

Clinical Trial A5055

Installation of required packages and functions.

```
source("tmecArpRCO.R")
source("utils_tmecArpRCO.R")

library(mvtnorm)
library(mnormt)
library(lmec)
library(tmvtnorm)
library(msm)
library(ggplot2)
library(tcltk)
library(numDeriv)
library(MASS)
library(base)
library(expm)
library(ARpLMEC)
library(Rcpp)
library(MomTrunc)
library(TTmoment)
```

Reading and setting the dataset

```
#####
# Dataset A5055      #
#####

data1 <- read.csv("dataA5055.csv")

attach(data1)
data1 <- subset(data1, !is.na(cd4))
subjects <- unique(data1$patid)
cluster <- c(match(data1$patid,subjects))
m <- length(subjects)
N <- length(cluster)
y1 <- c(data1$logrna)
y2.1 <- c(data1$cd4)
x <- c(data1$day)
tem <- c(data1$day)
treat <- data1$arm
nj <- matrix(0,m,1)

for (j in 1:m){nj[j]=sum(cluster==j)}
```

```

cc          <- (data1$rna<50)+0
y1[y1<=log10(50)] <- log10(50)

#####
# Excluding Subjects 4 and 8      #
#####

for(i in c( 4,8))
{ y1[cluster==i]      = NA
  y2.1[cluster==i]    = NA
  x[cluster==i]       = NA
  tem[cluster==i]     = NA
  treat[cluster==i]   = NA
  cc[cluster==i]      = NA
  nj[i]               = NA
  cluster[cluster==i]= NA }

y1      <- as.vector(na.omit(y1))
y2.1    <- as.vector(na.omit(y2.1))
x        <- as.vector(na.omit(x))
tem      <- as.vector(na.omit(tem))
treat    <- as.vector(na.omit(treat))
cc       <- as.vector(na.omit(cc))
nj       <- as.vector(na.omit(nj))
cluster  <- as.vector(na.omit(cluster))

subjetos=unique(cluster)
for(i in 1:length(subjetos))
{
  cluster[cluster==subjetos[i]]=i
}

m <- length(nj)
N <- length(cluster)

#####
# Design Matrix      #
#####

xx1    <- cbind(rep(1,length(y1)),x,treat,y2.1^0.5,treat*x)
zz1    <- cbind(1,x)
cc1    <- cc
nj1    <- nj
y1     <- y1
tempo1 <- tem

#####
# Profiles Plot      #
#####

datas  <- cbind(cluster,treat,x,y1,cc,y2.1)
nam_row <- as.character((1:312))
nam_col <- c("cluster","arm","day","logrna","cens","cd4")

```

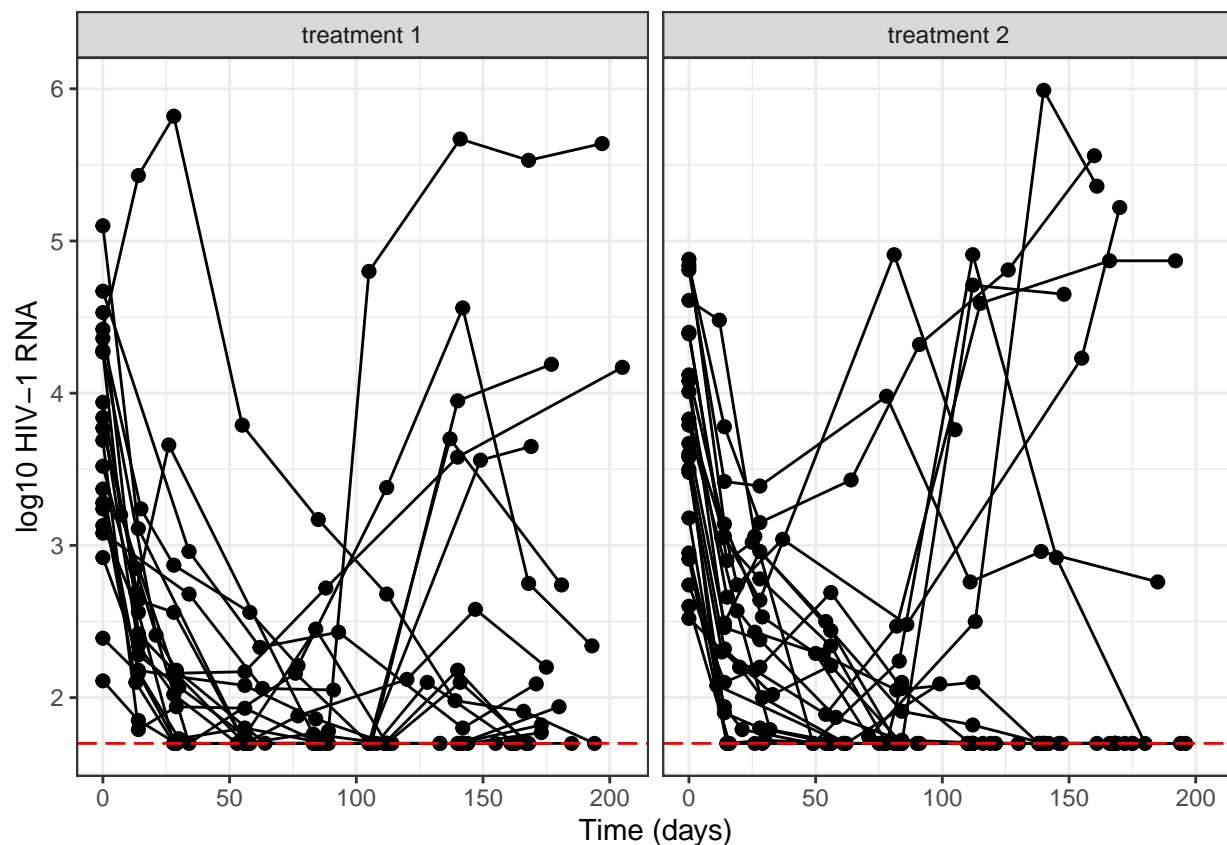
```

datas  <- matrix(datas,nrow=312,ncol=6,
                  dimnames=list(" "=nam_row," "=nam_col))
dados  <- as.data.frame(datas)
attach(dados, warn.conflicts = FALSE)
dados2 <- dados

dados2$arm[dados2$arm=="1"] <- "treatment 1"
dados2$arm[dados2$arm=="2"] <- "treatment 2"

grafico <- ggplot(dados2, aes(x=day,y=logrna,group = cluster))
grafico + geom_line() + geom_point(size = 2) +
  labs(x = "Time (days)", y="log10 HIV-1 RNA") +
  facet_wrap(~ arm) +
  geom_hline(yintercept=log10(50),colour="red",linetype ="longdash")+
  theme_bw()

