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UncertCalc: a web-based tool for measurement uncertainty calculation

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Abstract: This study presents UncertCalc, a web-based tool developed to facilitate measurement uncertainty calculations in laboratory settings. The application is supporting both Top-Down and Bottom-Up approaches. The Top-Down module performs ANOVA based estimation of within day repeatability and between day intermediate precision using multi day repeated measurements. The Bottom-Up module calculates the combined measurement uncertainty by incorporating user-defined uncertainty components. Both modules have graphical visualization of uncertainty contributions. The computational accuracy of UncertCalc was independently validated using Microsoft Excel and R, using randomly generated representative data for both Top-Down and Bottom-Up approaches. Results from these comparisons proved to be in perfect agreement across the different platforms, confirming that UncertCalc offers statistically reliable and fully traceable calculations, consistent with established analytical tools.
UncertCalc has been developed to provide a practical solution that enables a sound, accessible process of biochemical measurement methods according to ISO/IEC 17025.

Keywords: Measurement uncertainty; top-down approach; bottom-up approach; ANOVA; biochemistry; web application.

1. Introduction

Measurement uncertainty is crucial for the estimation of the accuracy and reliability of tests in an analytical laboratory. MU in clinical chemistry, where results directly influence medical decisions, calls for proper understanding and calculation. It gives the interval within which the true value of a test result is expected to fall. Thus, it has a direct influence on the interpretation of results and subsequent medical decisions. Proper estimation of MU is required for laboratory accreditation and is a key quality indicator for both laboratory performance and in vitro diagnostic (IVD) systems [1-3]. Failure to meet pre-determined APS for uncertainty may lead to misdiagnosis, treatment errors, and risks associated with patient safety [4]. In this regard, uncertainty is not only about the variability of instruments, but it also includes sample preparation, environmental conditions, calibration sources, and analytical methods.

According to the ISO/IEC 17025 standard, measurement uncertainty should be estimated for all methods, and, thus, it is an inherent part of routine practice [5]. There are two main approaches described in the literature. The Top-Down approach, based on field data and long term performance monitoring, recently gained wide acceptance for routine biochemical analyses due to its reflection of real laboratory conditions by considering natural result variation directly. The "top-down" approach, utilizing internal quality control and calibrator data, is widely recommended in routine clinical laboratories because of its practicality and applicability according to ISO 20914 guidelines [3]. The Bottom-Up approach involves

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identification, modeling, and mathematical combination of all individual components of uncertainty and requires more detailed and theoretical analysis [6].

The factors contributing to measurement uncertainty include, among others, instrument imprecision, calibration procedures, sample preparation, environmental conditions, and lot to lot variability of reagents. Standardization of MU assessment remains a task because of methodological diversity among laboratories and the requirement for harmonized, clinically based analytical performance specifications.

Several factors relate to MU in clinical chemistry, instrumental imprecision, sample handling and preparation, environmental variability, calibration processes, and reagent inconsistencies. Besides the aforementioned challenges regarding both compliance with the regulations and its critical role in practice, standardization of MU assessment remains a challenge due to methodological variability across laboratories, differences in instrumentation, and the lack of universally harmonized, outcome based analytical performance specifications (APS). Table 1 summarizes the main features of measurement uncertainty in the framework of clinical chemistry regarding its major contributors, clinical relevance, and challenges toward standardization. This overview emphasizes that there is a real need to implement practical, accurate, standardized tools for MU estimation to support reproducibility, compliance with accreditation standards, and, finally, improved patient care.

Table 1. Key Aspects of Measurement Uncertainty in Clinical Chemistry

Aspect	Description and Relevance	Citation
Accreditation Requirement	ISO 15189 mandates MU estimation for all quantitative results	[1]
Main Contributors to MU	Instrument imprecision, calibration, sample preparation, environmental factors, reagent lot changes	[4]
Clinical Impact	Inadequate MU can lead to misdiagnosis, errors, and patient safety risks	[7]
Standardization Challenges	Variability in methods; need for harmonized, outcome-based APS	[8]

Accurate and standardized estimation of measurement uncertainty (MU) is essential for ensuring reliable test results, supporting laboratory accreditation, and minimizing risks of diagnostic errors. Tools that facilitate practical calculation and visualization of uncertainty, while adhering to international standards, are therefore critical.

