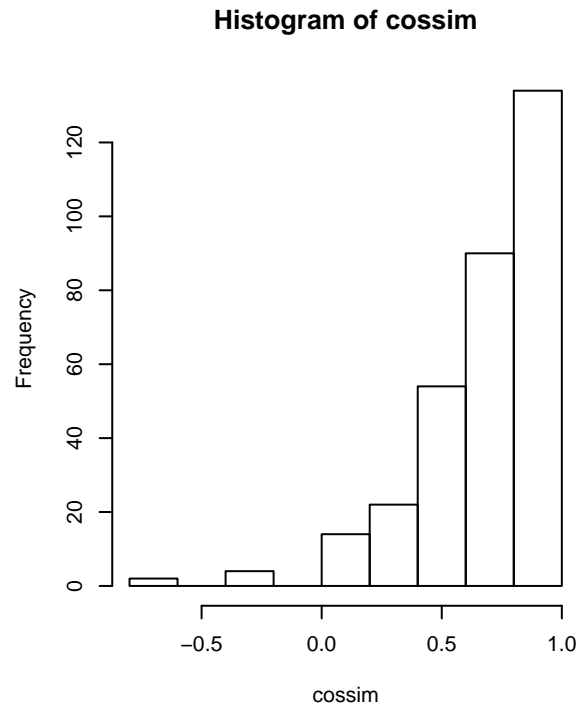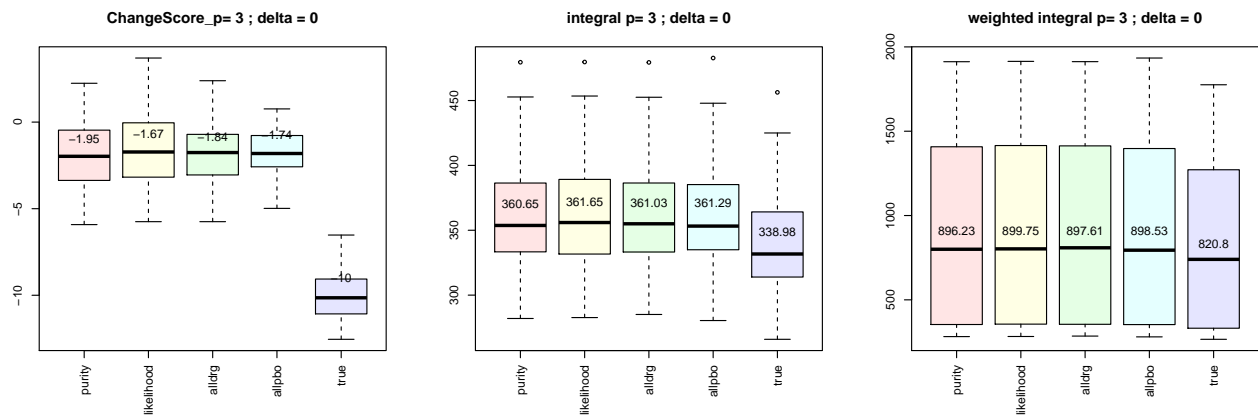
Scenario 2, $\delta = 0$