```



Getting initial values from the UNC-N-LMEC model

```

lm1.un1 <- ARpMMEC.est(y =y1 , x = xx1, z = zz1, tt = tempo1, cc =cc1,
  nj = nj1, struc = "UNC", typeModel = "Normal",
  error = 0.00001, MaxIter = 10)

```

```

##
## -----
## DEC censored mixed-effects models

```

```

## -----
##
## Case = UNC
## Distribution = Normal
## Subjects = 42 ; Observations = 312
##
## -----
## Estimates
## -----
##
## - Fixed effects
##
##           Est      SE          IConf(95%)
## beta 1  4.205 0.067    < 4.074 , 4.336 >
## beta 2 -0.003 0.009    < -0.021 , 0.015 >
## beta 3  0.270 0.248    < -0.216 , 0.756 >
## beta 4 -0.099 0.027    < -0.152 , -0.046 >
## beta 5 -0.001 0.005    < -0.011 , 0.009 >
##
##
## - Sigma^2
##
##           Est      SE          IConf(95%)
## Sigma^2 0.733 0.075    < 0.586 , 0.88 >
##
##
## - Autoregressives parameters
##
## NULL
##
## - Random effects
##
##           Est      SE          IConf(95%)
## Alpha 11  0.337 0.202    < 0 , 0.733 >
## Alpha 12 -0.004 0.005    < -0.014 , 0.006 >
## Alpha 22  0.000 0.000    < 0 , 0 >
##
##
## -----
## Model selection criteria
## -----
##
##           Loglik      AIC      BIC
## Value -366.292 750.585 784.272
##
## -----
## Details
## -----
##
## Convergence reached? = FALSE
## Iterations = 10 / 10
## Processing time = 20.71864 secs

```

```

betasI <- as.vector(lm1.un1$FixEffec$Est)
sigma2I <- lm1.un1$Sigma2$Est
alphasI <- diag(2)
phi1I <- 0.1
phi2I <- 1
LL1 <- rep(-Inf,length(y1))
LU1 <- as.vector(y1)

initial1 <- list(betas=betasI,sigma2=sigma2I,alphas=alphasI,
                phi1=phi1I,phi2=phi2I,nu=150)

```

Preliminary analysis

```

#####
# Fit of the N-LMEC model without correlation structures #
#####

fitN <- tmec.DEC(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
                LL=LL1,LU=LU1,initial=initial1,struc="unc",
                nu.fixed=TRUE,iter.max=500,precision=1e-4)

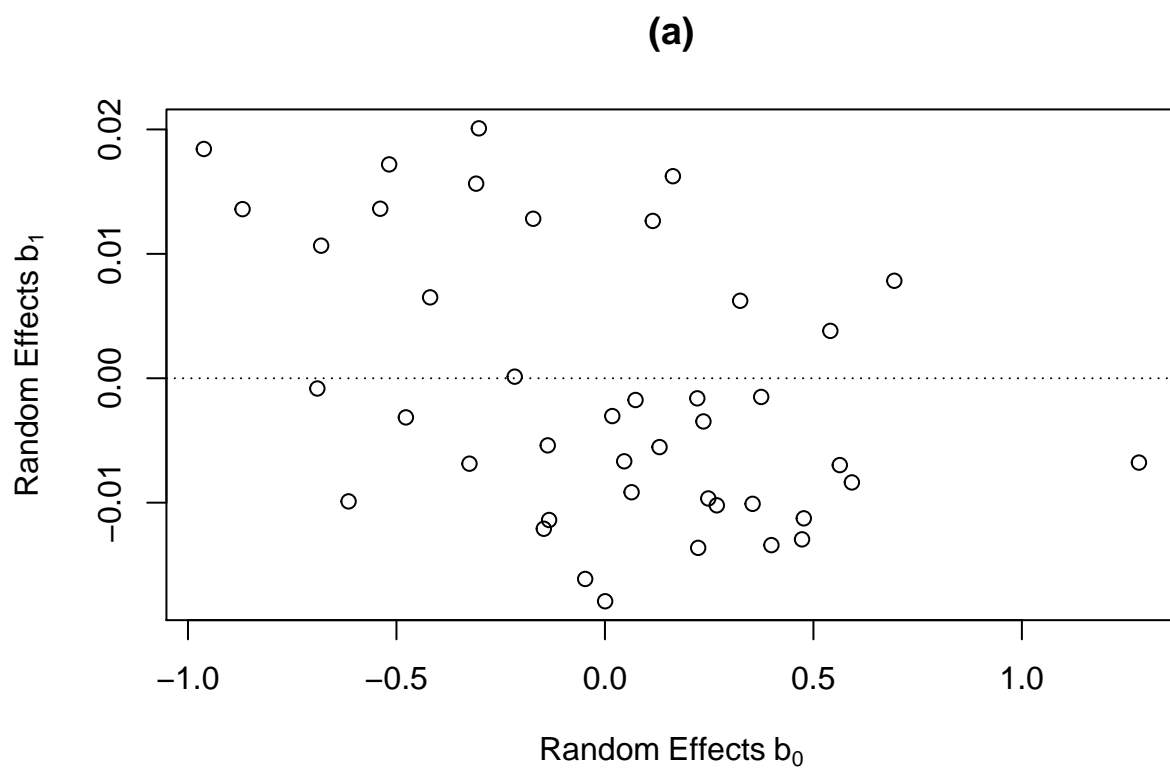
#####
# Residuals of the N-LMEC model without correlation structures #
#####

res <- fitY<-rep(0,length(y1))
efectob<- matrix(0,length(nj),2)
for (i in 1:length(nj)){
  efectob[i,] = fitN$Subi[(((i-1)*2)+1) : (i*2),i]
  resi = fitN$yog[(sum(nj[1:i-1])+1) : (sum(nj[1:i]))]-
        xx1[(sum(nj[1:i-1])+1) : (sum(nj[1:i])),]%*%fitN$beta1

  res[(sum(nj[1:i-1])+1) : (sum(nj[1:i]))] = ((fitN$sigmae)^(-0.5))*resi
  fitY[(sum(nj[1:i-1])+1) : (sum(nj[1:i]))]= xx1[(sum(nj[1:i-1])+1):(sum(nj[1:i]))
        ,]%*%fitN$beta1+ zz1[(sum(nj[1:i-1])
        +1):(sum(nj[1:i])),]%*%efectob[i,]
}

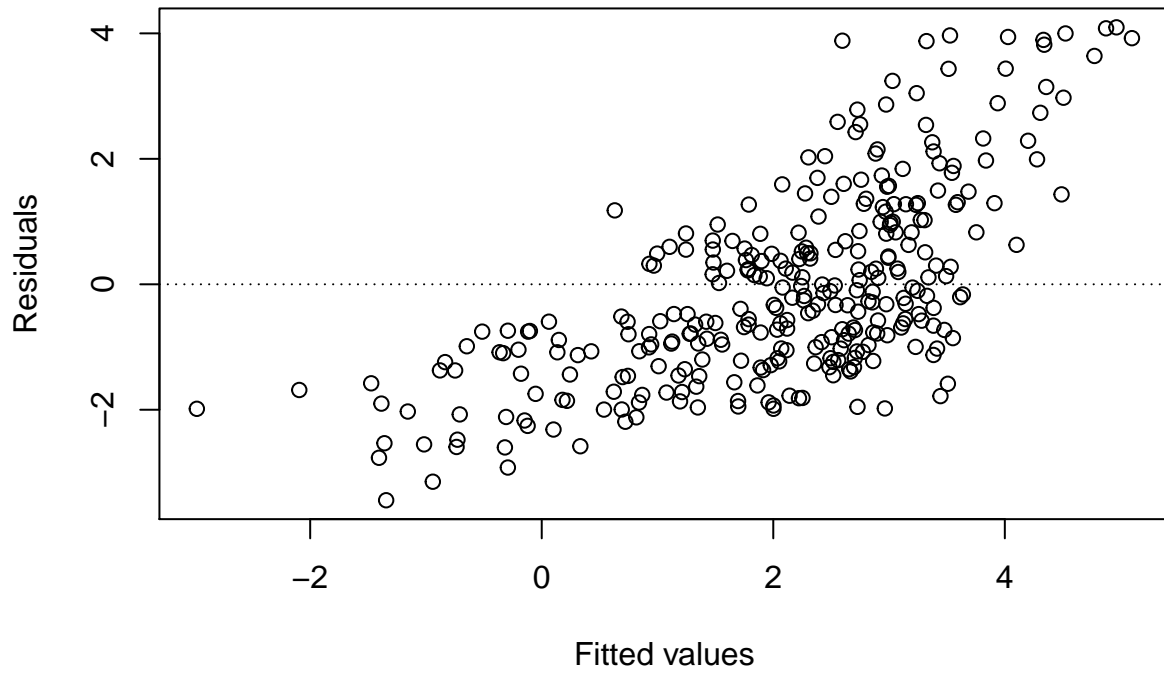
plot(efectob[,1],efectob[,2],xlab=expression(Random~Effects~b[0]),
     ylab=expression(Random~Effects~b[1]),main = "(a)")
abline(h=0, lty=3)

