How to accept the equivalence of two measurement methods?

Comparison and improvements of the Bland and Altman's approach and errors-in-variables regressions

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Motivation

Two measurement devices are often available to measure a same quantity of interest

NIR instruments in agronomy - chemistry - Clinical biology …

Real examples from consultancy:

Red-cross, devices in a hospital (cyst volume,…), pigmentation, concrete,…

Questions - Goals

Questions

- Are the measurements given by the two devices « equivalent » ?
- Is there a bias between the methods ?
- Do the two methods have the same precision ?
- Can one method be sustituted by the other ?

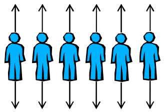
Goals

- Propose two procedures to compare two measurement methods
  - *Error-in-variables models*
  - *Bland and Altman's approach*
- Present the basic approaches, discuss their qualities and limitations and propose improvements
- Illustrations on a case study and on simulations

Outline of the talk

- **Precise problem definition**
- Bland-Altman approach – Tolerance Interval
- Errors-in-variables regresions approach
- Correlated Errors-in-variables regressions approach

The systolic blood pressure data



Patient	Sphygometer 'J'			Semi automatic 'S'		
i	J1	J2	J3	S1	S2	S3
1	100	106	107	122	128	124
2	108	110	108	121	127	128
…	…	…	…	…	…	…
i	X_{i1}	X_{i2}	X_{i3}	Y_{i1}	Y_{i2}	Y_{i3}
…	…	…	…	…	…	…
84	106	98	100	137	135	134
85	122	112	112	121	123	128

<u>S</u>ystolic <u>b</u>lood <u>p</u>ressure in mmHg

Bland JM, Altman DG. Measuring agreement in method Comparison studies. Stat Methods Med Res. 1999; 8:135-160

Typical experiment and notations

- Two « instruments » A and B are compared
- N « samples » are chosen and measured

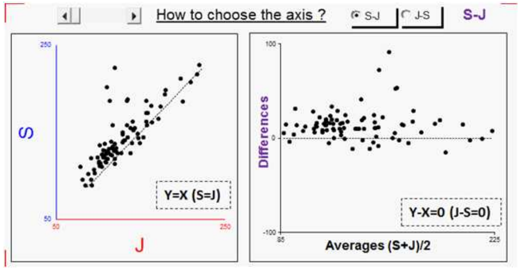
  « sample » = real sample, or subject
- Each sample is measured m_X and m_Y times on devices A and B

  X_{ij} = j_{th} measure of sample i for instrument A (Y_{ij} for B)
- Repeated measures of the same sample are averaged to X_i and Y_i which are paired data
- **m_X and m_Y are often equal to 1** (unreplicated data)
- There is **no** « real » **reference value** for what is measured.

  X_i is compared to Y_i and vice-versa (and NOT to a reference value)

Patient	Sphygometer 'J'			Semi automatic 'S'				
i	J1	J2	J3	S1	S2	S3	J	S
1	100	106	107	122	128	124	104,3	124,7
2	108	110	108	121	127	128	108,7	125,3
…	…	…	…	…	…	…	…	…
i	X_{i1}	X_{i2}	X_{i3}	Y_{i1}	Y_{i2}	Y_{i3}	X_i	Y_i

General principle of the two approaches



Error-in-variables regressions

- Y are plotted versus X
- A line Y = $\alpha+\beta$X is fitted
- The estimated line is compared to the equivalence line **Y=X** by hypothesis testing

Blant-Altman approach

- Averages (Y_i + X_i)/2 and differences Y_i – X_i are computed and displayed
- Look at the aspect of the scatter plot
- A calculated « agreement interval » is compared to an acceptance interval **[-Δ,Δ]**

