



TITLE: Bayesian prediction intervals for genetic toxicology assays using historical control data

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ABSTRACT: Data interpretation in genetic toxicology studies requires both biological and statistical assessment, with OECD guidelines for the testing of chemicals providing the regulatory framework while themselves evolving in precision through cross-disciplinary exchange. Statistical aspects are relevant for both assay acceptability and genotoxicity assessment, complementing the evaluation of biological relevance.

Historical control databases are required to define control intervals for comparisons regarding the current negative control and the positive control response (assay acceptability) as well as the effect of a test substance (additional criterion in genotoxicity assessment).

As one possible specification, we develop prediction intervals, explicitly named in a recent guideline, utilizing individual historical measurement data to predict individual future observations and derived statistics such as group means (often considered in test reports) and their ratios (especially to evaluate the positive control response).

Applications focus on assays with count data, specifically the in-vitro and in-vivo micronucleus tests as well as the Ames test, where random experiment effects and overdispersion within experiments render conventional binomial, Poisson or approximative Gaussian models inappropriate.

We therefore calculate prediction intervals using Bayesian generalized linear mixed models implemented in the R package *brms*, which respect the endpoint's distribution and hierarchical data structure, accommodate additional variability and prospectively allow for covariates or temporal correlation. Several individual future observations are predicted simultaneously to respect their correlation.

BRIEF SPEAKER BIO: Jonathan Rathjens - Early Development Statistics, Evidenze Germany GmbH, Essen, Germany

Jonathan Rathjens is a biostatistician working for the pharmaceutical industry in non-clinical statistics with a focus on research, toxicology as well as R development and automation.