```



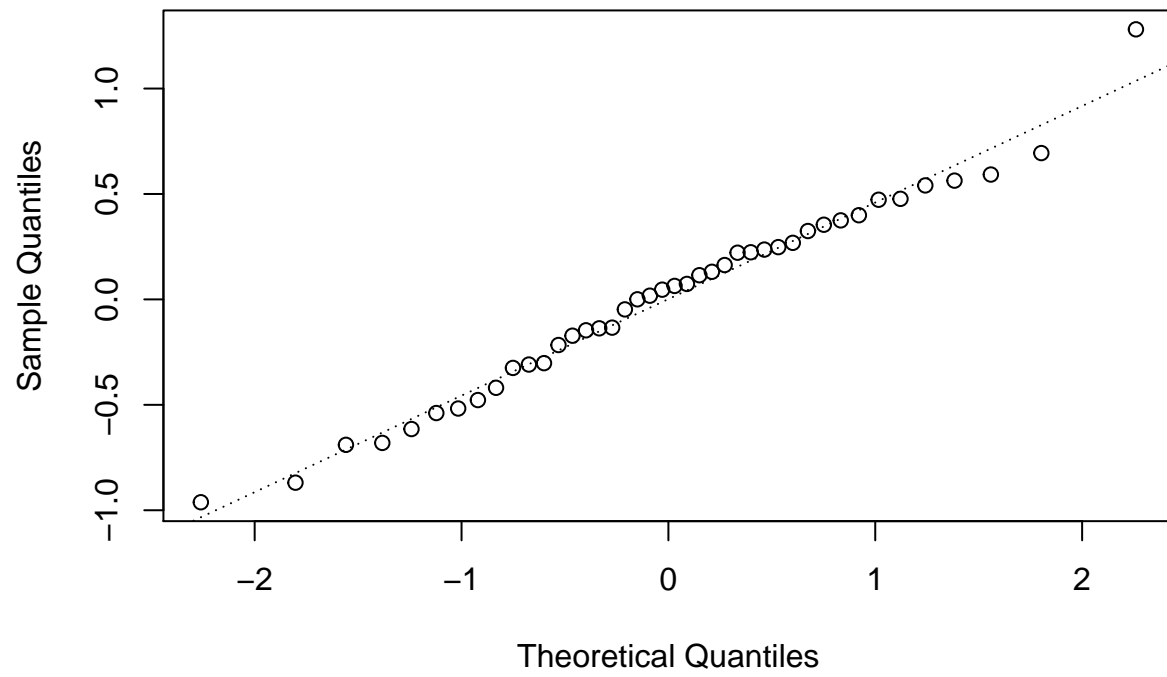
```
plot(fitY,res,xlab= "Fitted values", ylab= "Residuals", main="(b)")  
abline(h=0, lty=3, col=9)
```

(b)