Addressing the lack of such tools, UncertCalc was developed as a user friendly, web-based application that integrates both Top Down and Bottom Up approaches, enabling laboratories to evaluate measurement uncertainty effectively, visualize contributing factors, and generate comprehensive reports in compliance with ISO/IEC 17025. Recent studies report that the absence of accessible tools often leads to calculation mistakes, inconsistent reporting, and time inefficiency. By providing a standardized, practical solution with a comprehensive statistical infrastructure, UncertCalc allows laboratory personnel to perform uncertainty calculations quickly, reproducibly, and with minimal error [6]. (available at: https://uncertcalc.streamlit.app/).

2. Experimental

2.1. Materials and Methods

2.1.1. Software Architecture

UncertCalc is implemented in Python and utilizes modern scientific computing libraries. The user interface is built with the Streamlit framework, allowing access via web browsers without installation [9, 10]. Data processing and mathematical computations are performed using NumPy and Pandas; statistical analyses use SciPy, graphical outputs are generated with matplotlib, and PDF reporting is handled via ReportLab. This architecture supports the implementation of established mathematical approaches for uncertainty analysis in analytical measurements.

2.1.2. Top-Down Uncertainty Calculation

The Top-Down approach evaluates long-term performance of measurement systems based on routine daily quality control (QC) data, commonly applied in clinical chemistry laboratories. It follows statistical principles described in ISO/IEC 5725 and Eurachem guidelines [11, 12]. UncertCalc performs Top-Down uncertainty estimation by first calculating daily repeated-measurement means and standard deviations, followed by determining the overall mean across all measurements. Between-day and within-day variance components are then separated using one-way ANOVA, and these variance components are computed in accordance with ISO/IEC 5725. Based on these components, the combined standard uncertainty is derived, and finally, the expanded uncertainty is calculated assuming a coverage factor of $k = 2$.

In an attempt to ensure that the statistical estimates are robust, UncertCalc proposes a preliminary step of outliers detection. Box plots of the dataset are visually explored and the IQR rule follows, $Q3 \pm 1.5 \times IQR$, flagging questionable data as erroneous or unrepresentative. This is important because such outliers have the potential to inflate artificially both the within-day and between-day variance components which are estimated by ANOVA and will therefore provide an unreliable expanded uncertainty U.

2.1.3. Bottom-Up Uncertainty Calculation

The Bottom-Up approach identifies all individual uncertainty components affecting the measurement process and combines them mathematically. Each component can be expressed as absolute (u) or relative (%u) uncertainty. Component combination follows the root sum of squares method as described in the GUM [13].

UncertCalc supports three data entry modes, providing flexibility for different laboratory workflows. In Manual Mode, users can enter measurement data day by day, allowing precise control over each dataset. Paste Mode enables direct transfer of values from Excel or LIMS systems, streamlining data import for larger studies. Validation Mode allows users to compare calculated uncertainties with predefined reference values, supporting method verification and quality assurance processes.

2.1.4. Results and Reporting

Results are exported as PDF reports, including ANOVA tables, variance components, total uncertainty values, and Bottom-Up component contribution charts (Figure 1).

2.2. Method Validation Using Excel and R 4.5.1

To verify the computational accuracy of UncertCalc, an independent validation study was performed using two commonly accepted analytical platforms, Microsoft Excel and the R statistical programming environment. The analysis included both Top-Down and Bottom-Up uncertainty calculations using randomly generated representative component data. All calculations were repeated across platforms to ensure consistency.

The supporting file includes both the raw input data (randomly generated for demonstration) and the calculated uncertainty results, allowing full traceability and reproducibility of the validation process (Supporting file).

