

Analysis of Data from Method Comparison Studies Using R, merror, and OpenMx



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Introduction

Method comparison studies are used to compare the measurements made of the same quantity using different instruments, monitors, devices or methods. Researchers often try to compare the measurements made by just two devices, in some cases using regression analysis. As is well known, when both devices are subject to measurement error (ME), regression analysis presents a distorted view of the actual bias (or shows bias when none exists). Analogously, correlation is often used to describe the agreement even though correlation only measures linear association and cannot provide any insight into agreement of the two instruments. Other researchers resort to the use of Bland-Altman plots (paired differences versus paired averages). This approach is useful if there is good agreement but provides no way to determine the cause of poor agreement.

A more fruitful and general approach is provided by using the classic ME model (Jaech, 1985):

$$X_{ij} = \alpha_i + \beta_j \mu_j + \epsilon_{ij}$$

where μ_j denotes the "true" but unknown value of the j^{th} item being measured (often assumed to be Normally distributed with mean $\bar{\mu}$ and standard deviation σ_i), X_{ij} denotes the observed measurement from instrument i for item j , α_i and β_j describe the bias introduced by the instrument (assumed to be a linear function of μ), and ϵ_{ij} denotes a Normally distributed random error of instrument i and item j with mean of 0 and standard deviation of σ_i . The instrument imprecision adjusted for differences in scale is given by σ_i/β_j . The ME model can be described using a path diagram with μ as a latent variable and X_i as manifest variables, and represented as a structural equation model (SEM). SEM path analysis readily explains the deficiencies of using only two devices and the necessity of including repeats and/or 3 or more devices. SEMs can easily include repeated measurements, or, for example as in ophthalmology, having measurements from both eyes. Parameter estimates can be made using the method of moments (MOM) or the method of maximum likelihood (ML). Using these estimates, calibration equations relating measurements from different instruments can be easily derived.

The **merror** package (Bilonick, 2003) provides the function `ncb.od` (non-constant bias, original data) for computing ML estimates of the ME imprecision standard deviations for unclustered data and least squares estimates of β_i . The function `lrt` tests whether $\beta_i = \beta_j$. For clustered data, the more flexible **OpenMx** (SEM) package (Boker, et al., 2010) can be used for ML estimates of any desired (functions of) model parameters. When using **OpenMx** for ME models, **merror** can be used to provide good starting values for the parameter estimates.

The calibration equation relating any two methods i and j is then:

$$X_i = \left(\alpha_i - \alpha_j \frac{\beta_i}{\beta_j} \right) + \frac{\beta_i}{\beta_j} X_j$$

If $X = \ln(Y)$, then:

$$Y_i = e^{\left(\alpha_i - \alpha_j \frac{\beta_i}{\beta_j} \right)} Y_j^{\frac{\beta_i}{\beta_j}} = k Y_j^{\frac{\beta_i}{\beta_j}}$$

These methods are illustrated using data from an from air pollution study. Structural equation modeling can be easily extended to clustered data. For example, in ophthalmic studies, typically both eyes of each subject are measured. Separate correlated latent variables for each eye can be included in the SEM. SEMs can also accommodate correlation between the random errors of different methods.

Example - merror

The covariance matrix, means, and standard deviations for the log-transformed elemental carbon measurements made using thermal optical transmittance (TOT) and thermal optimal reflectance (TOR) by the Upper Ohio River Valley Project (UO) and Allegheny County Health Department (AC) for collocated existing (E) and archived (A) PM_{2.5} samples are shown in the table below:

Covariance	UO.A.Q.TOT	UO.E.Q.TOR	AC.E.Q.TOT
UO.A.Q.TOT	0.2371	0.1735	0.1668
UO.E.Q.TOR	0.1735	0.1902	0.1272
AC.E.Q.TOT	0.1668	0.1272	0.4076
Mean	-0.7799	-0.0093	-1.1611
SD	0.4869	0.4362	0.6384

