How to run a longitudinal GEE model with very large datasets in a reasonable amount of CPU time

Ellen Hertzmark and Donna Spiegelman

August 23, 2012

Abstract

This document contains instructions on how to run mixed (repeated measures) models for longitudinal data using a whole Channing cohort.

Keywords: SAS, mixed models, repeated measures

1 Motivation

Until now, people interested in longitudinal analysis with continuous outcomes have been sampling their data to make them runnable in PROC MIXED. This is NOT NECESSARY. In fact, with a bit of tweaking, PROC MIXED runs quite efficiently, even with a very large data set and a large number of repeated measures.

2 Setting up the data

Suppose you have the typical Channing dataset, with a record for each person-questionnaire cycle. It is already sorted by subject and time period.

If you have another type of dataset, you must sort it by subject and the index for the repeated measures.

If the data are sorted by the subject id, there is no need to make the subject a class variable. This saves a lot of memory when you

run the PROC MIXED.

Furthermore, in the example below we specify DDFM=BW (degrees of freedom method = Between-Within), which also makes things run faster.

Note that in the example below, where BMI is modeled in relation to protein intake, 49357 observations are deleted because of missing data (17109 with missing BMI or diet data in period 1, 17624 missing both in period 2, and 14624 missing both in period 3). Even though data are missing, it is important to keep all observations from subjects who have any data in the dataset, if the covariance structure is different at or between different times, such as when the working variance-covariance structure is unstructured (TYPE=UN), because they are needed to keep the place of each observation within the subject, so that the (1, 2) place in the covariance matrix will always be the relation between periods 1 and 2, and never between 1 and 3 (if 2 is missing) or between 2 and 3 (if 1 is missing).

We recommend using the empirical option to avoid requiring multivariate normality for valid inference.

3 Examples

Here is an example of models for the continuous outcome BMI with 3 time periods.

3.1 Random intercept and random slope for one predictor

First we specify a covariance with a random intercept and a random slope for timepd. The partial .saslog is shown.

```
how much memory a step used */
5
9
           data rs;
           infile indat;
10
           input id 1-6 bmi 8-18 aprot91a 20-25 timepd 27;
11
12
           proc sort data=rs; by id; run;
13
26
27
           title2 'random intercept, and slope for timepd';
28
           proc mixed data=rs;
29
           model bmi=aprot91a timepd/s ddfm=bw;
30
           random intercept timepd/type=un subject=id;
31
           run;
NOTE: 49357 observations are not included because of missing values.
NOTE: Convergence criteria met.
NOTE: The PROCEDURE MIXED printed pages 1-2.
NOTE: PROCEDURE MIXED used (Total process time):
     real time
                         20.18 seconds
                         14.98 seconds
     user cpu time
                         3.84 seconds
      system cpu time
     Memory
                                        8233k
     Page Faults
                                        210
     Page Reclaims
                                        0
     Page Swaps
     Voluntary Context Switches
                                        1116
     Involuntary Context Switches
                                        799
     Block Input Operations
                                        230
     Block Output Operations
                                        21403
```

So the first model, with one random slope, used about 19 seconds of (user+system) cpu and about 8 megabytes of memory. Here is the output.

/udd/stleh/helpme/yli/mixedmod.sas
random intercept, and slope for timepd

12:14 Wednesday, August 16, 2006

The Mixed Procedure

Model Information

| Data Set | | WORK.RS | |
|-----------|----------|---------|--|
| Dependent | Variable | bmi | |

Covariance Structure Unstructured

Subject Effect id
Estimation Method ML
Residual Variance Method Profile
Fixed Effects SE Method Empirical
Degrees of Freedom Method Between-Within

Dimensions

| Covariance | Parameters | 4 |
|---------------------|---------------|-------|
| ${\tt Columns\ in}$ | X | 3 |
| ${\tt Columns\ in}$ | Z Per Subject | 2 |
| Subjects | | 84073 |
| Max Obs Per | r Subject | 3 |

Number of Observations

| Number | of | ${\tt Observations}$ | Read | 252219 |
|--------|----|----------------------|----------|--------|
| Number | of | Observations | Used | 202862 |
| Number | of | Observations | Not Used | 49357 |

Iteration History

| Iteration | Evaluations | -2 Log Like | Criterion |
|-----------|-------------|-----------------|-----------|
| 0 | 1 | 1303435.3381153 | |

| 1 | 3 | 1049443.8409174 | 0.00071731 |
|---|---|-----------------|------------|
| 2 | 1 | 1049179.5513401 | 0.00001630 |
| 3 | 1 | 1049173.9505007 | 0.0000001 |
| 4 | 1 | 1049173.9469250 | 0.00000000 |

Convergence criteria met.

