**Fitting mixed effects models in R**

There are several packages available for fitting mixed effects models in R; in this course we will use two: nlme and lme4. The two packages were designed to do different things, though there is some overlap. Here I discuss a few of the similarities and differences. Please note that this is not intended to replace the (very well documented) manuals of either package.

The lme() function (nlme) is “nicer” for fitting two-level models because you can get (approximate, Wald) p-values. (Please note that there is a huge controversy about whether or not these should be used, but: they do correspond with the p-values one gets out of SPSS or SAS.) Covariance pattern models are also easier to fit with lme() (in fact, I do not know how to fit them with lmer()).

I find lmer() function (lme4) to be more intuitive for fitting three-level linear models. And the nlme package does not have the possibility of fitting *generalized* linear mixed effects models, so here we need the glmer() function in the lme4 package.

|  |  |  |
| --- | --- | --- |
|  | nlme | lme4 |
| Description (manual) | “Fit and compare *Gaussian* linear and nonlinear mixed-effects models.” | “Fit *linear and generalized linear* mixed-effects models.” |
| Function for *linear* mixed effects models | lme() function, produces objects of class “lme” | lmer() function, produces objects of class “mer” |
| Function for models with correlated errors (CPMs) (Day 2) | gls() |  |
| Function for *generalized* linear mixed effects models (Day 4) |  | glmer() |
| LME function usage | lme(fixed, data, random, correlation, weights, subset, method,  na.action, control, contrasts = NULL, keep.data = TRUE) | lmer(formula, data = NULL, REML = TRUE, control = lmerControl(), start = NULL, verbose = 0L, subset, weights, na.action, offset, contrasts = NULL, devFunOnly = FALSE, ...) |
| Wald DF, p-values | Gives approx DF & Wald p-values | No DF, p-values |
| Confidence intervals for coefficients | intervals() function in nlme package works with lme class objects, gives approximate (Wald) CIs | confint() function in lme4 package works with mer class objects, gives profile likelihood CIs |

**Examples** of linear mixed effects models fit in both packages. (Please note that some output has been removed or truncated (in numbers after the decimal) to get it to fit in the tables below.)

Two-level model (London schools example, “complete” model with child- and school-level variables from lecture), with 95% confidence intervals:

|  |  |
| --- | --- |
| nlme | lme4 |
| > sch.lme.4 <- lme(**fixed**=normexam ~standlrt + factor(gender)+ factor(schgend) + factor(schav), **random**=~standlrt | school, data=london, **method**="ML") | > sch.lmer.4 <- lmer(normexam ~standlrt + factor(gender)+ factor(schgend) + factor(schav) **+**  **(standlrt | school)**, data=london, **REML**=FALSE) |
| > summary(sch.lme.4)  Value Std.Err DF t-value p-value  (Intercept) -0.2647 0.08159 3992 -3.244 0.0012  standlrt 0.5515 0.02006 3992 27.482 0.0000  factor(gender)1 0.1671 0.03385 3992 4.937 0.0000  factor(schgend)2 0.1869 0.09777 60 1.912 0.0606  factor(schgend)3 0.1570 0.07780 60 2.018 0.0481  factor(schav)2 0.0668 0.08534 60 0.783 0.4363  factor(schav)3 0.1742 0.09876 60 1.764 0.0827 | > summary(sch.lmer.4)  Estimate Std. Error t value  (Intercept) -0.2647 0.08152 -3.248  standlrt 0.5515 0.02005 27.506  factor(gender)1 0.1671 0.03382 4.942  factor(schgend)2 0.1869 0.09769 1.914  factor(schgend)3 0.1570 0.07774 2.020  factor(schav)2 0.0668 0.08528 0.784  factor(schav)3 0.1742 0.09868 1.766 |
| > intervals(sch.lme.4)  Approximate 95% confidence intervals  Random Effects:  Level: school  lower upper  sd((Intercept)) 0.215731 0.32805  sd(standlrt) 0.089186 0.16485  cor((Intercept),standlrt) 0.119052 0.75175  Within-group standard error:  lower upper  0.7255056 0.7583129  (Intercept) -0.424598124 -0.1049332  standlrt 0.512238511 0.5908655  factor(gender)1 0.100821935 0.2334407  factor(schgend)2 -0.008444022 0.3823808  factor(schgend)3 0.001513856 0.3125173  factor(schav)2 -0.103688945 0.2374648  factor(schav)3 -0.023116161 0.3716462 | > confint(sch.lme.4\_lmer)  Computing profile confidence intervals  2.5 % 97.5 %  .sig01 0.2169442740 0.33052844  .sig02 0.1302120618 0.76803678  .sig03 0.0866341406 0.16259019  .sigma 0.7256200612 0.75844018  (Intercept) -0.4325035512 -0.09853867  standlrt 0.5109739060 0.59117563  factor(gender)1 0.1007931950 0.23346717  factor(schgend)2 -0.0073268125 0.38149357  factor(schgend)3 0.0007774215 0.31257546  factor(schav)2 -0.1072451061 0.24419861  factor(schav)3 -0.0405219334 0.39009438 |