Outline of the talk

Precise problem definition

➢ **Bland-Altman approach – Tolerance Interval**

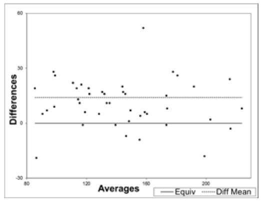
Errors-in-variables regresions approach

Correlated Errors-in-variables regressions approach

Bland and Altman approach

- Principle
  - Compute and plot the Averages $(Y_i + X_i)/2$ (X-axis) and differences $D_i = Y_i – X_i$ (Y-axis)
  - Look at the aspect of the scatter plot
  - Compute the « agreement interval » and compare to an acceptance interval $[-\Delta,\Delta]$
- Equivalence, agreement

  Ideally, the agreement interval is included inside the acceptance interval which means that the observed differences are not significantly higher than a practical threshold (the acceptance interval)



Intervals given by Bland & Altman, SBP data

- The agreement interval given by Bland & Altman

  Compute the differences, their mean and variance $D_i = Y_i - X_i$

  $$\bar{D} = \frac{1}{N}\sum_{i=1}^{N} D_i \qquad S_D^2 = \frac{1}{N-1}\sum_{i=1}^{N}(D_i - \bar{D})^2 \longrightarrow \boxed{\bar{D} \pm 1{,}96 \cdot S_D}$$

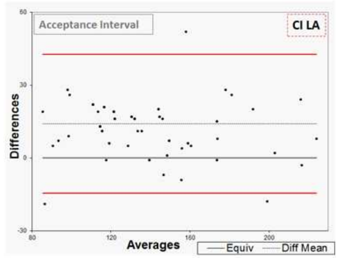
- And its Confidence interval

  $$(\bar{D} \pm 1{,}96 \cdot S_D) \pm t_{N-1;1-\alpha/2} \cdot S_D \sqrt{\frac{1}{N} + \frac{1{,}96^2}{2(N-1)}}$$

- Add if necessary the acceptance interval $[-\Delta,\Delta]$

  For example [-10;10] (mmHg)

- Improvements
  - Tolerance Intervals
  - A better estimation of a regression line



Tolerance interval (TI)

- Principle

  Define an interval which has given probability to contain a given proportion of the future difference

  $$P(a < Y_i - X_i < b) > \pi$$

  But the distribution of Y_i - X_i is unkwown $\quad Y_i - X_i = \sim iN(D_i, \sigma^2_{\upsilon_i})$

- Solution: tolerance intervals (« horizontal »)

  « beta » expectation tolerance interval

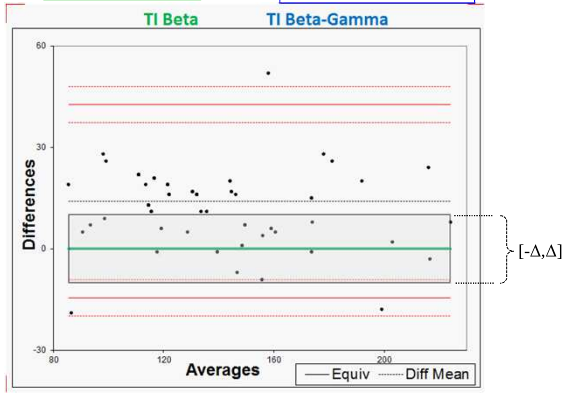
  $$\boxed{\bar{D} \pm t_{N-1;1-\alpha/2} \cdot S_D \sqrt{1 + \frac{1}{N}}}$$

  beta-gamma tolerance interval

  $$\boxed{\bar{D} \pm z_{1-\alpha/2} \cdot S_D \sqrt{1 + \frac{1}{N}} \sqrt{\frac{N-1}{\chi^2_{N-1;1-\gamma}}}}$$

