Towards Optimal Mixing: Enabling Autonomous Experimentation via Quantitative Emulsion Assessment

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1. Introduction

In recent years, interest in automation and autonomous experiments has grown, aiming to enhance the efficiency of materials research and development and advance the exploration of optimal conditions [1, 2, 3, 4]. Particularly in new material development and formulation, mixing operations such as blending and kneading significantly impact properties through microstructure formation, making the realization of *optimal mixing* indispensable [5, 6, 7].

To enable autonomous optimization (a closed-loop process of condition proposal → execution → evaluation → subsequent condition proposal), the experimental system must satisfy two fundamental requirements: (i) reproducible control of the mixing operation and (ii) rapid, non-destructive quantitative evaluation of the mixing state. Reliable quantitative evaluation provides an objective metric that can serve as the objective function for machine-learning models to predict and propose improved operating conditions. While the former can be readily implemented using existing technologies [8, 9, 10, 11], the latter is highly system-dependent, and no versatile online evaluation metric has yet been established. Consequently, mixing processes still rely heavily on the tacit knowledge and experiential judgment of skilled operators.

This challenge is particularly pronounced in emulsion systems, which represent one of the most important and sensitive classes of mixing processes. In these systems, initially separate liquids are blended and progressively transformed into viscous, structured fluids. Such processes are widely encountered in applications such as food products, pharmaceuticals, cosmetics, and chemical formulations (*e.g.*, mayonnaise, hand creams, paints) [12, 7].

In emulsification, mixing conditions directly determine droplet size, size distribution, and number density, which in turn govern stability and functional performance. As a result, even subtle differences in mixing history can lead to large variations in the final emulsion state. Despite this strong dependence on mixing, evaluation of emulsification is often performed subjectively, based on visual appearance or empirical experience, or through offline measurements that are unsuitable for real-time feedback [13, 14, 15, 7].

In this study, we address this challenge by introducing a *novel mixing evaluation metric designed for emulsion systems that can be measured in real time during the mixing process*. The proposed metric quantitatively captures the temporal evolution of the mixing state, rather than relying solely on post-process characterization of the final emulsion. Consequently, it serves as an effective interface between experimental operations and machine-learning models, enabling systematic learning of the relationships between mixing conditions and material states. This capability provides a foundation for incorporating optimal mixing operations into closed-loop optimization frameworks for autonomous experimentation.

2. Related work

Quantitative metrics in self-driving laboratories In self-driving laboratories (SDLs), machine learning models autonomously selects subsequent experiments based on accumulated experimental data, making the definition of quantitative objectives essential for closed-loop learning and decision-making. Prior studies have formulated experimental goals as scalar metrics to be optimized, enabling autonomous control across a wide range of domains. Early SDL implementations demonstrated this paradigm in materials synthesis and optimization, targeting quantitative performance metrics such as carbon nanotube growth rates and charge-carrier mobility through Bayesian-optimization-driven autonomous experimentation [16, 2]. Similar metric-driven frameworks have been applied to chemical reaction and catalyst discovery, optimizing measurable outcomes including reaction yield, selectivity, and photocatalytic hydrogen evolution rates [1, 17, 18], as well as to solid-state synthesis via metrics such as phase purity and synthesis success probability [19]. Building on this established paradigm, our work introduces a systematic quantification of mixing, enabling mixing-related metrics to be optimized within autonomous experimental frameworks.

Quantitative metrics for emulsification states In previous studies on emulsions, closed-loop optimization using machine learning was attempted to automate condition exploration [20]. However, these evaluation criteria are artificially imposed, and the framework for judgment still relies on skilled personnel. The applicability is limited to specific systems (*e.g.*, reaction systems, compositions), meaning online quantitative evaluation metrics independent of composition—such as those for different oil-water systems or surfactant systems—are not yet sufficiently established. In this study, we propose a metric that can be generally applied to emulsions, enabling system-independent quantitative evaluation.

3. Methods

To quantitatively evaluate emulsification states, we focused on light scattering. Emulsification states are governed by droplet size and number density; consequently, both the intensity of light scattering and its wavelength dependence vary with the state [7]. Using a dip probe capable of real-time measurements, we acquired visible to near-infrared absorption spectra (*i.e.*, the wavelength dependence of absorbance), which reflect light scattering. We then propose a processing method to convert these spectra into a scalar metric, enabling quantitative evaluation of emulsification states.

