Scholars Journal of Engineering and Technology
Abbreviated Key Title: Sch J Eng Tech
ISSN 2347-9523 (Print) | ISSN 2321-435X (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

# AI and Physics-Guided Multimodal Chemical Measurement: Unifying Spectroscopy, Chromatography–Mass Spectrometry, Electrochemical Sensing, and Chemical Imaging Via Data Fusion from Molecules to Materials and Devices

Ubaid Ullah Khan[1], Muhammad Umair[2], Ali Hamza Zahid[3], Maryam Aziz[4], Muhammad Umar Farooq Ahmad Kharl[5], Muhammad Aftab[6], Huraira Sayam[6], Muhammad Umer Farooq[7], Shariq Hassan[8], Waheed Zaman Khan[9,10*]

[1]College of Ecology and Environment, Chengdu University of Technology, Chengdu 610059, Sichuan, China
[2]Centre of Excellence in Solid State Physics, University of the Punjab, Lahore, Pakistan
[3]Department of Chemistry, The Islamia University of Bahawalpur, Punjab, Pakistan
[4]Department of Chemistry, University of Education, Lahore, Punjab 54770, Pakistan
[5]Department of Chemical Engineering, COMSATS University Islamabad, Lahore Campus, Pakistan
[6]Department of Chemical Engineering, University of Engineering and Technology (UET), Peshawar, Pakistan
[7]Department of Chemistry, University of Engineering and Technology (UET), Lahore 54590, Pakistan
[8]Department of Chemistry, University of Agriculture, Faisalabad, Punjab, Pakistan
[9]Department of Physics, Division of Science and Technology, University of Education, Lahore, Punjab 54770, Pakistan
[10]Phystech School of Aerospace Technology, Moscow Institute of Physics and Technology (MIPT), Dolgoprudny, Moscow Region 141700, Russian Federation

**DOI:** https://doi.org/10.36347/sjet.2026.v14i01.002 | **Received:** 22.10.2025 | **Accepted:** 27.12.2025 | **Published:** 05.01.2026

***Corresponding author:** Waheed Zaman Khan
Phystech School of Aerospace Technology, Moscow Institute of Physics and Technology (MIPT), Dolgoprudny, Moscow Region 141700, Russian Federation

**Abstract** **Review Article**

AI-enabled chemistry is rapidly moving from single-instrument modeling to multimodal chemical measurement, where spectroscopy, chromatography–mass spectrometry, electrochemical sensing, and chemical imaging jointly constrain the same underlying chemical state. This review synthesizes how data fusion (low-, mid-, and high-level) can unify heterogeneous signals from molecules to materials and devices, and why physics guidance is essential for models that remain reliable under matrix effects, instrument drift, and cross-laboratory transfer. We discuss practical fusion architectures, hybrid mechanistic–learning models, and uncertainty-aware inference that converts predictions into decision-ready measurement results. A central theme is that multimodal AI must be evaluated as an analytical procedure: calibration, figures of merit, cross-modality consistency checks, and uncertainty budgets must be reported with the same discipline expected in analytical chemistry. We map common AI tasks by modality (peak deconvolution, spectral unmixing, retention-time prediction, MS annotation, EIS parameter estimation, image segmentation) and show representative case studies spanning pharma/biomedicine, food/environmental sensing, operando catalysis, energy devices, and polymer/materials quality control. Finally, we outline future directions: standardized multimodal benchmarks, interoperable metadata and formats, real-time closed-loop experimentation, greener miniaturized platforms, and trustworthy AI practices that support regulatory acceptance and deployment. Overall, multimodal measurement is converging toward a new paradigm: quantitative, uncertainty-aware, and deployable chemical inference from fused evidence rather than isolated instrument readouts.

**Keywords:** Multimodal data fusion; analytical chemistry; physics-guided AI; chemometrics; spectroscopy; LC–MS/GC–MS; electrochemical impedance spectroscopy (EIS); chemical imaging; uncertainty quantification; method validation; calibration transfer; operando characterization.

## 1. INTRODUCTION

Chemical science increasingly operates in regimes where no single instrument can provide a complete, decision-ready description of a sample. Real samples are multicomponent, heterogeneous, and dynamic: they may contain isomers and trace impurities, exist as multiphase formulations, evolve during reactions, or display nanoscale spatial structure that controls macroscopic function. In such settings, an analytical result is rarely just “a spectrum” or “a

**Citation:** Ubaid Ullah Khan *et al*. AI and Physics-Guided Multimodal Chemical Measurement: Unifying Spectroscopy, Chromatography–Mass Spectrometry, Electrochemical Sensing, and Chemical Imaging Via Data Fusion from Molecules to Materials and Devices. Sch J Eng Tech, 2026 Jan 14(1): 10-40.

chromatogram"; it is an inference about identity, quantity, structure, dynamics, and spatial context that must remain defensible under matrix effects, instrument drift, and incomplete observability. These realities motivate a shift from single-technique workflows toward multimodal chemical measurement, where complementary modalities jointly constrain the interpretation and reduce ambiguity through cross-validation and shared physical consistency checks. Practical evidence of this direction appears across application areas from correlative chemical imaging in tissues (combining vibrational spectroscopy with mass spectrometry imaging) to multimodal hyperspectral approaches where rich spectral–spatial data demand advanced multivariate interpretation. (Tuck *et al.,* 2020; de Juan, 2025).

At the core of this shift is data fusion: the deliberate integration of heterogeneous measurements into a single inferential pipeline. A widely used framing distinguishes low-level fusion (combining raw signals), mid-level fusion (combining extracted features), and high-level fusion (combining decisions or model outputs). This taxonomy is particularly useful in chemistry because different instruments produce data with different noise structures, dimensionalities, and physical meanings making "how" and "where" fusion occurs as important as "what" is fused (Smolinska *et al.,* 2019). In parallel, the chemometrics community has developed multi-block (multi-source) data analysis to integrate distinct but related datasets while preserving block-specific structure and avoiding naïve concatenation; contemporary reviews emphasize its role in tasks ranging from visualization and prediction to calibration transfer in multi-instrument settings (Mishra *et al.,* 2021). In other words, multimodal analytics is not merely a technological trend; it is a methodological response to the reality that chemical information is distributed across measurement physics and must be recombined in statistically and physically coherent ways (Smolinska *et al.,* 2019; Mishra *et al.,* 2021).

This review focuses on a modern, broadly applicable multimodal stack spectroscopy, chromatography–mass spectrometry, electrochemical sensing, and chemical imaging because together they span much of the chemical information space (molecular structure, composition, interfacial kinetics, and spatial heterogeneity). Spectroscopy interrogates light–matter interactions to report functional groups, bonding environments, electronic structure, and (in some cases) surface chemistry. Chromatography–mass spectrometry (e.g., LC–MS, GC–MS and related "hyphenated" methods) couples separation with molecular identification/quantification, offering powerful deconvolution of complex mixtures where overlapping spectral features alone may be insufficient (Patel *et al.,* 2010). Electrochemical sensing adds access to interfacial processes and kinetics that are central to catalysis, corrosion, biosensing, and energy materials; for example, electrochemical impedance spectroscopy (EIS) is widely treated as a key method for probing interfacial properties and reaction/transport contributions, with modern tutorials emphasizing both theory and practical interpretation pitfalls (Lazanas *et al.,* 2023). Chemical imaging (including hyperspectral imaging, vibrational mapping, and mass spectrometry imaging) adds the spatial dimension often essential when function depends on microstructure, phase segregation, or localized chemistry. Recent treatments highlight that hyperspectral imaging uniquely combines spatial and chemical information but typically requires strong chemometric and modeling support to become operational in process and applied contexts (de Juan, 2025). The power of multimodality becomes especially clear in correlative workflows: for instance, multimodal imaging approaches integrating vibrational spectroscopies with mass spectrometry imaging have been reviewed as a route to multi-scale, multi-omic chemical insight in tissues illustrating how modalities compensate for each other's limitations (Tuck *et al.,* 2020).

However, simply collecting more data does not guarantee better chemical knowledge. Multimodal measurement is fundamentally an inverse problem: instruments report signals shaped by physics (e.g., convolution with an instrument response, transport limitations, ionization efficiency, scattering, and background contributions), while analysts seek latent chemical variables (composition, structure, states, rate constants, maps). Without principled inference, multimodal workflows can amplify bias, propagate artifacts across modalities, or create "agreement" that is merely shared systematic error. This is why the integration of physics-guided modeling with AI is increasingly positioned as the modern solution: physics provides constraints, interpretability, and extrapolation structure; AI offers flexible function approximation, automated feature extraction, and scalable fusion across high-dimensional signals. The broader scientific literature describes physics-informed machine learning as an approach that integrates data with mathematical/physical models (for example by embedding governing laws or constraints into learning), particularly valuable when data are noisy, sparse, or expensive (Karniadakis *et al.,* 2021). In analytical chemistry terms, this translates to using physically meaningful priors and constraints such as non-negativity of concentrations, mass/charge balance, known line-shape families, diffusion-limited kinetics, or instrument-response-aware forward models so that learned representations remain chemically plausible and more transferable across instruments, batches, and matrices (Karniadakis *et al.,* 2021).

Equally important, chemistry is a quantitative science, and quantification requires metrology. Claims based on multimodal fusion must be anchored to established analytical performance concepts selectivity, sensitivity, detection capability, and uncertainty. For example, IUPAC defines the limit of detection (LOD) as derived from the smallest measured signal that can be detected with reasonable certainty for a given analytical procedure (IUPAC Gold Book, "limit of detection"). Beyond detection, uncertainty must be estimated and communicated in ways that reflect not just instrument noise but the full chain including sampling, calibration, model choice, and fusion strategy. Eurachem's guidance on quantifying uncertainty in analytical measurement provides structured approaches (including use of validation data and component-based uncertainty models), while Eurachem's method validation guide emphasizes "fitness for purpose" as the organizing principle for whether a method (or fused workflow) is suitable for its intended decision context (Eurachem/CITAC QUAM, 2012; Eurachem Method Validation Guide, 2025). In multimodal pipelines, these principles must be extended from "single-instrument method validation" to workflow validation, because fusion introduces new failure modes: leakage between training/validation sets, unrecognized modality drift, inconsistent preprocessing, or non-identifiable parameterizations where multiple chemical explanations fit the fused signals equally well (Mishra *et al.,* 2021; Smolinska *et al.,* 2019).

The final modern requirement is reproducible, interoperable data practice, especially because multimodal studies depend on metadata-rich datasets and the ability to reuse or reanalyze results. The FAIR Guiding Principles Findability, Accessibility, Interoperability, and Reusability—were explicitly formulated to support machine-actionable reuse of digital assets and to apply not only to "data" but also to the algorithms, tools, and workflows that generated them (Wilkinson *et al.,* 2016). For multimodal chemistry, FAIR-aligned practice is not administrative overhead; it is what enables calibration transfer, cross-laboratory benchmarking, and trustworthy AI development under realistic drift and domain shift.

Scope and contribution of this review. Building on these motivations, this review synthesizes an AI- and physics-guided framework for multimodal chemical measurement that unifies spectroscopy, chromatography–mass spectrometry, electrochemical sensing, and chemical imaging through data fusion. Figure 1 will introduce the end-to-end pipeline from sampling and raw signals to quantitative "chemical truth" with uncertainty bounds. Table 1 will summarize what each modality family measures, the scales it operates on, and its typical failure modes. Figure 2 will map chemical questions (identity–quantity–structure–dynamics–spatial context) to optimal modality combinations across molecular-to-device scales. Figure 3 will compare low-, mid-, and high-level fusion blueprints and their practical trade-offs. Finally, the review will emphasize validation and uncertainty as the analytical backbone anchored in IUPAC definitions and Eurachem guidance so that multimodal/AI claims remain quantitatively defensible, reproducible, and fit for purpose (IUPAC Gold Book; Eurachem/CITAC QUAM, 2012; Eurachem Method Validation Guide, 2025).

**Table 1: Modality cheat sheet**

| **Modality family** | **Primary information** | **Typical output** | **Strengths** | **Common failure modes** | **Best practice anchor** |
|---|---|---|---|---|---|
| Vibrational spectroscopy (IR, NIR, Raman) | Functional groups, mixture fingerprints | Spectrum (intensity vs wavenumber) | Fast, non-destructive, field/PAT-friendly | Baseline/scatter, fluorescence, temperature sensitivity, instrument drift | Chemometrics with robust preprocessing + external validation |
| Chromatography (LC/GC) | Separation in time, resolves mixtures/isomers | Chromatogram, retention times | Reduces interference, supports quant workflows | RT drift, co-elution, sample prep variability | RT alignment + standards + system suitability |
| Mass spectrometry (MS, MS/MS) | Mass-to-charge, fragmentation patterns | Mass spectra, peak tables | High sensitivity, structural clues | Matrix effects, ion suppression, annotation ambiguity | Internal standards + blanks + confirmation logic |
| Electrochemical sensing (CV/DPV/ amperometry) | Redox activity, selective sensing chemistry | Current vs potential/time | Portable, low power, rapid | Fouling, cross-sensitivity, temperature/ionic strength effects | Calibration in realistic matrices + drift monitoring |
| Electrochemical impedance (EIS) | Kinetics/transport separation via frequency response | Nyquist/Bode, fitted parameters | Diagnoses processes, aging, interfaces | Non-unique fits, unstable spectra, wrong equivalent models | Physically constrained fitting + QC checks |
| Chemical imaging (HSI, Raman mapping, MSI) | Spatial composition and heterogeneity | Pixel spectra, chemical maps | Links chemistry to morphology/ performance | Registration errors, illumination bias, pixel leakage | Sample-level splits, map QC, registration reporting |

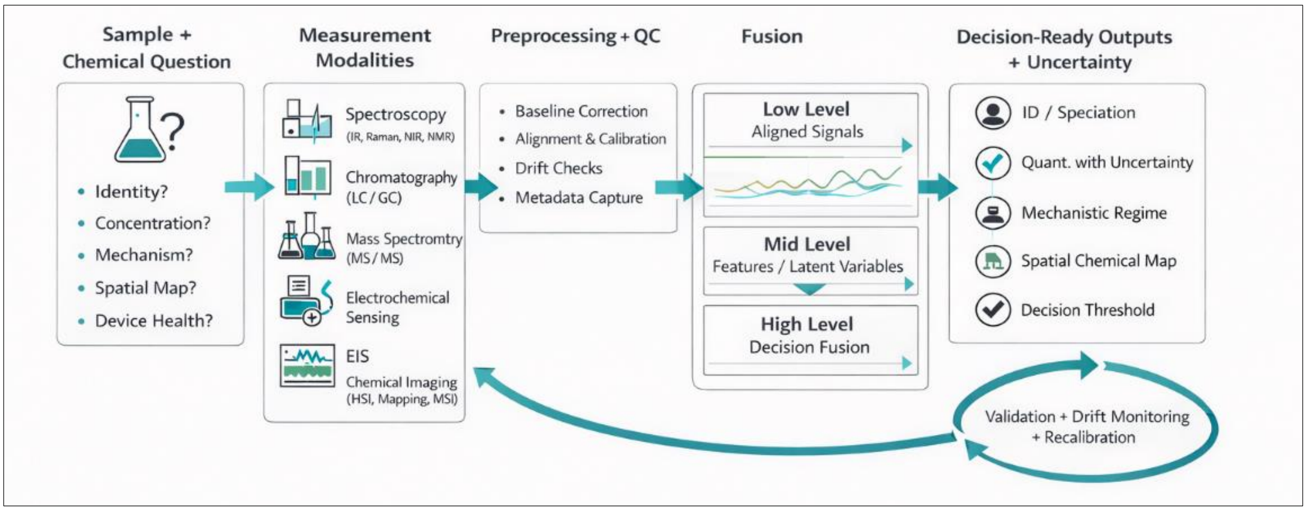

**Figure 1: Multimodal Chemical Measurement and Data Fusion: From Sample to Decision-Ready Chemistry with Uncertainty**

Figure 1 summarizes an end-to-end multimodal measurement pipeline in which complementary analytical modalities constrain a shared latent chemical state, and fusion converts heterogeneous signals into decision-ready outputs with explicit uncertainty. The fusion abstraction levels (low, mid, high) reflect a commonly used framework for integrating multi-source chemical data, while FAIR-aligned data stewardship underpins reproducibility and reuse.

## 2. Physics foundations shared across modalities

### 2.1 Measurement starts with a model

A rigorous measurement begins by defining the measurand, meaning the particular quantity intended to be measured (for example, concentration of an analyte in a matrix, surface coverage of a functional group, diffusion coefficient, or an interfacial charge transfer resistance). The IUPAC Gold Book definition is concise: a measurand is a "particular quantity subject to measurement." (IUPAC Gold Book, "measurand").

Across spectroscopy, chromatography, electrochemical sensing, and chemical imaging, instruments do not directly output the measurand. Instead, they output signals that are generated by physical interactions and then modified by the instrument. A useful unifying view is the forward model: a mapping from underlying chemical state to measured data, typically written as a function plus noise (for example, signal = instrument response applied to chemical state + noise). This framing is central in measurement science because it clarifies where error and uncertainty enter and why different modalities can disagree even on the same sample (JCGM 100:2008).

**Two universal components shape every modality's signal:**

- Instrument response / line shape. Spectrometers do not record infinitely sharp transitions; they record broadened features governed by an instrument line shape (for example Gaussian, Lorentzian, Voigt, and in Fourier-transform methods, dependence on apodization). IUPAC explicitly defines instrument line shape and notes these standard idealized forms and parameters (IUPAC Gold Book, "instrument line shape").
- Noise. Any inference depends on the ratio of signal to noise. IUPAC defines signal-to-noise ratio as the power of signal divided by the power of noise and notes practical RMS forms commonly used in measurement (IUPAC Gold Book, "signal-to-noise ratio").

This immediately links physics to analytical performance: if two methods disagree, the cause often lies in different response functions, different noise structures, and different sensitivities to the sample matrix.

### 2.2 Detection, resolution, and the "information budget" of an experiment

Even before data fusion or AI, measurement quality is constrained by detection capability and resolution. IUPAC defines the limit of detection (LOD) as derived from the smallest measure that can be detected with reasonable certainty for a given analytical procedure (IUPAC Gold Book, "limit of detection"). Classic analytical chemistry work also emphasizes that LOD is not a single universal constant; it depends on the statistical decision rule and the blank distribution, making the operational definition and validation design important (Long & Winefordner, 1983).