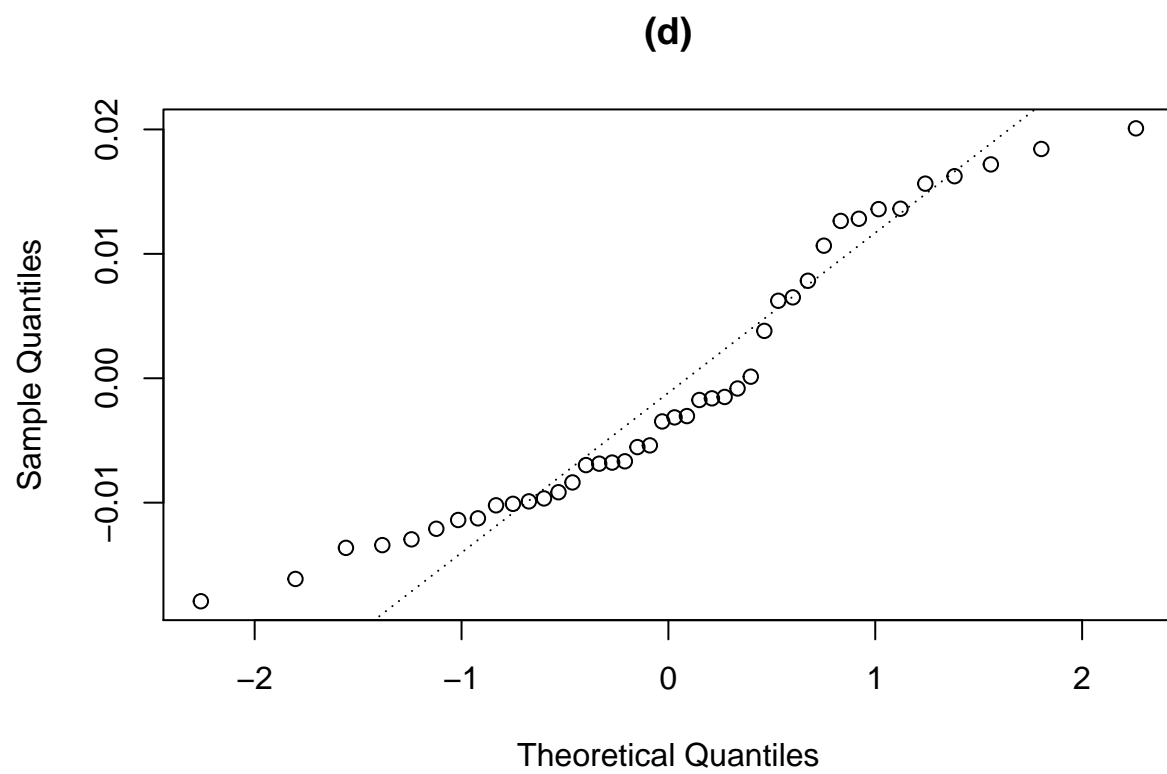


```
qqnorm(effectob[,1], main = "(c)")  
qqline(effectob[,1], lty=3)
```

(c)

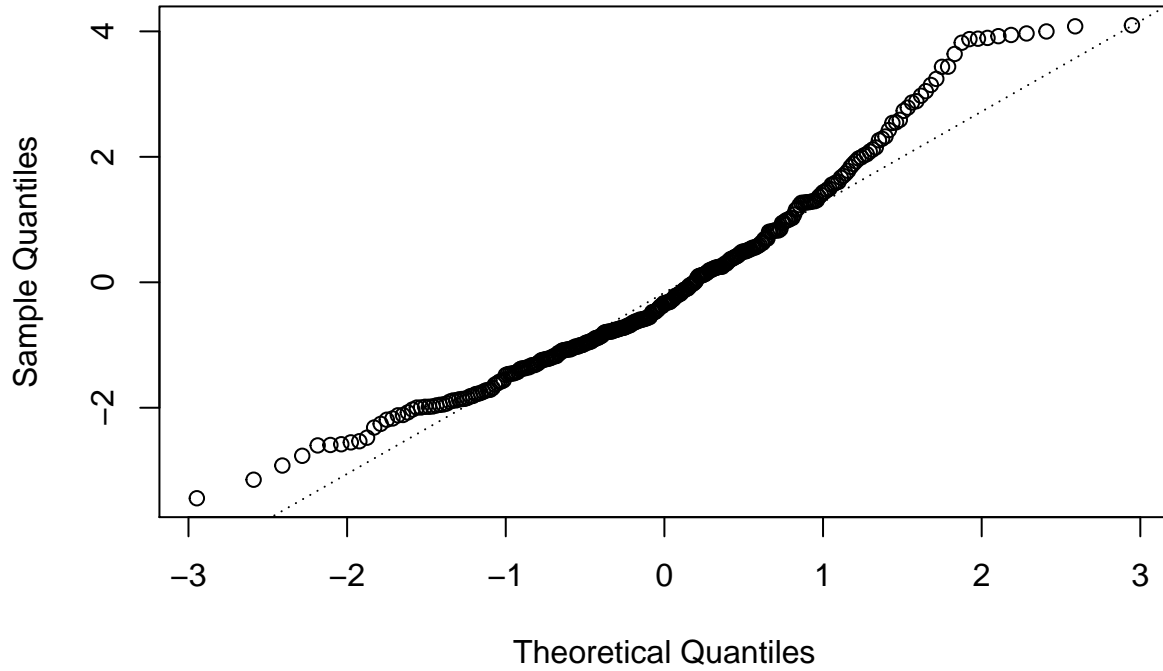


```
qqnorm(effectob[,2], main = "(d)")  
qqline(effectob[,2], lty=3)
```

```
qqnorm(res ,main = "(e)")  
qqline(res, lty=3)
```

(e)



Fit of the t-LMEC model under different correlation structures

```
#####  
# Initial values #  
#####  
  
initial1 <- list(betas=betasI,sigma2=sigma2I,alphas=alphasI,phi1=phi1I,  
                phi2=phi2I,nu=3)  
  
#####  
# Fitted t-LMEC models #  
#####  
  
model1T1 <- tmec.DEC(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj1,ttc=tempo1,  
                    LL=LL1,LU=LU1,initial=initial1,struc="unc",  
                    nu.fixed=FALSE,iter.max=500,precision=1e-4)  
model1T2 <- tmec.DEC(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,  
                    LL=LL1,LU=LU1,initial=initial1,struc="dec",  
                    nu.fixed=FALSE,iter.max=500,precision=1e-4)  
model1T3 <- tmec.DEC(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,  
                    LL=LL1,LU=LU1,initial=initial1,struc="ar",  
                    nu.fixed=FALSE,iter.max=500,precision=1e-4)  
model1T4 <- tmec.DEC(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,  
                    LL=LL1,LU=LU1,initial=initial1,struc="sym",  
                    nu.fixed=FALSE,iter.max=500,precision=1e-4)
```

```

model1T5 <- tmec.Arp(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
  LL=LL1,LU=LU1,initial=initial1,Arp=1,
  nu.fixed=FALSE,iter.max=500,precision=1e-4)
model1T6 <- tmec.Arp(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
  LL=LL1,LU=LU1,initial=initial1,Arp=2,
  nu.fixed=FALSE,iter.max=500,precision=1e-4)
model1T7 <- tmec.Arp(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
  LL=LL1,LU=LU1,initial=initial1,Arp=3,
  nu.fixed=FALSE,iter.max=500,precision=1e-4)

#####
# Parameters estimates #
#####

Table1Betas <- cbind(model1T1$beta1,model1T2$beta1,model1T3$beta1,
  model1T4$beta1,model1T5$beta1,model1T6$beta1,
  model1T7$beta1)
Table1sigmae <- cbind(model1T1$sigmae,model1T2$sigmae,model1T3$sigmae,
  model1T4$sigmae,model1T5$sigmae,model1T6$sigmae,
  model1T7$sigmae)
Table1D <- cbind(model1T1$dd,model1T2$dd,model1T3$dd,model1T4$dd,
  model1T5$dd,model1T6$dd,model1T7$dd)
Table1Phi1 <- cbind(0,model1T2$phi1,model1T3$phi1,model1T4$phi1,
  model1T5$phi,model1T6$phi[1],model1T7$phi[1])
Table1Phi2 <- cbind(0,model1T2$phi2,model1T3$phi2,model1T4$phi2,
  0,model1T6$phi[2],model1T7$phi[2])
Table1Phi3 <- cbind(0,0,0,0,0,0,model1T7$phi[3])
Table1Nu <- cbind(model1T1$nu,model1T2$nu,model1T3$nu,model1T4$nu,
  model1T5$nu,model1T6$nu,model1T7$nu)

tableTlmec<-round(rbind(Table1Betas,Table1sigmae,Table1D,Table1Phi1,
  Table1Phi2,Table1Phi3,Table1Nu),4)

colnames(tableTlmec) <- c("UNC","DEC","DEC(AR)","SYM","AR(1)","AR(2)","AR(3)")
row.names(tableTlmec) <- c("beta0","beta1","beta2","beta3","beta4","sigma2",
  "alpha11","alpha12","alpha22","phi1","phi2","phi3","nu")

print(tableTlmec)

