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TECHNICAL REPORT

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TITLE: Statistical analysis of interlaboratory studies. XXIX. A simple and accurate replacement for the Horwitz rule.

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ABSTRACT: Sample data from an article related to the Horwitz formula is statistically reanalyzed, and a hypothetical simpler model for reproducibility standard deviation proposed: It is asserted that the $\log_{10}$ transform of quantitative method results has a normal distribution with a constant reproducibility standard deviation of 0.05. The model is suggested as a more physical and more accurate replacement for the Horwitz rule in assessing adequacy of quantitative method precision, and works remarkably well for concentrations below 0.01. Statistical analysis of the $\log_{10}$ transformed data will also eliminate the frequent outlier problem often encountered at very low concentrations. The model equivalently suggests the untransformed data will have a constant relative reproducibility standard deviation of 0.115.

KEYWORDS: 1) HORWITZ 2) REPRODUCIBILITY
3) REPEATABILITY 4) PERFORMANCE

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INTRODUCTION

Horwitz [1,2] discovered an empirical relationship between the reproducibility standard deviation SD_R of a laboratory measurement and the mean concentration (C) of an analyte. This rule resulted from a straight line fit of $\log_{10}(SD_R)$ vs. $\log_{10}(C)$. The fitted coefficients of this line were simplified to the resulting Horwitz formula

$$SD_R = 0.02\ C^{0.85} \qquad (1)$$

This rule and its "rule of thumb" ad hoc approximation of the standard deviation of repeatability SD_r as

$$SD_r = (2/3)\ SD_R \qquad (2)$$

has been used to assess the acceptability of a method of quantitation of an analyte [2], with acceptable values falling within 0.5 to 2.0 times the values predicted from eqs.(1) and (2).

Problems with the Horwitz rules have been encountered for concentrations below those originally investigated by Horwitz, particularly at the ppb and ppt ranges. For these concentrations, methods appear anomalously more precise than expected, with a Horwitz ratio sometimes only a few percent, well below the 0.5 suggested as the minimum allowed.

In what follows, a reanalysis of the data used by Horwitz is carried out, and a new, simpler formula for reproducibility obtained. This simpler formula extends indefinitely to low concentrations, suggests a statistical model for error, and fits the data as well or better than the Horwitz formula.

DATA

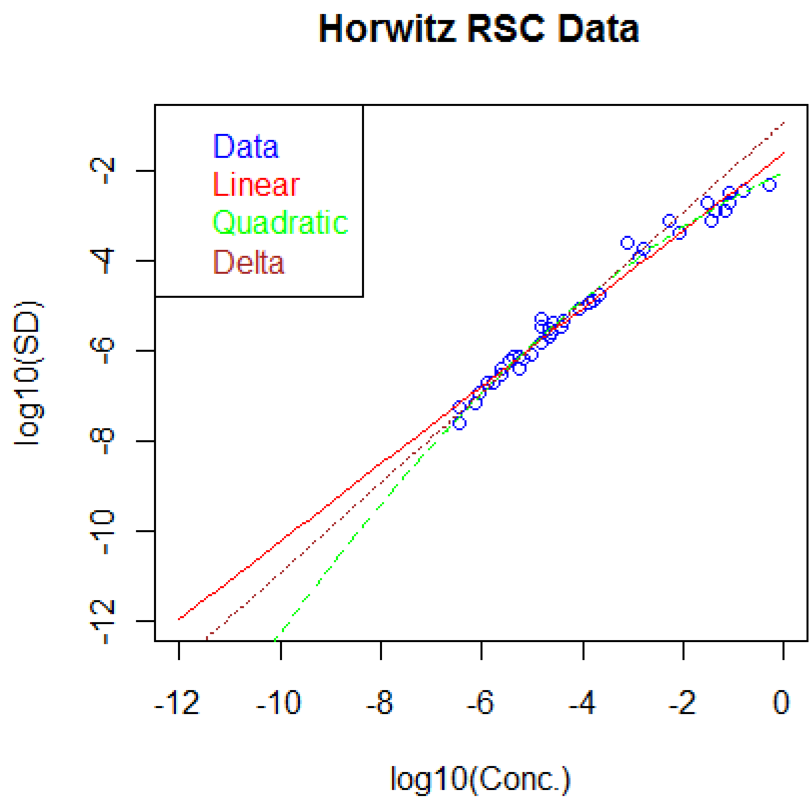
The data used for comparison was that included in Fig. 3 of Thomspon [3]. The points from this figure were digitized by computer into individual data, of which there were 40.

