first order (straight line) regression the true alues of the intercept α and the slope β are independent of each other but their estimated alues $\hat{a}$ and $\hat{\beta}$ are not independent. This can be appreciated isuall b considering the straight lines joining all the indi idual pairs of points; those ith a large slope ill ha e a small intercept and vice versa, so the correlation bet een $\hat{a}$ and $\hat{\beta}$ is negati e and possibl substantial. This correlation has important consequences hen the estimated coefficients are used for significance testing in the interpretation of the regression line.

but we can calculate a joint distribution for them. This often paints a rather different picture of the valid inferences that can be drawn. This is best seen in a diagram showing the limit of the joint distribution as an ellipse.

Fig. 2 illustrates the effect of the dependence on the outcome for the calibration shown in Fig. 1. Point A in Fig. 2 shows the values of the estimated coefficients. Points B and C show example reference pairs of values defining illustrative joint null hypotheses, that is,

$$H_0\text{: } \alpha = \alpha_{\text{ref}} \text{ and } \beta = \beta_{\text{ref}}.$$

Point B falls within both of the individual 95% confidence intervals, so the regression coefficients (Point A) might naively be taken as showing no significant difference from the reference values. Crucially, however, point B falls outside the ellipse defining the joint confidence region, and the joint null is therefore properly rejected at 95% confidence. Point C, in contrast, falls outside the two individual confidence intervals, so might be taken as significantly different and rejected on both counts. However, it is clearly within the joint 95% confidence region and therefore the null hypothesis is not rejected.

These examples serve as an illustration for interpreting joint confidence regions but, for calibration purposes, an analyst would usually be interested in testing only the single null hypothesis that the intercept was zero, $\alpha = 0$. A zero intercept is useful as it means that the signal is proportion to the concentration. In any event, the slope of the graph is usually set at an arbitrary value. In Fig. 2 we see that zero is comfortably within the confidence limits (−82.5, 118.9) for the separate intercept estimate.

Comparison of two procedures for bias

In this section we consider the comparison between paired results from two analytical procedures applied to numerous different test materials. Translational bias would be present if $\alpha \neq 0$, rotational bias if $\beta \neq 1$. At first sight it seems as though we should test

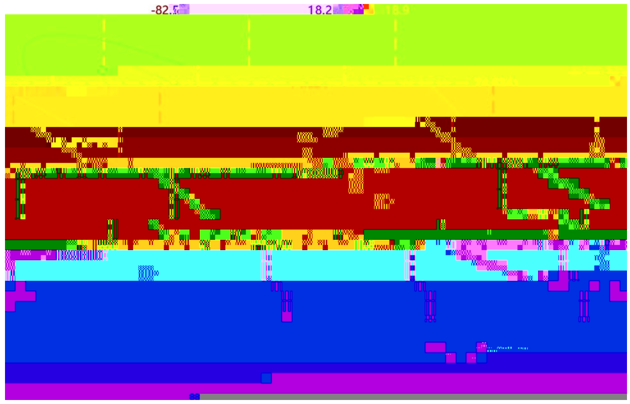

Fig. 2 Outcome of regression on data from Fig. 1, showing the regression coefficients (Point A), their individual 95% confidence limits (outer dashed lines), the limit of the 95% joint confidence region (blue ellipse), and two example joint null hypotheses (points B, C).

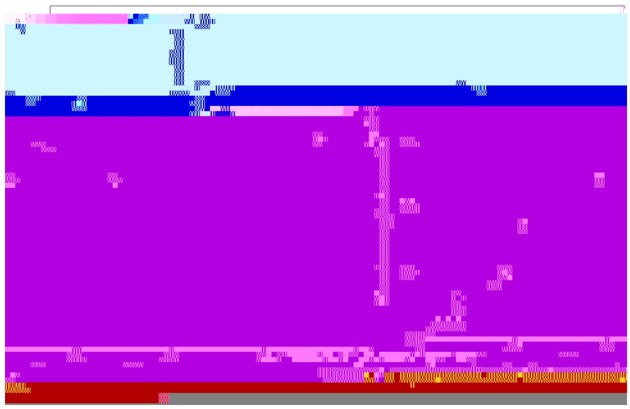

Fig. 3 Data (blue solid circles) from a comparison between an experimental field method and a laboratory reference method for the determination of uranium in stream water (excluding values above 100 ng ml^{-1}). Each point is from a separate source of water. Here the laboratory method is assumed to have the smaller variance and is treated as the independent variable. Data (from AMC Datasets) can be found at http://www.rsc.org/images/Uranium_in_stream%20water_tcm18-57750.txt.

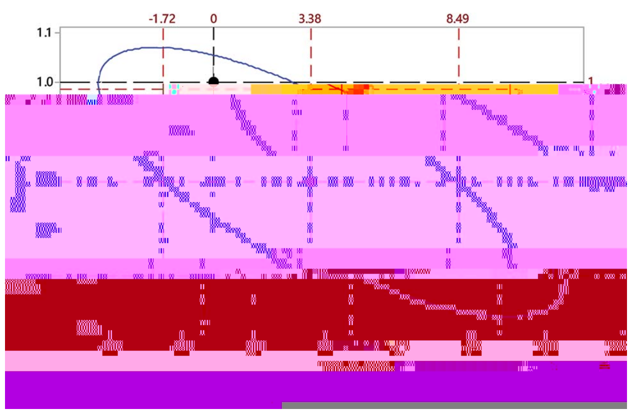

Fig. 4 Outcome of regression on data from Fig. 3, showing the regression coefficients (central point), their individual 95% confidence limits (outer red dashed lines), the limit of the joint 95% confidence region (blue ellipse), and a joint null hypothesis H_0: ($\alpha = 0$ and $\beta = 1$) (black dashed lines and point).

the respective null hypotheses separately. However, because of the correlation between the coefficients we can validly test only the joint outcome for inferring bias (or its absence) between the analytical procedures. In such cases we can formulate a joint null hypothesis, namely,

$$H_0\text{: } (\alpha = 0 \text{ and } \beta = 1).$$

Random variation aside, that is what we would expect if there were no bias at all.

Fig. 3 shows some results from a comparison of a laboratory-based reference method and a square error. This is a quadratic equation in $\tilde{\beta}$ with roots

By inserting any appropriate value of $\tilde{\alpha}$, we obtain two real values of