The `ncb.od` (non-constant bias, original data) function from the **merror** package can be used to compute maximum likelihood estimates of the measurement error model parameters:

```
> library(merror)
> options(width=140)

> round(tab <- ncb.od(log(EC))$sigma.table,2)
      n sigma se.sigma alpha.cb alpha.ncb beta    df chisq.1 chisq.u lb ub
uo_a_q_tot 42 0.10  0.14  -0.13  0.01 1.21 0.46  0.00  3.27 0.04 176.70
uo_e_q_tot 42 0.24  0.13  0.64  0.59 0.93 22.56 11.38 37.51 0.18  0.33
ac_e_q_tot 42 0.53  0.25  -0.51  -0.58 0.89 40.02 24.45 59.37 0.43  0.68
Process    42 0.39  0.19    NA    NA  NA 35.57 21.01 53.91 0.32  0.51

# Note: ncb.od constrains the product of the beta's to equal 1!

> tab$beta/tab$beta[1] # Fixing the first beta to equal 1 instead!
[1] 1.0000000 0.7628350 0.7331638      NA

> lrt(EC)$p.value #Warning messages not shown
[1] 9.454714e-05

> lrt(log(EC))$p.value
[1] 0.2720464
```

The `lrt` (likelihood ratio test) function from the **merror** package can be used to test the equality of the β estimates. The very small p-value for the untransformed elemental carbon measurements and the much larger p-value for the log-transformed measurements support the choice of transformation.

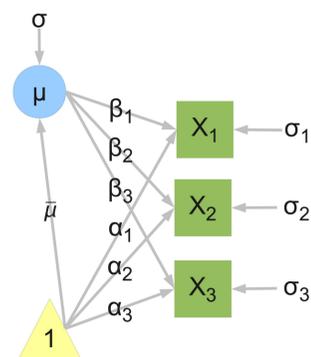


Figure 1: Path diagram for simple measurement error model represented as a structural equation model. Manifest (observed) variables are shown as squares while a circle indicates a latent (unobserved) variable - the "true" quantity we are attempting to measure. The triangle denotes the inclusion of the intercepts and latent variable mean.

Example - OpenMx

The simple measurement error model for the three measurements can be represented as a structural equation model or SEM (Figure 1). The SEM can be described by three matrices: 1) the A matrix describes the relations among the latent and observed variables, 2) the S matrix describes the error covariances, and 3) the F matrix "filters" the latent variable from the observed variables. For this model, the A , S , and F matrices are:

$$A = \begin{bmatrix} 0 & 0 & 0 & 0 \\ \beta_1 & 0 & 0 & 0 \\ \beta_2 & 0 & 0 & 0 \\ \beta_3 & 0 & 0 & 0 \end{bmatrix}, S = \begin{bmatrix} \sigma^2 & 0 & 0 & 0 \\ 0 & \sigma_1^2 & 0 & 0 \\ 0 & 0 & \sigma_2^2 & 0 \\ 0 & 0 & 0 & \sigma_3^2 \end{bmatrix}, \text{ and } F = \begin{bmatrix} 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

with the inverse of the identity matrix minus A being:

$$(I - A)^{-1} = \begin{bmatrix} 1 & 0 & 0 & 0 \\ \beta_1 & 1 & 0 & 0 \\ \beta_2 & 0 & 1 & 0 \\ \beta_3 & 0 & 0 & 1 \end{bmatrix}$$

The resulting covariance model is then:

$$F(I - A)^{-1}S(I - A)^{-1}F' = \begin{bmatrix} \beta_1^2\sigma^2 + \sigma_1^2 & \beta_1\beta_2\sigma^2 & \beta_1\beta_3\sigma^2 \\ \beta_1\beta_2\sigma^2 & \beta_2^2\sigma^2 + \sigma_2^2 & \beta_2\beta_3\sigma^2 \\ \beta_1\beta_3\sigma^2 & \beta_2\beta_3\sigma^2 & \beta_3^2\sigma^2 + \sigma_3^2 \end{bmatrix}$$

and means model is:

$$E \begin{bmatrix} X_1 \\ X_2 \\ X_3 \end{bmatrix} = F(I - A)^{-1}\alpha = \begin{bmatrix} 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} 1 & 0 & 0 & 0 \\ \beta_1 & 1 & 0 & 0 \\ \beta_2 & 0 & 1 & 0 \\ \beta_3 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} \bar{\mu} \\ \alpha_1 \\ \alpha_2 \\ \alpha_3 \end{bmatrix} = \begin{bmatrix} \alpha_1 + \beta_1\bar{\mu} \\ \alpha_2 + \beta_2\bar{\mu} \\ \alpha_3 + \beta_3\bar{\mu} \end{bmatrix}$$