```

##	UNC	DEC	DEC(AR)	SYM	AR(1)	AR(2)	AR(3)
## beta0	4.0445	4.0443	4.1077	4.0560	4.0471	4.0444	4.1446
## beta1	-0.0046	-0.0046	-0.0041	-0.0045	-0.0046	-0.0047	-0.0042
## beta2	0.3438	0.3441	0.3783	0.3382	0.3451	0.3454	0.3471
## beta3	-0.0888	-0.0887	-0.0955	-0.0897	-0.0890	-0.0889	-0.0981
## beta4	-0.0037	-0.0036	-0.0041	-0.0035	-0.0039	-0.0039	-0.0037
## sigma2	0.4958	0.4919	0.5406	0.5365	0.2909	0.2890	0.1802
## alpha11	0.2383	0.2374	0.2284	0.2152	0.2386	0.2379	0.2416
## alpha12	-0.0018	-0.0018	-0.0020	-0.0019	-0.0018	-0.0018	-0.0020
## alpha22	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
## phi1	0.0000	0.1061	0.8993	0.0620	0.6449	0.7401	0.2865
## phi2	0.0000	0.9980	1.0000	0.0000	0.0000	-0.4325	0.0959
## phi3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	-0.7872
## nu	4.5110	4.2730	5.4342	4.3559	4.5567	4.2991	7.3481

```
#####
# Standard errors #
#####

SET <- round(cbind(sqrt(diag(solve(model1T1$Infbetas))),
                    sqrt(diag(solve(model1T2$Infbetas))),
                    sqrt(diag(solve(model1T3$Infbetas))),
                    sqrt(diag(solve(model1T4$Infbetas))),
                    sqrt(diag(solve(model1T5$Infbetas))),
                    sqrt(diag(solve(model1T6$Infbetas))),
                    sqrt(diag(solve(model1T7$Infbetas))))),4)

colnames(SET) <- c("UNC", "DEC", "DEC(AR)", "SYM", "AR(1)", "AR(2)", "AR(3)")
row.names(SET) <- c("beta0", "beta1", "beta2", "beta3", "beta4")

print(SET)

##          UNC      DEC DEC(AR)      SYM  AR(1)  AR(2)  AR(3)
## beta0 0.4997 0.5013  0.5187 0.5088 0.5030 0.5007 0.5392
## beta1 0.0072 0.0072  0.0073 0.0072 0.0072 0.0072 0.0076
## beta2 0.2484 0.2491  0.2607 0.2527 0.2501 0.2490 0.2714
## beta3 0.0193 0.0193  0.0198 0.0195 0.0194 0.0193 0.0201
## beta4 0.0048 0.0048  0.0049 0.0048 0.0048 0.0048 0.0050

#####
# Information criterias #
#####

Table1AIC <- cbind(model1T1$AIC,model1T2$AIC,model1T3$AIC,
                   model1T4$AIC,model1T5$AIC,model1T6$AIC,
                   model1T7$AIC)
Table1BIC <- cbind(model1T1$BIC,model1T2$BIC,model1T3$BIC,
                   model1T4$BIC,model1T5$BIC,model1T6$BIC,
                   model1T7$BIC)
Table1loglik <- cbind(model1T1$loglik,model1T2$loglik,model1T3$loglik,
                     model1T4$loglik,model1T5$loglik,model1T6$loglik,
                     model1T7$loglik)

CriteriasT <- rbind(Table1loglik,Table1AIC,Table1BIC)
colnames(CriteriasT) <- c("UNC", "DEC", "DEC(AR)", "SYM", "AR(1)", "AR(2)", "AR(3)")
row.names(CriteriasT) <- c("loglik", "AIC", "BIC")

print(CriteriasT)

##          UNC      DEC  DEC(AR)      SYM      AR(1)      AR(2)      AR(3)
## loglik -355.8039 -355.8885 -350.7299 -356.0035 -355.5502 -355.5399 -353.1112
## AIC      731.6078 735.7771 723.4598 734.0071 733.1004 735.0798 732.2224
## BIC      769.0378 780.6931 764.6328 775.1801 774.2734 779.9959 780.8815
```