Scenario 2, $\delta = 0$, coefficient estimation

Histogram of cossim

Scenario 2, $\delta = 100$

ChangeScore_p= 3 ; delta = 100

integral p= 3 ; delta = 100
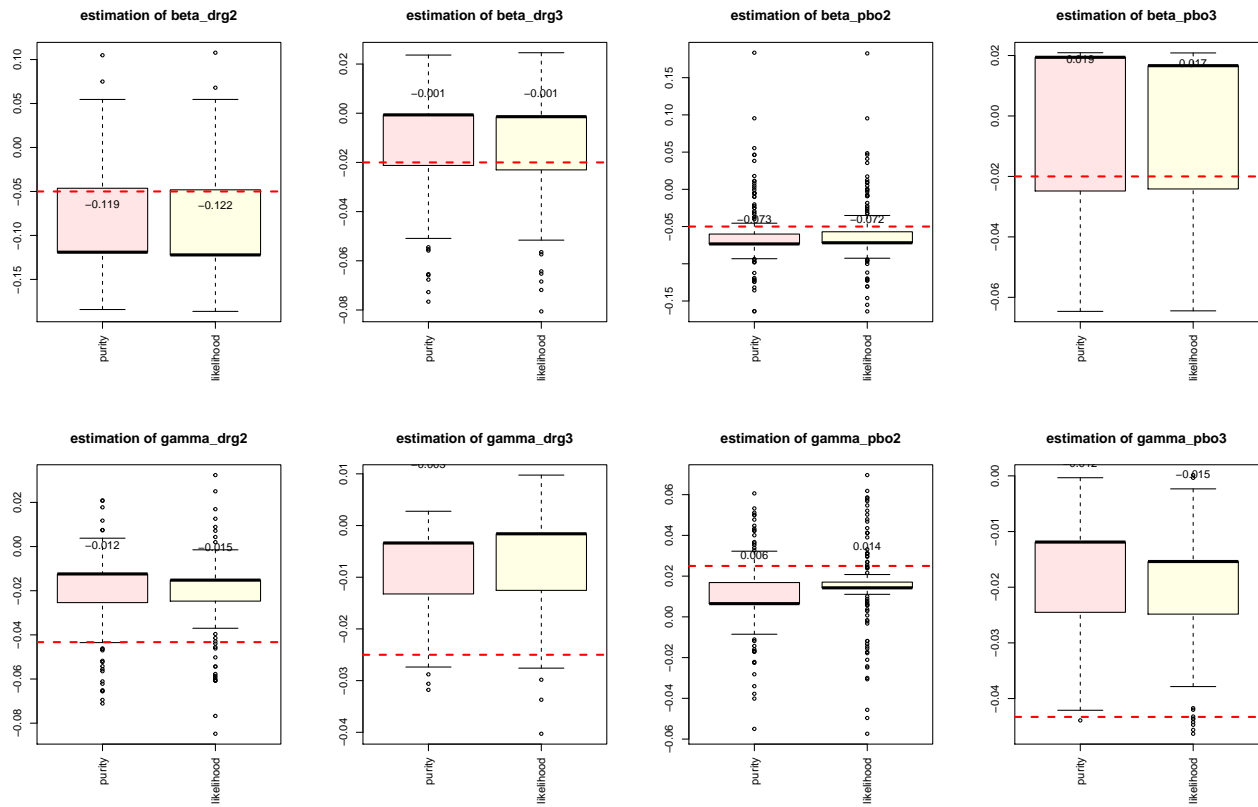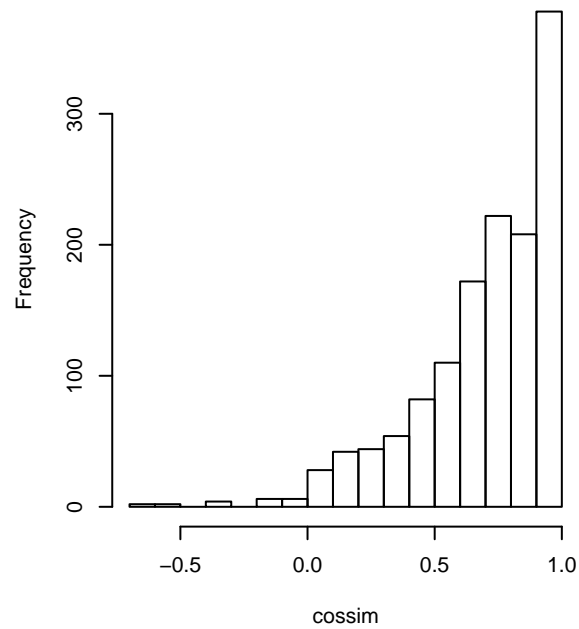
weighted integral p= 3 ; delta = 100
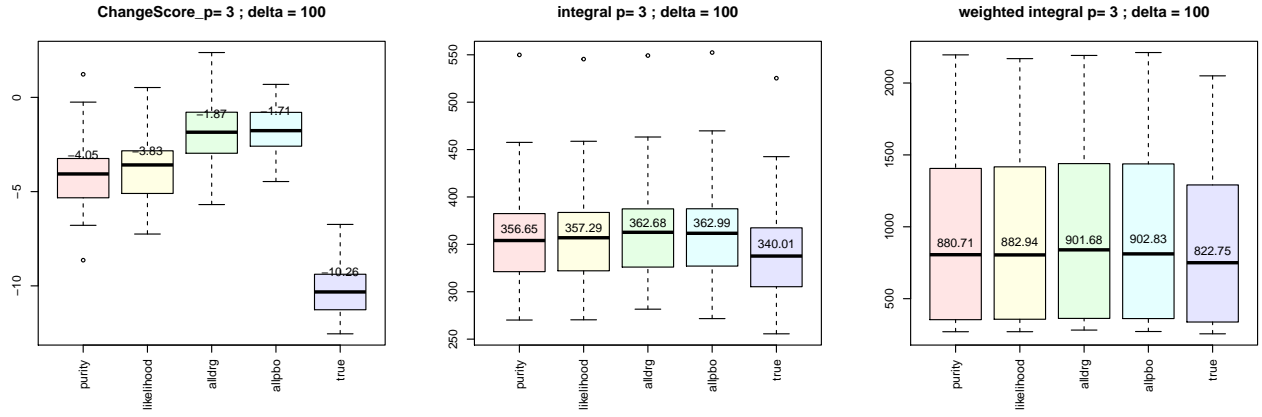
Scenario 2, $\delta = 100$, coefficient estimation