Resolution limits are modality-specific, but the pattern is universal: improving one dimension often costs another (for example spatial resolution versus signal-to-noise, or temporal resolution versus spectral resolution). This is not only practical experience; it is quantifiable in imaging contexts where signal-to-noise and spatial resolution are analyzed together as coupled performance metrics (Gureyev *et al.,* 2024). In spectroscopy, instrument line shape and apodization choices literally change the recorded line profile and thus influence peak fitting and quantitative extraction (IUPAC Gold Book, “instrument line shape”).

A modern multimodal workflow should treat every experiment as having an information budget: the best fusion strategy is often not “collect everything,” but “collect complementary constraints,” meaning measurements that reduce ambiguity in the inverse problem rather than duplicating the same limitation in different forms.

### 2.3 Transport and kinetics

Many analytical signals are not purely “spectral fingerprints.” They are shaped by transport, mixing, and kinetics. The simplest example is diffusion. IUPAC defines the diffusion coefficient as the proportionality constant relating flux to the concentration gradient in Fick’s law form (IUPAC Gold Book, “diffusion coefficient”). This matters because diffusion sets characteristic times for separation, equilibration, interfacial flux, and reaction progress.

In chromatography, band broadening is fundamentally a transport and mass-transfer problem. IUPAC defines plate height (HETP) as the column length divided by the plate number, a standard efficiency metric used across chromatographic modes (IUPAC Gold Book, “plate height”; IUPAC Recommendations 1993). The classic van Deemter rate-theory treatment explicitly identifies sources of nonideality (including longitudinal diffusion and resistance to mass transfer) as causes of peak broadening (van Deemter, Zuiderweg & Klinkenberg, 1956). This is why multimodal fusion that combines chromatography with spectroscopy or mass spectrometry is not just “more identification.” It is also a physics-based way to separate overlapping chemical states so that downstream inverse problems become better posed.

In electrochemical sensing, transport and kinetics are inseparable. Electrochemical impedance spectroscopy (EIS), for example, is explicitly used to disentangle contributions from processes such as charge transfer, double-layer behavior, and mass transport by analyzing frequency-dependent response. Modern tutorials emphasize the theoretical basis of EIS and the interpretation pitfalls that arise when different physical processes can produce similar impedance features (Lazanas *et al.,* 2023). IUPAC’s recommendations on electrochemical methods further standardize the terminology and classification of electroanalytical techniques, reinforcing that consistent definitions are necessary before quantitative comparison or fusion across studies (Pingarrón *et al.,* 2020; IUPAC Recommendations 2019/2020).

A practical implication across modalities is that “matrix” is not an abstract nuisance. IUPAC defines matrix effect as the combined effect of all components other than the analyte on the measurement of the quantity, and distinguishes it from a specific interference when a single component is identifiable (IUPAC Gold Book, “matrix effect”). This definition applies equally well to ion suppression in LC-MS, fluorescence background in Raman, adsorption and fouling in electrochemical sensors, and scattering or absorption artifacts in imaging.

### 2.4 The inverse problem view

Most chemical measurements are inverse problems: you observe data and infer the latent chemical quantities that produced them. Inverse problems are often ill-posed, meaning small noise or modeling errors can cause large changes in the inferred solution, or multiple solutions can fit the same data. A standard statistical and computational framework treats inversion as inference under uncertainty, often Bayesian in form, explicitly highlighting how prior knowledge and complementary information improve stability (Kaipio & Somersalo, 2005).

**Two concepts matter especially for a multimodal review:**

- **Identifiability.** Even with perfect computation, parameters may not be uniquely determined from the available observations. Classic identifiability literature frames this as a uniqueness problem for fitted parameters given observations (Vajda *et al.,* 1989). In practice, poor identifiability is common in kinetics, spectroscopy peak fitting, equivalent-circuit extraction from EIS, and deconvolution of overlapping chromatographic peaks.
- **Regularization.** Because inverse problems are commonly ill-posed, stable estimation requires constraints or priors (for example smoothness, sparsity, non-negativity, or physically meaningful bounds). Modern surveys describe regularization as a key tool to introduce prior knowledge and obtain robust approximations to ill-posed inverses, with strong emphasis on variational and nonlinear methods that connect naturally to modern learning approaches (Benning & Burger, 2018).

This is exactly where multimodal design becomes scientific rather than descriptive. Adding a second modality helps when it provides independent constraints that shrink the set of feasible explanations and improves identifiability. Adding a second modality hurts when it shares the same confounder (for example the same matrix effect) or introduces correlated errors without modeling them.

### 2.5 Uncertainty is not optional: propagation, correlation, and traceable reporting across a fused workflow

For multimodal fusion to be credible in analytical chemistry, it must carry uncertainty through the full pipeline. The Guide to the Expression of

Uncertainty in Measurement (GUM) formalizes how measurement results should be expressed with associated uncertainty and describes evaluation using a measurement model and propagation principles (JCGM 100:2008). For complex or nonlinear models, the GUM supplements extend the framework using Monte Carlo propagation of distributions through the measurement model (JCGM 101:2008).

In analytical chemistry practice, Eurachem's QUAM guide provides detailed guidance on identifying uncertainty sources, combining them, and reporting expanded uncertainty in a way aligned with laboratory competence and comparability expectations (Eurachem/CITAC QUAM, 2012). The key point for multimodal studies is correlation: modalities often share common inputs (sample preparation, calibration standards, environmental conditions), so uncertainties are not independent. GUM explicitly treats uncertainty as arising through a model with input quantities, and correlated inputs can propagate to correlated outputs, which matters directly when fusing results (JCGM 100:2008; JCGM 101:2008).

Finally, this physics and metrology foundation explains why "AI alone" is insufficient for high-stakes chemical claims. Physics-informed machine learning explicitly targets the integration of data with physical or mathematical models, including in forward and inverse problems, as a route to improve generalization and reliability when data are limited or noisy (Karniadakis *et al.,* 2021). In a multimodal chemical context, this translates to models that respect constraints such as non-negativity of concentrations, physically valid line shapes, mass-balance structure, and transport-limited kinetics, while still leveraging AI to learn complex mappings and perform scalable fusion.

**Table 2: Minimum preprocessing + alignment steps needed before fusion**

| Modality | Minimum preprocessing | Alignment step | QC signals to report |
|---|---|---|---|
| IR/NIR/Raman | Baseline correction, scatter correction/normalization, smoothing (if justified) | Wavenumber calibration (if needed) | Replicate agreement, drift trend, outlier rate |
| LC/GC | Peak picking/integration, baseline correction | Retention-time alignment | System suitability, RT shift, internal standard recovery |
| MS/MS | Mass calibration, peak detection, de-isotoping (if used), blank subtraction | m/z alignment across runs | Mass error ppm, blank features, ID confidence metrics |
| Electrochem sensing | Baseline drift correction, temperature compensation (if applicable) | Time alignment with other streams | Response stability, fouling indicators, calibration residuals |
| EIS | Noise screening, unstable spectrum rejection | Time alignment to operating condition | Fit residuals, parameter bounds, replicate consistency |
| Imaging/maps | Denoising, illumination correction, normalization | Spatial registration to reference image | Registration error, sample-level split integrity |

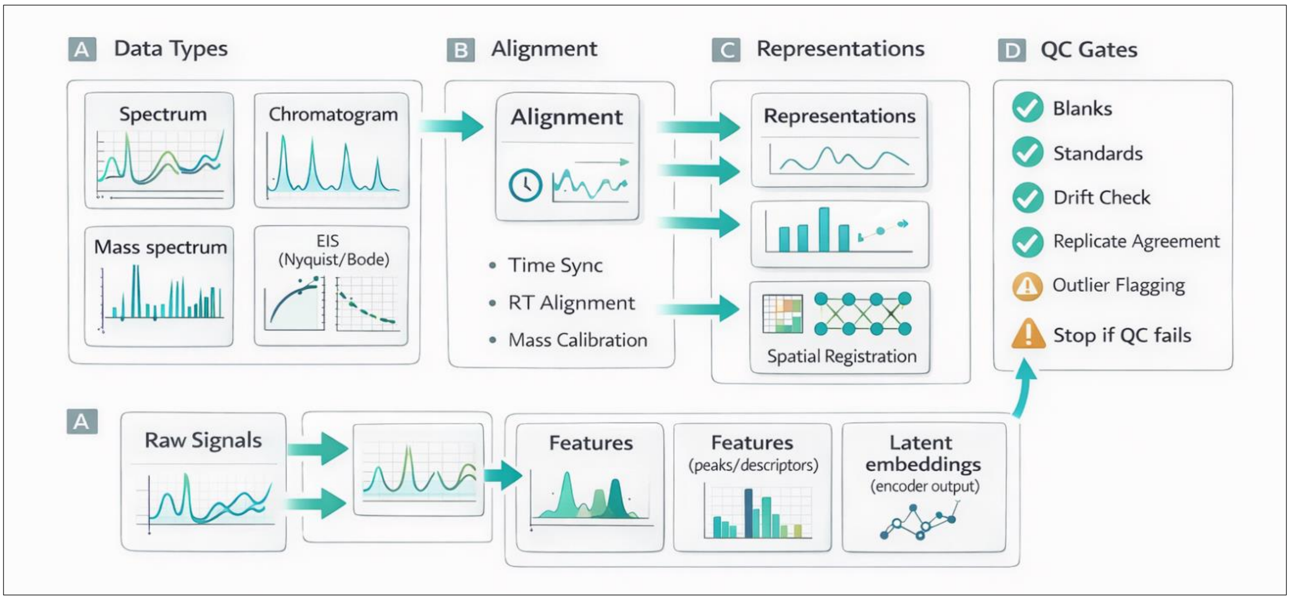

Figure 2: Making Heterogeneous Chemistry Comparable: Data Representations, Alignment, and Quality Control Across Modalities

Figure 2 highlights why multimodal fusion succeeds or fails: heterogeneous signals must be converted into comparable representations through alignment (time, mass, space) and quality control gates that prevent drift, leakage, and nonphysical artifacts from propagating into fused decisions.

## 3. The four modality families: what they measure, where they fail, and why they complement each other

### 3.1 Spectroscopy (bonding, structure, electronic states, and surfaces)

Spectroscopy is best treated as a measurement family defined by its physics: it studies physical systems through the electromagnetic radiation with which they interact, or that they produce. This definition is formalized in the IUPAC Gold Book and is broad enough to include vibrational, electronic, and surface sensitive methods used across chemistry and physics. (IUPAC Gold Book).

Vibrational spectroscopy includes infrared and Raman methods, which are central to analytical chemistry because they provide chemically interpretable fingerprints of functional groups, bonding environments, and lattice vibrations. IUPAC defines infrared spectroscopy as a measurement principle of vibrational spectroscopy using infrared radiation, and notes that without qualification it usually refers to the mid infrared region, approximately 2.5 to 25 micrometers, corresponding to 4000 to 400 inverse centimeters. (IUPAC Gold Book). Raman spectroscopy is defined by IUPAC as a vibrational spectroscopy principle based on Raman scattering, where Raman scattered light is shifted relative to the incident light by vibrational energies. (IUPAC Gold Book). These definitions matter in a multimodal review because they clarify why IR and Raman often behave differently on the same sample: IR intensity is governed largely by changes in dipole moment, while Raman intensity is governed largely by changes in polarizability as emphasized in IUPAC terminology for Raman scattering. (IUPAC Gold Book).

Electronic spectroscopy includes absorption and emission methods. Fluorescence is formally defined in the IUPAC Gold Book as luminescence that occurs essentially only during irradiation by electromagnetic radiation. (IUPAC Gold Book). This definition highlights why fluorescence can be extremely sensitive for trace analysis and imaging, but also why it can be unstable in real matrices, because the measured signal depends not only on concentration but also on quenching pathways, optical attenuation, and excitation conditions. In multimodal workflows, fluorescence or UV Vis signals often become more reliable when anchored to independent quantitative methods such as chromatography mass spectrometry, or when constrained by physics guided calibration models.

Nuclear magnetic resonance is a structurally powerful modality that often functions as both a qualitative and quantitative anchor. IUPAC defines nuclear magnetic resonance spectroscopy and explicitly notes its use for structure determination of organic molecules and for quantification. (IUPAC Gold Book). In multimodal design, NMR often complements chromatography mass spectrometry by providing orthogonal structural evidence and quantitative composition without relying on ionization efficiency, while chromatography mass spectrometry often complements NMR by improving sensitivity and resolving trace components.

Surface and electronic state spectroscopy provides the most direct bridge to condensed matter physics and materials chemistry. X ray photoelectron spectroscopy is defined by IUPAC as any technique in which a sample is bombarded with X rays and photoelectrons are detected as a function of energy, with ESCA referring to using this technique to identify elements, concentrations, and chemical state within the sample. (IUPAC Gold Book). The multimodal implication is that surface sensitive signals can be chemically decisive but not always representative of the bulk, so fusing surface spectroscopy with bulk spectroscopy, separations, or spatial mapping can prevent over interpretation.

In short, spectroscopy is fast and chemically rich, but it frequently faces overlapping bands, baseline artifacts, and matrix effects. These limitations are exactly why the next three modality families are not optional in a modern quantitative workflow.

### 3.2 Chromatography plus mass spectrometry (mixture resolution, identity, and trace quantification)

Chromatography is the primary way analytical chemistry converts mixture complexity into interpretable signals. A key organizing parameter is the retention factor, defined by IUPAC as a measure of the time a component resides in the stationary phase relative to the time it resides in the mobile phase, expressing how much longer it is retarded compared with traveling at the mobile phase velocity. (IUPAC Gold Book). In multimodal terms, chromatography improves identifiability because it turns one difficult inverse problem, such as overlapping spectral features, into a better posed problem by separating contributions across time before detection.

Mass spectrometry then provides highly specific molecular information through ion formation and mass analysis. IUPAC mass spectrometry terminology recommendations describe mass spectrometry as the study of matter through the formation of gas phase ions that are detected and characterized by their mass and charge, and they exist specifically to standardize interpretation across rapidly evolving instruments and methods. (IUPAC Recommendations 2013). The quantity used to label ion signals is commonly written as mover z. IUPAC clarifies that mover z denotes a dimensionless quantity formed by dividing the mass number of an ion by its charge number, and notes that the traditional phrase mass to charge ratio is historically used but technically imperfect. (IUPAC Gold Book).

The most important limitation for chromatography mass spectrometry in quantitative work is not lack of sensitivity, but matrix dependence. IUPAC defines matrix effect as the combined effect of all sample components other than the analyte on the measurement of the quantity, and distinguishes this from a specific interference when one component can be identified as causing the effect. (IUPAC Gold Book). Modern reviews and guidance emphasize that matrix effects can arise throughout the analytical process and are a major source of bias, particularly in workflows involving complex sample preparation and detection steps such as LC MS. (Williams, 2023). Recent LC MS focused literature also details practical approaches to assess matrix effect, including post column infusion and spiking approaches, reinforcing that quantitative LC MS is inseparable from explicit matrix effect assessment. (Fu *et al.,* 2024).

In multimodal fusion, chromatography mass spectrometry often functions as a quantitative anchor and identity validator for models trained on faster or cheaper modalities such as spectroscopy or electrochemical sensors. It also provides the reference labels needed for supervised learning and calibration, while physics guided constraints and uncertainty models prevent overfitting to instrument specific artifacts.

### 3.3 Electrochemical sensing (interfaces, kinetics, and selective detection)

Electrochemical sensing interrogates chemical systems through electrical signals governed by interfacial thermodynamics, reaction kinetics, and mass transport. It is uniquely powerful for chemistry where electron transfer, adsorption, or ionic processes define function, such as catalysis, corrosion, energy materials, and biosensing. Among electrochemical tools, electrochemical impedance spectroscopy is widely used because it separates processes by frequency response and can, when carefully modeled, distinguish charge transfer from transport and capacitive contributions. A modern tutorial in ACS Measurement Science Au explicitly provides theoretical background, principles, and applications of EIS and discusses how interpretation can fail when models are underconstrained or misapplied. (Lazanas & Prodromidis, 2023).

Electrochemical measurements are also highly exposed to matrix effects in the IUPAC sense. Changes in ionic strength, pH, dissolved oxygen, and co reactive species can shift potentials or alter currents, while electrode fouling and surface reconstruction change response over time. These issues often produce drift that is hard to diagnose from electrochemistry alone, which is why multimodal validation is so important. Surface spectroscopy such as XPS can verify chemical state changes at electrodes, vibrational spectroscopy can track functional group evolution in films, and chromatography mass spectrometry can confirm which dissolved species actually correlate with electrochemical signals. This kind of cross checking is the difference between a sensor that appears selective in a controlled solution and a sensor that remains reliable in real samples.

### 3.4 Chemical imaging (spatially resolved chemistry from microstructure to devices)

Chemical imaging extends chemical measurement into space, producing maps of chemical composition or state rather than a single bulk value. This is essential when heterogeneity controls behavior, such as phase segregation in polymers, active site distributions in catalysts, degradation fronts in batteries, or spatial microenvironments in tissues.

Hyperspectral imaging is one of the most general chemical imaging formats because it combines spatial information with spectral information, effectively creating a spectrum per pixel. A recent perspective in Analytical and Bioanalytical Chemistry describes hyperspectral imaging as a very complete analytical measurement enclosing rich spatial and chemical information, but also emphasizes that it requires powerful data analysis tools for interpretation and for practical implementation in process analytical technology contexts. (de Juan, 2025). This aligns naturally with the AI plus physics theme of this review, because unmixing and quantifying pixelwise chemical information requires both physically meaningful spectral models and robust statistical learning.

Mass spectrometry imaging maps spatial chemical distributions on complex surfaces and tissues, providing high molecular specificity. A recent Analytical Chemistry review states that MSI maps spatial distributions of chemicals on chemically complex surfaces and highlights its sensitivity and information richness, which is why it is widely used in spatial biology and materials contexts. (Körber, 2025). At the same time, MSI has fundamental tradeoffs between spatial resolution and sensitivity. A widely cited MSI review explains that improving spatial resolution decreases the sampled area per pixel, producing an inherent tradeoff with sensitivity. (Buchberger *et al.,* 2017).

Because no single imaging modality optimizes spatial resolution, molecular specificity, throughput, and quantification simultaneously, multimodal imaging has become a major direction. A multimodal imaging mass spectrometry review describes how MSI technologies have been integrated with other analytical modalities such as microscopy, spectroscopy, and even electrochemistry in what is now termed multimodal imaging, and discusses the promise and challenges of integration. (Neumann *et al.,* 2020). This multimodal trend is also visible in recent studies integrating Raman spectroscopy with MSI on the same section to combine complementary chemical contrasts. (Tóth *et al.,* 2025).