Covariance Parameter Estimates

| Cov Parm | Subject | Estimate |
|----------|---------|----------|
| UN(1,1) | id | 31.3619 |
| UN(2,1) | id | 0.05804 |
| UN(2,2) | id | 0.6954 |
| Residual | | 1.9588 |

Fit Statistics

| -2 Log Likelihood | 1049174 |
|--------------------------|---------|
| AIC (smaller is better) | 1049188 |
| AICC (smaller is better) | 1049188 |
| BIC (smaller is better) | 1049253 |

Null Model Likelihood Ratio Test

| DF | Chi-Square | Pr > ChiSq |
|----|------------|------------|
| 3 | 254261.39 | <.0001 |

/udd/stleh/helpme/yli/mixedmod.sas 12:14 Wednesday, August 16, 2006 2 random intercept, and slope for timepd

The Mixed Procedure

Solution for Fixed Effects

| | | Standard | | | |
|-----------|----------|----------|------|---------|---------|
| Effect | Estimate | Error | DF | t Value | Pr > t |
| _ | | | | | |
| Intercept | 21.5501 | 0.08191 | 82E3 | 263.10 | <.0001 |
| aprot91a | 0.05662 | 0.001273 | 82E3 | 44.47 | <.0001 |
| timepd | 0.5905 | 0.005225 | 12E4 | 113.02 | <.0001 |

Type 3 Tests of Fixed Effects

| Effect | Num DF | Den DF | F Value | Pr > F |
|----------|-----------|-----------|---------|--------|
| aprot91a | 1 | 82E3 | 1977.40 | <.0001 |
| timepd | 1 | 12E4 | 12773.9 | <.0001 |

3.2 Random intercepts and slopes for two predictors

Now we specify a covariance with a random intercept and random slopes for timepd and protein intake (aprot91a).

| 32 | |
|----|---|
| 33 | title2 'random intercept, random slopes for timepd and aprot91a'; |
| 34 | <pre>proc mixed data=rs method=ml empirical;</pre> |
| 35 | <pre>model bmi=aprot91a timepd/s ddfm=bw;</pre> |
| 36 | random intercept aprot91a timepd/type=un subject=id; |
| 37 | run; |

 ${\tt NOTE:}\ 49357\ {\tt observations}\ {\tt are}\ {\tt not}\ {\tt included}\ {\tt because}\ {\tt of}\ {\tt missing}\ {\tt values.}$

NOTE: Convergence criteria met.

NOTE: The PROCEDURE MIXED printed pages 3-4.

NOTE: PROCEDURE MIXED used (Total process time):

real time 27.25 seconds user cpu time 22.51 seconds system cpu time 3.69 seconds

Memory 10283k
Page Faults 0
Page Reclaims 0
Page Swaps 0
Voluntary Context Switches 1074
Involuntary Context Switches 1081
Block Input Operations 0
Block Output Operations 19391

This model, with 2 random slopes, used about 26 seconds of (user+system) cpu and about 10 megabytes of memory. The output is

/udd/stleh/helpme/yli/mixedmod.sas 12:14 Wednesday, August 16, 2006 random intercept, random slopes for timepd and aprot91a

The Mixed Procedure

Model Information

Data Set WORK.RS
Dependent Variable bmi

Covariance Structure Unstructured

Subject Effect id
Estimation Method ML
Residual Variance Method Profile
Fixed Effects SE Method Empirical
Degrees of Freedom Method Between-Within

Dimensions

Covariance Parameters 7
Columns in X 3
Columns in Z Per Subject 3
Subjects 84073

Number of Observations

| Number o | of | ${\tt Observations}$ | Read | 252219 |
|----------|----|----------------------|----------|--------|
| Number o | of | Observations | Used | 202862 |
| Number o | of | Observations | Not Used | 49357 |

Iteration History

| Iteration | Evaluations | -2 Log Like | Criterion |
|-----------|-------------|-----------------|------------|
| 0 | 1 | 1303435.3381153 | |
| 1 | 3 | 1048888.8981202 | 0.00074013 |
| 2 | 1 | 1048616.0334194 | 0.00001751 |
| 3 | 1 | 1048610.0144801 | 0.0000001 |
| 4 | 1 | 1048610.0102814 | 0.00000000 |

Convergence criteria met.

Covariance Parameter Estimates

| Cov Parm | Subject | Estimate |
|----------|---------|----------|
| UN(1,1) | id | 17.5010 |
| UN(2,1) | id | 0.08272 |
| UN(2,2) | id | 0.000735 |
| UN(3,1) | id | 0.6342 |
| UN(3,2) | id | -0.00861 |
| UN(3,3) | id | 0.6946 |
| Residual | | 1.9591 |

Fit Statistics

| -2 Log Likelihood | 1048610 |
|--------------------------|---------|
| AIC (smaller is better) | 1048630 |
| AICC (smaller is better) | 1048630 |
| BIC (smaller is better) | 1048723 |

Null Model Likelihood Ratio Test

| DF | Chi-Square | Pr > ChiSq |
|----|------------|------------|
| 6 | 254825.33 | <.0001 |

/udd/stleh/helpme/yli/mixedmod.sas 12:14 Wednesday, August 16, 2006 4 random intercept, random slopes for timepd and aprot91a

The Mixed Procedure

Solution for Fixed Effects

| | | Standard | | | |
|-----------|----------|----------|------|---------|---------|
| Effect | Estimate | Error | DF | t Value | Pr > t |
| | | | | | |
| Intercept | 21.6098 | 0.08011 | 82E3 | 269.75 | <.0001 |
| aprot91a | 0.05572 | 0.001244 | 82E3 | 44.80 | <.0001 |
| timepd | 0.5905 | 0.005222 | 12E4 | 113.07 | <.0001 |

Type 3 Tests of Fixed Effects

| Effect | Num DF | Den DF | F Value | Pr > F |
|----------|-----------|-----------|---------|--------|
| aprot91a | 1 | 82E3 | 2007.12 | <.0001 |
| timepd | 1 | 12E4 | 12785.5 | <.0001 |

4 Credits

Written by Donna Spiegelman and Ellen Hertzmark for the Channing Lab. Questions and comments may be directed to Ellen Hertzmark, stleh@channing.harvard.edu, (617) 432-4597.