estimation of beta_drg2

estimation of beta_drg3

estimation of beta_pbo2

estimation of beta_pbo3

estimation of gamma_drg2

estimation of gamma_drg3

estimation of gamma_pbo2

estimation of gamma_pbo3

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Histogram of cossim
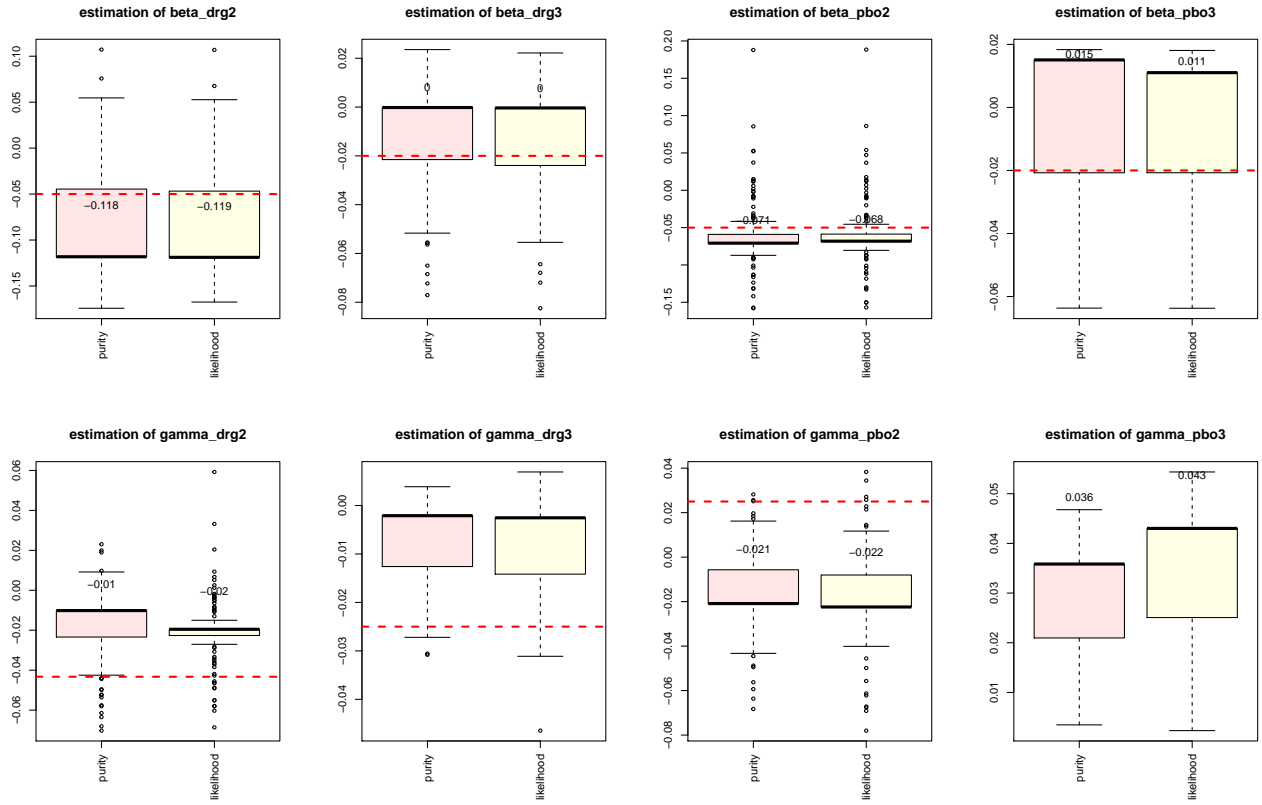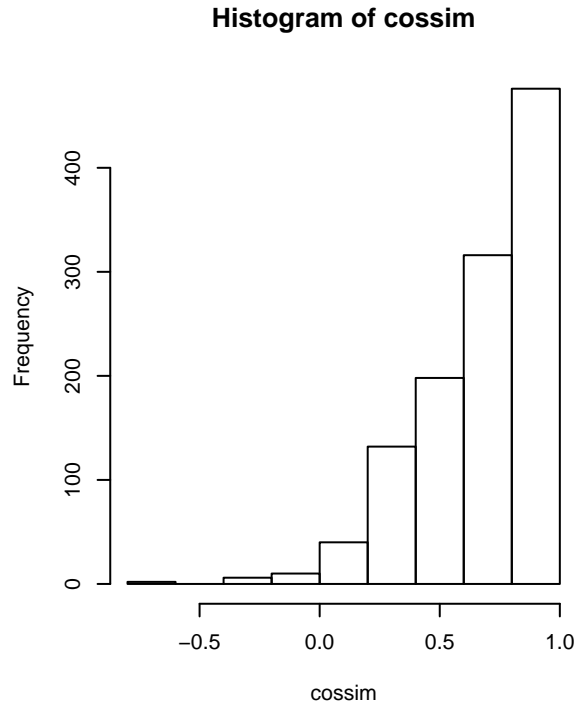
Relationship between purity-criteria and likelihood-criteria