### 3.5 Why these four families together approximate quantitative chemical truth

These modality families were chosen because together they cover most of the chemical information space with minimal redundancy. Spectroscopy provides rapid, physics grounded signatures of bonding and state and is standardized in its conceptual definition by IUPAC. Chromatography plus mass spectrometry resolves mixtures, supports identification and trace quantification, and is grounded in standardized definitions for retention behavior and mass spectrometric terminology. Electrochemical sensing adds direct access to interfacial kinetics and transport constrained processes and is strongly supported by modern interpretive guidance for tools such as EIS. Chemical imaging adds spatial context, with hyperspectral imaging and MSI explicitly recognized as chemically rich but analysis intensive modalities, motivating AI assisted interpretation and fusion.

A rigorous multimodal workflow uses this complementarity to reduce non uniqueness in inference. Chromatography mass spectrometry can anchor identity and concentration labels for calibration. Spectroscopy can provide fast screening and mechanistic signatures. Electrochemistry can test interfacial hypotheses and kinetic constraints. Imaging can reveal heterogeneity that would bias bulk results and can localize chemistry to specific structures. The next section builds on this foundation by explaining how these heterogeneous signals are fused at the raw, feature, or decision levels and how physics guided AI makes fusion more interpretable and transferable.

**Table 3: Fusion strategy decision guide (low vs mid vs high)**

| Fusion level | What is fused | When it is best | Strength | Weakness | Example in chemistry |
|---|---|---|---|---|---|
| Low-level | Aligned raw signals | Tight synchronization and stable instruments | Max information retained | Brittle to missing data and misalignment | Time-synced operando streams fused as one model |
| Mid-level | Features/latent variables | Most lab settings; easier alignment | Strong performance with manageable complexity | Feature design can bias results | LC–MS peak tables + spectroscopy latent variables |
| High-level | Decisions/scores | Field deployment, missing modalities, variable quality | Robust and modular | Can lose fine-grained info | Electrochem screen + Raman confirm + decision fusion |

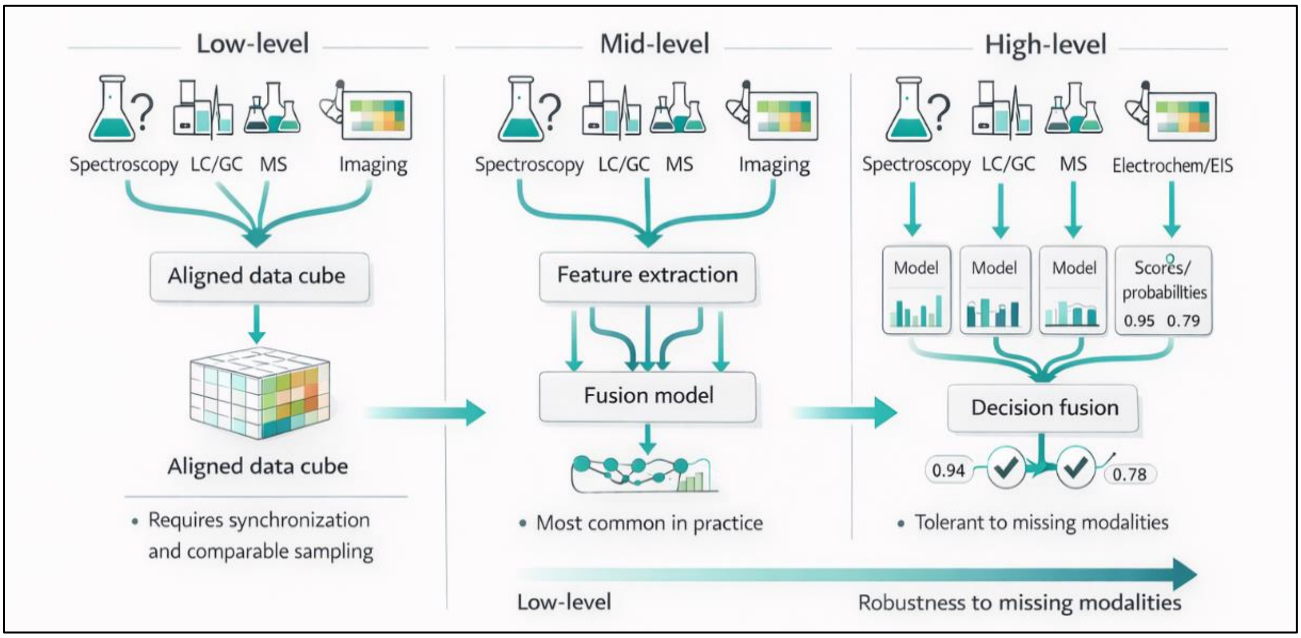

**Figure 3: Low-, Mid-, and High-Level Fusion in Multimodal Chemistry: When to Use Which**

Figure 3 compares low-, mid-, and high-level fusion, emphasizing the trade-off between information richness and robustness to missing modalities, and illustrating how the same analytical stack can be fused at different abstraction levels depending on synchronization, data quality, and deployment constraints.

## 4. Data fusion architectures for multimodal chemical measurement

Multimodal chemical measurement produces heterogeneous data blocks that differ in dimensionality (scalar metadata, 1D spectra, 2D chromatograms, 3D hyperspectral cubes, time series), noise structure, dynamic range, and sampling rate. The core purpose of data fusion is to combine these blocks so the final model captures complementary chemical information while controlling redundancy and modality specific artifacts (Smolinska *et al.,* 2019). In practice, the architecture you choose is inseparable from experimental design decisions such as sample pairing, replication, randomization, instrument calibration, and how you encode metadata and reference values because these choices determine whether the fused signal is chemically meaningful or simply a larger space for confounding (Westad & Marini, 2015; Lopez *et al.,* 2023).

### 4.1 Sample alignment, synchronization, and the "shared object" requirement

Most fusion strategies assume that different modalities describe the same underlying objects (the same sample, batch, location, time window, or process state). If objects are not aligned, concatenation or joint modeling can create spurious correlations that look predictive but do not generalize (Lopez *et al.,* 2023). Alignment can be trivial (same vial measured by NMR and LC MS) or difficult (linking operando electrochemistry time series to intermittent chromatographic fractions, or mapping chemical images to bulk spectra). When temporal structure exists, the alignment problem becomes a design and validation problem: the correct unit for cross validation is often the higher-level grouping (batch, day, patient, reactor run) rather than individual scans, otherwise leakage inflates performance (Westad & Marini, 2015; Király & Tóth, 2025).

A practical implication is that fusion should be described in terms of an explicit fusion index: what constitutes one "row" in the fused analysis (sample, pixel, peak, time slice) and how it maps across instruments. Reporting this mapping is not optional in multimodal analytical chemistry because it determines the chemical meaning of "features" and "labels" (Smolinska *et al.,* 2019; Westad & Marini, 2015).

### 4.2 Taxonomy of fusion levels: low, mid, high, plus sustainable and kernel fusion

Chemometrics commonly organizes multimodal fusion into low level, mid-level, and high-level strategies, with extensions such as sustainable mid-level fusion and kernel-based fusion (Smolinska *et al.,* 2019). This taxonomy is useful because it links directly to how chemical information is represented.

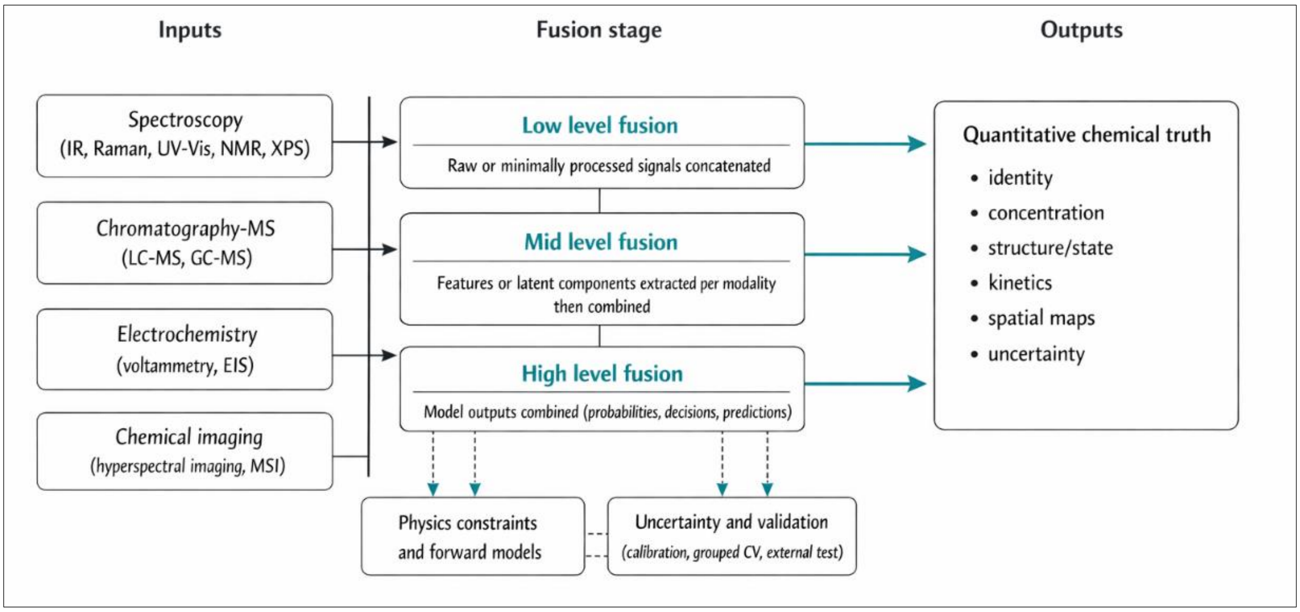

**Figure 3. Taxonomy of fusion architectures for AI and physics-guided multimodal chemical measurement.**

Fusion levels follow the low-, mid-, and high-level framing commonly used in chemometrics and data fusion literature, with deep fusion represented as intermediate representation fusion inside learned models (Smolinska *et al.,* 2019; Stahlschmidt *et al.,* 2022; Jiao *et al.,* 2024).

**Table 4: Comparison of fusion levels for multimodal chemical measurement**

| Fusion level | What is fused | Typical implementations in chemistry | Main strengths | Main risks and failure modes | Best used when | Minimum validation and reporting you must include |
|---|---|---|---|---|---|---|
| Low level fusion (early fusion) | Raw or minimally processed variables from each modality combined into one joint matrix (or tensor) | Simple concatenation then PCA, PLS, PLS-DA, SVM, RF; multiway extensions when you truly have matched multiway structure | Preserves fine cross modality relationships; can maximize information if blocks are well aligned | Dominance of large blocks or high-variance modalities; scaling choices can change the model; spurious correlations if samples are misaligned; missingness becomes difficult; high risk of leakage if preprocessing uses full dataset | Modalities are tightly synchronized (same sample/time), similar scale or carefully scaled, and you have enough samples for the joint dimension | Define the shared unit (sample, pixel, time slice); specify block scaling and centering choices; do leakage safe preprocessing inside CV; use grouped CV if batches exist; include an external test set when possible |
| Mid-level fusion (feature fusion) | Features or latent variables extracted separately per modality, then combined | Feature extraction by PCA, PLS scores, peak tables, targeted biomarkers, PARAFAC components, MCR-ALS profiles, summary descriptors; then concatenation and modeling | Reduces noise and dimensionality; features can be chemically meaningful; easier handling of missing modalities; often more stable than low level | Feature extraction can discard weak but important information; feature choices can inject bias; different feature pipelines can break comparability; interpretation can become unclear if features are not documented | Each modality has different dimension and noise structure (spectra, LC-MS peaks, EIS descriptors, image features), or when interpretability is needed | Fully document feature engineering; justify number of components (when using decompositions); perform feature extraction within training folds; report feature stability and uncertainty |
| High level fusion (decision fusion) | Outputs of modality-specific models fused (predictions, probabilities, decisions) | Voting, weighted averaging, stacking meta-models, Bayesian decision fusion, ensemble learning | Most robust to heterogeneous data; each modality can use its best model; easier to deploy and update one modality without retraining all | Loses some cross modality interaction information; can hide conflicts; weights can overfit if tuned improperly; requires calibrated probabilities for principled weighting | Modalities have different reliability, coverage, or missingness; deployment settings where not all sensors always available | Report calibration of probabilities; show performance per modality and fused; evaluate robustness under missing modality scenarios |
| Kernel fusion (similarity fusion) | Similarity matrices (kernels) per modality combined | Kernel PLS-DA, multiple kernel learning; fusion in kernel space | Handles nonlinear relationships; avoids variable scaling issues by fusing similarities; often works with very different data types | Kernel choice and hyperparameters can dominate; interpretability is harder; risk of optimistic tuning if nested CV not used | Strong nonlinear structure or incomparable feature spaces across modalities | Nested CV for kernel and hyperparameter selection; sensitivity analysis on kernel settings; report how kernels are built |
| Deep fusion (intermediate representation fusion) | Learned modality-specific embeddings fused within a joint neural architecture | Separate encoders for spectra, chromatograms, images, time series; fusion layers via concatenation, attention, gating; hybrid early plus late fusion | Captures complex cross modality interactions; strong for large datasets; can integrate raw and engineered features | Data hungry; can learn shortcuts; difficult interpretability; domain shift and drift can break models | Very large datasets or strong augmentation and external validation; when interactions across modalities are essential | Strict separation of train and test by batch or study; uncertainty or confidence calibration; ablation studies per modality; external validation across time or instrument |

Key foundations supporting the table: low, mid, high fusion definitions and extensions including kernel based fusion (Smolinska *et al.,* 2019); scaling impact in chemometric component models (Bro & Smilde, 2003); example of kernel space fusion in metabolomics (Smolinska *et al.,* 2012); deep multimodal fusion categories and fusion layer placement (Stahlschmidt *et al.,* 2022; Jiao *et al.,* 2024); validation pitfalls and proper strategies (Westad & Marini, 2015; Lopez *et al.,* 2023).

### 4.3 Low level fusion (early fusion): concatenation with careful scaling and structure preservation

Low level fusion merges modalities before modeling, typically by concatenating variables into one matrix. It is attractive because it can preserve subtle cross modality relationships, but it is also fragile: blocks with many variables or large variance can dominate unless block scaling is handled deliberately (Smolinska *et al.,* 2019). In chemical data, centering and scaling are not cosmetic. They define what variation is considered comparable across instruments and can change the latent structure learned by PCA, PLS, and multiway extensions (Bro & Smilde, 2003).

A robust low-level workflow usually includes (i) within block preprocessing that respects instrument physics (baseline correction, alignment, denoising), (ii) inter block scaling or weighting to prevent dominance, and (iii) explicit handling of missingness because real multimodal studies often have incomplete modality coverage (Smolinska *et al.,* 2019). Architectures that formalize low level fusion as a symmetric combination of blocks have been discussed as "frameworks for low level data fusion," emphasizing that fusion is not only concatenation but also a choice of equivalence between measurements (Smilde, 2019).

### 4.4 Mid-level fusion (feature fusion): chemically meaningful representations as the fusion interface

Mid-level fusion first transforms each modality into a reduced representation and then merges these representations. In chemometrics this is often called feature level fusion and is motivated by the idea that feature extraction removes modality specific noise and compresses signals into chemically interpretable components (Smolinska *et al.,* 2019; Casian *et al.,* 2022).

Feature extraction can be done with unsupervised decompositions (PCA, ICA, MCR ALS), supervised latent variable models (PLS variants), or multiway tensor models when data are naturally multi-dimensional. Multiway analysis is particularly important for chemical measurement because many instruments produce structured arrays such as excitation emission matrices, hyphenated separations with spectral detection, or time resolved spectroscopy. PARAFAC is a widely used multiway decomposition in chemometrics and has tutorial treatments emphasizing its ability to generalize PCA to higher order arrays and recover chemically meaningful profiles under appropriate conditions (Bro, 1997). Model complexity diagnostics such as CORCONDIA have been proposed to assess the appropriateness of PARAFAC component numbers, which is crucial when features become the fusion interface (Bro & Kiers, 2003).

For complex mixtures and hyphenated data, mid-level fusion can also be built around multivariate curve resolution. Reviews of MCR ALS highlight how bilinear decompositions and constraints can extract pure contributions from chromatographic data and related analytical signals (Mazivila *et al.,* 2022). In metabolomics, MCR ALS has been used for knowledge integration across CE MS and LC MS, including strategies that explicitly implement low level merging before MCR ALS to exploit a common spectral mode (Ortiz Villanueva *et al.,* 2017).

### 4.5 High level fusion (decision fusion): combining predictions, probabilities, or decisions

High level fusion combines outputs from separate modality specific models, such as class probabilities, concentration predictions, or decision scores. This approach is often more robust to heterogeneity because each modality can use its best suited preprocessing and model family, and fusion can be performed by voting, weighted averaging, stacking, or Bayesian decision rules (Smolinska *et al.,* 2019).

Decision fusion becomes especially relevant when modalities have different coverage or reliability. For example, Bayesian based decision fusion has been used to combine NIR and Raman based classifiers by integrating evidence from modality specific PLS DA models, illustrating a concrete route to uncertainty aware weighting at the decision stage (Xu *et al.,* 2022).

### 4.6 Multiblock chemometrics: shared, unique, and orthogonal variation as a design principle

Beyond low, mid, and high-level categories, modern chemometrics treats multimodal measurement as a multiblock problem: a set of matrices measured on the same objects. Reviews on multiblock data analysis emphasize tasks ranging from visualization and exploration to predictive modeling and calibration transfer, with many methods designed to separate predictive variation from block specific structured noise (Mishra *et al.,* 2021).

A central idea is that blocks can share common chemical variation but also contain distinct information. A unifying linear algebra framework for common and distinct components in data fusion has been proposed, clarifying terminology and linking methods such as O2PLS style decompositions and related approaches (Smilde *et al.,* 2017).

Sequential strategies are also important when blocks have natural priority, for example cheap high throughput sensors first, expensive confirmatory measurements second. Sequential and orthogonalized PLS methods formalize this by extracting information block by block while controlling overlap, and have been discussed for multiblock regression and related modeling goals (Næs *et al.,* 2021).

For symmetric multiblock settings, OnPLS extends O2PLS concepts to more than two blocks, extracting globally predictive and orthogonal components; OnPLS has also been applied with variable influence diagnostics for interpretable multiomics and other multiblock studies (Löfstedt *et al.,* 2011; Reinke *et al.,* 2018).

### 4.7 Kernel based and nonlinear fusion: fusing similarity rather than raw variables

When relationships across modalities are nonlinear or the feature spaces are incomparable, kernel-based fusion provides an alternative: each modality is mapped to a kernel (a similarity matrix between samples) and kernels are combined before modeling (Smolinska *et al.,* 2019).

A worked example is fusion in kernel space for metabolomics based on proton NMR and GC MS, where optimized kernels were merged and analyzed with kernel PLS DA, yielding performance improvements over common mid-level fusion in that study (Smolinska *et al.,* 2012).