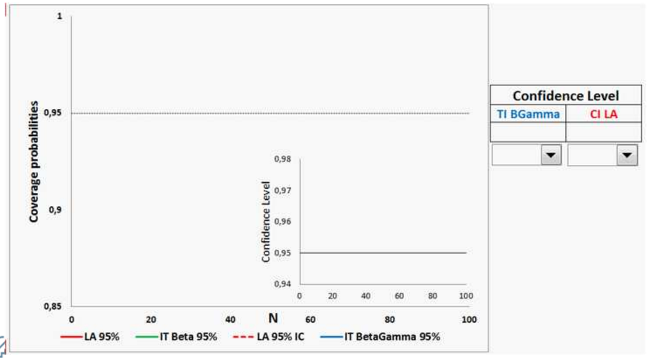
‘Horizontal’ Tolerance interval, SBP data

$$\boxed{\bar{D} \pm t_{N-1;1-\alpha/2} \cdot S_D \sqrt{1 + \frac{1}{N}}} \qquad \boxed{\bar{D} \pm z_{1-\alpha/2} \cdot S_D \sqrt{1 + \frac{1}{N}} \sqrt{\frac{N-1}{\chi^2_{N-1;1-\gamma}}}}$$



Coverage probabilities Tolerance Interval

- Simulate 10000 samples (N from 5 to 100, unreplicated data) under equivalence with known distribution for the differences $D_i = Y_i - X_i$
- For each simulated sample, compute the proportion of « new » differences inside each intervals and compare



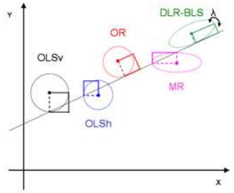
Outline of the talk

Precise problem definition

Bland-Altman approach – Tolerance Interval

➢ **Errors-in-variables regresions approach**

Correlated Errors-in-variables reg



Errors-in-variables models approach in (X,Y) plot

- Principle
  - Plot Y versus X
  - Fit a line Y = α + β X
  - Compare the estimtated line to Y=X equivalence line

- Equivalence definition

  The two methods are « equivalent » if

  α = 0 (no constant bias) and

  β = 1 (no proportionnal bias)

- Statistical problems
  - Fit a line taking into account the errors in both variables
  - Set up an appropriate hypothesis test procedure to test α=0 and β=1

Statistical model (unreplicated data)

Error in variables model

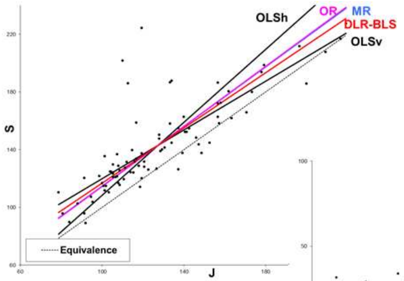
$$X_i = \xi_i + \delta_i$$
$$Y_i = \eta_i + \nu_i$$
$$\begin{pmatrix}\delta_i \\ \nu_i\end{pmatrix} \sim iN\left(\begin{pmatrix}0 \\ 0\end{pmatrix}, \begin{pmatrix}\sigma^2_{\delta_i} & 0 \\ 0 & \sigma^2_{\nu_i}\end{pmatrix}\right)$$
$$\lambda_{XY} = \sigma^2_\nu / \sigma^2_\delta$$
$$\eta_i = \alpha_{XY} + \beta_{XY}\xi_i$$
$$Y_i = \underset{=0}{\hat\alpha_{XY}} + \underset{=1}{\hat\beta_{XY}} X_i + e_{XYi}$$

Under Ho : Equivalence

Bland Altman Model

$$\frac{X_i + Y_i}{2} = \frac{\xi_i + \eta_i}{2} + \frac{\delta_i + \nu_i}{2}$$
$$Y_i - X_i = (\eta_i - \xi_i) + (\nu_i - \delta_i)$$
$$\lambda = \frac{\sigma^2_\delta + \sigma^2_\nu}{(\sigma^2_\delta + \sigma^2_\nu)/4} = 4$$
$$\eta_i - \xi_i = \alpha_{BA} + \beta_{BA}(\eta_i + \xi_i)/2$$
$$Y_i - X_i = \hat\alpha_{BA} + \hat\beta_{BA}(X_i + Y_i)/2 + e_{BAi}$$
$$\underset{=0}{\alpha_{BA}} = \frac{2\alpha_{XY}}{1+\beta_{XY}} \text{ and } \underset{=0}{\beta_{BA}} = \frac{2\beta_{XY} - 2}{1+\beta_{XY}}$$