When $\delta = 0$

Plots: purity v.s. α (2 dimension)
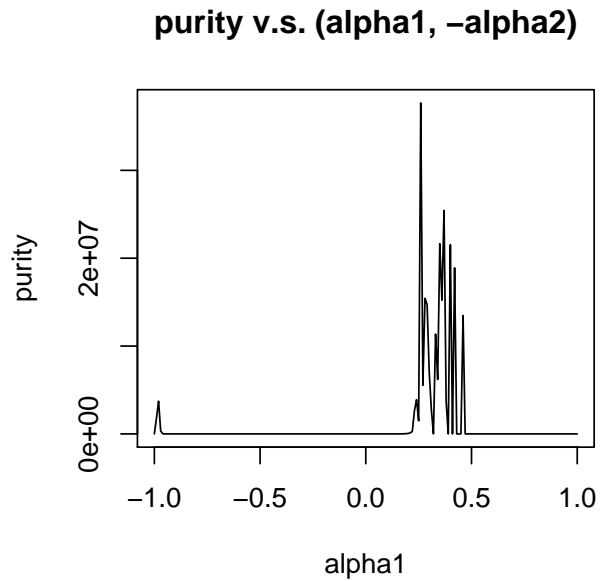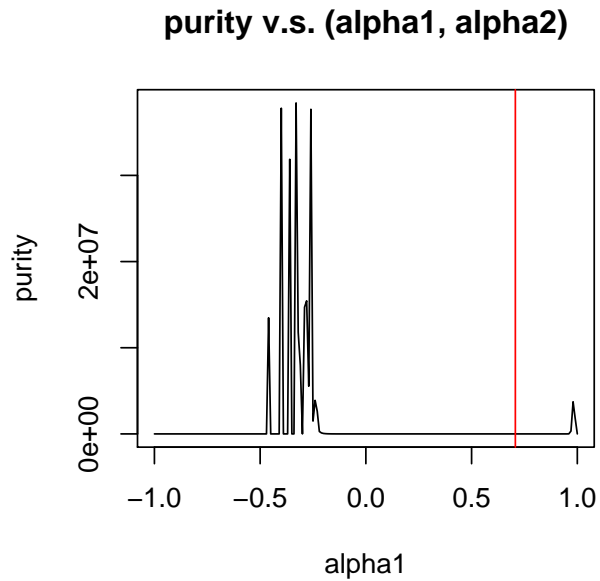
If we substitude extreme value as 0, 8b
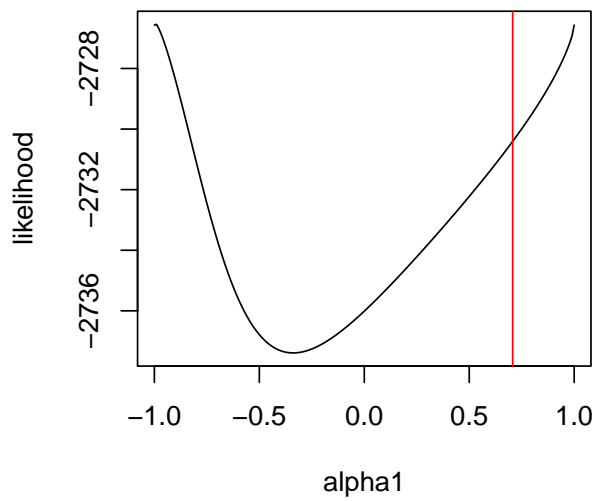