Fit of the N-LMEC model under different correlation structures

```
#####
# Initial values #
```

```
#####

initial1 <- list(betas=betasI,sigma2=sigma2I,alphas=alphasI,phi1=phi1I
                ,phi2=phi2I,nu=150)

#####
# Fitted t-LMEC models #
#####

model1N1<- tmec.DEC(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
                    LL=LL1,LU=LU1,initial=initial1,struc="unc",
                    nu.fixed=TRUE,iter.max=500,precision=1e-4)
model1N2<- tmec.DEC(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
                    LL=LL1,LU=LU1,initial=initial1,struc="dec",
                    nu.fixed=TRUE,iter.max=500,precision=1e-4)
model1N3<- tmec.DEC(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
                    LL=LL1,LU=LU1,initial=initial1,struc="ar",
                    nu.fixed=TRUE,iter.max=500,precision=1e-4)
model1N4<- tmec.DEC(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
                    LL=LL1,LU=LU1,initial=initial1,struc="sym",
                    nu.fixed=TRUE,iter.max=500,precision=1e-4)
model1N5<- tmec.Arp(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
                    LL=LL1,LU=LU1,initial=initial1,Arp=1,
                    nu.fixed=TRUE,iter.max=500,precision=1e-4)
model1N6<- tmec.Arp(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
                    LL=LL1,LU=LU1,initial=initial1,Arp=2,
                    nu.fixed=TRUE,iter.max=500,precision=1e-4)
model1N7<- tmec.Arp(y=y1,cc=cc1,x=xx1,z=zz1,nj=nj,ttc=tempo1,
                    LL=LL1,LU=LU1,initial=initial1,Arp=3,
                    nu.fixed=TRUE,iter.max=500,precision=1e-4)

#####
# Parameters estimates #
#####

Table1Betas    <- cbind(model1N1$beta1,model1N2$beta1,model1N3$beta1,
                        model1N4$beta1,model1N5$beta1,model1N6$beta1,
                        model1N7$beta1)
Table1sigmae   <- cbind(model1N1$sigmae,model1N2$sigmae,model1N3$sigmae,
                        model1N4$sigmae,model1N5$sigmae,model1N6$sigmae,
                        model1N7$sigmae)
Table1D        <- cbind(model1N1$dd,model1N2$dd,model1N3$dd,model1N4$dd,
                        model1N5$dd,model1N6$dd,model1N7$dd)
Table1Phi1     <- cbind(0,model1N2$phi1,model1N3$phi1,model1N4$phi1,
                        model1N5$phi,model1N6$phi[1],model1N7$phi[1])
Table1Phi2     <- cbind(0,model1N2$phi2,model1N3$phi2,model1N4$phi2,0,
                        model1N6$phi[2],model1N7$phi[2])
Table1Phi3     <- cbind(0,0,0,0,0,0,model1N7$phi[3])

tableNlmec     <- round(rbind(Table1Betas,Table1sigmae,Table1D,Table1Phi1,
                              Table1Phi2,Table1Phi3),4)

colnames(tableNlmec) <- c("UNC","DEC","DEC(AR)","SYM","AR(1)","AR(2)","AR(3)")
```

```
row.names(tableNlmec) <- c("beta0","beta1","beta2","beta3","beta4","sigma2",
                           "alpha11","alpha12","alpha22","phi1","phi2","phi3")
```

```
print(tableNlmec)
```

```
##          UNC      DEC DEC(AR)      SYM  AR(1)  AR(2)  AR(3)
## beta0    4.3668  4.3667  4.3430  4.3711  4.3657  4.3637  4.2908
## beta1   -0.0040 -0.0040 -0.0033 -0.0040 -0.0040 -0.0039 -0.0033
## beta2    0.3064  0.3064  0.3530  0.3056  0.3094  0.3085  0.3601
## beta3   -0.1097 -0.1097 -0.1127 -0.1102 -0.1100 -0.1099 -0.1123
## beta4   -0.0029 -0.0029 -0.0032 -0.0030 -0.0030 -0.0029 -0.0035
## sigma2   0.7134  0.7136  0.7246  0.7450  0.4132  0.4074  0.1926
## alpha11  0.3756  0.3756  0.3254  0.3459  0.3744  0.3763  0.2992
## alpha12 -0.0039 -0.0039 -0.0037 -0.0039 -0.0039 -0.0039 -0.0031
## alpha22  0.0002  0.0002  0.0002  0.0002  0.0002  0.0002  0.0002
## phi1     0.0000  0.1064  0.8993  0.0426  0.6551  0.7603  0.2785
## phi2     0.0000  0.9979  1.0000  0.0000  0.0000 -0.4809  0.0963
## phi3     0.0000  0.0000  0.0000  0.0000  0.0000  0.0000 -0.8128
```

```
#####
# Standard errors #
#####
```

```
SEN <- round(cbind(sqrt(diag(solve(model1N1$Infbetas))),
                   sqrt(diag(solve(model1N2$Infbetas))),
                   sqrt(diag(solve(model1N3$Infbetas))),
                   sqrt(diag(solve(model1N4$Infbetas))),
                   sqrt(diag(solve(model1N5$Infbetas))),
                   sqrt(diag(solve(model1N6$Infbetas))),
                   sqrt(diag(solve(model1N7$Infbetas)))),4)

colnames(SEN) <- c("UNC","DEC","DEC(AR)","SYM","AR(1)","AR(2)","AR(3)")
row.names(SEN) <- c("beta0","beta1","beta2","beta3","beta4")
```

```
print(SEN)
```

```
##          UNC      DEC DEC(AR)      SYM  AR(1)  AR(2)  AR(3)
## beta0  0.4966  0.4961  0.5007  0.4972  0.4982  0.4981  0.5182
## beta1  0.0073  0.0073  0.0073  0.0073  0.0073  0.0073  0.0075
## beta2  0.2564  0.2561  0.2613  0.2568  0.2571  0.2571  0.2671
## beta3  0.0187  0.0187  0.0186  0.0187  0.0188  0.0188  0.0191
## beta4  0.0047  0.0047  0.0047  0.0047  0.0047  0.0047  0.0048
```

```
#####
# Information criterias #
#####
```

```
Table1AIC1 <- cbind(model1N1$AIC,model1N2$AIC,model1N3$AIC,
                    model1N4$AIC,model1N5$AIC,model1N6$AIC,model1N7$AIC)
Table1BIC1 <- cbind(model1N1$BIC,model1N2$BIC,model1N3$BIC,
                    model1N4$BIC,model1N5$BIC,model1N6$BIC,model1N7$BIC)
Table1loglik1 <- cbind(model1N1$loglik,model1N2$loglik,model1N3$loglik,
                      model1N4$loglik,model1N5$loglik,model1N6$loglik,
                      model1N7$loglik)
```

```

CriteriasN      <- rbind(Table1loglik1,Table1AIC1,Table1BIC1)
colnames(CriteriasN) <- c("UNC","DEC","DEC(AR)","SYM","AR(1)","AR(2)","AR(3)")
row.names(CriteriasN) <- c("loglik","AIC","BIC")

print(CriteriasN)

```

```

##          UNC          DEC  DEC(AR)          SYM          AR(1)          AR(2)          AR(3)
## loglik -362.0229 -362.0222 -354.9770 -361.9947 -361.7953 -361.8760 -355.1145
## AIC      744.0458  748.0443  731.9539  745.9893  745.5905  747.7519  736.2290
## BIC      781.4758  792.9604  773.1270  787.1623  786.7636  792.6679  784.8880