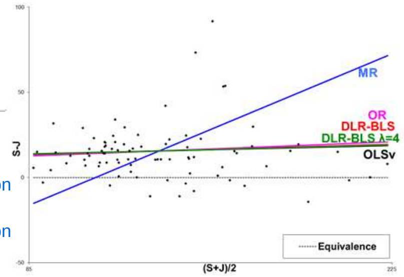
Regression lines for SBP data



The X,Y approach

The OLS lines are the « extreme » lines

The BLS is the most suitable regression



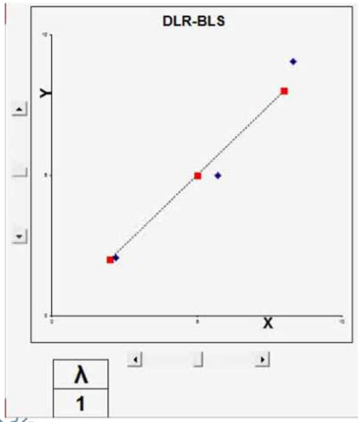
The B&A approach

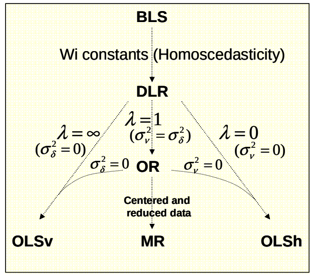
The most suitable regression is BLS with λ=4 ?

OLSh is the worst regression

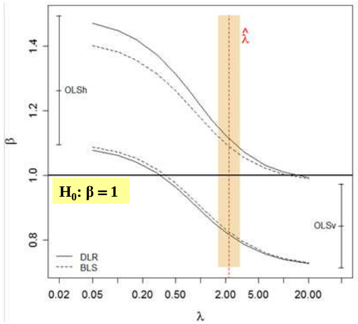
MR isn't a good idea

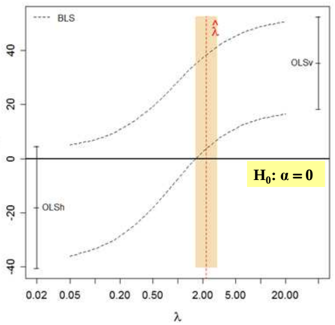
Regression methods comparison





Full Diagrams from the OLSv to the OLSh, CI

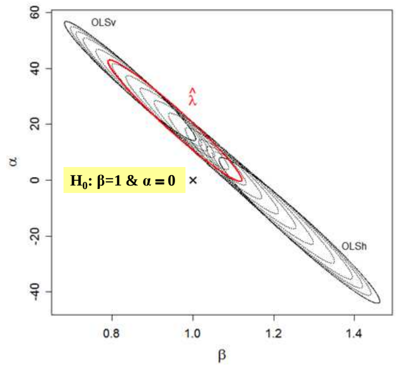




The hypothesis of no proportional bias isn't rejected

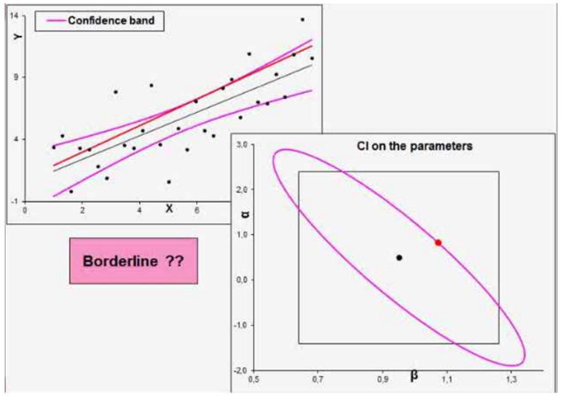
The hypothesis of no constant bias is borderline

