```
> library(Stat5303)
> counts <- read.table("kuehl3.dat.txt",header=TRUE)
```

We have triplicate particle counts on each of three filters from each of two manufacturers for a total of 18 counts.

```
> counts
   manu filter partcount
1     1      1      1.12
2     1      1      1.10
3     1      1      1.12
4     1      2      0.16
5     1      2      0.11
6     1      2      0.26
7     1      3      0.15
8     1      3      0.12
9     1      3      0.12
10    2      1      0.91
11    2      1      0.83
12    2      1      0.95
13    2      2      0.66
14    2      2      0.83
15    2      2      0.61
16    2      3      2.17
17    2      3      1.52
18    2      3      1.58
> counts <- within(counts, {manu <- as.factor(manu);filter<-as.factor(filter)})
> partcount.lmer <- lmer(partcount ~ 1 + (1|manu/filter),data=counts)
```

There are a couple of ways to set up the nested model (filter nested in manufacturer). The first is with slash notation: (1|manu/filter) means do the random effects (here just the intercept or constant) for manufacturer and for filter nested in manufacturer. In effect, the (1|manu/filter) expands to (1|manu) + (1|manu:filter).

```
> summary(partcount.lmer)
```

We get separate estimates for each of the three random effects as usual.

```
Linear mixed model fit by REML
Formula: partcount ~ 1 + (1 | manu/filter)
   AIC   BIC logLik deviance REMLdev
 15.41 18.97 -3.705    6.955   7.411
Random effects:
 Groups      Name        Variance Std.Dev.
 filter:manu (Intercept) 0.303311 0.55074
 manu        (Intercept) 0.103730 0.32207
 Residual                0.025389 0.15934
Number of obs: 18, groups: filter:manu, 6; manu, 2

Fixed effects:
            Estimate Std. Error t value
(Intercept)   0.7956     0.3222   2.469
```

> **`lmer(partcount ~ 1 + (1|manu) + (1|manu:filter),data=counts)`**

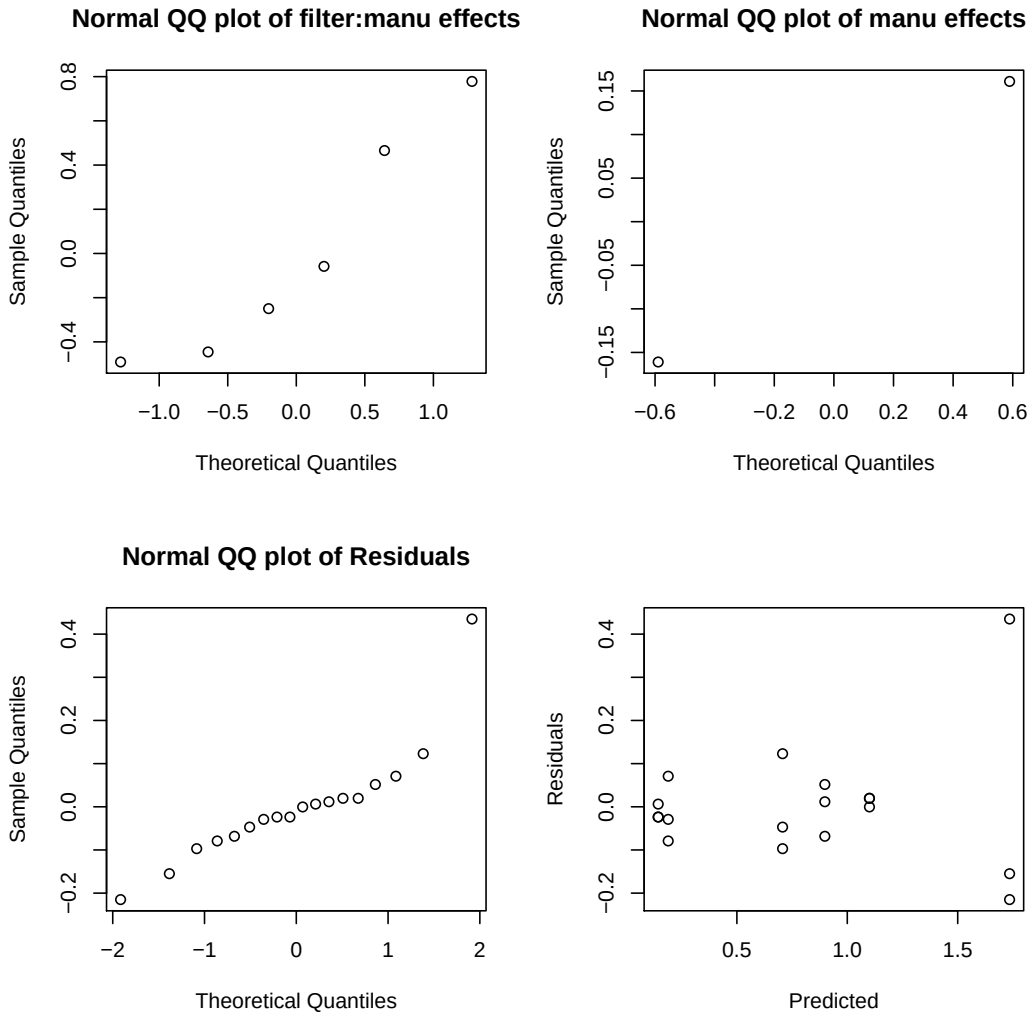
The other way to do it is to specifically set up the filter (nested in manufacturer) to have a separate effect for each manufacturer by filter combination. This fits the same model and gives the same output.

> **`par(mfrow=c(2,2))`**

The lmer.plot command is going to make four plots, one for each explicit random effect and two for residuals. I'm just saying to arrange them 2 by 2.

> **`lmer.plot(partcount.lmer)`**

And now we see a problem. There is increasing variability in the residuals. I know that the variance of counts can often be stabilized by square roots, so I'll try that. An alternative is to fit the random model as if it were a fixed model and do Box Cox. That is not "right," but it should help.