```

Residual analysis of the DEC(AR)-t-LMEC model

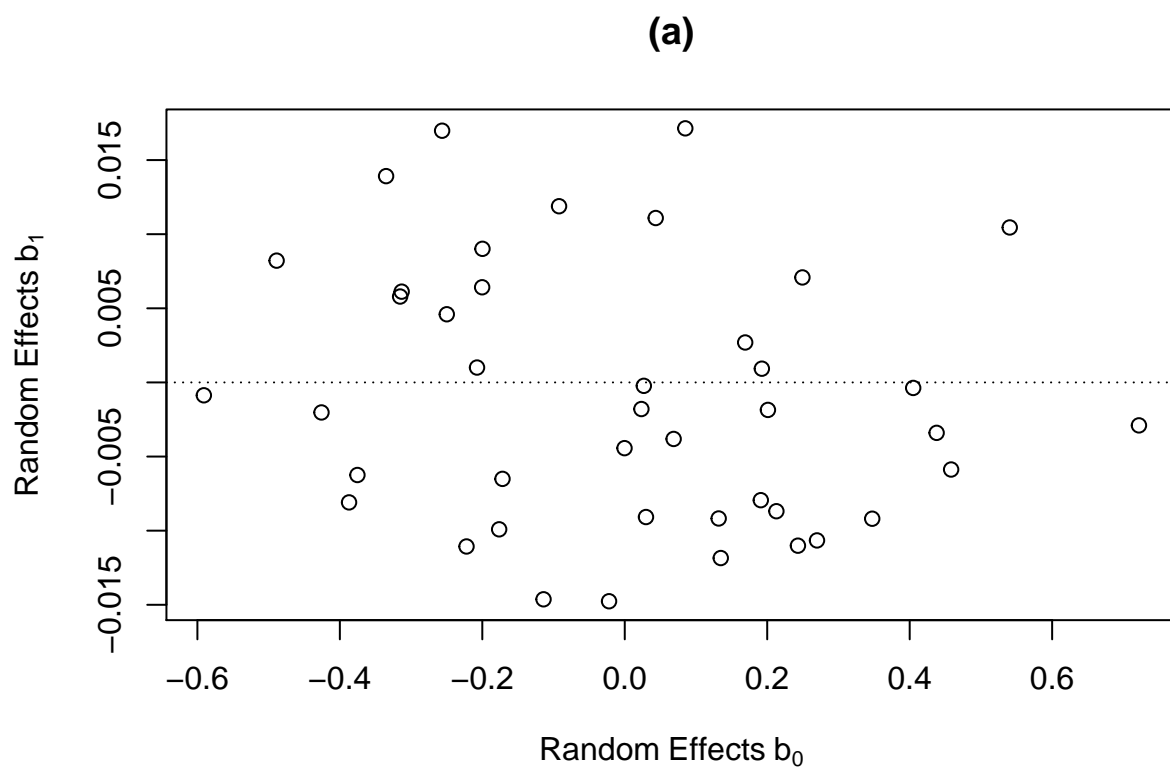
```

obj      <- model1T3
Di       <- matrix(0,dim(zz1)[2],dim(zz1)[2])
bet      <- obj$beta1
Di[upper.tri(Di, diag = T)] <- obj$dd
Di[lower.tri(Di, diag = T)] <- obj$dd
Di       <- round(Di,6)
sig      <- obj$sigmae
rese     <- Yi<- Ye<- vector(mode = "numeric", length = length(y1))
efectob  <- matrix(0,length(nj),2)
for (k in 1:length(nj)){
  tc      <- tem[(sum(nj[1:k-1])+1) : (sum(nj[1:k]))]
  bi      <- obj$ubi[(((k-1)*dim(zz1)[2])+1) : (k*dim(zz1)[2]), k]
  efectob[k,] <- bi
  Mq      <- MatDec(tc,obj$phi1,obj$phi2,"ar")
  Sii     <- zz1[(sum(nj[1:k-1])+1) : (sum(nj[1:k])),,]%*%Di%*%t(zz1[(sum(nj[1:k-1])+1) : (sum(nj[1:k])),,])+sig*Mq
  Sii     <- round(Sii,6)
  Mui     <- xx1[(sum(nj[1:k-1])+1) : (sum(nj[1:k])),,]%*%bet
  Yi      <- obj$yog[(sum(nj[1:k-1])+1) : (sum(nj[1:k]))]

  Ye[(sum(nj[1:k-1])+1) : (sum(nj[1:k]))] <- xx1[(sum(nj[1:k-1])+1) : (sum(nj[1:k])),,]%*%bet+zz1[(sum(nj[1:k-1])+1) : (sum(nj[1:k])),,]%*%bi
  rese[(sum(nj[1:k-1])+1) : (sum(nj[1:k]))] <- (sqrtm(solve(Sii))%*%(Yi-Mui))
}

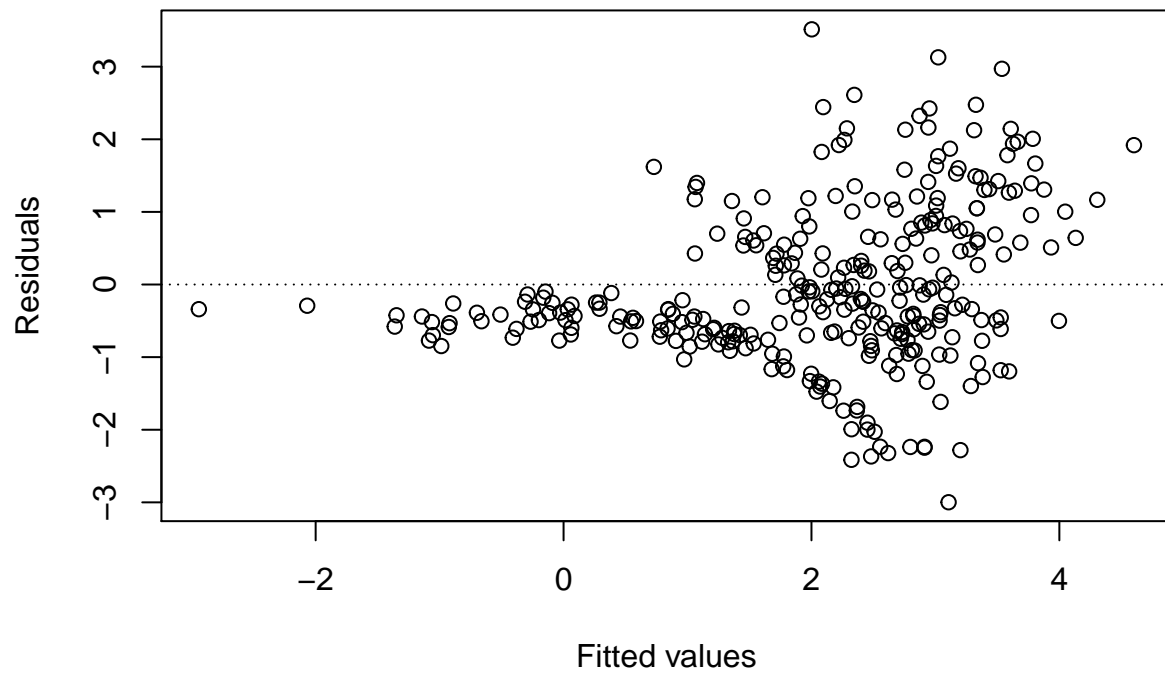
plot(efectob[,1],efectob[,2],xlab=expression(Random-Effects~b[0]),
     ylab=expression(Random-Effects~b[1]),main = "(a)")
abline(h=0, lty=3)