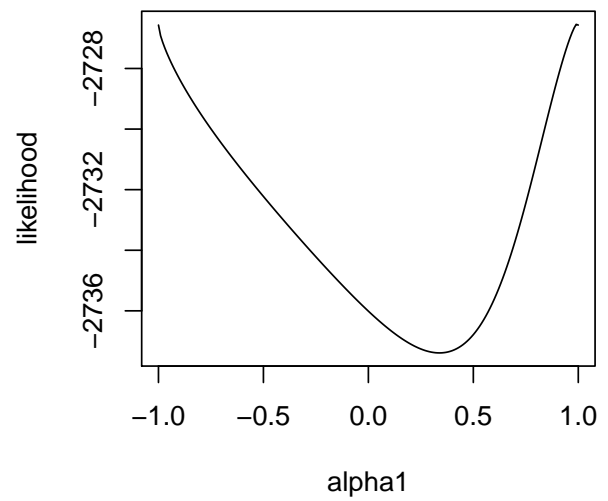## purity v.s. (alpha1, alpha2)
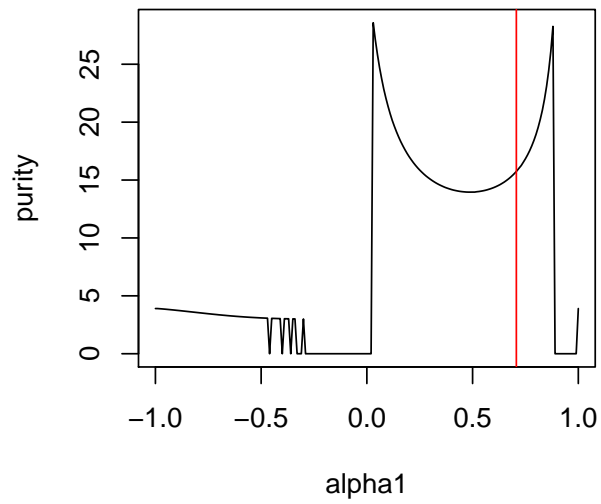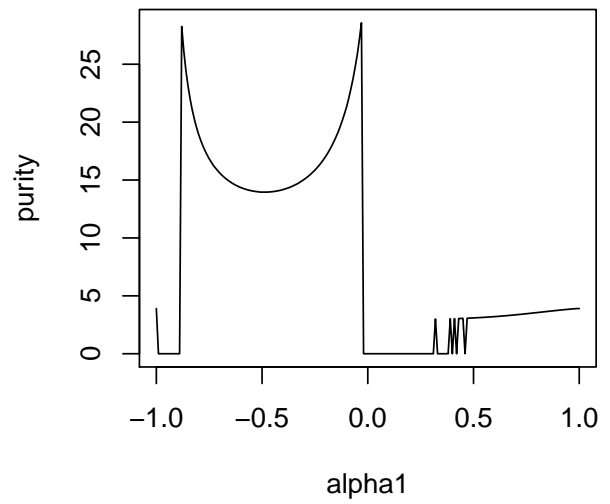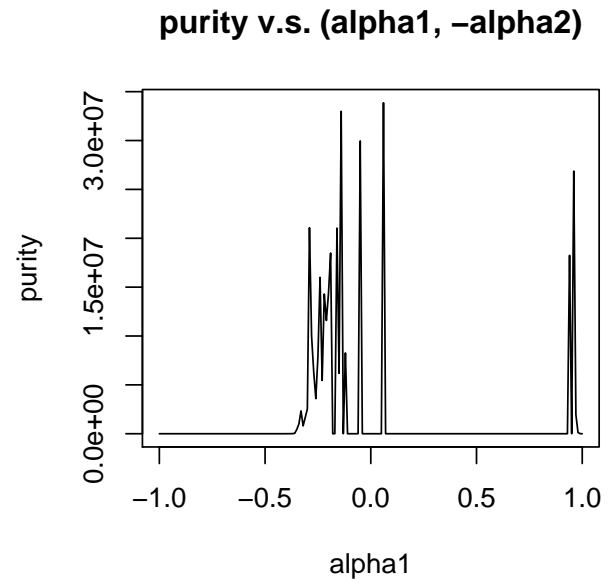