> **`tmp <- lm(partcount ~ manu/filter,data=counts)`**

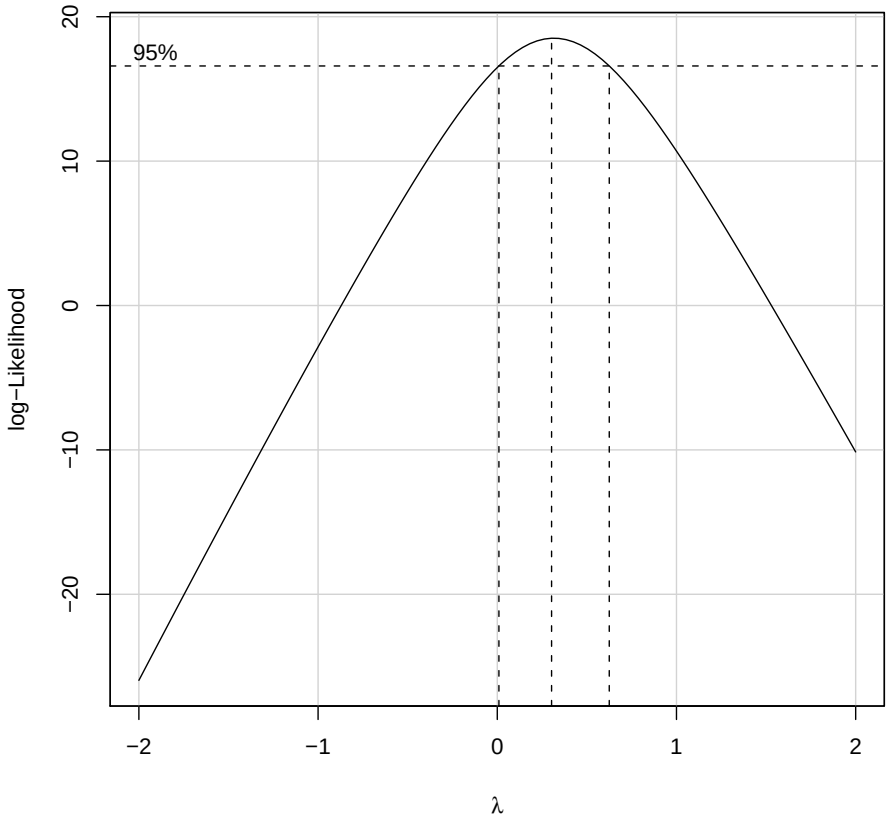
Looking at the residuals from the fixed effects model is not the same thing as looking at the residuals from the random effects model, but it should usually be close enough to be helpful.

> **`par(mfrow=c(1,1))`**

Put the graphics back to 1 by 1.

> **`boxCox(tmp)`**

Best looks like power .25 or .3, but .5 is well within the interval and is suggested by theory, so we'll use it.

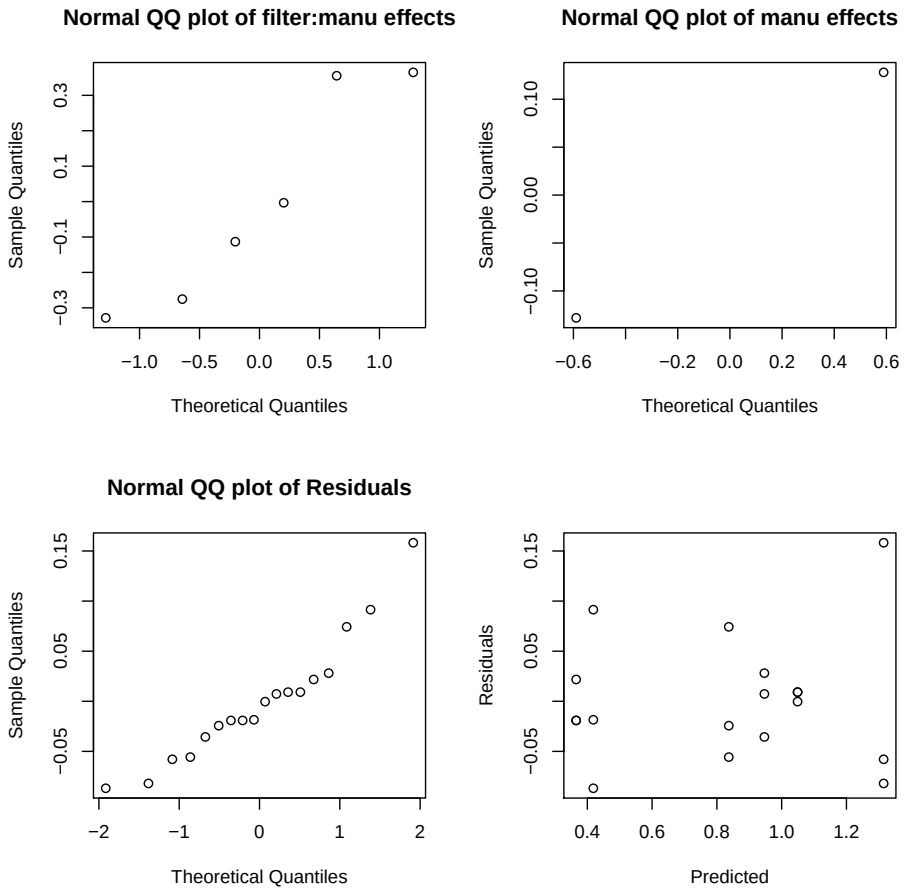


> **`rpc.lmer <- lmer(sqrt(partcount)~1 + (1|manu/filter),data=counts)`**

Let's try the square root. Note, it is possible to do the transformation within the lmer() statement.

```
> par(mfrow=c(2,2))
> lmer.plot(rpc.lmer)
```

OK, the residuals look better, so we'll work with the square root counts.




```
> par(mfrow=c(1,1))
> rpc.lmer
```

Filter variability is the largest (at about 20 times residual), and manufacturer variability is in between (at about 10 times residual). You would think those would both be very significant, but we only have two manufacturers (one df between), so we have very little information about manufacturer. We will see that manu is not significant.

```
Linear mixed model fit by REML
Formula: rootpartcount ~ 1 + (1 | manu/filter)
    AIC    BIC logLik deviance REMLdev
 -8.484 -4.922  8.242   -17.78  -16.48
Random effects:
 Groups      Name        Variance  Std.Dev.
 filter:manu (Intercept) 0.1054262 0.324694
 manu        (Intercept) 0.0543449 0.233120
 Residual                0.0053046 0.072833
Number of obs: 18, groups: filter:manu, 6; manu, 2

Fixed effects:
            Estimate Std. Error t value
(Intercept)   0.8219     0.2122   3.873
```

```
> rpc.manuonly.lmer <- lmer(sqrt(partcount) ~ 1 + (1|manu),data=counts)
```

To test terms using exactRLRT, we need the full model, the model with only the term of interest, and the full model less the term of interest. Since there are only two terms other than error in the model, the "only the term of interest" models are also the "without the term of interest" models for the other term.

```
> rpc.filteronly.lmer <- lmer(sqrt(partcount) ~ 1 + (1|manu:filter),data=counts)
> exactRLRT(rpc.filteronly.lmer,rpc.lmer,rpc.manuonly.lmer)
```

Here we test filter, and it is highly significant.

```
simulated finite sample distribution of RLRT.  (p-value based
on 10000 simulated values)

data:
RLRT = 27.8483, p-value < 2.2e-16
```

```
> exactRLRT(rpc.manuonly.lmer,rpc.lmer,rpc.filteronly.lmer)
```

