MEASUREMENT UNCERTAINTY IN ISOTHERMAL TITRATION CALORIMETRY

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Isothermal Titration Calorimetry (ITC) has a wide range of application in chemical and biochemical research. This method is based on the measurement of the heat effects of the studied process and allows to simultaneously determine several thermodynamic parameters in a single experiment. Several issues were previously reported in literature concerning metrological aspects of ITC [1], and more recent research [2] still emphasizes calibration and uncertainty evaluation in ITC as an ongoing problem.

In 2023 VNIIM calorimetry lab finished a project on improvement of the State Primary Standard of heat quantity in the field of solution and reaction calorimetry GET 133. A new calorimetric complex including a standard titration microcalorimeter (TMC) and a NanoITC SV microcalorimeter-comparator was developed that allowed to implement the ITC method and broaden the measurement capabilities of the GET 133 Primary Standard to the microcalorimetry range.

The goal of current work was to study and evaluate the uncertainty contributions based on the measurement model developed for the TMC considering its operating principle, which consists in determining the energy equivalent of the calorimeter ε in stationary mode and measuring the amount of heat Q released during the titration process. The contributions studied included instrumental sources from the characteristics of the measuring equipment and methodological sources from the experiment design, data analysis and interpretation.

The standard GUM approach [3] and the Monte Carlo method [4] were used to estimate combined standard and expanded uncertainties for determining the energy equivalent and measuring the amount of heat. As a result of microcalorimeter studies, the capability of realizing the unit of heat quantity in a range from 100 μJ to 5000 μJ with an expanded uncertainty from 1.2 % to 8.6 % was confirmed.

Our uncertainty estimates obtained using the “bottom-up” approach basing on the uncertainty components were compared with the “top-down” estimate based on the interlaboratory study results described in [1].

In perspective, the results of this study can be adapted to get more reliable uncertainty estimates for heat effects measured by commercial measuring instruments.

1. Velazquez-Campoy A. et al., *European Biophysics Journal*, 2021, 50, 429
2. Medos Z. et al., *Analytical Biochemistry*, 2024, 694, 115602
3. JCGM 100:2008. Evaluation of Measurement Data—Guide to the Expression of Uncertainty in Measurement, 1st ed., JCGM (2008)
4. JCGM 101:2008. Evaluation of measurement data — Supplement 1 to the “Guide to the expression of uncertainty in measurement” — Propagation of distributions using a Monte Carlo method, 1st ed., JCGM (2008)