Using **OpenMx**, this SEM can be coded as:

```
require(OpenMx)
manifests <- names(EC)
latents <- c("mu")
ecModel <- mxModel("log EC", type="RAM",
  manifestVars = manifests,
  latentVars = latents,
  mxPath(from=latents, to=manifests, free=c(F,T,T),
    values=c(1,NA,NA),
    labels=c("beta_1","beta_2","beta_3")),
  mxPath(from=manifests, arrows=2, lbound=0,
    labels=c("sigma2_1","sigma2_2","sigma2_3")),
  mxPath(from=latents, arrows=2, lbound=0, labels="sigma2"),
  mxPath(from="one", to=c(latents,manifests), arrows=1,
    free=c(F,T,T,T),
    values=c(mean(mean(log(EC))), 0, 0, 0),
    labels=c("mubar","alpha1","alpha2","alpha3")),
  mxData(cov(log(EC)), type="cov",
    numObs=dim(EC)[1], means=mean(log(EC))),
  mxAlgebra(sqrt(diag2vec(S)), name="P"),
  mxCI(c('A','S','M'))
)
results.ec <- mxRun(ecModel, intervals=T)
```

The calibration equations for elemental carbon ($\mu\text{g}/\text{m}^3$) were:

$$\begin{aligned} \text{UO.E.Q.TOR} &= 1.797 \text{ UO.A.Q.TOT}^{0.763} \\ \text{UO.A.Q.TOT} &= 0.464 \text{ UO.E.Q.TOR}^{1.311} \\ \text{AC.E.Q.TOT} &= 0.555 \text{ UO.A.Q.TOT}^{0.733} \\ \text{UO.A.Q.TOT} &= 2.234 \text{ AC.E.Q.TOT}^{1.364} \\ \text{AC.E.Q.TOT} &= 0.316 \text{ UO.E.Q.TOR}^{0.961} \\ \text{UO.E.Q.TOR} &= 3.317 \text{ AC.E.Q.TOT}^{1.040} \end{aligned}$$

and are plotted in Figure 2.

Calibration Curves

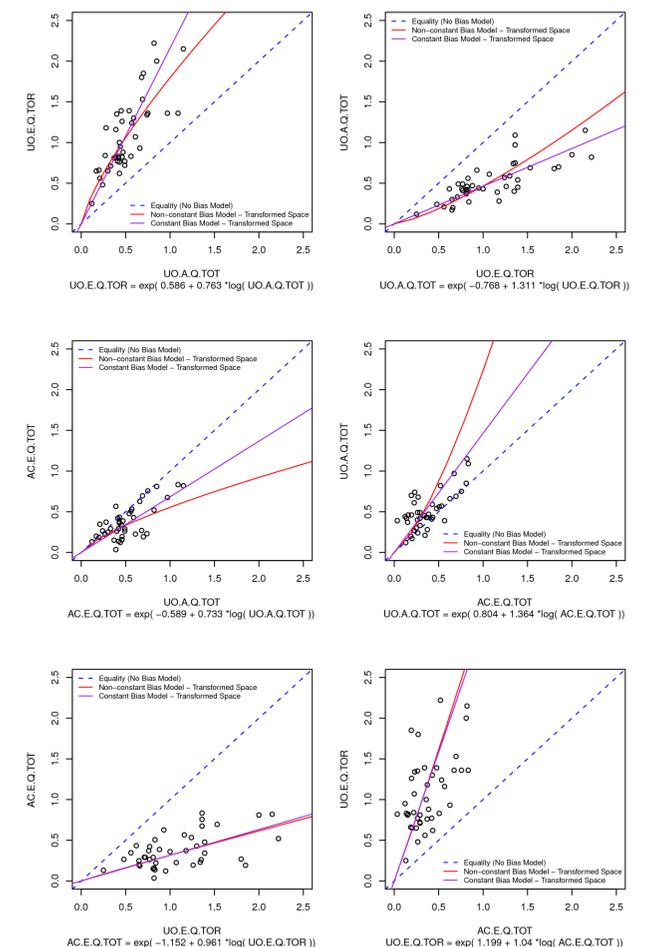


Figure 2: Calibration curves for elemental carbon.

References

- Richard A. Bilonick (2003). **merror**: Accuracy and Precision of Measurements. **R** package version 1.0. <http://www.r-project.org>
- Steven Boker, Michael Neale, Hermine Maes, Paras Metah, Sarah Kenny, Timothy Bates, Ryne Estabrook, Jeffrey Spies, Timothy Brick and Michael Spiegel (2010). **OpenMx**: The OpenMx Statistical Modeling Package. **R** package version 0.2.3-1006. <http://openmx.psyc.virginia.edu>
- John L. Jaech (1985). **Statistical Analysis of Measurement Errors**, John Wiley & Sons, New York.