Full Diagrams from the OLSv to the OLSh, joint-CI



The hypothesis of no bias is rejected whatever λ

Joint CI Ellipse or Confidence band

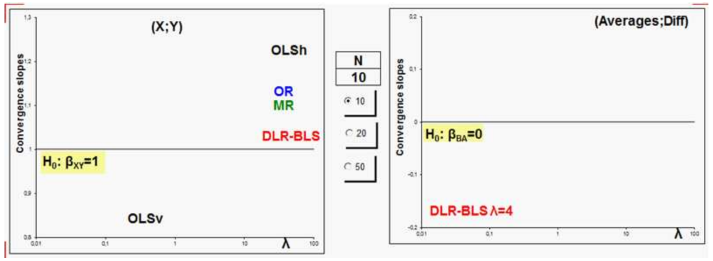


Bland & Altman's approach vs (X,Y) approach

- Error-in-variables regressions in (X,Y)
  - The BLS is the most suitable regression
  - Diagrams with the CI from OLSv to OLSh are very useful
  - The fitted line is compared to Y=X line
- Bland-Altman approach (Averages, Diff)
  - Is the BLS with λ=4 the most suitable regression?
  - Tolerance intervals are more appropriate than agreement interval
- Similarities
  - There is an « analogy » between both approaches
  - Tolerance intervals can also be applied with the (X,Y) approach (not shown in this presentation)
  - The « acceptance interval » [-Δ,Δ] in the Bland & Altman's approach becomes Y = X ± Δ with the (X,Y) approach (not shown in this presentation)
  - So, finally, what choice do we do? Regress in (X,Y) or in Bland & Altman's approach?

Bland & Altman's approach vs (X,Y) approach

Estimators bias under equivalence, example given for the slope

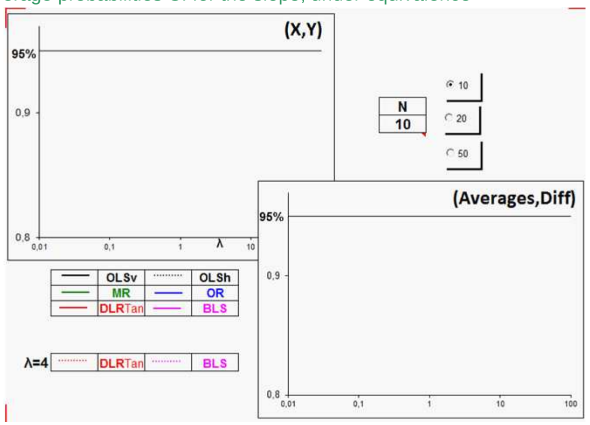


In (X,Y) approach, BLS is the most appropriate regression whatever λ but perform better with λ_{XY}>1

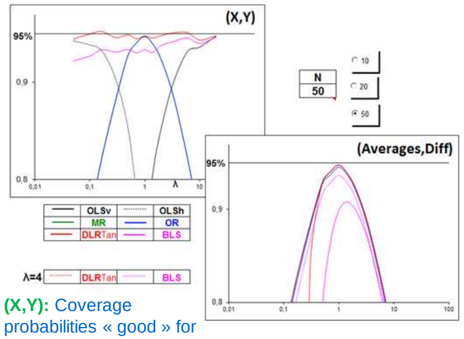
In the Bland & Altman's approach, all the regression perform « equally » at λ_{XY}=1 but the bias increases when λ_{XY} moves away from 1

Bland & Altman's approach vs (X,Y) approach

Coverage probabilities CI for the slope, under equivalence



Bland & Altman's approach vs (X,Y) approach



(X,Y): Coverage probabilities « good » for BLS when λ>1 (and excellent with the exact CI for the slope given by Tan)

Bland & Altman's approach: only good when λ_{XY}=1 otherwise the coverages probabilities collapse drastically!