### 4.8 Deep multimodal fusion: early, intermediate, late, and hybrid architectures

Deep learning literature often groups multimodal fusion into early fusion, intermediate fusion (sometimes called deep or representation fusion), late fusion, and hybrids, echoing the chemometrics taxonomy but implemented inside neural architectures (Jiao *et al.,* 2024).

A detailed review in biomedical multimodal fusion further distinguishes how fusion layers are placed and how joint representations are learned, and it discusses practical tradeoffs such as when early fusion fails to capture higher level cross modality relations versus when late fusion cannot model feature interactions (Stahlschmidt *et al.,* 2022).

For chemical measurement, deep fusion is most convincing when it respects physics and instrument structure, for example using modality specific encoders that preserve spectral smoothness, chromatographic peak locality, or image spatial correlations, followed by a controlled fusion module. Even when deep models are used, the same alignment, scaling, and validation principles from chemometrics still apply (Lopez *et al.,* 2023; Westad & Marini, 2015).

### 4.9 Preprocessing, block scaling, drift, and transfer: preventing fusion from amplifying artifacts

Fusion increases model capacity, which increases the risk that models learn instrument artifacts. Chemometric work on centering and scaling shows that preprocessing choices directly change the geometry of component models and can be generalized from two way to multiway data, making it a foundation for multimodal fusion pipelines (Bro & Smilde, 2003).

Dedicated studies on multiblock preprocessing propose workflows that explicitly consider intra block and inter block variation components, because naive preprocessing can overemphasize one block or distort shared structure (Campos *et al.,* 2020). Transfer across instruments and time is another key issue. Calibration transfer addresses how to adapt models between spectrometers and related settings, highlighting practical barriers such as the need for standard samples and the impact of instrument differences (Mishra *et al.,* 2021).

Sustainable mid-level fusion has been proposed to reduce the risk of discarding useful information during feature selection by introducing a recycling step for initially rejected variables, which is relevant when signals are weak or distributed across modalities (Geurts, 2017; Smolinska *et al.,* 2019).

### 4.10 Validation for fused models: leakage control, grouped resampling, and external generalization

Because fusion pipelines involve many choices (preprocessing, feature extraction, block weighting, model selection), validation must be nested and must treat preprocessing and feature selection as part of the trained model, otherwise leakage occurs. Tutorials emphasize that independent test sets are the most conservative assessment for calibration, while cross validation remains essential for rank selection and stability, especially under grouped data structures (Westad & Marini, 2015). Recent didactic work shows how wrong designed cross validation and external validation can produce models that look promising but fail on truly independent samples, stressing that hierarchical or dependent data structure must shape the validation strategy (Lopez *et al.,* 2023).

Work specifically raising awareness about data leakage and cross validation scaling in chemometric model validation further underlines how easily performance can be inflated when scaling or preprocessing uses information from held out folds (Király & Tóth, 2025).

## 5. Physics-guided AI: making models reliable, interpretable, and transferable

Physics-guided AI aims to merge data-driven learning with domain constraints so that predictions respect chemistry and measurement physics, remain stable under changing conditions, and provide uncertainty that is meaningful for decision-making. This matters most in multimodal analytical pipelines because each modality brings its own inductive biases, artifacts, and failure modes, and naive fusion can amplify these weaknesses instead of cancelling them. (Karniadakis *et al.,* 2021; Smolinska *et al.,* 2019).

### 5.1 Why purely data-driven models can break (shortcut learning, OOD failures)

Many high-performing ML models learn “shortcuts”, meaning they exploit spurious correlations that are predictive on a benchmark but not causally tied to the chemistry of interest, so performance collapses when conditions shift (Geirhos *et al.,* 2020). In chemical measurement this can look like a classifier that relies on batch-specific baseline shapes, a chromatography model that “recognizes” an instrument method ID, or a microscopy segmenter that keys on illumination differences rather than chemical contrast. These behaviors are a special case of dataset shift: when the joint distribution of inputs and outputs differs between training and deployment due to new instruments, columns, operators, reagents, temperature, drift, or sample composition changes (Quiñonero-Candela *et al.,* 2009).

Out-of-distribution (OOD) failures are common in chemistry workflows because the test regime often differs from the training regime in subtle ways: new matrices, new interferents, new operating points, or different preprocessing pipelines. Unless evaluation explicitly simulates these shifts, accuracy can be overestimated and models may fail when moved to a new lab or a new instrument. This is why validation strategy and leakage control are not “ML hygiene”, they are part of scientific correctness in fused analytical models (Westad & Marini, 2015; Lopez *et al.,* 2023; Király & Tóth, 2025).

Finally, streaming and long-term deployments add concept drift: the data-generating process changes over time (for example sensor aging or changing feedstock), so a model that was correct last month may degrade today. Surveys on concept drift emphasize that drift detection and adaptation need to be designed into operational ML systems, not added after failures occur (Gama *et al.,* 2014).

### 5.2 Physics constraints in ML

Physics constraints shape the hypothesis space so the model is encouraged (or forced) to obey rules that must hold regardless of dataset idiosyncrasies. In multimodal chemistry, constraints typically enter in three places: the chemistry (conservation and stoichiometry), the signal model (non-negativity and smoothness), and the instrument response (what the instrument can physically measure).

#### 5.2.1 Conservation and stoichiometry constraints

Chemical transformations and reactive systems are governed by conservation of mass and elements. Recent work shows how to enforce atom conservation as a hard constraint in neural models of chemical kinetics by inserting an element-balance layer, so outputs cannot violate conservation even if training data are noisy or incomplete (Döppel *et al.,* 2024). Similarly, hard-constrained neural architectures have been proposed to strictly enforce mass, energy, and element conservation in chemical source term prediction, which directly targets the common failure where flexible regressors create physically impossible species trends (Wang *et al.,* 2025).

These constraints generalize beyond kinetics: in quantitative spectroscopy, constraints can enforce that mixture fractions are non-negative and optionally sum to one; in separations and mass spectrometry, constraints can enforce that isotopic envelopes and adduct relationships follow known rules; in process analytical technology, constraints can enforce that material balances close across sensors. The key benefit is that constraints reduce shortcut learning because the model cannot “explain away” outcomes using physically impossible internal states (Karniadakis *et al.,* 2021).

#### 5.2.2 non-negativity, sparsity, and smoothness priors

Many chemical quantities are inherently non-negative (concentrations, absorbance contributions, abundance maps). Enforcing non-negativity is a classic route to interpretability, exemplified by non-negative matrix factorization, which yields parts-based, additive representations that align with mixture intuition (Lee & Seung, 1999). In hyperspectral Raman unmixing, modern approaches explicitly impose abundance non-negativity and related constraints to improve physical interpretability of recovered components (Georgiev *et al.,* 2024).

Sparsity priors are useful when only a few chemical sources, peaks, or reactions dominate, and they can stabilize ill-posed inversions (for example peak deconvolution or sparse mixture identification). Compressed sensing theory formalized how sparsity enables recovery from undersampled measurements, which motivated many modern sparse regularization strategies used in spectroscopy and imaging pipelines (Donoho, 2006). Smoothness priors are equally important: spectra and time-series often vary smoothly, and penalizing non-physical roughness can suppress noise amplification. A concrete example in infrared analysis is blind spectral deconvolution that estimates both latent spectrum and instrument response while using total-variation style regularization to control unrealistic oscillations (Liu *et al.,* 2024).

#### 5.2.3 Instrument-response-aware learning

Instrument effects are not nuisances; they define the forward map from chemical reality to measured data. If the model ignores this forward map, it can learn instrument-specific signatures that do not transfer. A simple but powerful practice is to encode measurement knowledge explicitly: incorporate instrument line shape concepts, detector saturation behavior, chromatographic peak models, or electrochemical circuit constraints. Even basic terminology like “instrument line shape” is formalized in IUPAC definitions, emphasizing that spectral features are shaped by the spectrometer response and processing choices (IUPAC, 2025).

In learning systems, instrument-response awareness can be implemented by (i) training on synthetic data generated from a forward model, (ii) adding a differentiable forward layer inside the network, or (iii) learning residual corrections around a known forward simulator. Blind infrared deconvolution methods that explicitly model the instrument response function illustrate the principle: you do not ask a neural model to “guess” the true spectrum without telling it how the instrument distorts the signal (Liu *et al.,* 2024).

### 5.3 Hybrid models: mechanistic core + learned residuals

Hybrid modeling treats first-principles physics and chemistry as the backbone and uses ML to learn what the mechanistic model misses: unmodeled kinetics, unknown parameters, nuisance effects, or systematic biases. In chemical engineering, hybrid science-guided ML has been reviewed as a structured family of strategies, including serial (mechanistic then ML), parallel (mechanistic plus ML residual), inverse/hybrid identification, and reduced-order surrogates, with clear discussion of when each approach is appropriate (Sharma & Liu, 2022).

This architecture is attractive for multimodal measurement because mechanistic parts can act as a shared “physics interface” across modalities. For example, a mechanistic reaction model can constrain feasible concentration trajectories while the spectroscopy and chromatography models learn modality-specific mappings to those latent states. The physics core improves extrapolation beyond the training window, while the learned residual captures systematic discrepancies such as temperature dependence, matrix effects, or sensor cross-sensitivity that are hard to model from first principles (Karniadakis *et al.,* 2021; Sharma & Liu, 2022).

### 5.4 Bayesian and probabilistic approaches for uncertainty-aware predictions

Uncertainty is essential in analytical chemistry because decisions are often threshold-based: pass/fail quality control, identity confirmation, or whether to trigger confirmatory measurement. Modern probabilistic ML distinguishes aleatoric uncertainty (noise inherent in the observations) from epistemic uncertainty (model uncertainty that can shrink with more data), and this separation helps interpret whether uncertainty is coming from poor measurement quality or from the model being outside its competence region (Kendall & Gal, 2017).

Bayesian deep learning methods provide practical approximations to epistemic uncertainty in neural networks. A well-known result is that dropout training can be interpreted as approximate Bayesian inference in deep Gaussian processes, enabling uncertainty estimates without redesigning the full architecture (Gal & Ghahramani, 2016). Gaussian processes themselves remain a strong probabilistic baseline for regression and calibration because they provide principled predictive distributions and are well-studied for scientific inference and surrogate modeling (Rasmussen & Williams, 2006).

For electrochemical impedance analysis, uncertainty-aware tools are becoming concrete: AutoEIS, for example, explicitly integrates Bayesian inference to automate equivalent-circuit modeling from EIS data, reflecting a broader trend toward probabilistic workflows that quantify parameter uncertainty instead of returning single-point fits (Sadeghi *et al.,* 2025).

### 5.5 Model governance: dataset bias, drift monitoring, documentation

Reliable physics-guided AI is not only about model equations; it requires governance so users can trust where the model works, where it fails, and how it was validated. Two widely adopted documentation frameworks are datasheets for datasets, which standardize how datasets are described (collection process, composition, intended use, limitations), and model cards, which standardize how trained models are reported (performance slices, ethical considerations, caveats, intended users) (Gebru *et al.,* 2018; Mitchell *et al.,* 2019).

For multimodal chemistry, governance should also include drift monitoring. Dataset shift is expected when deploying to a new instrument, method, or operator, and concept drift is expected in long-running processes. Drift surveys emphasize that drift detection is a defined task with established evaluation approaches, and it should be part of operational monitoring for analytical AI systems (Quiñonero-Candela *et al.,* 2009; Gama *et al.,* 2014).

A minimal governance package for your review can therefore recommend: (i) dataset documentation (datasheet), (ii) model documentation (model card), (iii) leakage-safe validation and grouped evaluation when batches or days are present, (iv) ongoing drift detection, and (v) recalibration or transfer procedures when drift is detected (Gebru *et al.,* 2018; Mitchell *et al.,* 2019; Lopez *et al.,* 2023).

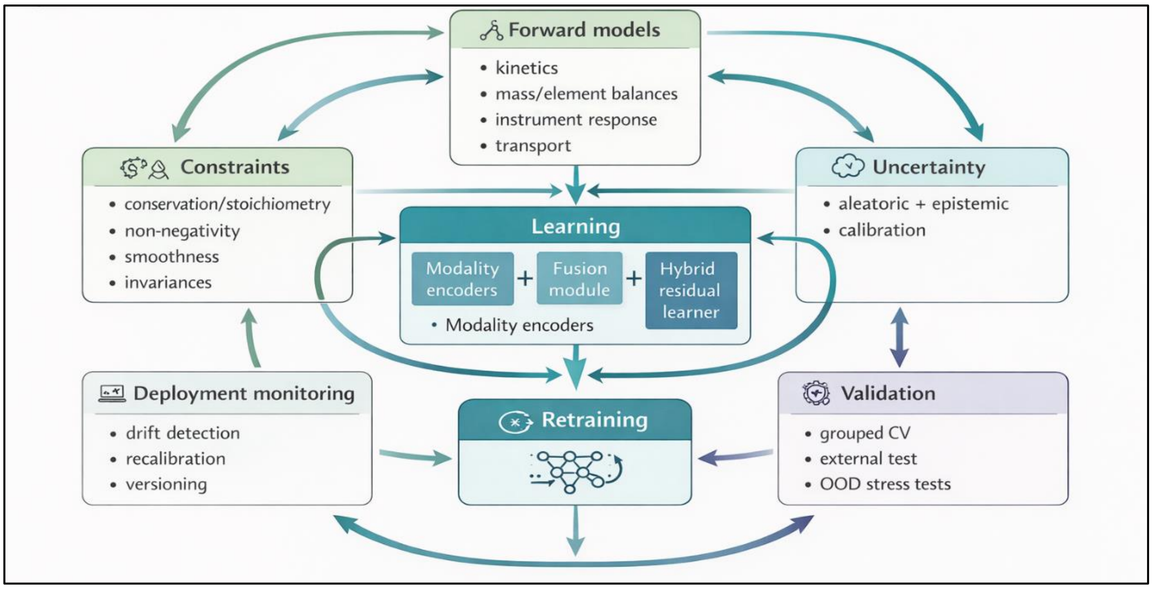

**Figure 4: Physics-Guided AI Workflow for Multimodal Chemistry: Forward Models + Constraints + Learning + Uncertainty Quantification + Validation**

**Table 5: AI Tasks by Modality: Typical Inputs, Targets, and Suitable Model Families (with Pros/Cons)**

| **Modality** | **Typical inputs** | **Common AI tasks** | **Typical targets** | **Suitable model families** | **Pros** | **Cons / failure modes** | **Physics-guided additions** |
|---|---|---|---|---|---|---|---|
| Spectroscopy (IR, Raman, UV-Vis, NMR) | 1D spectra; sometimes time-resolved or hyperspectral cubes | Baseline/denoise; peak picking and deconvolution; spectral unmixing; quantitative prediction | Peak positions/areas; component spectra; concentrations; uncertainty | PLS/PLS2; sparse regression; NMF; 1D CNN; autoencoders; Bayesian NNs | Fast, often interpretable with constraints; strong for quant | Shortcut learning on baseline/batch; instrument-specific artifacts; poor transfer without calibration | Non-negativity and smoothness priors (Lee & Seung, 1999); instrument line-shape and deconvolution models (IUPAC, 2025; Liu *et al.*, 2024) |
| Chromatography–MS (LC-MS, GC-MS) | Chromatograms; MS1 isotope patterns; MS/MS spectra; peak tables | Peak detection/deconvolution; retention time prediction; compound annotation; molecular networking | RT; peak identity; formula/ structure candidates; class labels | Gradient boosting; deep embeddings for spectra; graph models; kernel methods | High specificity when models use fragmentation rules and RT | Domain shift across columns/methods; false annotation confidence; missingness and batch effects | Physics/chemistry rules (isotopes, adducts); RT constraints; uncertainty-aware ranking; community curation |
| Electrochemistry (voltammetry, EIS) | Current–potential curves; Nyquist/Bode; time series | Denoise; state/parameter estimation; equivalent-circuit identification; inverse modeling | Circuit topology; R,C, diffusion params; state-of-health | Feature + tree models; 1D CNN; probabilistic inference; Bayesian methods | Strong for parameter inference; supports principled UQ | Non-uniqueness of circuit fits; overfitting to geometry; drift with aging | Conservation and monotonicity constraints; Bayesian inference for circuits (AutoEIS) |
| Chemical imaging (hyperspectral, MSI, microscopy) | 2D/3D images; hyperspectral cubes; MSI maps | Segmentation; unmixing; super-resolution/ deconvolution; spatial quantification | Chemical maps; class masks; spatial distributions | U-Net; transformers; NMF/ unmixing; physics-informed deconvolution | Captures spatial heterogeneity and microstructure | Illumination and instrument transfer issues; shortcut learning via background | Non-negativity and abundance constraints; PSF / instrument response models; spatial smoothness priors |
| Cross-modality fusion | Aligned blocks across modalities | Joint representation learning; decision fusion; OOD detection; calibration transfer | Robust predictions across instruments and labs | Multiblock methods; deep multimodal fusion; probabilistic stacking | Better robustness if modalities complement | Fusion can amplify confounding if alignment is wrong | Grouped validation; drift monitoring; physics interface as shared latent state |

Representative anchors: non-negativity foundations (Lee & Seung, 1999); instrument line shape concept (IUPAC, 2025); IR instrument-response deconvolution (Liu *et al.,* 2024); retention-time generalization challenges and methods (Zhang *et al.,* 2024); MS community curation and networking (Wang *et al.,* 2016); EIS deep learning and automated modeling (Doonyapisut *et al.,* 2023; Sadeghi *et al.,* 2025).

## 6. Validation, metrology, and uncertainty (the analytical chemistry backbone)

Multimodal data fusion becomes *analytical chemistry* only when it is treated as a measurement procedure: the measurand is defined, calibration establishes traceability, validation demonstrates fitness for intended use, and uncertainty is stated and propagated to decisions (JCGM, 2008; JCGM, 2012a; De Bièvre *et al.,* 2011). In this framing, "AI performance" is not enough; reviewers increasingly expect the same discipline used for analytical procedures, including validation characteristics and lifecycle thinking (ICH, 2023a; ICH, 2023b).

### 6.1 Calibration strategies across modalities (external, internal standard, standard addition)

Calibration connects instrument response to a quantity value that can be compared across time, instruments, and laboratories, so it is the first place where multimodal workflows either become trustworthy or become irreproducible (De Bièvre *et al.,* 2011; JCGM, 2012b). External calibration is straightforward and supports linearity/range claims, but it is vulnerable to matrix effects and drift when the calibration environment differs from real samples (ICH, 2023a; Thompson *et al.,* 2002). Internal standardization improves robustness when an internal standard tracks losses, injection variability, or signal fluctuations and is particularly important in workflows where instrument response is sensitive to sample composition (Thompson *et al.,* 2002). Standard addition is often the most defensible approach in severe matrix-effect regimes because the calibration is performed inside the sample matrix, reducing bias from suppression/enhancement and other matrix-dependent behavior (Thompson *et al.,* 2002; Ellison & Williams, 2012).