```

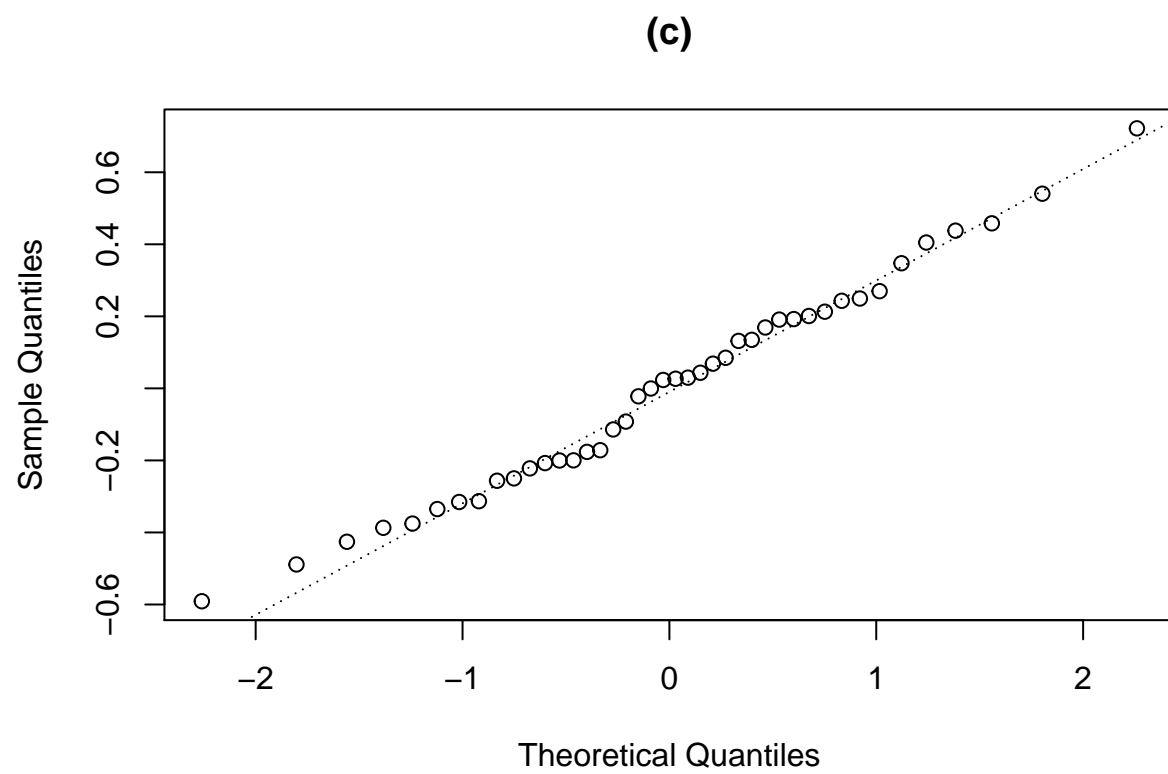


```
plot(Ye, rese, xlab= "Fitted values", ylab= "Residuals", main = "(b)")  
abline(h=0, lty=3, col=9)
```


(b)

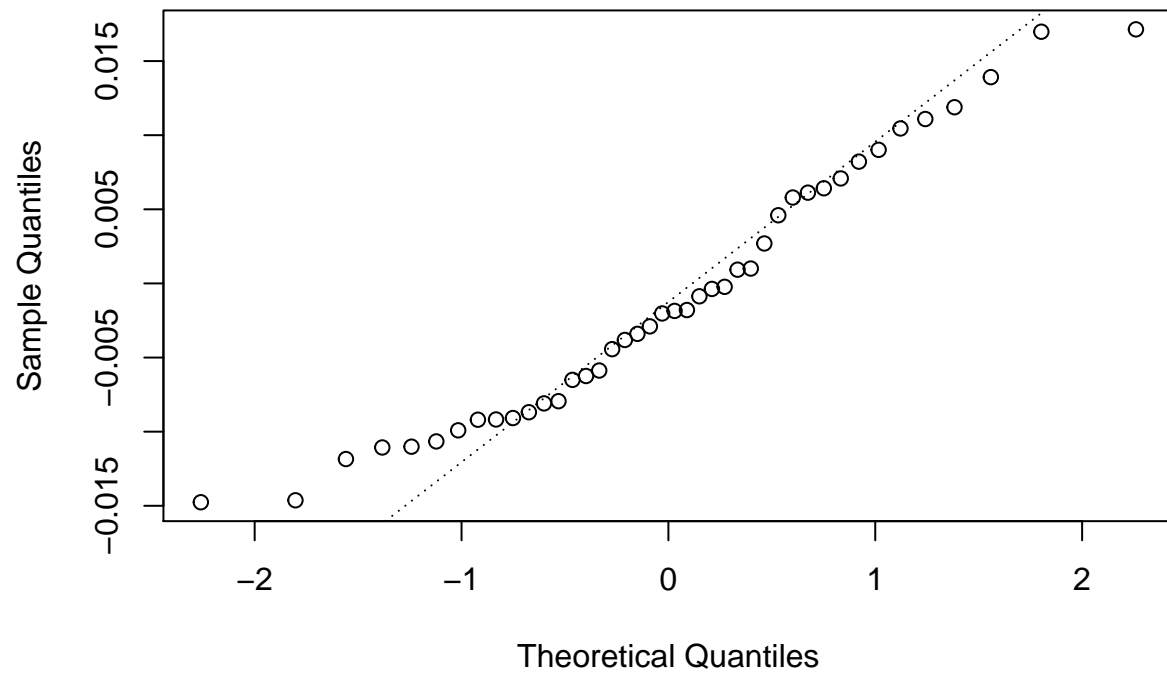


```
qqnorm(efectob[,1], main = "(c)")  
qqline(efectob[,1], lty=3)
```



```
qqnorm(effectob[,2],main = "(d)")  
qqline(effectob[,2], lty=3)
```

(d)



```
qqnorm(rese,main = "(e)")  
qqline(rese, lty=3)
```

(e)