2.3. Excel Based Validation

Excel spreadsheets were used to reproduce all statistical analyses performed in the study, including daily statistical summaries, one-way ANOVA, within-day and between-day variance components, the calculation of combined standard uncertainty (uc), and the estimation of expanded uncertainty. All formulas implemented in the Excel worksheets were manually inspected and verified to ensure full compliance with ISO/IEC 5725 and GUM guidelines.

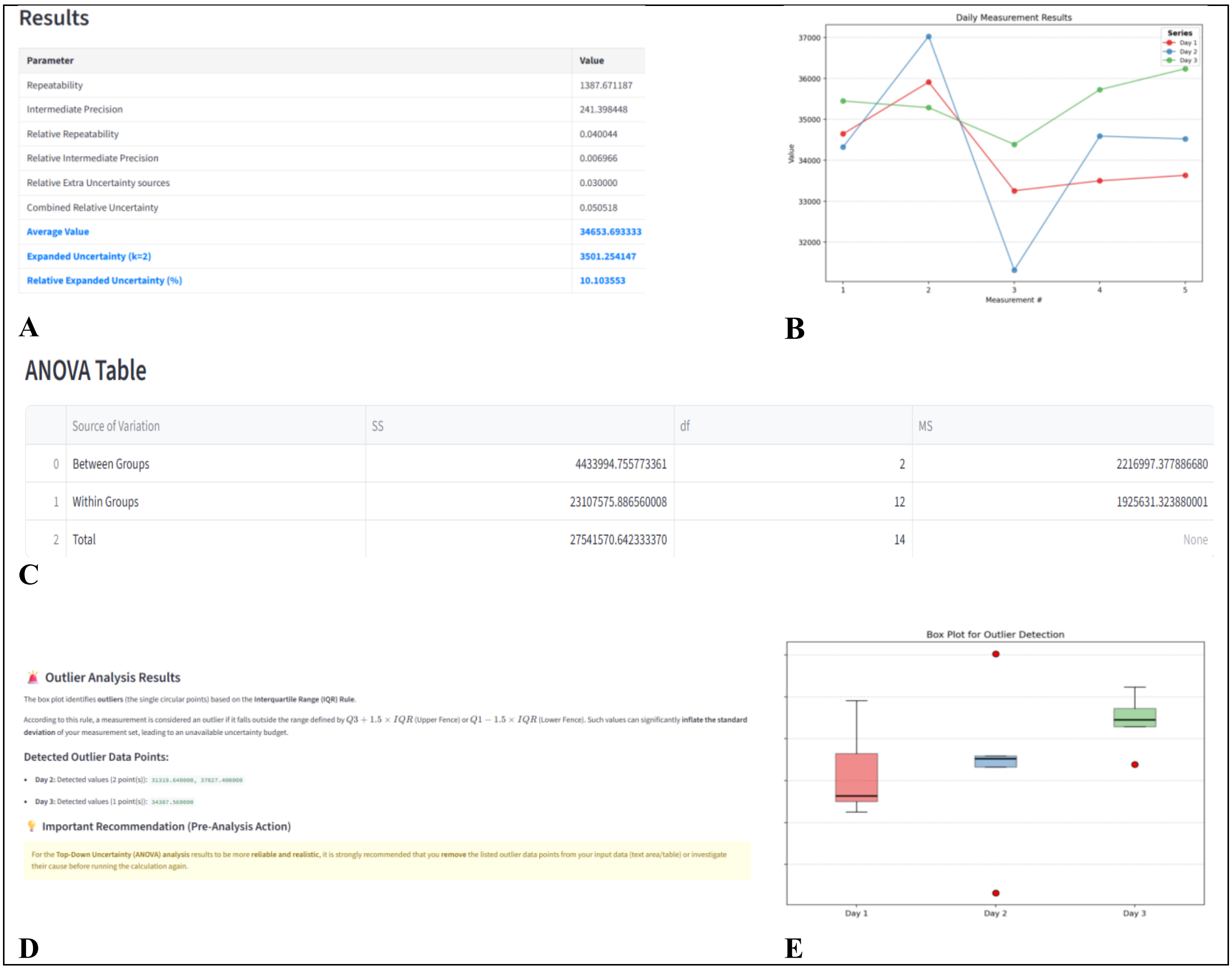

Figure 1. Screenshots of the application. (A) Measurement uncertainty results of the data; (B) Daily measurements of the data; (C) ANOVA results; (D) Outlier analysis results; (E) Box plot for outlier detection.