In multimodal studies, reviewers will look for an explicit calibration hierarchy: which modality provides the traceable anchor (often a separation–MS method or a certified reference method), how other modalities are cross-calibrated to it, and whether transfer is re-checked when instruments, operators, or batches change (De Bièvre *et al.,* 2011; ICH, 2023b). Whenever reference materials are used, good practice is to document how they were selected, handled, and applied to maintain comparability and traceability across runs (ISO, 2015; ISO, 2017a).

### 6.2 Figures of merit: selectivity, sensitivity, LOD/LOQ, precision, accuracy, robustness

Analytical figures of merit must be reported in a way that maps to established validation language. ICH validation guidance explicitly requires characterizing performance with core attributes such as specificity/selectivity, accuracy, precision, detection limit, quantitation limit, linearity, range, and robustness (ICH, 2023a). For detection and quantification, it is important to use consistent definitions. The classic statistical treatment of detection capability in analytical chemistry is often traced to Currie's framework, which clarifies how detection decisions depend on error probabilities and distributional assumptions (Currie, 1968). Later work discusses practical pitfalls and interpretation issues around IUPAC-aligned LOD definitions, highlighting how inconsistent practice can produce misleading comparability (Long & Winefordner, 1983). Related international terminology and guidance for detection capability are also covered in ISO standards (ISO, 1997).

Precision should be stated under clearly described conditions (repeatability vs intermediate precision), and accuracy should be treated as trueness plus precision rather than a single "error" number (ICH, 2023a; ISO/IEC, 2017). In fusion papers, the minimum expectation is to report figures of merit per modality and for the fused output, and to state whether fusion improved sensitivity/selectivity at the expense of robustness or interpretability (Westad & Marini, 2015; Lopez *et al.,* 2023).

### 6.3 Cross-modality consistency checks (does the fused result obey chemistry/physics?)

A unique advantage of multimodal chemistry is that different instruments constrain the same underlying chemical state through different physics. That advantage only becomes credible when authors explicitly show that the fused result obeys chemical and physical constraints and that modalities do not contradict each other beyond stated uncertainty (JCGM, 2008; Smolinska *et al.,* 2019). Practically, reviewers expect evidence of (i) scale consistency (units and calibration compatibility), (ii) constraint consistency (non-negativity for concentrations, mass or charge balance where relevant), and (iii) agreement diagnostics (residual plots and disagreement metrics showing when modalities diverge) (De Bièvre *et al.,* 2011; JCGM, 2008).

A simple but powerful pattern is to treat each modality as an independent measurement model and then test whether they converge on the same measurand within uncertainty. When they do not, the paper should explain whether the discrepancy is attributable to sampling, matrix effects, model bias, or instrument drift, rather than silently averaging disagreements through fusion (Ellison & Williams, 2012; Westad & Marini, 2015).

### 6.4 Uncertainty decomposition: sampling, instrument, model, fusion

Uncertainty is what converts a fused estimate into a defensible measurement result. The GUM framework formalizes uncertainty through a measurement model and propagation from input quantities to the output, using either analytical propagation or Monte Carlo methods when linear approximations are not appropriate (JCGM, 2008; JCGM, 2008a). In chemistry labs, Eurachem guidance operationalizes this into practical uncertainty budgets and emphasizes that uncertainty evaluation must be tied to fitness-for-purpose rather than theoretical completeness (Ellison & Williams, 2012; Bettencourt da Silva & Williams, 2015).

For multimodal fusion, a practical uncertainty budget should separate at least four components: sampling uncertainty, instrument/calibration uncertainty (per modality), model uncertainty (chemometrics/ML), and fusion uncertainty (introduced by combining modalities and any cross-calibration). Sampling uncertainty can dominate in real-world settings, and Eurachem guidance treats sampling as part of the measurement process rather than a pre-analytical footnote (Eurachem *et al.,* 2019). For compliance or pass/fail decisions, uncertainty must be connected to decision rules and statements of conformity; this is addressed both by metrology guidance on conformity assessment and by laboratory accreditation guidance used in ISO/IEC 17025 contexts (JCGM, 2012b; ILAC, 2019; ISO/IEC, 2017).

### 6.5 Reporting standards and reproducibility (what reviewers expect now)

Reviewers increasingly judge multimodal fusion manuscripts as method papers: they expect enough detail to reproduce the pipeline and to evaluate whether performance is real or inflated. At minimum, this means reporting calibration and validation elements aligned with analytical procedure guidance (ICH, 2023a; Thompson *et al.,* 2002) and describing model validation in a way that avoids leakage and respects grouping (batch, day, instrument, site) (Westad & Marini, 2015; Lopez *et al.,* 2023). For long-running or field-deployed systems, reviewers also expect drift control (QC samples, monitoring logic, recalibration triggers) because stability over time is part of “robustness” in practice (Thompson & Wood, 1995; ISO/IEC, 2017).

Reproducibility expectations now commonly extend beyond narrative description to structured sharing of data and metadata. FAIR principles are frequently used as the standard reference for how scientific data should be made reusable, and they are especially important in multimodal studies where hidden metadata debt prevents independent replication (Wilkinson *et al.,* 2016).

**Table 6: Multimodal Validation Checklist: Minimum Reporting Requirements for Reproducible Fusion Studies**

| **Checklist domain** | **Minimum reporting requirements** | **Key guidance anchor** |
|---|---|---|
| Measurand definition | Measurand, units, matrix definition, operating conditions, and how “ground truth” is established | JCGM (2008); De Bièvre *et al.,* (2011) |
| Sampling and handling | Sampling design, replicates, holding times, storage, transport, contamination controls | Eurachem *et al.,* (2019) |
| Sample preparation | Full workflow, blanks, spike recovery strategy, internal standards/standard addition if used | Thompson *et al.,* (2002); ICH (2023a) |
| Instrument settings | Instrument model/configuration, acquisition parameters, environment, QC schedule | ISO/IEC (2017) |
| Calibration strategy | External/internal standard/standard addition; model form; range; recalibration frequency | ICH (2023a); Ellison & Williams (2012) |
| Figures of merit | Selectivity, sensitivity, LOD/LOQ, precision, accuracy, robustness per modality + fused output | ICH (2023a); Currie (1968); ISO (1997) |
| Preprocessing | Exact preprocessing steps, parameters, software versions; alignment/normalization rules | Westad & Marini (2015) |
| Data splits and validation | Grouped splitting rules; nested CV if tuning; truly external test set when claiming transfer | Westad & Marini (2015); Lopez *et al.,* (2023) |
| Fusion description | Fusion level (data/feature/decision), rationale, ablation tests (drop-modality) | Smolinska *et al.,* (2019) |
| Drift control | Drift indicators, control charts/QC logic, recalibration triggers, versioning | Thompson & Wood (1995); ISO/IEC (2017) |
| Cross-modality consistency | Chemical/physical plausibility checks, disagreement metrics, residual analysis | JCGM (2008); De Bièvre *et al.,* (2011) |
| Uncertainty budget | Sampling + instrument + model + fusion components; propagation method; coverage statement | JCGM (2008); Ellison & Williams (2012); Eurachem *et al.,* (2019) |
| Decision rules | Guard bands/decision rule for compliance, statement of conformity, risk rationale | ILAC (2019); JCGM (2012b) |
| Data and code availability | Raw data, metadata schema, code/workflows, versioning; FAIR alignment | Wilkinson *et al.,* (2016) |

## 7. Representative application case studies (show power across many fields)

This section is designed to prove a single point: multimodal chemical measurement is not "more instruments," it is a way to *remove ambiguity* by combining orthogonal physical principles (separation, spectral fingerprints, electrochemical kinetics, and spatially resolved imaging) and then fusing the evidence with validation strategies that prevent overconfident failures. A useful framing is to decide, for each problem, whether you need low level fusion (combine aligned signals), mid-level fusion (combine engineered features or latent variables), or high-level fusion (combine decisions from separate models), and then to choose validation splits that reflect the real deployment scenario rather than random splits that leak information. (Smolinska *et al.,* 2019; Lopez *et al.,* 2023; Westad & Marini, 2015).

### 7.1 Pharmaceutical and biomedical: identity plus quantification in complex matrices (LC-MS plus spectroscopy plus ML)

In pharma and biomedical analysis, the central challenge is that complex matrices (plasma, serum, urine, tissue, formulated products) can distort signals at multiple stages, especially in mass spectrometry where ion suppression or enhancement changes the apparent analyte response. A dedicated matrix effects review emphasizes that these effects can arise throughout sample preparation and in GC-MS and LC-MS workflows, and they directly threaten accuracy, sensitivity, and reproducibility if not assessed and controlled. (Williams *et al.,* 2023).

For quantitative claims to be credible in regulated contexts, the method must be validated against recognized expectations for accuracy, precision, selectivity, and stability, and the study sample analysis must follow disciplined procedures. Regulatory guidance documents (FDA and ICH M10 related guidance) explicitly define validation elements and expectations for bioanalytical methods used for regulatory decisions, which is why this case study is ideal for showing how "AI plus multimodal" has to be paired with traceable validation and documentation. (FDA, 2024; FDA, 2018; EMA, 2022).

A strong multimodal strategy here uses LC-MS as the quantitative anchor while spectroscopy provides speed and non-destructive screening. Portable and handheld Raman and NIR are widely reviewed for in-process and quality-control testing of pharmaceutical products, typically relying on chemometrics for classification and prediction rather than single peak rules. (Deidda *et al.,* 2019). Process Analytical Technology reviews further explain how PAT supports quality-by-design style manufacturing by monitoring critical attributes in unit operations such as blending, granulation, tableting, and coating, which naturally creates a multimodal setting where signals must be integrated to support control decisions. (Kim *et al.,* 2021).

In writing this case study, emphasize the "reference to deployment" chain. LC-MS provides identity and quantification, spectroscopy provides rapid screening and process monitoring, and AI primarily functions as a calibration and transfer tool across batches, instruments, and sites. The most defensible fusion pattern is often mid-level fusion, where you combine LC-MS peak table features with spectroscopic latent variables, then validate using batch-wise or instrument-wise splits, aligned with predictive-model validation guidance for real-world generalization. (Smolinska *et al.,* 2019; Lopez *et al.,* 2023).

### 7.2 Environmental and food: trace contaminants and field deployable fusion (electrochemistry plus spectroscopy)

Environmental and food settings stress the system in different ways: targets can be trace level, samples are diverse and messy, and measurement may need to happen outside the lab. Reviews of electrochemical biosensors for on-site food safety emphasize the promise of rapid and low-cost detection, but they also highlight that complex matrices and minimal sample preparation make sensitivity and selectivity difficult, which is exactly where orthogonal sensing and fusion become valuable. (Hosseinikebria *et al.,* 2025). A complementary review on smart electrochemical sensors for foodborne hazards similarly frames the field around design strategies and persistent performance challenges in real matrices. (Dong *et al.,* 2025).

The multimodal argument is strongest when you show how electrochemistry and spectroscopy compensate for each other. Electrochemical sensors are excellent for fast response and portable deployment, while infrared or Raman-based approaches add a chemical fingerprint that can reduce false positives and improve specificity. A recent RSC review explicitly evaluates electrochemical sensing, infrared spectroscopy, hyperspectral imaging, SERS, and fluorescence sensing for food safety, highlighting that different technologies dominate under different constraints and that validation milestones matter. (Feng *et al.,* 2025).

Data fusion becomes the mechanism to turn "two imperfect sensors" into one reliable decision. A recent review dedicated to multi-source data fusion for food contaminant detection surveys how data from spectroscopy, imaging, and other modalities are combined and why the choice of fusion level and preprocessing determines whether performance transfers across sample types. (Adade *et al.,* 2024). In your narrative, you can motivate high level fusion for field programs, because it tolerates missing modalities and supports calibrated decision thresholds, while still allowing a lab confirmatory test (for example LC-MS) to close the loop when needed. This mapping from modality to fusion choice aligns with general data-fusion frameworks used across life science analytics. (Smolinska *et al.,* 2019).

### 7.3 Catalysis and surface chemistry (operando): intermediates and structure activity links (spectroscopy plus electrochemistry plus imaging)

Catalysis is the showcase domain for why multimodal must be "physics guided." Surface intermediates are transient, spatially heterogeneous, and strongly dependent on operating conditions, so conclusions drawn from a single probe are often underdetermined. A recent Chemical Reviews perspective on operando and in situ studies emphasizes that operando approaches are central for linking catalyst structure and reactivity, and it situates modern catalysis research around integrated characterization under working conditions. (Roldán Cuenya *et al.,* 2024).

The practical problem is that operando experiments can produce misleading certainty if the cell design, synchronization, or interpretation is weak. A best-practices article in Nature Communications makes this point directly, arguing that execution and interpretation determine how strong mechanistic conclusions can be and what uncertainties remain, which is why this article is ideal to cite when you justify design choices for fusion and validation. (Prajapati *et al.,* 2025).

A compelling multimodal template for this case study is to treat spectroscopy as the "intermediate and state" channel, electrochemistry as the "kinetics and transport" channel, and imaging as the "heterogeneity and structure" channel. When you describe fusion, emphasize that the goal is not to stack raw signals, but to fuse mechanistically meaningful descriptors (for example, spectral proxies for adsorbate coverage, electrochemical descriptors of charge transfer and mass transport, and image-derived activity hotspot metrics). This is a natural fit for mid-level fusion, followed by perturbation-based validation such as potential steps or reactant switching that must produce consistent cross-modal narratives, as recommended by operando best-practice guidance. (Prajapati *et al.,* 2025).

### 7.4 Energy materials and devices: batteries and corrosion (EIS plus imaging plus spectroscopy)

Energy devices highlight a different failure mode: standard electrochemical measurements provide global averages, but degradation is driven by local inhomogeneities, interfaces, and evolving microstructure. Electrochemical impedance spectroscopy is widely used because it can separate contributions from different processes in frequency space, but a major tutorial also stresses that interpretation must be physically grounded and that poor modeling can create convincing but incorrect parameter stories. (Lazanas & Prodromidis, 2023).

This is why imaging and spectroscopy matter. A recent review on operando imaging for batteries frames operando imaging as a way to connect micro and mesoscale evolution to macroscopic device performance, which directly supports the multimodal promise of linking structure, composition, and performance in real time rather than post-mortem inference. (Zhang *et al.,* 2024). Complementary research and reviews on local imaging in batteries further reinforce that spatially varying transport and reaction rates can self-amplify, making local observation essential for diagnosing and mitigating degradation. (Pollok *et al.,* 2025).

For corrosion, the same measurement logic applies, but the deployment context can be field structures and longtime horizons. A recent review focused on corrosion in reinforced concrete explains that EIS has expanded beyond laboratory studies toward field assessment, while still facing challenges that motivate improved analysis and interpretation. (Alexander *et al.,* 2025). In writing the case study, emphasize that fusion is not optional: EIS helps infer interfacial and transport behavior, imaging helps localize damage evolution, and spectroscopy helps identify chemical state changes and reaction products. The most defensible fusion here is often hybrid and physics guided: you use physically meaningful constraints for impedance interpretation and you validate across cells, temperatures, protocols, or exposure environments using validation strategies known to prevent optimistic leakage. (Lazanas & Prodromidis, 2023; Lopez *et al.,* 2023).

### 7.5 Polymer and materials QC: composition to morphology coupling (spectroscopy plus imaging plus chemometrics)

Polymers and formulated materials are an ideal "bridging" domain because the same chemical composition can yield different properties depending on morphology, phase separation, and spatial distribution of additives. A polymer characterization review focused on vibrational spectroscopy and chemical imaging summarizes how Raman, NIR, and mid-IR based approaches are used to characterize polymers in diverse forms and to capture behavior that is not visible to bulk assays. (Mukherjee & Gowen, 2015).

Chemical imaging is particularly important because morphology is often the hidden variable that drives performance. A classic Analytical Chemistry paper on Raman chemical imaging demonstrates noninvasive visualization of polymer blend architecture, providing a foundational reference for why spatially resolved spectroscopy is central for polymer QC and structure-property links. (Schaeberle *et al.,* 1995).

To make the topic modern, connect polymer QC to hyperspectral imaging and advanced chemometrics, where data volume and dimensionality demand learning-based analysis. A recent critical review positions hyperspectral imaging as a step beyond classical spectroscopic PAT tools by combining spatial and chemical information, while emphasizing that powerful data analysis is required for interpretation and industrial implementation. (de Juan & Rocha de Oliveira, 2025). In this case study, show that mid level fusion can combine spectral latent variables with spatial texture and morphology descriptors to predict QC endpoints, and that validation must hold out entire lots or production runs rather than pixels to avoid inflated performance, consistent with general chemometric validation guidance. (Westad & Marini, 2015).