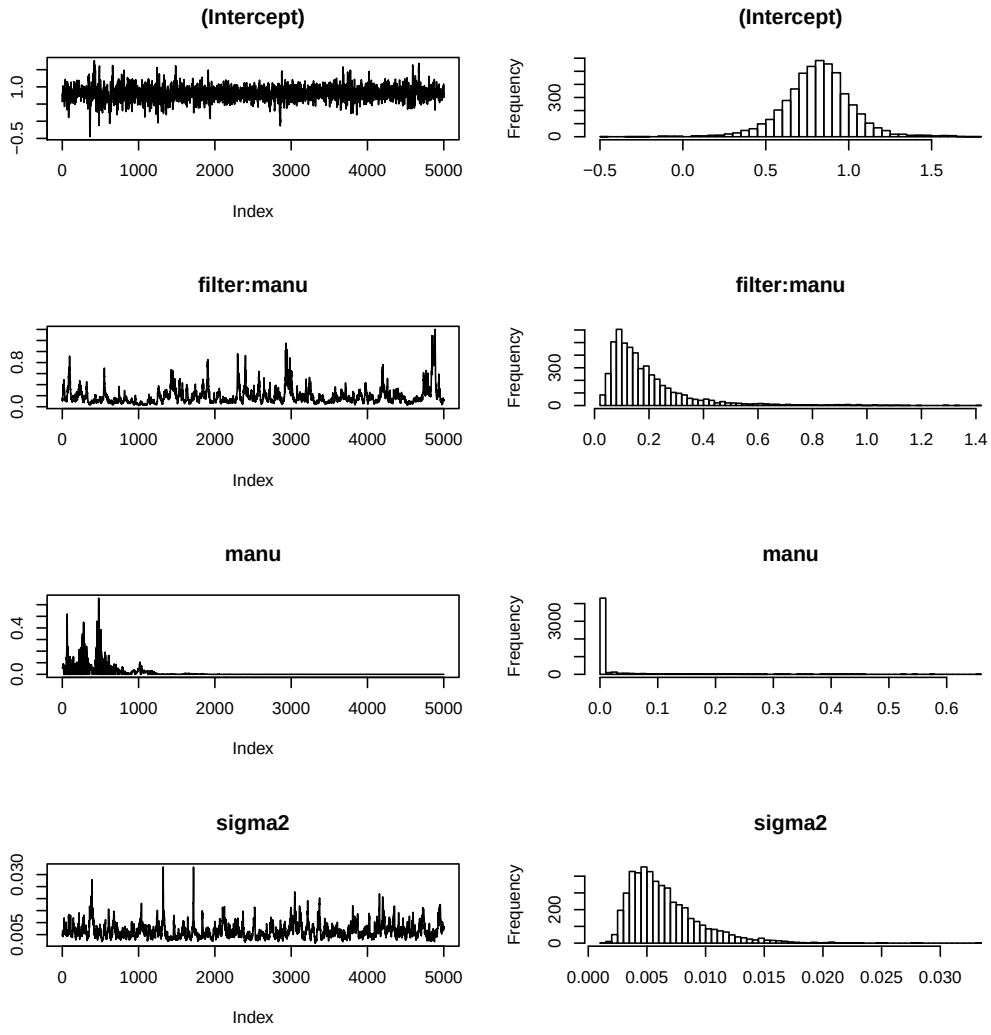
Here we test manufacturer, and it is not significant. As a point of comparison, these results agree very will with the old school way of doing things.

```
simulated finite sample distribution of RLRT.  (p-value based
on 10000 simulated values)

data:
RLRT = 0.4033, p-value = 0.1535
> rpc.mcmc5 <- lmer.mcmc(rpc.lmer,50000)
```

Let's get some MCMC samples to look at parameters.

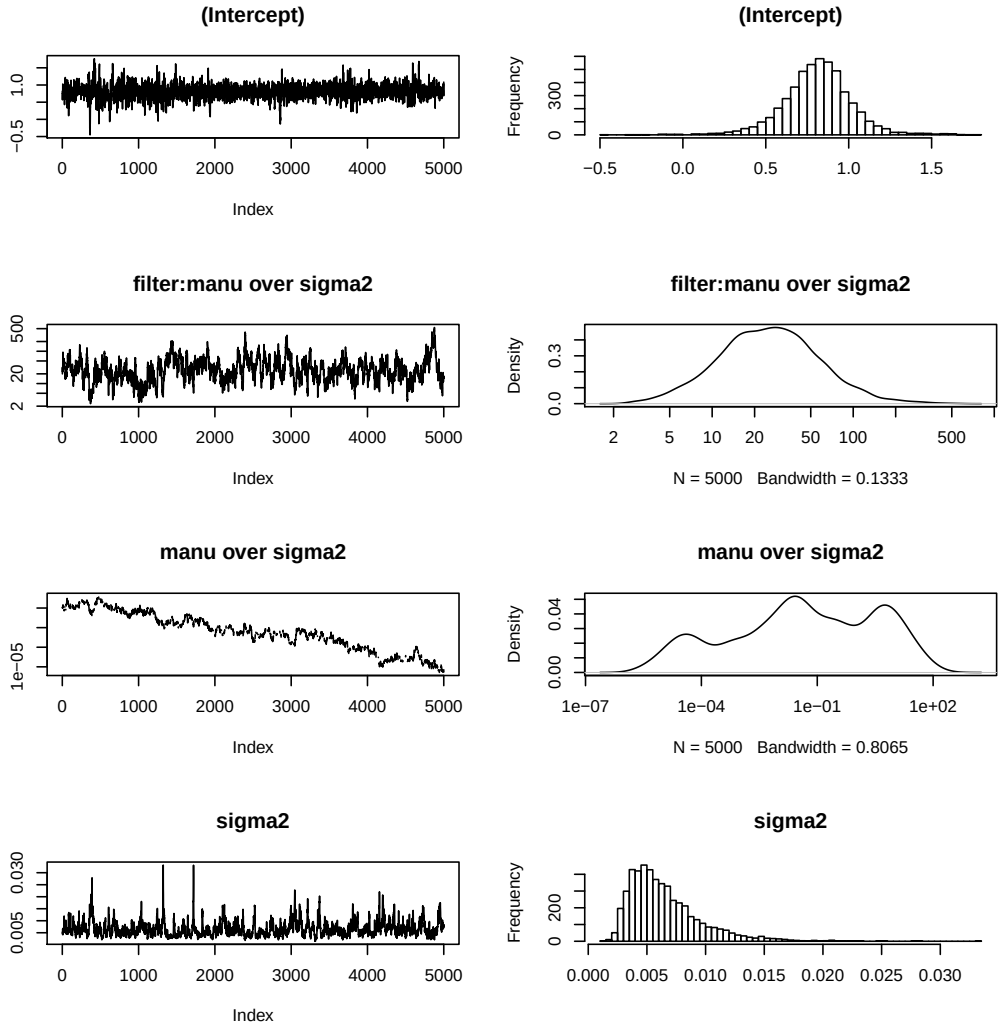
```
> par(mfrow=c(4,2))
> lmer.mcmc.plots(rpc.mcmc5)
```



> **lmer.mcmc.plots(rpc.mcmc5,log=TRUE)**

The plots look better yet if you plot the log of the ratio of a variance component to the error variance. Filter is fairly stable, and the manufacturer component is just going to zero, with gaps where the value is exactly zero (log of 0 not being defined). Witness the warning (since it only plots every tenth value, almost half of the values are zero).

```
Warning message:
In xy.coords(x, y, xlabel, ylabel, log) :
  2309 y values <= 0 omitted from logarithmic plot
```



> **lmer.mcmc.intervals(rpc.mcmc5)**

Here are the intervals. Zero is in the interval for manufacturer, but it could be big.

```
                lower       median      upper          SE
(Intercept) 0.373615419 8.177015e-01 1.21274913 0.210405186
filter:manu 0.043123936 1.437820e-01 0.62863391 0.152003545
manu        0.000000000 2.393180e-07 0.12465288 0.044364959
sigma2      0.002691776 5.779265e-03 0.01475100 0.003142901
```

```
> #
```