Three-level model (diastolic blood pressure trial example, longitudinal measurements within patients within centers):

|  |  |
| --- | --- |
| nlme\* | lme4 |
| > bp.3l.lme <- lme(fixed=dbp ~ visit + factor(treat)+ visit\*factor(treat) + dbp1, random=list(center=~1, patient = ~visit), data=bp, method="ML") | > bp.3l.lmer <- lmer(dbp ~ visit + factor(treat)+ visit\*factor(treat) + dbp1 + (visit|patient) + (1|center), data=bp, REML=F) |
| > summary(bp.3l.lme)  Linear mixed-effects model fit by maximum likelihood  Data: bp  AIC BIC logLik  7492.422 7552.371 -3734.211  Random effects:  Formula: ~1 | center  (Intercept)  StdDev: 2.111865  Formula: ~visit | patient %in% center  Structure: General positive-definite, Log-Cholesky parametrization  StdDev Corr  (Intercept) 7.111208 (Intr)  visit 0.699357 -0.549  Residual 5.749893  Fixed effects: dbp ~ visit + factor(treat) + visit \* factor(treat) + dbp1  Value Std.Err DF t-value  (Intercept) 47.5547 8.9224 801 5.3298  visit -0.5796 0.1565 801 -3.7020  factor(treat)B -1.5914 1.5989 256 -0.9952  factor(treat)C -3.2687 1.5867 256 -2.0600  dbp1 0.4795 0.0856 256 5.5998  visit:factor(treat)B 0.0563 0.2219 801 0.2540  visit:factor(treat)C 0.0425 0.2189 801 0.1941 | > summary(bp.3l.lmer)  Linear mixed model fit by maximum likelihood ['lmerMod']  Formula: dbp ~ visit + factor(treat) + visit \* factor(treat) + dbp1 + (visit | patient) + (1 | center)  Data: bp  AIC BIC logLik deviance df.resid  7492.4 7552.4 -3734.2 7468.4 1080  Random effects:  Groups Name Variance Std.Dev. Corr  patient (Intercept) 50.5693 7.1112  visit 0.4891 0.6994 -0.55  center (Intercept) 4.4599 2.1119  Residual 33.0613 5.7499  Fixed effects:  Estimate Std. Error t value  (Intercept) 47.55472 8.89378 5.347  visit -0.57966 0.15608 -3.714  factor(treat)B -1.59140 1.59384 -0.998  factor(treat)C -3.26870 1.58165 -2.067  dbp1 0.47958 0.08537 5.618  visit:factor(treat)B 0.05638 0.22120 0.255  visit:factor(treat)C 0.04252 0.21829 0.195 |

\*Note that it is critical in a three-level model in nlme that you list the random effect(s) for the *highest* level first in the random option (in this example: center), and then for the next level (patient, nested within center). If you reverse these, R will assume centers are nested within patients – and you will get very odd results!