**Table 7: Application-to-Workflow Map: Recommended multimodal stacks for common chemical questions (concise)**

| Application area | Primary question | Recommended multimodal stack | Fusion level (typical) | Key validation step |
|---|---|---|---|---|
| Pharmaceutical & biomedical | Identity + accurate quant in complex matrices | LC–MS/MS (anchor) + Raman/NIR (rapid screen) ± NMR (structure) | Mid-level | Split/hold-out by batch or site; matrix-effect checks; external test set |
| Environmental & food | Trace contaminants with field-ready decisions | Electrochemical sensor + portable IR/Raman ± lab LC–MS confirm | High-level | Stress-test across matrix types and conditions; calibrated decision thresholds |
| Catalysis & surface chemistry (operando) | Intermediates + structure–activity links | Operando IR/Raman/XAS/EPR + electrochemistry + operando imaging | Mid-level (physics-guided) | Synchronization + perturbation tests (switching/steps); cross-modality consistency |
| Energy devices (batteries/supercaps) | Degradation diagnosis during operation | EIS + operando spectroscopy (Raman/XAS/IR) + operando imaging | Hybrid / Mid-level | Hold-out by cell/batch; test across temperature & protocol; drift monitoring |
| Corrosion monitoring | State and progression under real exposure | EIS + metadata (T, humidity, chloride) ± surface spectroscopy/imaging | High-level (deploy) / Mid-level (lab) | Time-split validation (past→future); field validation; recalibration plan |
| Polymers & materials QC | Blend ratio, phase separation, defects | IR/Raman + hyperspectral/Raman imaging + chemometrics | Mid-level | Hold-out by lot/run (not pixels); cross-instrument transfer test |
| Semiconductors & thin films | Surface state, contamination, uniformity | XPS/Raman + mapping/imaging ± MS for trace contaminants | Mid-level | Replicate locations; inter-operator reproducibility; registration error reporting |
| Bioprocess/PAT | Real-time CQAs and process control | Inline NIR/Raman + process sensors ± periodic LC/HPLC/LC–MS reference | High-level (control) / Mid-level (build) | Time-based splits (early→late); site transfer; drift alarms & recalibration |

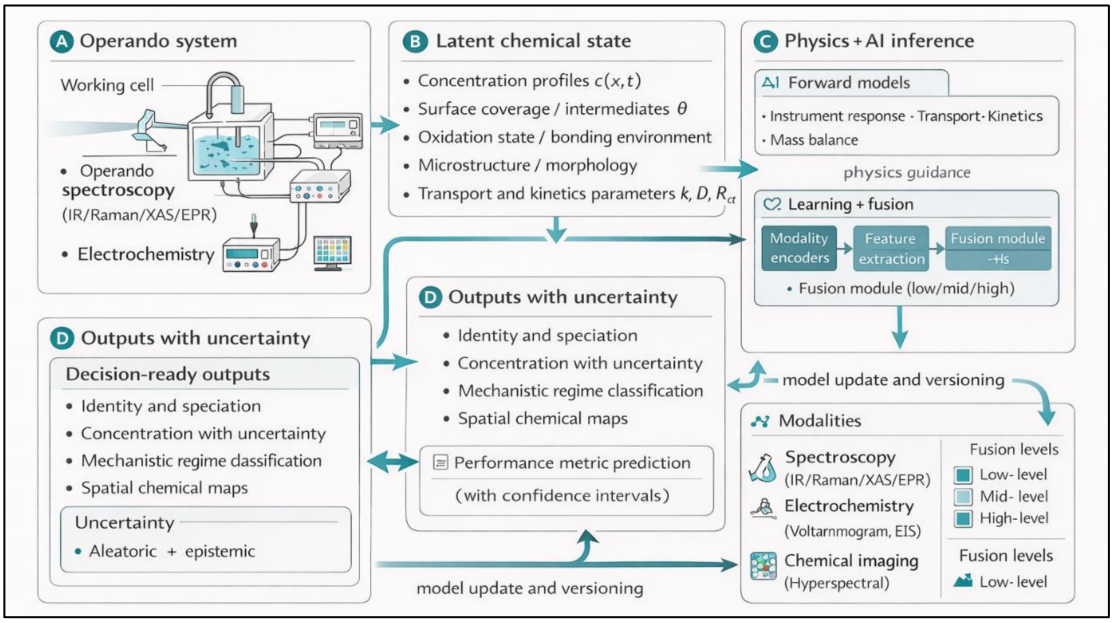

**Figure 5: End-to-End Operando Multimodal Case Study: Fusing Spectroscopy, Electrochemistry, and Chemical Imaging to Track Structure–Composition–Performance in a Working System**

## 8. Challenges and future directions

### 8.1 Standardized multimodal datasets and benchmark tasks

A major barrier to multimodal chemical intelligence is the lack of fusion-ready datasets where the *same samples* are measured across multiple modalities with consistent identifiers, raw data availability, and rich metadata. Without this, models often learn lab- or instrument-specific signatures instead of chemistry, and results become hard to reproduce or transfer. The FAIR principles (Findable, Accessible, Interoperable, Reusable) are widely used guidance for making datasets machine-actionable and reusable, which is exactly what multimodal benchmarking needs (Wilkinson *et al.,* 2016).

Community benchmarking already works well in sub-areas and can be extended to multimodal fusion. For example, the CASMI challenges created shared evaluation settings for small-molecule identification and exposed realistic failure modes that are hidden when studies use non-comparable metrics (Schymanski *et al.,* 2017). Likewise, open community platforms such as GNPS enable large-scale sharing and curation of MS/MS data and libraries, supporting reproducible comparisons of annotation pipelines (Wang *et al.,* 2016).

For "chemistry-wide" multimodal benchmarks, the next step is paired and synchronized repositories where raw data and metadata are preserved across techniques. Metabolomics infrastructure shows what is possible: MetaboLights explicitly archives raw experimental data and associated metadata (Haug *et al.,* 2013; Haug *et al.,* 2020). For imaging mass spectrometry, METASPACE supports metabolite annotation workflows and hosts large public collections that can be used to stress-test generalization (Palmer *et al.,* 2017; METASPACE, n.d.).

A modern direction is to define benchmark tasks that reflect real deployment: calibration transfer, drift-robust quantification, operando state estimation, and uncertainty-calibrated decisions across labs and instruments (not only average accuracy within one dataset). (Wilkinson *et al.,* 2016).

### 8.2 Interoperability: metadata, FAIR data, instrument formats and ontologies

Multimodal fusion often fails for simple reasons: missing metadata, inconsistent units, unknown preprocessing, and unclear provenance. FAIR explicitly elevates interoperability and reuse, implying that multimodal studies must capture enough structured context for both humans and machines (Wilkinson *et al.,* 2016).

Several communities already provide strong building blocks. In mass spectrometry, mzML is a widely adopted community standard for vendor-neutral MS data exchange (Martens *et al.,* 2011). In NMR, nmrML provides a vendor-agnostic open format designed for long-term archiving and reuse of NMR data (Schober *et al.,* 2018).

Beyond file formats, multimodal chemistry needs structured descriptions of the experiment itself. The ISA software suite was designed to support standards-compliant experimental annotation, including multi-technology studies and ontology-backed checklists (Rocca-Serra *et al.,* 2010). Complementary perspectives on interoperable bioscience data and "data commoning" further emphasize shared frameworks and incentives for standardized metadata (Sansone *et al.,* 2012).

For regulated and industrial workflows, enterprise-level interoperability efforts are also growing. The Allotrope Framework describes a standardized approach to storing analytical data plus instrument settings and contextual metadata to support integrity and downstream analytics (Allotrope Foundation, n.d.; Kayser & Lau, 2024). For cross-technique interchange and archiving, AnIML is an ASTM-linked standardization effort for analytical result data and metadata (ASTM International, n.d.).

A practical "future direction" message for your review is: treat interoperability as a design constraint, meaning minimum metadata fields, standard formats when available, controlled vocabularies for instrument and sample descriptors, and explicit provenance of preprocessing and calibration. (Wilkinson *et al.,* 2016; Rocca-Serra *et al.,* 2010).

### 8.3 Real-time fusion and closed-loop experimentation

The frontier is moving from offline data fusion to real-time inference that guides what the lab does next. Self-driving laboratories combine automation, online analytics, and algorithmic experiment selection to accelerate discovery and optimization (Tom *et al.,* 2024). In this setting, multimodal fusion becomes a control problem: each modality constrains a latent chemical state, and the system chooses the next action to reduce uncertainty or optimize objectives (Tom *et al.,* 2024).

Demonstrations show why these matters: a self-driving laboratory can efficiently explore trade-offs and move toward a Pareto front when multiple objectives compete (MacLeod *et al.,* 2022). For multimodal chemistry, the key research direction is "measurement-aware autonomy," where the platform selects the next measurement because it is maximally informative for the fused estimate (for example, spectroscopy for specificity, electrochemistry for kinetics, imaging for heterogeneity), rather than simply collecting everything all the time (Tom *et al.,* 2024).

### 8.4 Green and miniaturized analytics (portable multimodal platforms)

Sustainable measurement is increasingly a design requirement, not an optional add-on. The 12 principles of green analytical chemistry explicitly promote miniaturization, automation, and reducing reagent use, waste, and energy demand (Gałuszka *et al.,* 2013).

Portable spectroscopy is a strong example because it can reduce sampling logistics and enable in situ decisions when coupled to robust chemometrics. Reviews discuss how portable NIR supports nondestructive, online, or in situ analyses and highlight the central role of chemometrics for extracting reliable information from compact instruments (Gullifa *et al.,* 2023; Yan *et al.,* 2023). Portable Raman instrumentation is also expanding rapidly; reviews emphasize performance limits and the importance of careful validation and preprocessing for field deployment (Jehlička *et al.,* 2022).

Miniaturization at the platform level has deep roots in micro total analysis systems. The classic concept of miniaturized "total chemical analysis systems" proposed integrating analytical operations to reduce transport time and reagent consumption while enabling faster workflows (Manz *et al.,* 1990). The modern future direction is portable multimodal stacks (for example handheld spectroscopy plus electrochemical sensing) with on-device fusion that reports not only a prediction, but also uncertainty and an "out-of-scope" warning (Gałuszka *et al.,* 2013; Gullifa *et al.,* 2023).

### 8.5 Trustworthy AI: uncertainty, explainability, and regulatory acceptance

As multimodal AI shifts from papers to regulated or safety-relevant decisions, "trustworthy AI" must be operationalized as governance, evaluation, monitoring, and lifecycle management. The NIST AI Risk Management Framework (AI RMF 1.0) provides a lifecycle structure for managing AI risks and emphasizes continuous monitoring and governance rather than one-time model building (NIST, 2023).

Regulatory expectations around AI lifecycle documentation are becoming more explicit, especially for medical-device software. FDA's SaMD pages highlight ongoing guidance activity for AI-enabled device software functions and lifecycle considerations (FDA, 2025a; FDA, 2025b). In parallel, Good Machine Learning Practice principles (referenced by FDA and published by IMDRF) emphasize total product lifecycle thinking, transparency, and quality systems alignment (FDA, 2025c; IMDRF, 2025).

For chemistry and pharmaceutical analysis, method validation and lifecycle concepts provide strong analogies for multimodal AI validation. ICH Q2(R2) sets expectations for analytical procedure validation, and Q14 frames science- and risk-based analytical procedure development and maintenance (ICH, 2023a; ICH, 2023b). A clean future direction is "audit-ready multimodal AI": clearly defined intended use, locked preprocessing, uncertainty calibration, external validation under domain shift (new instruments, labs, matrices), and drift monitoring with controlled update pathways (NIST, 2023; ICH, 2023a).

## CONCLUSION

Multimodal chemical measurement is becoming a practical unifying layer across chemistry and physics because it links orthogonal signals to a common chemical reality: identity, concentration, structure/state, kinetics, and spatial heterogeneity. When designed well, fusion does not merely increase accuracy; it reduces ambiguity by forcing agreement between independent physical principles, so the final output is more robust to interference, drift, and instrument changes than any single modality alone. The strongest workflows therefore treat fusion as a *measurement strategy*, not a post-processing trick: the modalities are chosen to be complementary, the fusion level is kept as simple as possible, and models are built around a clearly defined decision (screening vs quantification vs mechanistic inference vs control).

A key message of this review is that the field will not achieve real-world impact without the analytical chemistry backbone. Multimodal AI must be calibrated, validated, and reported like an analytical procedure, including figures of merit per modality and for the fused output, explicit cross-modality consistency checks, and uncertainty budgets that separate sampling, instrument, model, and fusion components. Only then can fused results be compared across labs and time, used in conformity decisions, and trusted in regulated or safety-relevant settings. In parallel, physics-guided modeling and probabilistic inference are shifting multimodal AI from "high performance on a dataset" to transferable and uncertainty-aware predictions, enabling reliable deployment and safer automation.

Looking forward, the most exciting trajectory is the convergence of multimodal sensing, interoperability, and autonomy: standardized datasets and benchmark tasks will make comparisons fair; FAIR-aligned metadata and instrument formats will make fusion reproducible; real-time fusion will power closed-loop experimentation and self-driving labs; and miniaturized green platforms will move multimodal analytics from centralized facilities to field and production environments. The practical decision framework is: select an anchor modality for traceable quantification, add orthogonal modalities that constrain ambiguity, fuse at the simplest level that achieves robustness, and validate under realistic domain shift with uncertainty reporting. If this discipline becomes standard, the next decade will see multimodal workflows evolve from descriptive measurements into quantitative, uncertainty-aware, and deployable chemical intelligence.

# REFERENCES

- ASTM International. (2020, September 8). ASTM molecular spectroscopy and separation science committee continues work on proposed Analytical Information Markup Language (AnIML) standard.
- Azcárate, S. M., Ríos-Reina, R., Amigo, J. M., & Goicoechea, H. C. (2021). Data handling in data fusion: Methodologies and applications. TrAC Trends in Analytical Chemistry, 143, 116355. https://doi.org/10.1016/j.trac.2021.116355
- Benning, M., & Burger, M. (2018). Modern regularization methods for inverse problems. Acta Numerica, 27, 1–111. https://doi.org/10.1017/S0962492918000016
- Bettencourt da Silva, R., & Williams, A. (Eds.). (2015). Eurachem/CITAC guide: Setting and using target uncertainty in chemical measurement. Eurachem/CITAC.
- Bro, R. (1997). PARAFAC. Tutorial and applications. Chemometrics and Intelligent Laboratory Systems. https://doi.org/10.1016/S0169-7439(97)00032-4
- Bro, R., & Kiers, H. A. L. (2003). A new efficient method for determining the number of components in PARAFAC models. Journal of Chemometrics, 17(5), 274–286. https://doi.org/10.1002/cem.801
- Bro, R., & Smilde, A. K. (2003). Centering and scaling in component analysis. Journal of Chemometrics, 17(1), 16–33. https://doi.org/10.1002/cem.773
- Buchberger, A. R., DeLaney, K., Johnson, J., & Li, L. (2018). Mass spectrometry imaging: A review of emerging advancements and future insights. Analytical Chemistry, 90(1), 240–265. https://doi.org/10.1021/acs.analchem.7b04733
- Campos, E. P., Reis, M. S., & Li, W. (2020). Data preprocessing for multiblock modeling and data fusion. Chemometrics and Intelligent Laboratory Systems, 199, 103959. https://doi.org/10.1016/j.chemolab.2020.103959
- Cantwell, H. (Ed.). (2025). Blanks in method validation (2nd ed.). Eurachem.
- Cantwell, H. (Ed.). (2025). Eurachem guide: The fitness for purpose of analytical methods: A laboratory guide to method validation and related topics (3rd ed.). Eurachem.
- Cantwell, H. (Ed.). (2025). The fitness for purpose of analytical methods: A laboratory guide to method validation and related topics (3rd ed.). Eurachem.
- Casian, T., Nagy, B., Kovács, B., Galata, D. L., Hirsch, E., & Farkas, A. (2022). Challenges and opportunities of implementing data fusion in process analytical technology—A review. Molecules, 27(15), 4846. https://doi.org/10.3390/molecules27154846
- Currie, L. A. (1968). Limits for qualitative detection and quantitative determination: Application to radiochemistry. Analytical Chemistry, 40(3), 586–593. https://doi.org/10.1021/ac60259a007
- Currie, L. A. (1968). Limits for qualitative detection and quantitative determination: Application to radiochemistry. Analytical Chemistry, 40(3), 586–593. doi:10.1021/ac60259a007
- De Bièvre, P., Dybkaer, R., Fajgelj, A., & Hibbert, D. B. (2011). Metrological traceability of measurement results in chemistry: Concepts and implementation (IUPAC Technical Report). Pure and Applied Chemistry, 83(10), 1873–1935. https://doi.org/10.1351/PAC-REP-07-09-39
- De Bièvre, P., Dybkaer, R., Fajgelj, A., & Hibbert, D. B. (2011). Metrological traceability of measurement results in chemistry: Concepts and implementation (IUPAC Technical Report). Pure and Applied Chemistry, 83(10), 1873–1935. doi:10.1351/PAC-REP-07-09-39
- de Juan, A., & Rocha de Oliveira, R. (2025). Hyperspectral image and chemometrics: A step beyond classical spectroscopic PAT tools. Analytical and Bioanalytical Chemistry. Advance online publication. doi:10.1007/s00216-025-06154-x
- de Juan, A., & Rocha de Oliveira, R. (2025). Hyperspectral image and chemometrics. A step beyond classical spectroscopic PAT tools. Analytical and Bioanalytical Chemistry. Advance online publication. https://doi.org/10.1007/s00216-025-06154-x
- Donoho, D. L. (2006). Compressed sensing. IEEE Transactions on Information Theory, 52(4), 1289–1306. https://doi.org/10.1109/TIT.2006.871582
- Doonyapisut, D., Kim, B., Kim, J. K., Lee, E., & Chung, C.-H. (2023). Deep generative learning for exploration in large electrochemical impedance dataset. Engineering Applications of Artificial Intelligence, 126(Part C), 107027. https://doi.org/10.1016/j.engappai.2023.107027
- Döppel, F. A., & Votsmeier, M. (2024). Robust mechanism discovery with atom conserving chemical reaction neural networks. Proceedings of the Combustion Institute, 40(1–4), 105507. https://doi.org/10.1016/j.proci.2024.105507
- Ellison, S. L. R., & Williams, A. (Eds.). (2012). Eurachem/CITAC guide: Quantifying uncertainty in analytical measurement (3rd ed.). Eurachem.
- Ellison, S. L. R., & Williams, A. (Eds.). (2012). Eurachem/CITAC guide: Quantifying uncertainty in analytical measurement (3rd ed.). Eurachem. (ISBN 978-0-948926-30-3)
- Ellison, S. L. R., & Williams, A. (Eds.). (2012). Eurachem/CITAC guide: Quantifying uncertainty in analytical measurement (3rd ed.). Eurachem/CITAC.
- Ellison, S. L. R., & Williams, A. (Eds.). (2012). Eurachem/CITAC guide: Quantifying uncertainty in analytical measurement (3rd ed.). Eurachem/CITAC.
- Ellison, S. L. R., & Williams, A. (Eds.). (2019). Eurachem/CITAC guide: Metrological traceability

in analytical measurement (2nd ed.). Eurachem/CITAC.