Outline of the talk

- Precise problem definition
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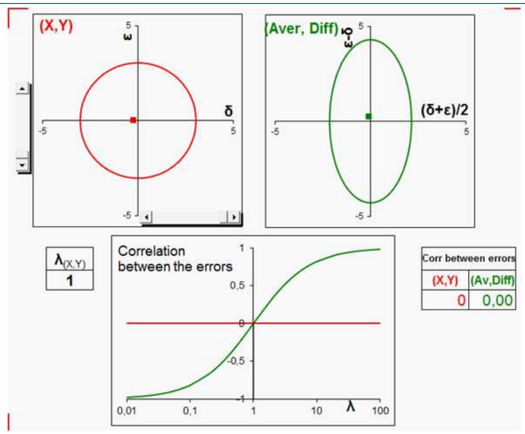
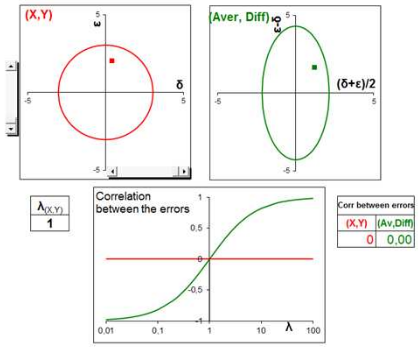
- Errors-in-variables regresions approach
- ➢ **Correlated Errors-in-variables regressions**

Bland & Altman's approach: errors-structure



Bland & Altman's approach: error structure

The errors terms are independant in the (X,Y) approach but dependant in the Bland & Altman's approach (with λ_{BA}=4)

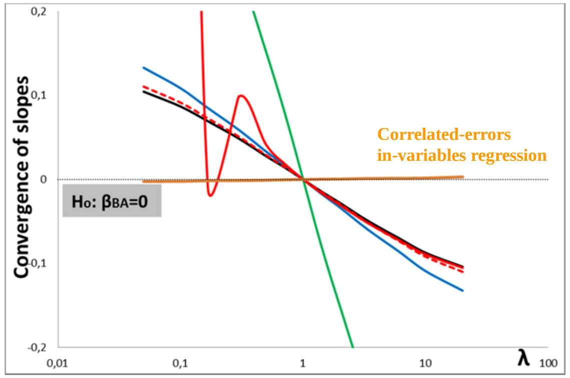


The more λ moves away from 1, the more the correlation between the errors in averages and differences in the Bland & Altman's approach increases!

The only way to regress correctly in the Bland & Altman's approach is to take into account this correlation

B&A's approach taking into account correlation between errors

Estimators bias under equivalence, example given for the slope, N=50



Full Diagrams in (X,Y) plot vs B&A plot

Diagram for the slope (X,Y) plot

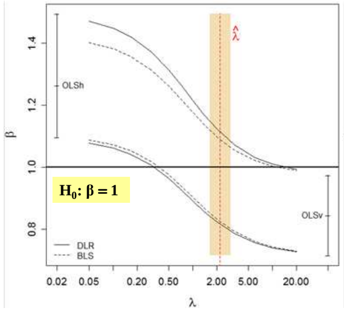


Diagram for the slope B&A plot

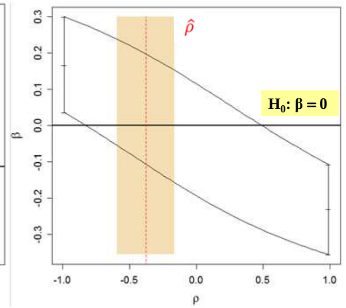


Diagram from $\lambda = 0$ to ∞ in a (X,Y) plot
and from $\rho = -1$ to 1 (correlation between the errors) in a B&A plot
If λ is unknown in a (X,Y) plot, ρ is unknown in a B&A plot

Conclusion and Further work

- Conclusions - remarks
  - BLS is the most suitable regression to take into account errors on both axis, heteroscedasticity (and correlation between the errors if necessary)
  - Bland & Altman's approach is probably the most applied method, widely used and very well known
  - To regress in a Bland & Altman's plot, the correlation between the errors terms must be taken into account
  - The tolerance intervals are very useful to compare with an « acceptance interval »
  - λ is an important parameter in a (X,Y) plot while it's equal to 4 in a B&A plot where the correlation between the errors is important
- Work in progress
  - Correlated errors in variables regressions and (exact-)CI and TI