Simulation

Suppose we generate a data set as following:

```
##   subj        X1         X2 tt      w_drg      w_pbo        fd1        fd2
## 1    1 0.5768541 -0.2587745  0 0.2249162 0.2249162 2.891554 -0.3190356
## 2    1 0.5768541 -0.2587745  1 0.2249162 0.2249162 2.891554 -0.3190356
## 3    1 0.5768541 -0.2587745  2 0.2249162 0.2249162 2.891554 -0.3190356
## 4    1 0.5768541 -0.2587745  3 0.2249162 0.2249162 2.891554 -0.3190356
## 5    1 0.5768541 -0.2587745  4 0.2249162 0.2249162 2.891554 -0.3190356
## 6    1 0.5768541 -0.2587745  6 0.2249162 0.2249162 2.891554 -0.3190356
##         fd3       fp1        fp2       fp3    yi_drg   yi_pbo        y       int1
## 1 0.2665183 1.714478 -0.6931485 0.1199219  2.586166 1.698288 1.698288 0.5768541
## 2 0.2665183 1.714478 -0.6931485 0.1199219  4.350818 2.085088 2.085088 0.5768541
## 3 0.2665183 1.714478 -0.6931485 0.1199219  3.709400 1.629090 1.629090 0.5768541
## 4 0.2665183 1.714478 -0.6931485 0.1199219  3.711872 1.308231 1.308231 0.5768541
## 5 0.2665183 1.714478 -0.6931485 0.1199219  3.665005 1.779612 1.779612 0.5768541
## 6 0.2665183 1.714478 -0.6931485 0.1199219 11.696931 2.654913 2.654913 0.5768541
##       slop1       cov1       int2      slop2       cov2
## 1 0.0000000  0.0000000 -0.2587745  0.0000000  0.0000000
## 2 0.5768541  0.5768541 -0.2587745 -0.2587745 -0.2587745
## 3 1.1537082  2.3074164 -0.2587745 -0.5175490 -1.0350981
## 4 1.7305623  5.1916868 -0.2587745 -0.7763236 -2.3289707
## 5 2.3074164  9.2296654 -0.2587745 -1.0350981 -4.1403924
## 6 3.4611245 20.7667472 -0.2587745 -1.5526471 -9.3158828
```

where

- X1, X2 shows the value of two predictors

- tt presents the time in the trial

- w_drg and w_pbo are the true $\alpha'_{drg}x, \alpha'_{pbo}x$ values.

- (fd1, fd2, fd3) are the coefficients for the trajectory (intercept, slope, concavity) is the subject is in drug group.

- (fp1, fp2, fp3) are the coefficients for the trajectory (intercept, slope, concavity) is the subject is in placebo group.

- yi_drg and yi_pbo are the outcomes for drug treatment and placebo treatment

- trt is the group assignment and y is the observed outcome.

- X is the design matrix $X = (1, t, t^2), t = 0, 1, 2, 3, 4, 6, 8$

- int1 is the value of X1 $\times X[,1]$, slop1 is the value of X1 $\times X[,2]$, cov1 is the value of X1 $\times X[,3]$.

- int2 is the value of X2 $\times X[,1]$, slop2 is the value of X2 $\times X[,2]$, cov2 is the value of X2 $\times X[,3]$.

To fit the unrestricted LME, we have the formula as

```
formula_full
```

```
## [1] "y~1+ tt + I(tt^2) + int1 + slop1 + cov1 + int2 + slop2 + cov2 + (1+ tt + I(tt^2) |subj)"
```

The LME

```
dat_pbo = data[data$trt == 1, ]; rownames(dat_pbo) = NULL
dat_drg = data[data$trt == 2, ]; rownames(dat_drg) = NULL
```

```
fit_pbo_est_full = lmer(formula_full,data = dat_pbo, REML = FALSE)
fit_drg_est_full = lmer(formula_full,data = dat_drg, REML = FALSE)
```

The loglikelihood in the models

```
summary(fit_pbo_est_full)$logLik
```

```
## 'log Lik.' -1539.87 (df=16)
```

```
summary(fit_drg_est_full)$logLik
```

```
## 'log Lik.' -1507.694 (df=16)
```

To fit the GEM LME, we have the function as

```
fit_pbo_est_si = lmer(y ~ tt + I(tt^2) + w_pbo + w_pbo * tt +
                      w_pbo * I(tt^2) + (tt + I(tt^2) |subj),
                      data = dat_pbo, REML = FALSE)
fit_drg_est_si = lmer(y ~ tt + I(tt^2) + w_drg + w_drg * tt +
                       w_drg * I(tt^2) + (tt + I(tt^2)|subj),
                      data = dat_drg, REML = FALSE)
```

The loglikelihood in the models

```
summary(fit_pbo_est_si)$logLik
```

```
## 'log Lik.' -1542.624 (df=13)
```

```
summary(fit_drg_est_si)$logLik
```

```
## 'log Lik.' -1507.912 (df=13)
```

Therefore the test statistics is

```
chis = as.numeric(summary(fit_pbo_est_full)$logLik + summary(fit_drg_est_full)$logLik -
                (summary(fit_pbo_est_si)$logLik + summary(fit_drg_est_si)$logLik))
chis = chis*2
chis
```

```
## [1] 5.943638
```

The p value is

```
1-pchisq(chis, df= (3*(p-1)-p)*2)
```

```
## [1] 0.05121008
```

For different dimension p, the likelihood ratio test can be conducted and we can get p values as

If we use df $= 2 \times (3p - p - 3)$,

p	2	3	4	5	6	7	8	9	10	11
p-value	0.051	0.071	0.033	0.002	0.006	0.025	0.684	0.048	0.001	0

p	12	13	14	15	16	17	18	19	20	21
p-value	0.008	0.055	0.008	0.033	0	0.025	0	0	0	0

p	22	23	24	25	26	27	28	29	30
p-value	0	0	0.006	0	0	0	0.002	0	0

Most of the p values are less than 0.05. Therefore, we tend to reject H0, that they do not share the same α. However, the true model is the GEM model. The results do not consistant with the true scenario.

If we use df $= 2 \times (3p - 3)$,

p	2	3	4	5	6	7	8	9	10	11
p-value	0.43	0.476	0.355	0.081	0.186	0.432	0.995	0.639	0.157	0.04

p	12	13	14	15	16	17	18	19	20	21
p-value	0.443	0.787	0.51	0.758	0.171	0.766	0.201	0.016	0.177	0.268

p	22	23	24	25	26	27	28	29	30
p-value	0.335	0.091	0.734	0.142	0.118	0.021	0.674	0.1	0.026

Most of the p values are larger than 0.05. Therefore, we tend to accept H0, that they share the same α.