2.4. R-Based Validation

R (version 4.5.1) was used to independently compute all relevant statistical parameters, including variance components obtained through ANOVA, the combined uncertainty calculated via the root-sum-of-squares method, the evaluation of uncertainty distributions, and agreement statistics.

3. Results and Discussion

The application provides high-accuracy calculations of measurement uncertainty employing both Top-Down and Bottom-Up approaches. The Top-Down module statistically interprets multi day repeated measurements, automatically producing ANOVA tables and accurately segregating within-day repeatability and between-day intermediate precision components. Because the ANOVA outputs are provided in a standard format, laboratory professionals can take results directly from the outputs without transferring data to external software applications. Full tabulation of the mathematical basis for calculations also allows users to review the methodology.

This graphical interface also enables users to add more uncertainty components in absolute or percentage form, where the system updates the calculations dynamically. This makes it very useful for laboratory specialists who want to evaluate the impact of different uncertainty components on the results.

Incorporating a preliminary outlier detection step greatly enhances the reliability of the Top-Down uncertainty estimation. The use of box plot visualization in combination with the IQR criterion provides effective identification of anomalous data points that do not reflect the true performance of the measurement system. Excluding such outliers prevents artificial inflation of either the within-day or between-day variance components calculated by one-way ANOVA.

The Bottom-Up module presents the contribution of each component to the total uncertainty, using detailed graphical representation that clearly depicts their relative weights. This helps the user immediately identify the dominant sources of uncertainty in the measurement process and target process improvement efforts. Graphical presentation of uncertainty components facilitates monitoring and reporting by quality management units.

One-way ANOVA was conducted using daily measurements to test homogeneity between the three days. Table 2 presents the comparison of Excel and application -based calculations of SS, df, and MS. Results from both platforms are close to each other, and this confirms that the applied computational workflow gives correct estimates of variances.

Table 2. Comparison of One-Way ANOVA Sum of Squares Across Excel, UncertCalc, and R

Source	Excel SS	UncertCalc SS	R SS
Between Groups	4433999.457	4433994.756	4433994.756
Within Groups / Residuals	23107600.920	23107575.887	23107575.887
TOTAL	27541600.377	27541570.642	27541570.642

Representative daily measurements of the five analytes were used to validate the computational accuracy of UncertCalc. Both Excel and R were employed to calculate within-day and between-day variance components, combined standard uncertainty (uc), and expanded uncertainty ($U = k \cdot uc$, $k=2$). Table 2 shows the comparative results obtained from the three platforms, demonstrating agreement and confirming the reliability of the implemented algorithms.

Results obtained from Excel, R, and UncertCalc showed same results for all parameters in the Top-down uncertainty model. Both combined and expanded uncertainties were consistent across all platforms, confirming that UncertCalc produces fully traceable and statistically reliable calculations comparable to standard analytical tools (Table 3).

Table 2. Top-down approach: cross-platform comparison of uncertainty components (Excel, UncertCalc, and R)

Parameter	Excel	UncertCalc	R script
Mean value	34653.69	34653.69	34653.69
Repeatability (ur)	1387.67	1387.67	1387.67
Intermediate precision (uip)	241.40	241.40	241.40
Relative extra uncertainty	0.0300	0.0300	0.0300
Combined relative uncertainty	0.0500	0.0505	0.0505
Combined absolute (u_c)	**1750.63**	**1750.63**	**1750.63**
Expanded uncertainty (k=2)	**3501.25**	**3501.25**	**3501.25**
Relative expanded uncertainty (%)	**10.10**	**10.10**	**10.10**

The bottom-up uncertainty analysis was performed using three independent approaches, a custom R script, Microsoft Excel, and the UncertCalc software. The results from all three methods were found to be identical when rounded to the same number of significant digits. Specifically, the combined relative uncertainty was 0.014967 and the expanded uncertainty (U, with k=2 and a reference value of 10) was 0.299333 across all platforms. This complete agreement confirms the consistency and reliability of the bottom-up uncertainty calculation, regardless of the computational tool used (Table 4).