purity v.s. (alpha1, −alpha2)

Likelihood

likelihood v.s. (alpha1, alpha2)

likelihood v.s. (alpha1, −alpha2)

$\delta = 100$

purity v.s. (alpha1, alpha2)

purity v.s. (alpha1, −alpha2)

If we substitude extreme value as 0,

purity v.s. (alpha1, alpha2)
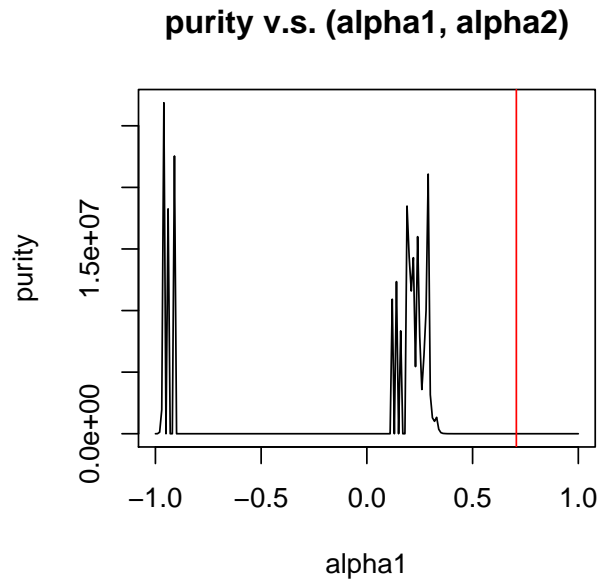
purity v.s. (alpha1, −alpha2)

