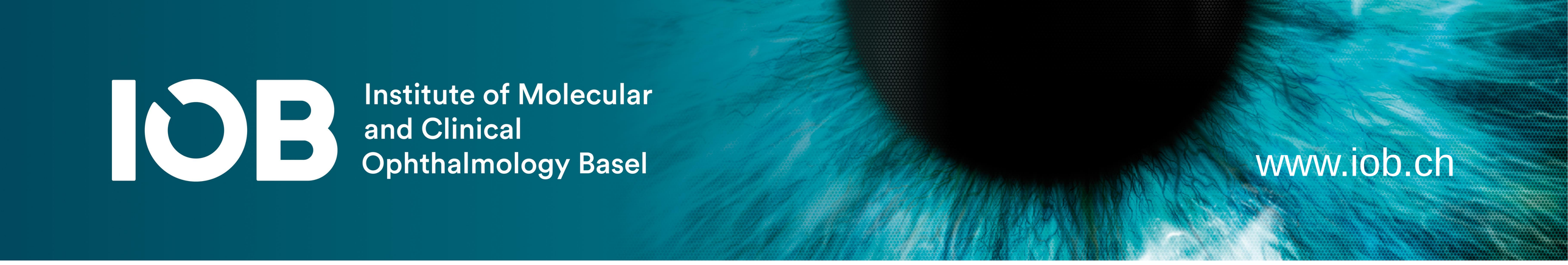

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Correlations in Ophthalmology (e.g., when measuring both eyes)

Disregarding the correlations among data points usually leads to slightly less efficient estimates and much too short confidence intervals. Novel statistical methods for correlation analysis based on a bivariate random effects model and multilevel parametric bootstrapping have been implemented in the `R` package `corre` (correlations with random effects).

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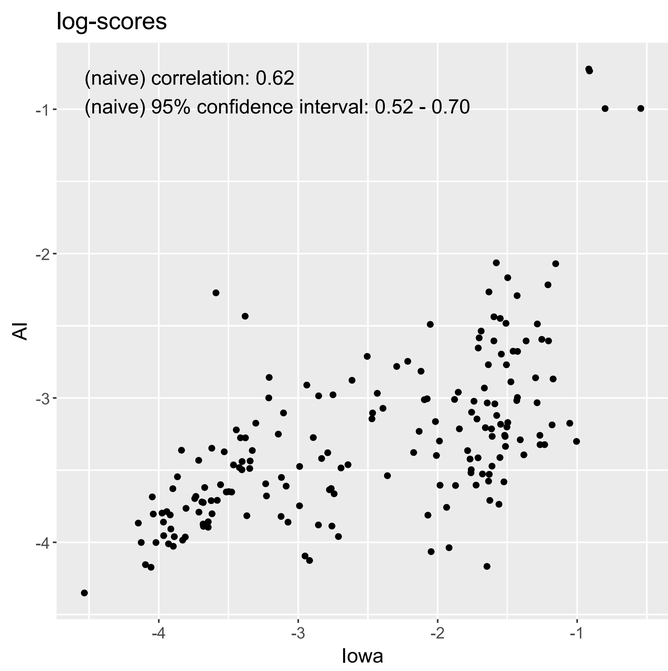
Example: correlation of log-scores

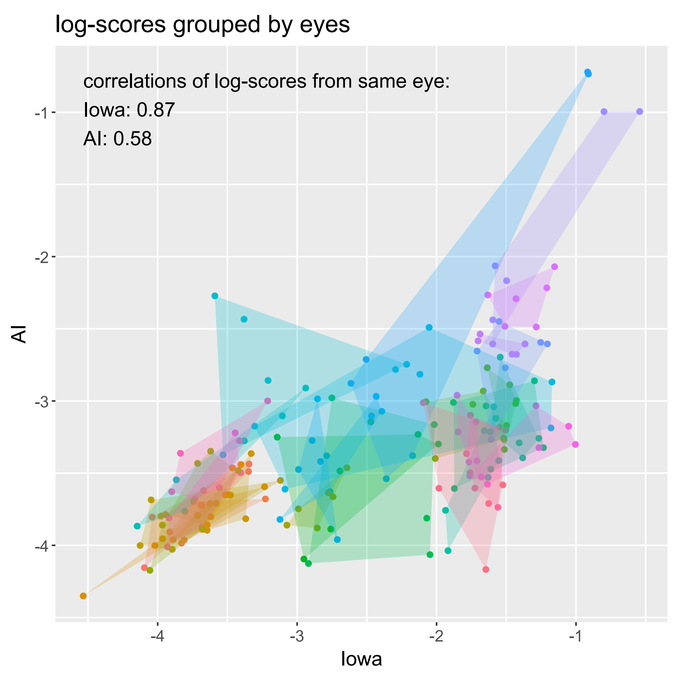
Comparison of two segmentation algorithms (with manual corrections) for OCT images from the **EyeConic** study: 184 data points, 31 eyes, 19 patients, 2 graders.