Table 3. Bottom-Up Approach: Cross-Platform Comparison of Uncertainty Components (Excel, UncertCalc, and R)

Parameter	Excel	UncertCalc	R Script
Balance (Uncertainty)	0.012000	0.012000	0.012000
Calibration (Uncertainty)	0.004000	0.004000	0.004000
Repeatability (Uncertainty)	0.008000	0.008000	0.008000
Combined Uncertainty	0.014967	0.014967	0.014967
Expanded Uncertainty (U, k=2)	0.299333	0.299333	0.299333

UncertCalc is a tool that contributes to the standardization and acceleration of measurement uncertainty calculations in analytical laboratories. Compared to other tools reported in the literature, it stands out for both its comprehensive methodological infrastructure and user friendly web-based interface. While some commercial and open source solutions focus solely on the Bottom-Up approach, and others offer limited support for Top-Down calculations, UncertCalc integrates both approaches on a single platform, addressing this gap [14].

A major strength of the application is the Top-Down module's full compliance with the statistical methods defined in ISO/IEC 5725 and Eurachem guidelines. By using multi day measurement data to separate repeatability and intermediate precision components, it provides a major advantage for long term performance monitoring in biochemistry laboratories. Unlike many free software tools, which require additional data processing for ANOVA table generation, UncertCalc automates this step, reducing potential errors.

The Bottom-Up module presents component contributions graphically, which is in line with the requirement to provide transparency of the sources of uncertainty that has been emphasized repeatedly. Similarly, employing the root sum of squares method according to the GUM guidelines means that the calculations are based on internationally accepted theoretical principles, thus offering higher methodological traceability than other existing tools.

A few limitations of the application are to be noted. Although the web-based nature offers considerable advantages in terms of accessibility, some institutions may have internet access restrictions because of information security policies. Software can be installed on local servers, but this may necessitate additional IT infrastructure in some laboratories.

4. Conclusions

UncertCalc is an online, user-friendly, and scientifically compliant software created to meet increasing demands for measurement uncertainty analysis. Although uncertainty calculations are by nature complex and very time-consuming, this application simplifies processes while offering practical functionality.

Conformity of the software with the requirements of ISO/IEC 17025, with both modules of Top-Down and Bottom-Up calculations, contributes greatly to standardizing measurement uncertainty in clinical chemistry laboratories. The real multi-day field data applied in the Top-Down module enable reliable estimates that reflect real conditions in a laboratory. By providing both approaches within the same platform, UncertCalc offers flexibility to the user in the method of choice.

While web-based access offers many advantages, in many laboratories access may be limited based on security policy [15]. The ability to run UncertCalc on local or isolated networks reduces these concerns. Results are provided in a user-friendly format, and the automation of the calculations minimizes the possibility of errors; however, there is some risk that the user will interpret results without understanding the statistical model upon which the results are based. Incorporating educational notes and warnings, and descriptions of methodological choices, are ways to ensure that the user does not simply produce results but also understands the basis for methods applied.

In conclusion, UncertCalc provides complete functionality for scientific computing while combining practical usability. Therefore, it contributes highly to the evaluation of measurement uncertainty in clinical chemistry laboratories. Its conformity with ISO/IEC 17025 and integration of Top-Down and Bottom-Up approaches make it versatile across different needs of laboratories. The future versions, with their offline availability, will have enhanced reporting capabilities and automated data integration, thus extending their applicability further.

Supporting Information

Supporting information accompanies this paper on http://www.acgpubs.org/journal/ journal-of-chemical-metrology

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