We can also get intervals for functional combinations of these variables. For example, suppose that we want the correlation between two observations on the same filter. These observations would share the same random manufacturer and filter random effects (α_i and $\beta_{j(i)}$, but they would have their own error ϵ_{ijk}. Thus the correlation would be $(\sigma^2_\alpha + \sigma^2_\beta)/(\sigma^2_\alpha + \sigma^2_\beta + \sigma^2)$.
What we do is just produce the same functional combination of the variables from the MCMC output, and then find the middle 95 (or whatever) percent.

```
> m <- rpc.mcmc5$mcmcout
```

There is a component in the output of lmer.mcmc() called mcmcout. The component is a matrix with one row for every tenth MCMC trial and one column for every parameter.

```
> dim(m)
```

We had 50,000 MCMC reps, so 5,000 rows in m. There are four parameters (the intercept and three variance components filter:manu, manu, and sigma2), so m has four columns.

```
[1] 5000    4
```

```
>colnames(rpc.mcmc5$mcmcout)
```

If you need a reminder about the order of the columns, look at the column labels.

```
[1]  "(Intercept)"  "filter:manu"  "manu"       "sigma2"
```

```
> ratio <- (m[,2]+m[,3])/(m[,2]+m[,3]+m[,4])
```

The ratio we are looking for is the sum of the second and third columns (filter:manu and manu) divided by the sum of the last three columns (all the variance components).

```
> .025*5000
```

For a 95% confidence interval we're going to want to go in 2.5% on each end, so we'll want the 125th smallest and the 125th biggest ratio.

```
[1] 125
> ratio.sorted <- sort(ratio)
```

Sort the ratios.

```
> ratio.sorted[c(125,5000-125)]
```

Get 125th biggest and smallest for our interval, which runs from .88 to .996.
As it happens, the smallest ratio occurred on simulation 2361, and the largest on simulation 35951, but that is not very useful.

```
     2361     35951
0.8816339 0.9965386
```

```
> rpcb.lmer <- lmer(sqrt(partcount) ~ manu + (1|manu:filter),data=counts)
```

What if there really are only two manufacturers? In that case we are hardly taking a random sample, we are looking at all of them. We should now fit manufacturer as a fixed effect, but filters would still be random nested in manufacturer.

```
> summary(rpcb.lmer)
```

Note that we have a fixed coefficient for the first manufacturer, and only random effects for filter and residuals. In this nicely balanced case the error and filter estimated effects are the same as in the fully random model.

```
Linear mixed model fit by REML
Formula: rootpartcount ~ manu + (1 | manu:filter)
    AIC   BIC logLik deviance REMLdev
 -8.221 -4.66   8.11   -20.72  -16.22
Random effects:
 Groups      Name        Variance  Std.Dev.
 manu:filter (Intercept) 0.1054262 0.324694
 Residual                0.0053046 0.072833
Number of obs: 18, groups: manu:filter, 6

Fixed effects:
            Estimate Std. Error t value
(Intercept)   0.8219     0.1337   6.149
manu1        -0.2122     0.1337  -1.588

Correlation of Fixed Effects:
      (Intr)
manu1 0.000
```

```
> anova(rpcb.lmer)
```

anova() for an lmer model with fixed effects gives an F test statistic for each fixed term. Unfortunately, it doesn't give a denominator df and thus gives no p-value. We would get a p-value if we had used lme() instead of lmer(). The issue is that it is easier to get an appropriate denominator degrees of freedom for these tests when there is only nesting of random effects. lme() only does nesting, so it gives a denominator df. lmer() does crossing as well as nesting, and lmer() does not try to get a denominator df, even in cases where there is only nesting.

```
Analysis of Variance Table
     Df   Sum Sq  Mean Sq F value
manu  1 0.013373 0.013373  2.5209
```

```
> rpcb.mcmc5 <- lmer.mcmc(rpcb.lmer,50000)
```

Do the MCMC.

```
> lmer.mcmc.anova(rpcb.mcmc5)
```

I have written a function that will take the MCMC output and do an "anova" on the fixed effect.

In the "old school" analysis, the t-value for manu1 we saw above (-1.588) would have 4 degrees of freedom. Computing a two-sided p-value with that df gives us 0.19, which is just about what we got here.

```
                chisq Df MC p-value
(Intercept) 18.818904  1     0.0034
manu         1.315096  1     0.2018
```

```
> lmer.KR.anova(rpcb.lmer)
```

I also have another testing method for fixed effects that uses some approximations due to Kenward and Rogers. KR was designed to give approximate results that are familiar and comfortable and will usually agree with "old school" approaches in simple cases.

```
           F df1 df2   p-value
manu 2.520925   1   4 0.1875383
```

```
> detach("package:lme4")
```

Let's look at what we can do using lme instead of lmer. We'll first get rid of the lme4 package, then we'll load in the nlme package. (I think lme4 and nlme sometimes step on each others toes.)

```
> library(nlme)
> filterinmanu <- with(counts,join(manu,filter))
```

We will for the moment treat manufacturer as fixed. lme() is happy to work with nested random factors, but it won't cross them. So in order to get something like manu:filter we need to combine it directly. The join function makes a new factor combining all the levels of two factors.

```
> rpc.lme <- lme(rootpartcount ~ manu,random=~1|filterinmanu,data=counts)
```

When using lme you first describe the fixed parts like in a fixed only model, and then you put the random parts in a separate argument. Note that in the random= argument there is no "response" on the left hand side of the tilde. Don't ask me why.

```
> summary(rpc.lme)
```

The parameter estimates and other outputs are the same here as they were for the lmer model, but lme is willing to give a p-value for fixed effects.

```
Linear mixed-effects model fit by REML
 Data: NULL
        AIC       BIC   logLik
  -8.221371 -5.131016 8.110685

Random effects:
 Formula: ~1 | filterinmanu
        (Intercept)   Residual
StdDev:    0.324694 0.07283274

Fixed effects: rootpartcount ~ manu
                Value Std.Error DF   t-value p-value
(Intercept)  0.821899 0.1336628 12  6.149050  0.0000
manu1       -0.212222 0.1336628  4 -1.587742  0.1875
 Correlation:
      (Intr)
manu1 0

Standardized Within-Group Residuals:
       Min         Q1        Med         Q3        Max
-1.1728581 -0.4687896 -0.1102852  0.2743776  2.1534105

Number of Observations: 18
Number of Groups: 6
> anova(rpc.lme)
```

lme() is willing to have a go at p-values for testing fixed terms (but recall that it only handles nested chains of random terms).

```
            numDF denDF  F-value p-value
(Intercept)     1    12 37.81081  <.0001
manu            1     4  2.52093  0.1875
```

```
> detach("package:nlme");attach(lme4)
```

Let's get back to lme4.

```
> soils <- read.table("kuehl5.dat.txt",header=TRUE)
```

Data from problem 5-7 of Kuehl (1994 Duxbury). Fifteen fields are chosen at random. Two subsections are chosen at random from each field. Soil porosity is measured at a random location of each subsection; some subsections are measured at two locations.
Field and subsection are random, with subsection nested in field. The data set is not balanced.

```
> soils <- within(soils, {field <- as.factor(field);
 section <- as.factor(section);sect <- as.factor(sect)})
```

```
> soils
```