- Ettre, L. S. (1993). Nomenclature for chromatography (IUPAC Recommendations 1993). Pure and Applied Chemistry, 65(4), 819–872. https://doi.org/10.1351/pac199365040819
- Eurachem, EUROLAB, CITAC, Nordtest, & RSC Analytical Methods Committee. (2019). Measurement uncertainty arising from sampling: A guide to methods and approaches (2nd ed.). Eurachem.
- Eurachem/CITAC, EUROLAB, Nordtest, & Royal Society of Chemistry Analytical Methods Committee. (2019). Measurement uncertainty arising from sampling: A guide to methods and approaches (2nd ed.).
- FDA. (2025a, March 25). Artificial intelligence in software as a medical device. U.S. Food and Drug Administration.
- FDA. (2025b, December 2024; page updated 2025). Good machine learning practice for medical device development: Guiding principles. U.S. Food and Drug Administration.
- Fu, Y., Li, W., & Picard, F. (2024). Assessment of matrix effect in quantitative LC–MS bioanalysis. Bioanalysis, 16(12), 631–634. https://doi.org/10.4155/bio-2024-0047
- Gal, Y., & Ghahramani, Z. (2016). Dropout as a Bayesian approximation: Representing model uncertainty in deep learning. In M. F. Balcan & K. Q. Weinberger (Eds.), Proceedings of the 33rd International Conference on Machine Learning (ICML 2016) (Vol. 48, pp. 1050–1059). PMLR. https://arxiv.org/abs/1506.02142
- Gałuszka, A., Migaszewski, Z. M., & Namieśnik, J. (2013). The 12 principles of green analytical chemistry and the SIGNIFICANCE mnemonic of green analytical practices. TrAC Trends in Analytical Chemistry, 50, 78–84. https://doi.org/10.1016/j.trac.2013.04.010
- Gama, J., Žliobaitė, I., Bifet, A., Pechenizkiy, M., & Bouchachia, A. (2014). A survey on concept drift adaptation. ACM Computing Surveys, 46(4), Article 44. https://doi.org/10.1145/2523813
- Gebru, T., Morgenstern, J., Vecchione, B., Vaughan, J. W., Wallach, H., Daumé III, H., & Crawford, K. (2021). Datasheets for datasets. Communications of the ACM, 64(12), 86–92. https://doi.org/10.1145/3458723
- Geirhos, R., Jacobsen, J.-H., Michaelis, C., Zemel, R., Brendel, W., Bethge, M., & Wichmann, F. A. (2020). Shortcut learning in deep neural networks. Nature Machine Intelligence, 2, 665–673. https://doi.org/10.1038/s42256-020-00257-z
- Geurts, B. P., Engel, J., Rafii, B., Blanchet, L., & Buydens, L. M. C. (2016). Improving high-dimensional data fusion by exploiting the multivariate advantage. Chemometrics and Intelligent Laboratory Systems, 156, 231–240. https://doi.org/10.1016/j.chemolab.2016.05.010
- Gullifa, G., *et al.,* (2023). Portable NIR spectroscopy: The route to green analytical chemistry. Frontiers in Chemistry. https://doi.org/10.3389/fchem.2023.1214825
- Gureyev, T. E., Paganin, D. M., & Quiney, H. M. (2024). Signal-to-noise and spatial resolution in in-line imaging. 1. Basic theory, numerical simulations and planar experimental images. Journal of Synchrotron Radiation, 31(4), 896–909. https://doi.org/10.1107/S1600577524003886
- Haug, K., *et al.,* (2020). MetaboLights: A resource evolving in response to the needs of its scientific community. Nucleic Acids Research.
- Haug, K., Salek, R. M., Conesa, P., Hastings, J., de Matos, P., Rijnbeek, M., … Steinbeck, C. (2013). MetaboLights: An open-access general-purpose repository for metabolomics studies and associated metadata. Nucleic Acids Research, 41(Database issue), D781–D786. https://doi.org/10.1093/nar/gks1004
- Horai, H., Arita, M., Kanaya, S., Nihei, Y., Ikeda, T., Suwa, K., *et al.,* (2010). MassBank: A public repository for sharing mass spectral data for life sciences. Journal of Mass Spectrometry, 45(7), 703–714. https://doi.org/10.1002/jms.1777
- ICH. (2023a). ICH Q2(R2): Validation of analytical procedures (Guideline, Step 4). International Council for Harmonisation.
- ICH. (2023b). ICH Q14: Analytical procedure development (Guideline, Step 4). International Council for Harmonisation.
- International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. (2023). ICH harmonised guideline: Validation of analytical procedures Q2(R2) (Final version; adopted 1 November 2023).
- International Council for Harmonisation. (2023). Analytical procedure development (ICH Guideline Q14). ICH.
- International Council for Harmonisation. (2023). Validation of analytical procedures (ICH Guideline Q2(R2)). ICH.
- International Laboratory Accreditation Cooperation. (2019). Guidelines on decision rules and statements of conformity (ILAC-G8:09/2019). ILAC.
- International Laboratory Accreditation Cooperation. (2019). ILAC-G8:09/2019: Guidelines on decision rules and statements of conformity.
- International Organization for Standardization, & International Electrotechnical Commission. (2010). Conformity assessment: General requirements for proficiency testing (ISO/IEC 17043:2010). ISO.
- International Organization for Standardization, & International Electrotechnical Commission. (2017). General requirements for the competence of testing and calibration laboratories (ISO/IEC 17025:2017). ISO.

- International Organization for Standardization, & International Electrotechnical Commission. (2017). General requirements for the competence of testing and calibration laboratories (ISO/IEC 17025:2017). ISO.
- International Organization for Standardization. (1997). Capability of detection: Part 1: Terms and definitions (ISO 11843-1:1997). ISO.
- International Organization for Standardization. (1997). Capability of detection—Part 1: Terms and definitions (ISO 11843-1:1997). ISO.
- International Organization for Standardization. (2012). Water quality: Estimation of measurement uncertainty based on validation and quality control data (ISO 11352:2012). ISO.
- International Organization for Standardization. (2015). Reference materials: Good practice in using reference materials (ISO Guide 33:2015). ISO.
- International Organization for Standardization. (2015). Reference materials—Good practice in using reference materials (ISO Guide 33:2015). ISO.
- International Organization for Standardization. (2016). General requirements for the competence of reference material producers (ISO 17034:2016). ISO.
- International Organization for Standardization. (2017). Guidance for the use of repeatability, reproducibility and trueness estimates in measurement uncertainty evaluation (ISO 21748:2017). ISO.
- International Organization for Standardization. (2017). Reference materials: Guidance for characterization and assessment of homogeneity and stability (ISO Guide 35:2017). ISO.
- International Organization for Standardization. (2017). Reference materials—Guidance for characterization and assessment of homogeneity and stability (ISO Guide 35:2017). ISO.
- International Organization for Standardization. (2022). Statistical methods for use in proficiency testing by interlaboratory comparison (ISO 13528:2022). ISO.
- International Organization for Standardization. (2023). Accuracy (trueness and precision) of measurement methods and results: Part 1: General principles and definitions (ISO 5725-1:2023). ISO.
- International Organization for Standardization. (2024). Reference materials: Contents of certificates, labels and accompanying documentation (ISO 33401:2024). ISO.
- International Union of Pure and Applied Chemistry. (2019). Compendium of Chemical Terminology (the Gold Book). https://doi.org/10.1351/goldbook
- International Union of Pure and Applied Chemistry. (2025). Fluorescence. In IUPAC Compendium of Chemical Terminology (the “Gold Book”) (Version 5.0.0). https://doi.org/10.1351/goldbook.F02453
- International Union of Pure and Applied Chemistry. (2025). Infrared spectroscopy. In IUPAC Compendium of Chemical Terminology (the “Gold Book”) (Version 5.0.0). https://doi.org/10.1351/goldbook.08618
- International Union of Pure and Applied Chemistry. (2025). Mass-to-charge ratio. In IUPAC Compendium of Chemical Terminology (the “Gold Book”) (Version 5.0.0). https://doi.org/10.1351/goldbook.M03752
- International Union of Pure and Applied Chemistry. (2025). Matrix effect. In IUPAC Compendium of Chemical Terminology (the “Gold Book”) (Version 5.0.0). https://doi.org/10.1351/goldbook.M03759
- International Union of Pure and Applied Chemistry. (2025). Nuclear magnetic resonance spectroscopy. In IUPAC Compendium of Chemical Terminology (the “Gold Book”) (Version 5.0.0). https://doi.org/10.1351/goldbook.08218
- International Union of Pure and Applied Chemistry. (2025). Raman spectroscopy. In IUPAC Compendium of Chemical Terminology (the “Gold Book”) (Version 5.0.0). https://doi.org/10.1351/goldbook.08669
- International Union of Pure and Applied Chemistry. (2025). Retention factor. In IUPAC Compendium of Chemical Terminology (the “Gold Book”) (Version 5.0.0). https://doi.org/10.1351/goldbook.R05359
- International Union of Pure and Applied Chemistry. (2025). Spectroscopy. In IUPAC Compendium of Chemical Terminology (the “Gold Book”) (Version 5.0.0). https://doi.org/10.1351/goldbook.S05848
- International Union of Pure and Applied Chemistry. (2025). X-ray photoelectron spectroscopy. In IUPAC Compendium of Chemical Terminology (the “Gold Book”) (Version 5.0.0). https://doi.org/10.1351/goldbook.X06716
- International Union of Pure and Applied Chemistry. (n.d.). Detection limit. In IUPAC compendium of chemical terminology (Gold Book). https://doi.org/10.1351/goldbook.D01629
- International Union of Pure and Applied Chemistry. (n.d.). Diffusion coefficient (D01719). In IUPAC Compendium of Chemical Terminology (the “Gold Book”). https://doi.org/10.1351/goldbook.D01719
- International Union of Pure and Applied Chemistry. (n.d.). Instrument line shape (08257). In IUPAC Compendium of Chemical Terminology (the “Gold Book”). https://doi.org/10.1351/goldbook.08257
- International Union of Pure and Applied Chemistry. (n.d.). Limit of detection (L03540). In Compendium of Chemical Terminology (the IUPAC Gold Book). Retrieved December 25, 2025. doi:10.1351/goldbook.L03540
- International Union of Pure and Applied Chemistry. (n.d.). Limit of detection (L03540). In IUPAC Compendium of Chemical Terminology (the “Gold Book”). https://doi.org/10.1351/goldbook.L03540

- International Union of Pure and Applied Chemistry. (n.d.). Limit of detection. In IUPAC compendium of chemical terminology (Gold Book). https://doi.org/10.1351/goldbook.L03540
- International Union of Pure and Applied Chemistry. (n.d.). Limit of quantification. In IUPAC compendium of chemical terminology (Gold Book). https://doi.org/10.1351/goldbook.08022
- International Union of Pure and Applied Chemistry. (n.d.). Matrix effect (M03759). In IUPAC Compendium of Chemical Terminology (the "Gold Book"). https://doi.org/10.1351/goldbook.M03759
- International Union of Pure and Applied Chemistry. (n.d.). Measurand (M03789). In IUPAC Compendium of Chemical Terminology (the "Gold Book"). https://doi.org/10.1351/goldbook.M03789
- International Union of Pure and Applied Chemistry. (n.d.). Plate height (P04693). In IUPAC Compendium of Chemical Terminology (the "Gold Book"). https://doi.org/10.1351/goldbook.P04693
- International Union of Pure and Applied Chemistry. (n.d.). Signal-to-noise ratio (08282). In IUPAC Compendium of Chemical Terminology (the "Gold Book"). https://doi.org/10.1351/goldbook.08282
- Jiao, T., *et al.,* (2024). A comprehensive survey on deep learning multi-modal fusion methods, technologies and applications. Computer Modeling in Engineering & Sciences, 80(1).
- Joint Committee for Guides in Metrology. (2008). Evaluation of measurement data: Guide to the expression of uncertainty in measurement (JCGM 100:2008). https://www.bipm.org/documents/20126/2071204/JCGM_100_2008_E.pdf
- Joint Committee for Guides in Metrology. (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 (JCGM 101:2008). https://www.bipm.org/documents/20126/2071204/JCGM_101_2008_E.pdf
- Joint Committee for Guides in Metrology. (2008). Evaluation of measurement data: Guide to the expression of uncertainty in measurement (JCGM 100:2008). BIPM.
- Joint Committee for Guides in Metrology. (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 (JCGM 101:2008). BIPM.
- Joint Committee for Guides in Metrology. (2008). Evaluation of measurement data: Guide to the expression of uncertainty in measurement (JCGM 100:2008). BIPM.
- Joint Committee for Guides in Metrology. (2008). Evaluation of measurement data—Supplement 1 to the GUM: Propagation of distributions using a Monte Carlo method (JCGM 101:2008). BIPM.
- Joint Committee for Guides in Metrology. (2012). Evaluation of measurement data: The role of measurement uncertainty in conformity assessment (JCGM 106:2012). BIPM.
- Joint Committee for Guides in Metrology. (2012). Evaluation of measurement data—The role of measurement uncertainty in conformity assessment (JCGM 106:2012). BIPM.
- Joint Committee for Guides in Metrology. (2012). International vocabulary of metrology: Basic and general concepts and associated terms (VIM) (3rd ed.; JCGM 200:2012). BIPM. https://doi.org/10.59161/JCGM200-2012
- Joint Committee for Guides in Metrology. (2012). International vocabulary of metrology—Basic and general concepts and associated terms (VIM) (3rd ed.; JCGM 200:2012). BIPM.
- Kaipio, J., & Somersalo, E. (2005). Statistical and computational inverse problems. Springer. https://doi.org/10.1007/b138659
- Karniadakis, G. E., Kevrekidis, I. G., Lu, L., Perdikaris, P., Wang, S., & Yang, L. (2021). Physics-informed machine learning. Nature Reviews Physics, 3(6), 422–440. doi:10.1038/s42254-021-00314-5
- Karniadakis, G. E., Kevrekidis, I. G., Lu, L., Perdikaris, P., Wang, S., & Yang, L. (2021). Physics-informed machine learning. Nature Reviews Physics, 3(6), 422–440. https://doi.org/10.1038/s42254-021-00314-5
- Karniadakis, G. E., Kevrekidis, I. G., Lu, L., Perdikaris, P., Wang, S., & Yang, L. (2021). Physics-informed machine learning. Nature Reviews Physics, 3, 422–440. https://doi.org/10.1038/s42254-021-00314-5
- Kayser, H., & Lau, M. L. (2024). Growing value of data standardization: Allotrope Foundation Connect Workshop Proceedings. Drug Discovery Today, 29(6), 103988. https://doi.org/10.1016/j.drudis.2024.103988
- Kendall, A., & Gal, Y. (2017). What uncertainties do we need in Bayesian deep learning for computer vision? In Advances in Neural Information Processing Systems 30 (NeurIPS 2017) (pp. 5574–5584). Curran Associates. https://arxiv.org/abs/1703.04977
- Khan, S., Ali, F., Khan, W. Z., Adnan, M., & others. (2025, November). AI-driven and quantum-informed design of functional nanomaterials: Bridging catalysis, drug discovery, and sustainable environmental remediation. Scholars Journal of Physics Mathematics and Statistics, 12(9), 389–418. doi:10.36347/sjpms.2025.v12i09.002
- Khan, W. Z. (2017, April). Efficacy and safety of intense pulsed light in acne treatment: A meta analysis.
- Khan, W. Z. (2024, December). Across the spectrum: Imaging and spectroscopy [Raw data]. ResearchGate.

- Khan, W. Z. (2024, December). Advancing perovskite solar cells: Addressing stability, scalability, and environmental challenges.
- Khan, W. Z. (2024, December). Exploring the frontiers of material science for energy sustainability, breakthroughs in batteries, smart electronics, renewable energy systems, and next-generation electric mobility solutions.
- Khan, W. Z. (2025, August). Brain-targeted delivery and redox-responsive release of protein drugs via polymeric nanoparticles (PLGA-PEG): A targeted and controlled approach. Annual Methodological Archive Research Review, 1(05), 152–164. doi:10.5281/zenodo.16312259
- Khan, W. Z. (2025, August). Unified intelligence: Integrating AI, chemistry, physics, and engineering for breakthroughs in nanomaterials, biotechnology, and energy. doi:10.5281/zenodo.16438394
- Khan, W. Z. (2025, February). Laser technology: New innovations in laser design and optical systems for advanced applications in materials and energy research. doi:10.5281/zenodo.14770605
- Khan, W. Z. (2025, February). Nanotechnology for perovskite solar cells: Advances and challenges in high efficiency, stability, and cost-effective fabrication. doi:10.5281/zenodo.14913631
- Khan, W. Z. (2025, February). Synthesis and characterization of La-doped BNBT lead-free ceramics with enhanced piezoelectric and dielectric properties. doi:10.5281/zenodo.15046638
- Khan, W. Z. (2025, January). Advanced engineering of ZnO nanoparticles for biomedical and environmental applications: New approaches to synthesis, characterization, and functionalization.
- Khan, W. Z. (2025, January). Advancing diagnostic medical physics: Innovations in imaging, radiation therapy, and AI-driven healthcare solutions.
- Khan, W. Z. (2025, January). Advancing double perovskites: Key materials for next generation energy harvesting, storage, and optoelectronic applications. doi:10.5281/zenodo.14770877
- Khan, W. Z. (2025, January). Atomic nuclei to nanostructures: The role of nuclear physics in shaping modern materials science and nanotechnology. doi:10.5281/zenodo.14789142
- Khan, W. Z. (2025, July). Next-generation materials discovery using DFT and multiscale modeling: A pathway for quantum simulation, semiconductor innovation, and energy storage advancements. doi:10.5281/zenodo.16312340
- Khan, W. Z. (2025, July). Theoretical design and optoelectronic analysis of lead-free $CsPbX_3/Cs_2SnX_6$ core-shell perovskite nanocrystals for enhanced stability and charge dynamics.
- Khan, W. Z. (2025, May). Targeted delivery and responsive release of protein drugs to the brain using GSH-responsive $SiO_2$ nanoparticles (Thesis for MS Physics). ResearchGate.
- Khan, W. Z. (2025, May). Theoretical design, electronic, optical and thermoelectric properties of functional double perovskite oxides $Na_2NiMnO_6$ and $Na_2MgMnO_6$ for energy and photocatalytic applications.
- Khan, W. Z. (2025, November). Cross-disciplinary research gaps in physical, chemical, and environmental sciences: A roadmap for integration, innovation, and sustainability.
- Khan, W. Z. (2025, September). An interdisciplinary review of modern computer science's role in advancing engineering innovations and sustainable solutions. International Journal of Innovative Science and Research Technology, 10(08), 1612–1625. doi:10.5281/zenodo.16438438
- Khan, W. Z. (2025, September). Multifunctional nanomaterials as catalysts and environmental remediation tools. doi:10.5281/zenodo.16438360
- Khan, W. Z., & others. (2025, August). Perovskite solar cell efficiency via tunable Ag nanoparticle-integrated $SnO_2$: A DFT-assisted stability and conductivity optimization. Scholars Journal of Physics Mathematics and Statistics, 12(7), 274–289. doi:10.36347/sjpms.2025.v12i07.002
- Khan, W. Z., & others. (2025, October). Role of spin-orbit coupling and many-body effects in optical and band structure properties of lead-free perovskite $Rb_2TlBiX_6$ (X = Cl, Br, I). Scientific Reports, 15(1). doi:10.1038/s41598-025-07568-x
- Khan, W. Z., & others. (2025, September). First demonstration of lead-free double perovskite $Cs_2NaBiI_6$ as a dual-function electrode for high-performance long-life photo-rechargeable lithium-ion batteries with superior solar-to-power conversion. Macromolecular Rapid Communications. doi:10.1002/marc.202400594
- Khan, W. Z., Haseeb, M., Khan, S. N., Falk, M., & others. (2025, April). Quantum materials: Key to advancing quantum computing by enhancing stability, scalability, and error resistance through superconductors, topological insulators, and 2D materials for scalable systems. doi:10.5281/zenodo.15180740
- Király, T., & Tóth, Z. (2025). Being aware of data leakage and cross-validation scaling in chemometric model validation. Journal of Chemometrics, 39, e70082. https://doi.org/10.1002/cem.70082
- Korber, A., Anthony, I. G. M., & Heeren, R. M. A. (2025). Mass spectrometry imaging. Analytical Chemistry, 97(29), 15517–15549. https://doi.org/10.1021/acs.analchem.4c05249
- Lazanas, A. C., & Prodromidis, M. I. (2023). Electrochemical impedance spectroscopy—A tutorial. ACS Measurement Science Au, 3(3), 162–193. doi:10.1021/acsmeasuresciau.2c00070
- Lazanas, A. C., & Prodromidis, M. I. (2023). Electrochemical impedance spectroscopy: A tutorial. ACS Measurement Science Au, 3(3), 162–