Likelihood

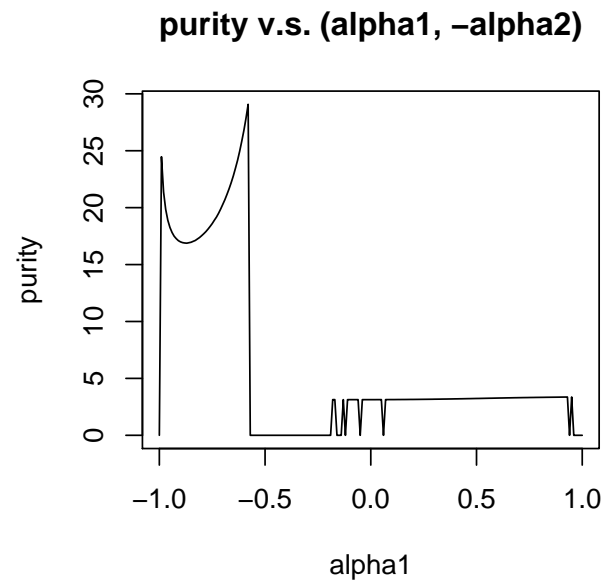**likelihood v.s. (alpha1, alpha2)**

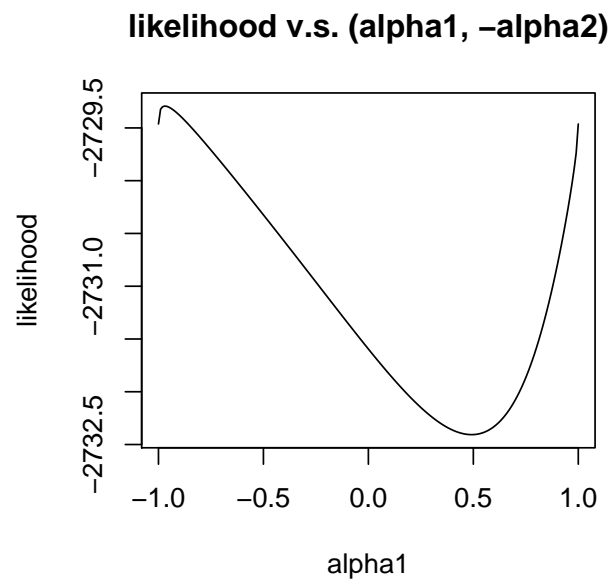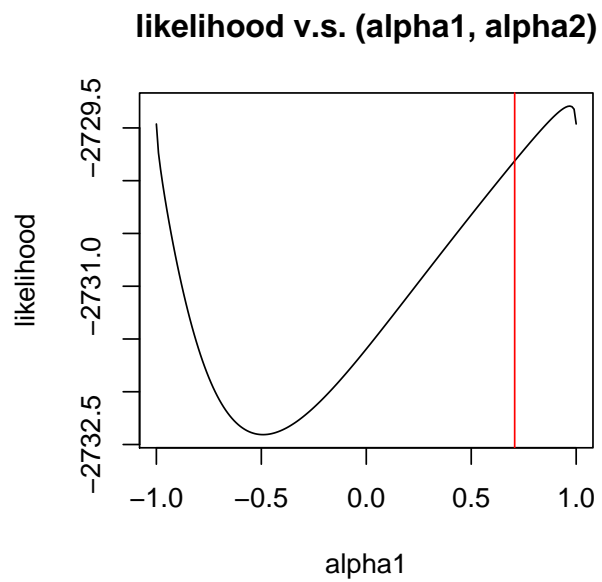**likelihood v.s. (alpha1, −alpha2)**
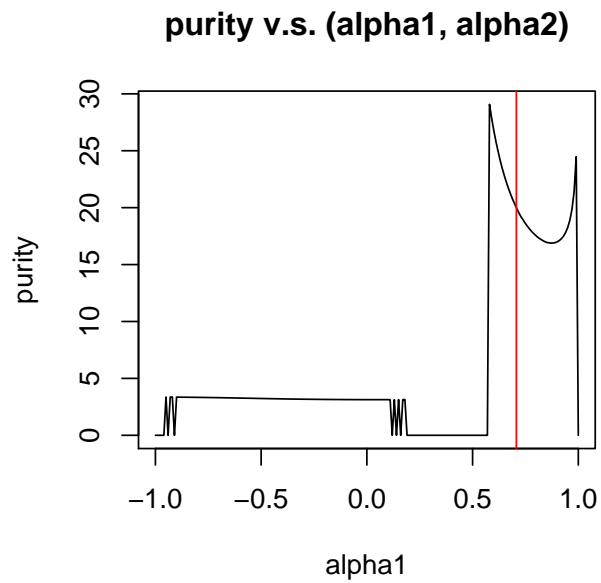
use the fixed value of β, Γ, D

−likelihood/(n/4) v.s. purity

——	likelihood
——	purity