Note that the variable section enumerates all the sections, but the variable sect is 1 or 2 within each field.

```
   field section sect porosity
1      1       1    1    3.846
2      1       1    1    3.712
3      1       2    2    5.629
4      1       2    2    2.021
5      2       3    1    5.087
6      2       4    2    4.621
7      3       5    1    4.411
8      3       6    2    3.357
9      4       7    1    3.991
10     4       8    2    5.766
11     5       9    1    5.677
12     5      10    2    3.333
13     6      11    1    4.355
14     6      11    1    6.292
15     6      12    2    4.940
16     6      12    2    4.810
17     7      13    1    2.983
18     7      14    2    4.396
19     8      15    1    5.603
20     8      16    2    3.683
21     9      17    1    5.942
22     9      18    2    5.014
23    10      19    1    5.143
24    10      20    2    4.061
25    11      21    1    3.835
26    11      21    1    2.964
27    11      22    2    4.584
28    11      22    2    4.398
29    12      23    1    4.193
30    12      24    2    4.125
31    13      25    1    3.074
32    13      26    2    3.483
33    14      27    1    3.867
34    14      28    2    4.212
35    15      29    1    6.247
36    15      30    2    4.730
```

```
> fit1 <- lmer(porosity~1+(1|field/sect),data=soils)
```

Fit the model with sect nested within field.

```
> fit2 <- lmer(porosity~1+(1|field) + (1|section),data=soils)
```

Fit the model with field and section. Since section enumerates all the sections individually, we don't need to do "nesting" in the model. We'll get the same results.

```
> fit1
```

There is some evidence of field to field variabilty, but the section within field is estimated at zero.

```
Linear mixed model fit by REML
Formula: porosity ~ 1 + (1 | field/sect)
   AIC   BIC logLik deviance REMLdev
 110.6 116.9 -51.28    100.9   102.6
Random effects:
 Groups     Name        Variance Std.Dev.
 sect:field (Intercept) 0.000000 0.00000
 field      (Intercept) 0.059483 0.24389
 Residual               0.935989 0.96747
Number of obs: 36, groups: sect:field, 30; field, 15

Fixed effects:
            Estimate Std. Error t value
(Intercept)   4.4037     0.1741   25.29
```

```
> fit2
```

As hoped, same results this way.

```
Linear mixed model fit by REML
Formula: porosity ~ 1 + (1 | field) + (1 | section)
   AIC   BIC logLik deviance REMLdev
 110.6 116.9 -51.28    100.9   102.6
Random effects:
 Groups   Name        Variance Std.Dev.
 section  (Intercept) 0.000000 0.00000
 field    (Intercept) 0.059483 0.24389
 Residual             0.935989 0.96747
Number of obs: 36, groups: section, 30; field, 15

Fixed effects:
            Estimate Std. Error t value
(Intercept)   4.4037     0.1741   25.29
```

```
> fit.nofield <- lmer(porosity ~ 1 + (1|field:sect),data=soils)
> fit.onlyfield <- lmer(porosity ~ 1 + (1|field),data=soils)

> exactRLRT(fit.onlyfield,fit1,fit.nofield)
```

Test of field effect is not significant.

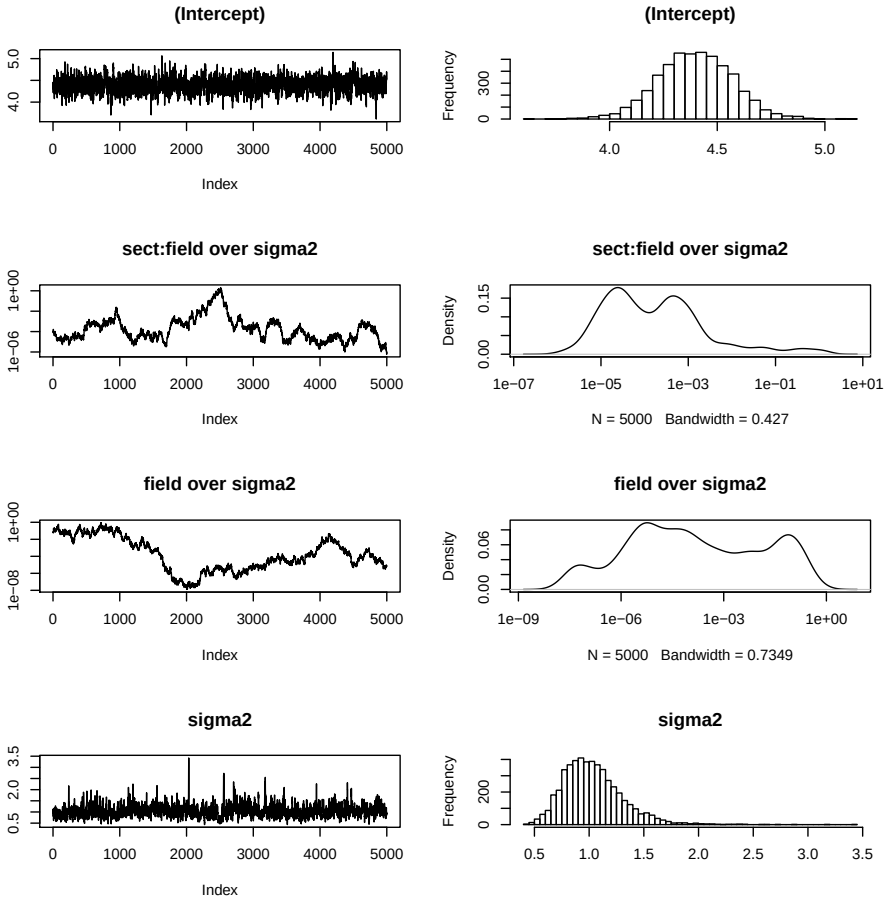
```
simulated finite sample distribution of RLRT.  (p-value based
on 10000 simulated values)

data:
RLRT = 0.1197, p-value = 0.3388
```

```
> fit1.mcmc <- lmer.mcmc(fit1,50000)
> lmer.mcmc.plots(fit1.mcmc,log=TRUE)
```

Even 50,000 is not enough for this to have settled down entirely. Lot's of zeros showing up.

```
Warning messages:
1: In xy.coords(x, y, xlabel, ylabel, log) :
  2524 y values <= 0 omitted from logarithmic plot
2: In xy.coords(x, y, xlabel, ylabel, log) :
  2348 y values <= 0 omitted from logarithmic plot
```



```
> lmer.mcmc.intervals(fit1.mcmc)
```