Datum	$\log_{10}(C)$	$\log_{10}(SD_R)$	$\log_{10}(C) - \log_{10}(SD_R)$
1	-6.44	-7.61	1.17
2	-6.46	-7.25	0.79
3	-6.11	-7.17	1.06
4	-6.03	-6.97	0.94
5	-5.87	-6.71	0.84
6	-5.76	-6.71	0.95
7	-5.60	-6.53	0.93
8	-5.62	-6.40	0.78
9	-5.45	-6.24	0.79
10	-5.37	-6.16	0.79
11	-5.27	-6.14	0.87

12	-5.27	-6.40	1.13
13	-5.17	-6.19	1.02
14	-5.02	-6.09	1.07
15	-4.83	-5.85	1.02
16	-4.83	-5.47	0.64
17	-4.83	-5.31	0.48
18	-4.65	-5.70	1.05
19	-4.63	-5.62	0.99
20	-4.65	-5.52	0.87
21	-4.59	-5.41	0.82
22	-4.40	-5.49	1.09
23	-4.36	-5.36	1.00
24	-4.07	-5.10	1.03
25	-3.87	-4.95	1.08
26	-3.78	-4.90	1.12
27	-3.66	-4.77	1.11
28	-3.10	-3.60	0.50
29	-2.88	-3.91	1.03
30	-2.79	-3.76	0.97
31	-2.26	-3.14	0.88
32	-2.07	-3.40	1.33
33	-1.52	-2.72	1.20
34	-1.44	-3.14	1.70
35	-1.37	-2.91	1.54
36	-1.17	-2.91	1.74
37	-1.09	-2.72	1.63
38	-1.06	-2.52	1.46
39	-0.80	-2.47	1.67
40	-0.28	-2.31	2.03

RESULTS

Consider the following graph:



The blue points indicate the data.

The red line is a straight line fit of $\log_{10}(SD_R)$ to $\log_{10}(C)$ for the entire dataset, with a slope of 0.86 (corresponding to Horwitz' 0.85) and intercept -1.62, whose antilog is 0.024 (corresponding to Horwitz' 0.02).

It is obvious that the data exhibit slight curvature, so the green quadratic curve was fit, with resulting form

$$\log_{10}(SD_R) \quad = \quad -2.07 + 0.503 \log_{10}(C) - 0.052 \log_{10}(C)^2 \qquad (3)$$

Within the range of the data, eq.(2) fits noticeably better than the straight line by any statistical measure (AIC, BIC, residual standard error, R^2).

However, it is unphysical to believe either the straight line or the quadratic will extrapolate correctly to very low concentrations. The straight line become increasingly pessimistic with respect to precision, with a slope that is too low because it is leveraged down by the highest concentration curvature. The quadratic predicts remarkably increasing precision as the concentration drops, which no physical mechanism can explain.

To allow extrapolation with any accuracy, a model must have a basis in a physical mechanism. An additional column has been added to the table of data above, showing the difference between $\log_{10}(C)$ and $\log_{10}(SD_R)$. This column was added to allow a visual check of the simple model that the reproducibility error is distributed as a lognormal distribution (i.e., $\log_{10}(C)$ is normally distributed with a constant standard deviation). If the distribution is lognormal, then the relative standard deviation $RSD_R = SD_R / C$ will be approximately constant, or, equivalently, $\log_{10}(C) - \log_{10}(SD_R)$ will be approximately constant.

Examination of the last column of the table above indicates that, for $\log10(C) < -2$, the values average remarkably close to 1.0 (actual: 0.94), corresponding to a $RSD_R = 0.115$. As this value is small compared to 1.0, this indicates the constant standard deviation of $\log_{10}(C)$ is $0.115 / \ln(10) = 0.050$, a remarkably simple result.

The brown curve in the figure above is that of

$$\log_{10}(SD_R) = \log_{10}(C) - 0.94 \qquad (C < 0.01) \qquad (4)$$

which may be considered a simpler alternative to the Horwitz relation of eq.(1).

Examination of the plot indicates the brown curve interpolates the data points with $\log_{10}(C) < -2$ more accurately than the Horwitz curve, and the implied constant $RSD_R = 0.115$ does not result in anomalous or unphysical values at very low concentrations.

In addition, the model suggests that $\log_{10}(C)$ is the natural experimental variable, and this variable has a normal distribution with $SD_R = 0.05$. Thus collaborative experiments should be analyzed and reported with respect to $\log_{10}(C)$ and not solely with respect to concentration directly.

SETTING PERFORMANCE CRITERIA

The new rule suggests the following performance criteria for an interlaboratory study on a quantitative method:

1. The experiment should be statistically analyzed in the transformed variable $\log_{10}$(result). This will also eliminate problems with outliers found too frequently at low concentrations (due to skewness of the untransformed variable's distribution).

2. The repeatability SD_r and reproducibility SD_R should be estimated in the usual way for the transformed results.

3. The 95% confidence interval on SD_R should include the value 0.05.

4. Assuming repeatability standard deviation averages no more than 2/3 the reproducibility standard deviation, the 95% confidence interval on SD_r should include the value 0.033, if $SD_r > 0.033$.

5. The 95% confidence interval for mean bias (candidate method result - reference result) should fall entirely within ($-SD_R$, $+SD_R$).

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