193. https://doi.org/10.1021/acsmeasuresciau.2c00070

- Lazanas, A. C., & Prodromidis, M. I. (2023). Electrochemical impedance spectroscopy—A tutorial. ACS Measurement Science Au, 3(3), 162–193. https://doi.org/10.1021/acsmeasuresciau.2c00070
- Lee, D. D., & Seung, H. S. (1999). Learning the parts of objects by non-negative matrix factorization. Nature, 401, 788–791. https://doi.org/10.1038/44565
- Liu, T., Song, Y., Liu, H., Li, X., Ju, J., & Zou, S. (2024). MAP-based blind infrared spectral deconvolution via modified total variation regularization for mixture identification. Infrared Physics & Technology, 141, 105506. https://doi.org/10.1016/j.infrared.2024.105506
- Löfstedt, T., & Trygg, J. (2011). OnPLS—A novel multiblock method for the modelling of predictive and orthogonal variation. Journal of Chemometrics, 25(8), 441–455. https://doi.org/10.1002/cem.1388
- Long, G. L., & Winefordner, J. D. (1983). Limit of detection: A closer look at the IUPAC definition. Analytical Chemistry, 55(7), 712A–724A. https://doi.org/10.1021/ac00258a724
- Long, G. L., & Winefordner, J. D. (1983). Limit of detection: A closer look at the IUPAC definition. Analytical Chemistry, 55(7), 712A–724A. https://doi.org/10.1021/ac00258a724
- Long, G. L., & Winefordner, J. D. (1983). Limit of detection: A closer look at the IUPAC definition. Analytical Chemistry, 55(7), 712A–724A. doi:10.1021/ac00258a001
- Lopez, E., Etxebarria-Elezgarai, J., Amigo, J. M., & Seifert, A. (2023). The importance of choosing a proper validation strategy in predictive models: A tutorial with real examples. Analytica Chimica Acta, 1275, 341532. https://doi.org/10.1016/j.aca.2023.341532
- Lopez, E., Gorla, G., Etxebarria-Elezgarai, J., Amigo, J. M., & Seifert, A. (2025). The importance of choosing a proper validation strategy in predictive models. Part 2: Recipes for (avoiding) overfitting—A tutorial. Analytica Chimica Acta. Advance online publication. doi:10.1016/j.aca.2025.344838
- MacLeod, B. P., *et al.,* (2022). A self-driving laboratory advances the Pareto front for materials discovery. Nature Communications, 13, 995. https://doi.org/10.1038/s41467-022-28580-6
- Magnusson, B., & Örnemark, U. (Eds.). (2014). Eurachem guide: The fitness for purpose of analytical methods—A laboratory guide to method validation and related topics (2nd ed.). Eurachem.
- Magnusson, B., Näykki, T., Hovind, H., Krysell, M., & Sahlin, E. (2017). Handbook for calculation of measurement uncertainty in environmental laboratories (Nordtest Report TR 537, 4th ed.). Nordtest.
- Manz, A., Graber, N., & Widmer, H. M. (1990). Miniaturized total chemical analysis systems: A novel concept for chemical sensing. Sensors and Actuators B: Chemical. https://doi.org/10.1016/0925-4005(90)80209-I
- Martens, L., Chambers, M., Sturm, M., Kessner, D., Levander, F., Shofstahl, J., *et al.,* (2011). mzML: A community standard for mass spectrometry data. Molecular & Cellular Proteomics, 10(1), R110.000133. https://doi.org/10.1074/mcp.R110.000133
- Mazivila, S. J., & Santos, J. L. M. (2022). A review on multivariate curve resolution applied to spectroscopic and chromatographic data acquired during the real-time monitoring of evolving multi-component processes: From process analytical chemistry to analytics of biological systems. TrAC Trends in Analytical Chemistry, 157, 116698. https://doi.org/10.1016/j.trac.2022.116698
- Mishra, P., *et al.,* (2021). Recent trends in multi-block data analysis in chemometrics for multi-omics and multi-source data integration. Analytica Chimica Acta, 338001. https://doi.org/10.1016/j.aca.2021.338001
- Mishra, P., Roger, J.-M., Jouan-Rimbaud-Bouveresse, D., Biancolillo, A., Marini, F., Nordon, A., & Rutledge, D. N. (2021). Recent trends in multi-block data analysis in chemometrics for multi-source data integration. TrAC Trends in Analytical Chemistry, 137, 116206. doi:10.1016/j.trac.2021.116206
- Mitchell, M., Wu, S., Zaldivar, A., Barnes, P., Vasserman, L., Hutchinson, B., Spitzer, E., Raji, I. D., & Gebru, T. (2019). Model cards for model reporting. In Proceedings of the Conference on Fairness, Accountability, and Transparency (FAT '19)* (pp. 220–229). Association for Computing Machinery. https://doi.org/10.1145/3287560.3287596
- Murray, K. K., Boyd, R. K., Eberlin, M. N., Langley, G. J., Li, L., & Naito, Y. (2013). Definitions of terms relating to mass spectrometry (IUPAC Recommendations 2013). Pure and Applied Chemistry, 85(7), 1515–1609. https://doi.org/10.1351/PAC-REC-06-04-06
- Næs, T., *et al.,* (2021). Sequential and orthogonalized PLS regression for path modeling. Journal of Chemometrics, 35, e3243. https://doi.org/10.1002/cem.3243
- Nazar, M., Tabassam, M., Irfan, A., Liaqat, M., & others. (2025, April). DFT study of optoelectronic and thermoelectric properties of halide double perovskite $Rb_2TlSbX_6$ (X = Cl, Br, I) for solar cell applications. Scholars Journal of Engineering and Technology, 13(04), 208–222. doi:10.36347/sjet.2025.v13i04.002
- Neumann, E. K., Djambazova, K. V., Caprioli, R. M., & Spraggins, J. M. (2020). Multimodal imaging mass spectrometry: Next generation molecular

mapping in biology and medicine. Journal of the American Society for Mass Spectrometry, 31(12), 2401–2415. https://doi.org/10.1021/jasms.0c00232

- Neumann, S., *et al.,* (2025). MassBank: An open and FAIR mass spectral data resource. Nucleic Acids Research. https://doi.org/10.1093/nar/gkaf1193
- NIST. (2023). Artificial Intelligence Risk Management Framework (AI RMF 1.0) (NIST AI 100-1). https://doi.org/10.6028/NIST.AI.100-1
- Palmer, A., Phapale, P., Chernyavsky, I., Lavigne, R., Fay, D., Tarasov, A., *et al.,* (2017). FDR-controlled metabolite annotation for high-resolution imaging mass spectrometry. Nature Methods, 14(1), 57–60. https://doi.org/10.1038/nmeth.4072
- Patel, K. N., Patel, J. K., Patel, M. P., Rajput, G. C., & Patel, H. A. (2010). Introduction to hyphenated techniques and their applications in pharmacy. Pharmaceutical Methods, 1(1), 2–13. doi:10.4103/2229-4708.72222
- Pingarrón, J. M., Labuda, J., Barek, J., Brett, C. M. A., Camões, M. F., Fojta, M., & Hibbert, D. B. (2020). Terminology of electrochemical methods of analysis (IUPAC Recommendations 2019). Pure and Applied Chemistry, 92(4), 641–694. https://doi.org/10.1515/pac-2018-0109
- Quiñonero-Candela, J., Sugiyama, M., Schwaighofer, A., & Lawrence, N. D. (Eds.). (2009). Dataset shift in machine learning. MIT Press.
- Rafiq, M. N., Liaqat, M., Sadiqa, M., Shams, H., & others. (2025, April). Enhanced dielectric and piezoelectric properties of $BaTiO_3$-infused $K_{0.3}Na_{0.2}Bi_{0.5}TiO_3$ ceramics for high-frequency applications. doi:10.5281/zenodo.14956707
- Rasmussen, C. E., & Williams, C. K. I. (2006). Gaussian processes for machine learning. MIT Press.
- Reinke, S. N., Galindo-Prieto, B., Skotare, T., Broadhurst, D. I., Singhania, A., Horowitz, D., Djukanović, R., Hinks, T. S. C., Geladi, P., Trygg, J., & Wheelock, C. E. (2018). OnPLS-based multi-block data integration: A multivariate approach to interrogating biological interactions in asthma. Analytical Chemistry, 90(22), 13400–13408. https://doi.org/10.1021/acs.analchem.8b03205
- Rocca-Serra, P., Brandizi, M., Maguire, E., Sklyar, N., Taylor, C., Begley, K., *et al.,* (2010). ISA software suite: Supporting standards-compliant experimental annotation and enabling curation at the community level. Bioinformatics, 26(18), 2354–2356. https://doi.org/10.1093/bioinformatics/btq415
- Sansone, S. A., *et al.,* (2012). Toward interoperable bioscience data. Nature Genetics, 44(2), 121–126. https://doi.org/10.1038/ng.1054
- Schober, D., *et al.,* (2018). nmrML: A community supported open data standard for the description, storage, and exchange of NMR data. Analytical Chemistry. https://doi.org/10.1021/acs.analchem.7b02795
- Schymanski, E. L., *et al.,* (2017). Critical Assessment of Small Molecule Identification 2016: Automated methods. Journal of Cheminformatics, 9, 22. https://doi.org/10.1186/s13321-017-0207-1
- Smilde, A. K. (2019). A framework for low-level data fusion. In Data Fusion Methodology and Applications. Elsevier. https://doi.org/10.1016/B978-0-444-63984-4.00002-8
- Smilde, A. K., *et al.,* (2017). Common and distinct components in data fusion. Journal of Chemometrics, 31(7), e2900. https://doi.org/10.1002/cem.2900
- Smolinska, A., Engel, J., Szymanska, E., Buydens, L. M. C., & Blanchet, L. (2019). General framing of low-, mid-, and high-level data fusion with examples in the life sciences. In Data fusion methodology and applications (pp. 51–79). Elsevier. doi:10.1016/B978-0-444-63984-4.00003-X
- Smolinska, A., Engel, J., Szymanska, E., Buydens, L., & Blanchet, L. (2019). General framing of low-, mid-, and high-level data fusion with examples in the life sciences. In M. Cocchi (Ed.), Data fusion methodology and applications (Vol. 31, pp. 51–79). Elsevier. doi:10.1016/B978-0-444-63984-4.00003-X
- Smolinska, A., *et al.,* (2012). Interpretation and visualization of non-linear data fusion in kernel space: Study on metabolomic characterization of progression of multiple sclerosis. PLoS ONE, 7(6), e38163. https://doi.org/10.1371/journal.pone.0038163
- Smolinska, A., *et al.,* (2019). General framing of low-, mid-, and high-level data fusion with examples in life sciences. In Data Fusion Methodology and Applications. Elsevier. https://doi.org/10.1016/B978-0-444-63984-4.00004-1
- Stahlschmidt, S. R., Ulfenborg, B., & Synnergren, J. (2022). Multimodal deep learning for biomedical data fusion: A review. Briefings in Bioinformatics, 23(2), bbab569. https://doi.org/10.1093/bib/bbab569
- Thompson, M., & Wood, R. (1995). Harmonized guidelines for internal quality control in analytical chemistry laboratories (IUPAC Technical Report). Pure and Applied Chemistry, 67(4), 649–666. https://doi.org/10.1351/pac199567040649
- Thompson, M., & Wood, R. (1995). Harmonized guidelines for internal quality control in analytical chemistry laboratories (IUPAC Technical Report). Pure and Applied Chemistry, 67(4), 649–666. doi:10.1351/pac199567040649
- Thompson, M., Ellison, S. L. R., & Wood, R. (2002). Harmonized guidelines for single-laboratory validation of methods of analysis (IUPAC Technical

Report). Pure and Applied Chemistry, 74(5), 835–855. https://doi.org/10.1351/pac200274050835

- Thompson, M., Ellison, S. L. R., & Wood, R. (2002). Harmonized guidelines for single-laboratory validation of methods of analysis (IUPAC Technical Report). Pure and Applied Chemistry, 74(5), 835–855. doi:10.1351/pac200274050835
- Thompson, M., Ellison, S. L. R., & Wood, R. (2006). The international harmonized protocol for the proficiency testing of analytical chemistry laboratories (IUPAC Technical Report). Pure and Applied Chemistry, 78(1), 145–196. https://doi.org/10.1351/pac200678010145
- Tom, G., *et al.,* (2024). Self-driving laboratories for chemistry and materials science. Chemical Reviews. https://doi.org/10.1021/acs.chemrev.4c00055
- Toth, G., Kryska, A., Sroka-Bartnicka, A., & Lanekoff, I. (2025). Multimodal mass spectrometry–Raman imaging reveals solvent-dependent structural and chemical tissue alterations. Analytica Chimica Acta, 1371, 344425. https://doi.org/10.1016/j.aca.2025.344425
- Tuck, M., Blanc, L., Touti, R., Patterson, N. H., Van Nuffel, S., Villette, S., Taveau, J.-C., Römpp, A., Brunelle, A., Lecomte, S., & Desbenoit, N. (2021). Multimodal imaging based on vibrational spectroscopies and mass spectrometry imaging applied to biological tissue: A multiscale and multiomics review. Analytical Chemistry, 93(1), 445–477. doi:10.1021/acs.analchem.0c04595
- Vajda, S., Rabitz, H., Walter, E., & Lecourtier, Y. (1989). Qualitative and quantitative identifiability analysis of nonlinear chemical kinetic models. Chemical Engineering Communications, 83(1), 191–219. https://doi.org/10.1080/00986448908940662
- van Deemter, J. J., Zuiderweg, F. J., & Klinkenberg, A. (1956). Longitudinal diffusion and resistance to mass transfer as causes of nonideality in chromatography. Chemical Engineering Science, 5(6), 271–289. https://doi.org/10.1016/0009-2509(56)80003-1
- Wang, M., Carver, J. J., Phelan, V. V., Sanchez, L. M., Garg, N., Peng, Y., *et al.,* (2016). Sharing and community curation of mass spectrometry data with Global Natural Products Social Molecular Networking. Nature Biotechnology, 34(8), 828–837. https://doi.org/10.1038/nbt.3597
- Wang, M., Carver, J. J., Phelan, V. V., Sanchez, L. M., Garg, N., Peng, Y., *et al.,* (2016). Sharing and community curation of mass spectrometry data with Global Natural Products Social Molecular Networking. Nature Biotechnology, 34(8), 828–837. https://doi.org/10.1038/nbt.3597
- Wang, T., Yi, Y., Yao, J., Xu, Z.-Q. J., Zhang, T., & Chen, Z. (2025). Enforcing physical conservation in neural network surrogate models for complex chemical kinetics. Combustion and Flame, 275, 114105. https://doi.org/10.1016/j.combustflame.2025.114105
- Westad, F., & Marini, F. (2015). Validation of chemometric models: A tutorial. Analytica Chimica Acta, 893, 14–24. https://doi.org/10.1016/j.aca.2015.06.056
- Westad, F., & Marini, F. (2015). Validation of chemometric models—a tutorial. Analytica Chimica Acta, 893, 14–24. https://doi.org/10.1016/j.aca.2015.06.056
- Westad, F., & Marini, F. (2015). Validation of chemometric models—A tutorial. Analytica Chimica Acta, 893, 14–24. doi:10.1016/j.aca.2015.06.056
- Wilkinson, M. D., Dumontier, M., Aalbersberg, I. J. J., Appleton, G., Axton, M., Baak, A., Blomberg, N., Boiten, J.-W., da Silva Santos, L. B., Bourne, P. E., Bouwman, J., Brookes, A. J., Clark, T., Crosas, M., Dillo, I., Dumon, O., Edmunds, S., Evelo, C. T., Finkers, R., … Mons, B. (2016). The FAIR Guiding Principles for scientific data management and stewardship. Scientific Data, 3, 160018. doi:10.1038/sdata.2016.18
- Wilkinson, M. D., Dumontier, M., Aalbersberg, I. J., Appleton, G., Axton, M., Baak, A., *et al.,* (2016). The FAIR Guiding Principles for scientific data management and stewardship. Scientific Data, 3, 160018. https://doi.org/10.1038/sdata.2016.18 Nature+1
- Wilkinson, M. D., Dumontier, M., Aalbersberg, I. J., *et al.,* (2016). The FAIR guiding principles for scientific data management and stewardship. Scientific Data, 3, 160018. doi:10.1038/sdata.2016.18
- Williams, A., & Magnusson, B. (Eds.). (2021). Eurachem/CITAC guide: Use of uncertainty information in compliance assessment (2nd ed.). Eurachem/CITAC.
- Williams, M. L., Olomukoro, A. A., Emmons, R. V., Godage, N. H., & Gionfriddo, E. (2023). Matrix effects demystified: Strategies for resolving challenges in analytical separations of complex samples. Journal of Separation Science, 46(23), e2300571. https://doi.org/10.1002/jssc.202300571
- Xu, Y., *et al.,* (2022). Bayesian fusion model enhanced codfish classification using near infrared and Raman spectrum. Foods, 11(24), 4100. https://doi.org/10.3390/foods11244100
- Yan, H., *et al.,* (2023). Handheld near-infrared spectroscopy: State-of-the-art instrumentation and applications in material identification, food authentication, and environmental investigations. Biosensors, 11(5), 272.
- Zhang, X., *et al.,* (2024). A critical review on recent advances in retention time prediction: From conventional methods to deep learning. Communications Chemistry, 7, 24. https://doi.org/10.1038/s42004-024-01027-w