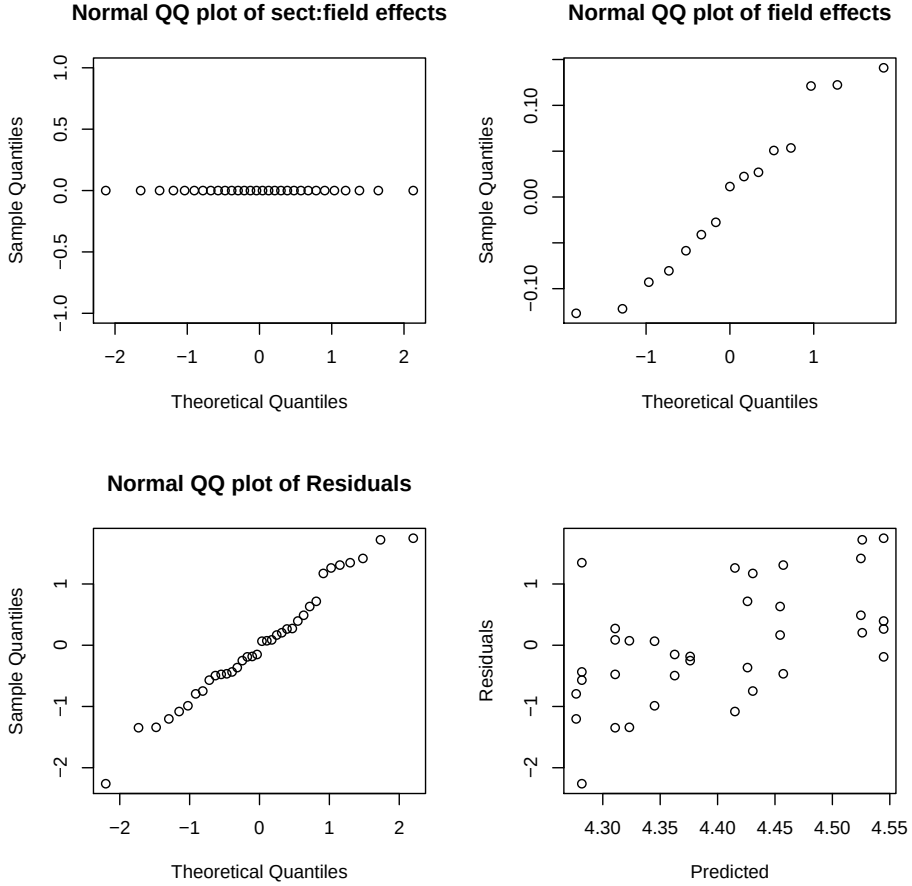
When we look at the intervals, they show the section and field variances not significantly different from zero.

```
                lower       median      upper         SE
(Intercept) 4.0429291 4.397537e+00 4.75294137 0.17593126
sect:field  0.0000000 0.000000e+00 0.08718555 0.03057076
field       0.0000000 1.497799e-10 0.03423929 0.01448301
sigma2      0.6527158 1.014978e+00 1.69588286 0.26718021
```

```
> par(mfrow=c(2,2))
> lmer.plot(fit1)
```

What the heck?!! Look at that last plot. It looks all the world like the field effects didn't really pick up al of the field to field variation, because there is still some trend in the residuals.

Well, guess what? In some cases, such as this one, random effects can be "shrunk" back towards zero. This happens more when the variance of the random effect is small compared to the error variance. In this case, residual variance is much larger than field variance, and field variance and and its random effects are being shrunk towards zero. This shows up in the residual plot as trend: negative random effects aren't negative enough (at least by what we're used to) and positive random effects aren't positive enough.



```
> fit3 <- lmer(porosity ~ field + (1|section),data=soils)
```

OK, now suppose that we are only worried about these 15 fields, and we're not thinking of them as sampled from some larger population. In this case, we would treat field as fixed. Note, we could also use (1|field:sect) for the random term.

```
> fit3
```

Section variance is still estimated at zero, but we now have individual estimates for the fields.

```
Linear mixed model fit by REML
Formula: porosity ~ field + (1 | section)
   AIC   BIC logLik deviance REMLdev
 110.8 137.7 -38.41     81.6   76.81
Random effects:
 Groups   Name        Variance Std.Dev.
 section  (Intercept) 0.00000  0.000
 Residual             0.96827  0.984
Number of obs: 36, groups: section, 30

Fixed effects:
            Estimate Std. Error t value
(Intercept)  4.42307    0.17043  25.952
field1      -0.62107    0.48871  -1.271
field2       0.43093    0.66980   0.643
field3      -0.53907    0.66980  -0.805
field4       0.45543    0.66980   0.680
field5       0.08193    0.66980   0.122
field6       0.67618    0.48871   1.384
field7      -0.73357    0.66980  -1.095
field8       0.21993    0.66980   0.328
field9       1.05493    0.66980   1.575
field10      0.17893    0.66980   0.267
field11     -0.47782    0.48871  -0.978
field12     -0.26407    0.66980  -0.394
field13     -1.14457    0.66980  -1.709
field14     -0.38357    0.66980  -0.573
...
```

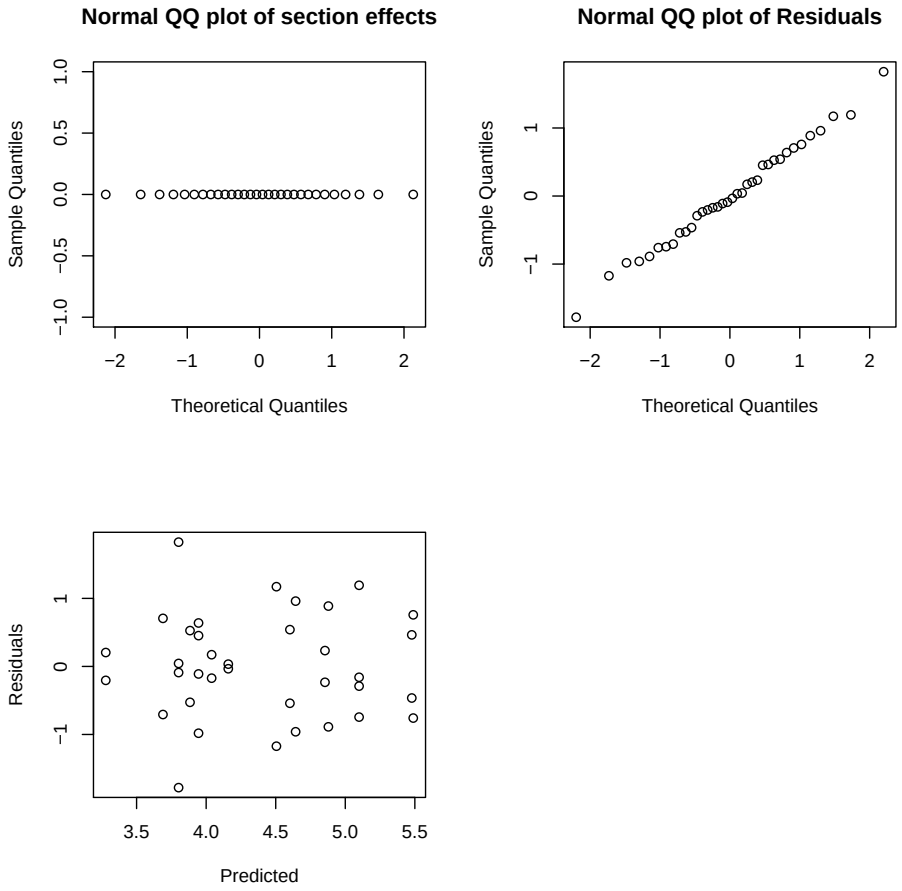
```
> fit2@ranef
```

Although we don't usually look at the actual estimated random effects, we can get them. For fit2, the first 30 (for section) are all zero, then we see the next 15 for field. Note that our best guess of these random effects is considerably smaller than what we would estimate if they were fixed effects (which we can see in the output of fit3).

```
 [1]  0.00000000  0.00000000  0.00000000  0.00000000  0.00000000
 [6]  0.00000000  0.00000000  0.00000000  0.00000000  0.00000000
[11]  0.00000000  0.00000000  0.00000000  0.00000000  0.00000000
[16]  0.00000000  0.00000000  0.00000000  0.00000000  0.00000000
[21]  0.00000000  0.00000000  0.00000000  0.00000000  0.00000000
[26]  0.00000000  0.00000000  0.00000000  0.00000000  0.00000000
[31] -0.12193305  0.05077171 -0.05859339  0.05353402  0.01142282
[36]  0.14095733 -0.08052279  0.02698198  0.12112617  0.02235933
[41] -0.09290314 -0.02758782 -0.12686202 -0.04106115  0.12231002
```

```
> par(mfrow=c(2,2))
> lmer.plot(fit3)
```