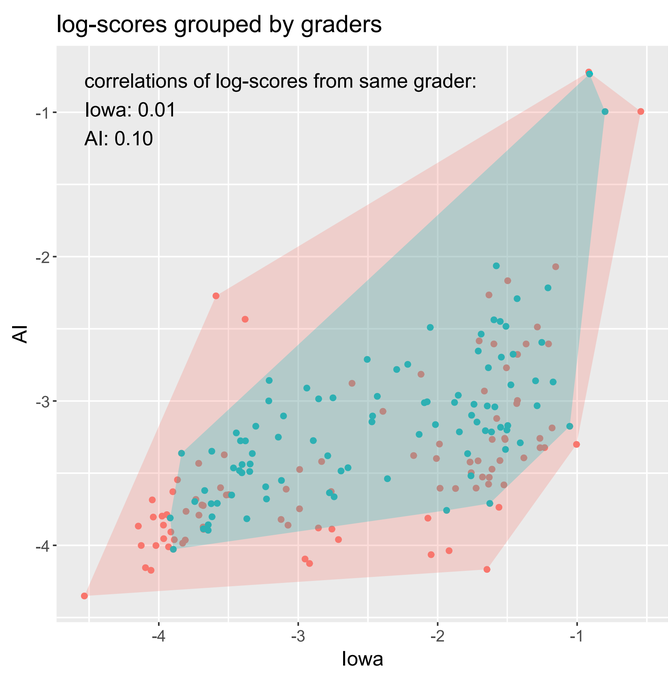
(Also 93 OCT images, but the information for grouping by OCT images is not completely available and anyway the grouping would be difficult to visualize.)

Data points from the same patient/eye/grader are correlated: are the (naive) correlation estimates still correct? No, in particular confidence intervals are too short (see below).

Questionable solutions, leading in general to loss of information and statistical power:
- data selection (e.g., selecting one eye per patient),
- data summary (e.g., averaging over the eyes of each patient).







Regression (asymmetric):

If we were interested in regression instead of correlation, we could fit an **LMM** (linear mixed model) with patient/eye/grader as random effects, e.g. in `R`:

```
lme4::lmer(AI ~ Iowa + (1|patient/eye) + (1|grader), logscores)
```

slope: 0.47, 95% confidence interval: 0.36 - 0.58

Without random effects (simple linear regression):
slope: 0.37, 95% confidence interval: 0.31 - 0.44

Simulation (10'000 replicates from LMM fit):
- RMSE (root mean square error):
  with random effects 0.054, without random effects 0.077
- actual coverage probability of nominal 95% confidence interval:
  with random effects 94%, without random effects 63%

Correlation (symmetric):

With the `R` package **`corre`** (Cattaneo, 2024+, version 1.0), correlations with patient/eye/grader as random effects can be calculated as well:

```
corre::corre(AI, Iowa, list(patient, patient:eye, grader), logscores)
```

correlation: 0.63, 95% confidence interval: 0.37 - 0.80

Without random effects (naive correlation):
slope: 0.62, 95% confidence interval: 0.52 - 0.70

Simulation (10'000 replicates from bivariate LMM fit):
- RMSE (root mean square error):
  with random effects 0.11, without random effects 0.12
- actual coverage probability of nominal 95% confidence interval:
  with random effects 97%, without random effects 55%