These residuals are more like what we expect, because the fixed effects are not being shrunk back like we were seeing when we treated field as a random effect.




```
> fit3.mcmc <- lmer.mcmc(fit3,50000)
> lmer.mcmc.plots(fit3.mcmc,log=TRUE)
```

We'll not show these here, as there are 34 plots!

```
> lmer.mcmc.intervals(fit3.mcmc)
```

We're seeing just a shade more variability here than in the output of fit3, but it's not much of a difference.

```
                lower     median     upper        SE
(Intercept)  4.0601051  4.4337112 4.7980495 0.1861582
field1      -1.6911292 -0.6149087 0.3774820 0.5221897
field2      -0.9437626  0.3796817 1.7097702 0.6722641
field3      -1.8665268 -0.4635144 0.9300701 0.7197178
field4      -1.1352510  0.4423249 1.8682280 0.7389921
field5      -1.2204997  0.1267372 1.5236367 0.6827920
field6      -0.3341452  0.6711747 1.6577772 0.5098678
field7      -2.0576945 -0.6869103 0.6575987 0.6880298
field8      -1.2219240  0.2083560 1.6960486 0.7245083
field9      -0.4384252  1.0215854 2.5466026 0.7242237
field10     -1.3230680  0.1579496 1.4900398 0.7114554
field11     -1.4628051 -0.4862379 0.5525603 0.5087946
field12     -1.6631675 -0.2712383 1.1628171 0.7115539
field13     -2.6236514 -1.1488082 0.2532431 0.7261034
field14     -1.8467741 -0.3947314 0.9866249 0.7059231
section      0.0000000  0.0000000 0.2154743 0.1101968
sigma2       0.5640519  0.9856555 2.0049233 0.3773852
> lmer.mcmc.anova(fit3.mcmc)
```

Here's how we test fixed effects. Field is not signficant.

```
               chisq Df MC p-value
(Intercept) 564.52447  1     0.0000
field        13.33335 14     0.4466
> lmer.KR.anova(fit3)
```

Alternative test for fixed effects, again not significant.

```
             F df1      df2   p-value
field 1.186108  14 4.334391 0.4717713
```

```
> glucose <- read.table("kuehl4.dat.txt",header=TRUE)
```

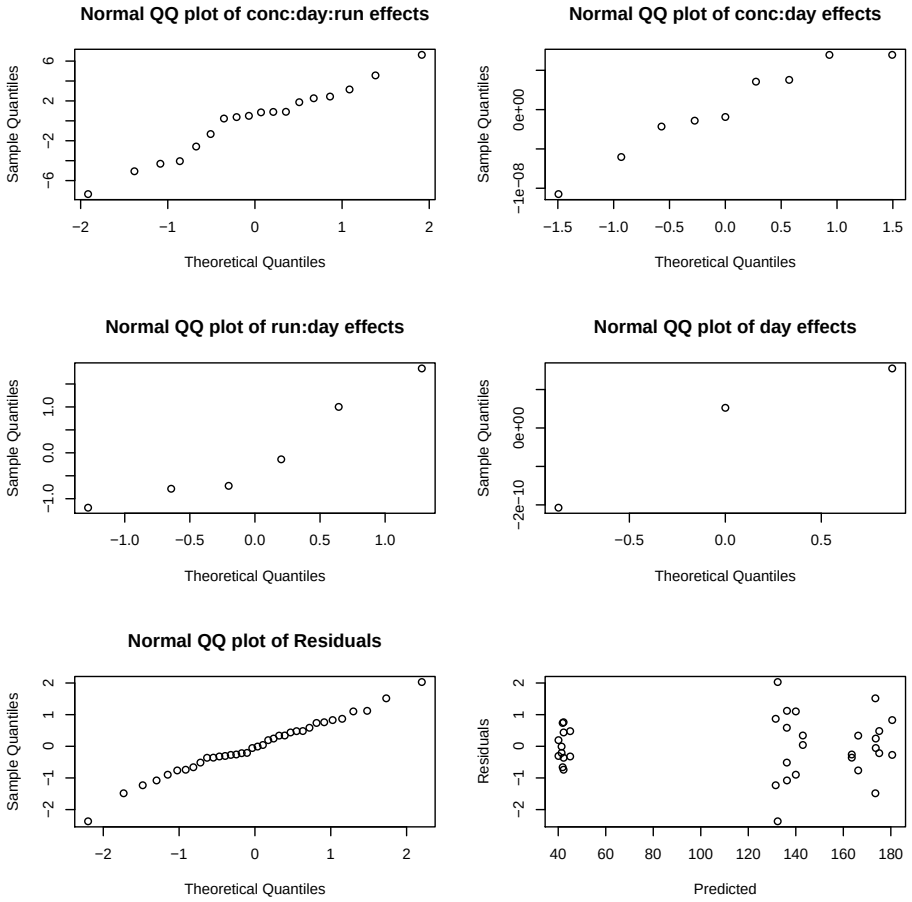
These are the data from Table 7.10 of Kuehl. We are investigating how well an instrument measures serum glucose. We measure at three fixed levels of glucose. The machine may work differently on different days, so we choose three days at random. Also, we will do two runs or batches on the machine each day. That is, do everything once, and then do it all over again. There may be a run effect nested in day. Finally, each concentration is measured twice during each run.

```
> glucose
   conc day rn     y
1     1   1  1  41.2
2     1   1  1  42.6
3     1   1  2  41.2
4     1   1  2  41.4
5     1   2  1  39.8
6     1   2  1  40.3
7     1   2  2  41.5
8     1   2  2  43.0
9     1   3  1  41.9
10    1   3  1  42.7
11    1   3  2  45.5
12    1   3  2  44.7
13    2   1  1 135.7
14    2   1  1 136.8
15    2   1  2 143.0
16    2   1  2 143.3
17    2   2  1 132.4
18    2   2  1 130.3
19    2   2  2 134.4
20    2   2  2 130.0
21    2   3  1 137.4
22    2   3  1 135.2
23    2   3  2 141.1
24    2   3  2 139.1
25    3   1  1 163.2
26    3   1  1 163.3
27    3   1  2 181.4
28    3   1  2 180.3
29    3   2  1 173.6
30    3   2  1 173.9
31    3   2  2 174.9
32    3   2  2 175.6
33    3   3  1 166.6
34    3   3  1 165.5
35    3   3  2 175.0
36    3   3  2 172.0
> glucose <- within(glucose,{conc <- factor(conc);
  day <- factor(day);run <- factor(rn)})
> glu.lmer <- lmer(y ~ conc + (1|day/run) + (1|conc:day) + (1|conc:day:run))
```

Concentration is fixed, and day and run are random. Run is nested in day, and everything else crosses.

```
> par(mfrow=c(3,2))
> lmer.plot(glu.lmer)
```

Hmmm, perhaps we should take the square root of these data.

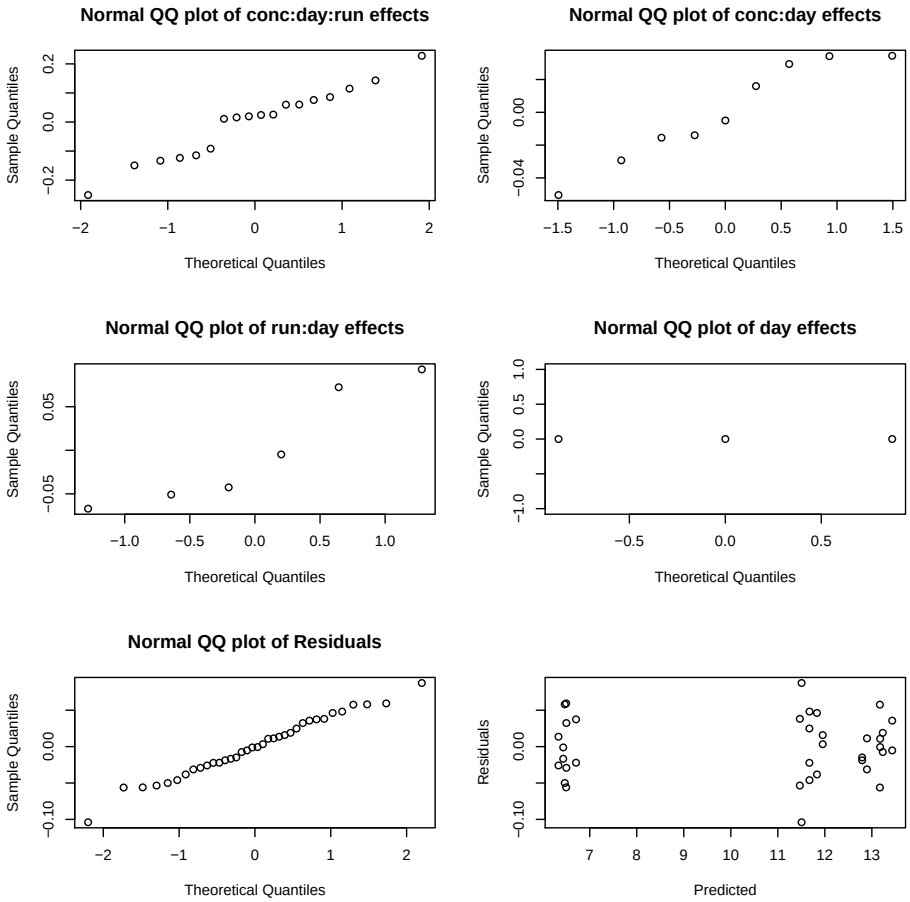



```
> rglu.lmer <-lmer(sqrt(y) ~ conc + (1|day/run) + (1|conc:day) + (1|conc:day:run),
   data=glucose)
```

So let's redo with square root concentration.

```
> lmer.plot(rglu.lmer)
```

This looks a bit better.



> **rglu.lmer**

We have little evidence that day has any effect, or that there is a difference in days by concentration. Concentration is significant (well, we haven't done the "right" test, but it's going to be significant). Run seems to have an effect, as does concentration by run. So every time we set up the apparatus we get a different answer, and the difference varies a lot by the concentration we happen to be measuring. This is not a reassuring finding.

```
Linear mixed model fit by REML
Formula: sqrt(y) ~ conc + (1 | day/run) + (1 | conc:day) + (1 | conc:day:run)
    AIC    BIC logLik deviance REMLdev
 -23.45 -10.78  19.72   -51.07  -39.45
Random effects:
 Groups       Name        Variance  Std.Dev.
 conc:day:run (Intercept) 0.0238342 0.154383
 conc:day     (Intercept) 0.0050494 0.071059
 run:day      (Intercept) 0.0092985 0.096429
 day          (Intercept) 0.0000000 0.000000
 Residual                 0.0031903 0.056483
Number of obs: 36, groups: conc:day:run, 18; conc:day, 9; run:day, 6; day, 3

Fixed effects:
            Estimate Std. Error t value
(Intercept) 10.43086    0.05936  175.72
conc1       -3.93972    0.06283  -62.70
conc2        1.25351    0.06283   19.95
```

```
Correlation of Fixed Effects:
      (Intr) conc1
conc1  0.000
conc2  0.000 -0.500
```

```
> rglu.norun <-lmer(sqrt(y) ~ conc + (1|day) + (1|conc:day) + (1|conc:day:run),
   data=glucose)
> rglu.runonly <- lmer(sqrt(y)~conc+(1|day:run),data=glucose)
> exactRLRT(rglu.runonly,rglu.lmer,rglu.norun)
```

Run is not significant.

```
simulated finite sample distribution of RLRT.  (p-value based
on 10000 simulated values)

data:
RLRT = 0.6062, p-value = 0.1763
```

```
> rglu.noconcrun <- lmer(sqrt(y) ~ conc + (1|day/run) + (1|conc:day),data=glucose)
> rglu.concrunonly <- lmer(sqrt(y) ~ conc + (1|conc:day:run),data=glucose)
> exactRLRT(glu.concrunonly, glu.lmer,glu.noconcrun)
```

Concentration by run is very significant.

```
simulated finite sample distribution of RLRT.  (p-value based on 10000
simulated values)

data:
RLRT = 25.1997, p-value < 2.2e-16
```

```
> rglu.mcmc <- lmer.mcmc(rglu.lmer,20000)
```

20000 may be a bit few.

```
> lmer.mcmc.intervals(rglu.mcmc)
```

Run by concentration is the only one that doesn't seem small compared to error, which fits with our tests.

```
                  lower        median         upper           SE
(Intercept)  10.331592534  1.043348e+01  1.053928e+01 5.286296e-02
conc1        -4.077867827 -3.933806e+00 -3.804056e+00 6.865053e-02
conc2         1.117605958  1.248936e+00  1.380883e+00 6.790569e-02
conc:day:run  0.015151192  3.548855e-02  9.333894e-02 1.945454e-02
conc:day      0.000000000  0.000000e+00  1.170940e-02 4.478276e-03
run:day       0.000000000  0.000000e+00  3.559134e-02 1.075606e-02
day           0.000000000  1.960372e-08  8.253208e-07 2.332330e-07
sigma2        0.001852617  3.309787e-03  8.419489e-03 1.628933e-03
```

```
> lmer.mcmc.anova(rglu.mcmc)
```

As anticipated, the concentrations differ.

```
               chisq Df MC p-value
(Intercept) 38934.758  1          0
conc         3456.903  2          0
```

```
> lmer.KR.anova(rglu.lmer)
```

Kenward and Rogers approximation agrees.

```
           F df1      df2      p-value
conc 1720.584   2 5.604631 1.530098e-08
```