A continuous spectrum contains a large amount of information, making it extremely difficult to determine a single score for uniformly evaluating emulsification states. To address this challenge, we propose a simple yet fundamentally effective analytical method: measuring spectral slope. In this method, we consider that white turbidity occurring as emulsification progresses is reflected in changes in the spectral shape. Insufficient emulsification results in a spectrum with strong wavelength dependence, but as emulsification progresses, light scattering increases and the spectrum becomes flatter. The physical basis of this approach is that, in insufficiently emulsified systems, single scattering dominates, resulting in pronounced wavelength-dependent features in the spectrum. As emulsification progresses and the droplet number density increases, multiple scattering becomes dominant, averaging out the wavelength dependence and causing the spectrum to become flatter. Given a spectrum $A(\lambda) = k\lambda^{-n}$, where $A(\lambda)$ represents the absorbance at wavelength λ, the wavelength dependence n is defined by

$$\log A(\lambda) = \log k - n \log \lambda. \tag{1}$$

By introducing logarithms, the scattering intensity scale and the spectral shape derived from wavelength dependence can be evaluated separately.

4. Experiments

To examine whether the proposed method can quantitatively and objectively evaluate the degree of mixing, we performed experiments using a simple model system consisting of water, oil, and a surfactant. Samples were mixed for predefined durations using an automated stirring device, and the experiments were repeated multiple times for each mixing time. For a given mixing time, a reliable evaluation method should yield similar values across repeated trials, with only small variability, whereas different mixing times should lead to clear differences in the evaluation values.

Fig. 1 shows the results of the quantitative evaluation obtained using the proposed method for different mixing durations (10, 15, 20, 25, and 30 min), where the experiment was repeated three times for each mixing time. The error bars represent the standard deviation of the evaluation values. As the mixing time increases, the evaluation metric exhibits a clear and systematic change, while the variability at each mixing time remains sufficiently small in comparison to this change. These results are consistent with the observed changes in appearance, rheological measurements, and microscopic observations, confirming the validity of this method. The experimental details are provided in Appendix A. These results confirm that the proposed method can reliably distinguish differences in the degree of mixing in a quantitative and objective manner.

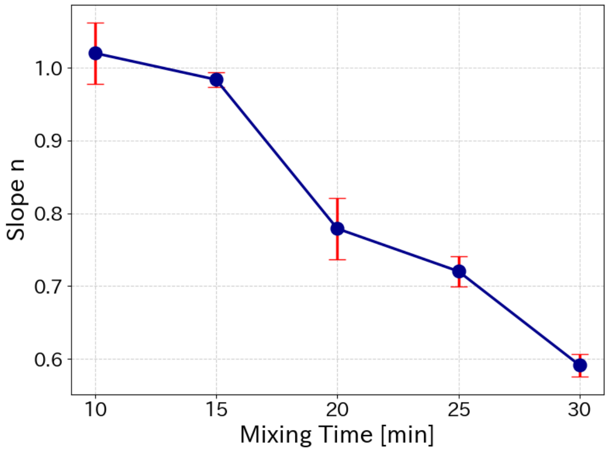

Fig. 1: Effect of Mixing Time on Spectral Slope at 550–650 nm

5. Discussions

This method enables non-destructive, in situ quantitative evaluation of the emulsification process. In future work, we will further validate this metric to establish it as a reliable indicator for various mixing states, such as slurries and pastes. By integrating this with robotic control for closed-loop optimization, we aim to realize an autonomous system that achieves optimal mixing in real time. Ultimately, this framework will serve as a versatile research platform that integrates evaluation, optimization, and autonomous operation across a wide range of material processes.

6. Conclusion

We focused on the fact that reliance on experts' tacit knowledge makes it difficult to objectively and quantitatively evaluate mixing states, which makes autonomous experimentation difficult. Therefore, we acquired transmission and reflection spectra in real time throughout emulsification and quantified the mixing state based on changes in light scattering. The proposed score enables comparison of mixed states on a consistent scale, making closed-loop optimization possible. This framework is expected to be extended to diverse material systems such as slurries and pastes, and applied to autonomous systems that independently explore the "optimal mixing method" for formulation and new material development.

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Appendix A. Experimental details

In this experiment, canola oil was used as the oil phase and Polysorbate 80 was used as the surfactant. To prepare reproducible samples with consistent conditions other than mixing time, THINKY MIXER (Model AR-100, Thinky) was used.

Measurement using a dip probe A fiber-type transmission probe (Model TP22, Thorlabs) connected to a UV-Vis/NIR spectrophotometer (Model V-770, JASCO) was used for spectral measurements. The probe tip is designed with an internal mirror that reflects light back through the sample. This allows for simultaneous detection of transmitted and backscattered light, capturing complete optical profile of the mixing state. Measurements were performed three times for each stirring time (10, 15, 20, 25, 30 minutes). The wavelength range was set to 400–800 nm, with a sampling interval of 5 nm, acquiring a total of 81 data points per spectrum.

Appearance observation Emulsions are thermodynamically unstable dispersed systems, and changes in their dispersion structure occur spontaneously when left to stand. Therefore, differences in emulsion stability can be evaluated by differences in appearance. We left the prepared samples to stand for one day and observed the degree of creaming and phase separation.

Rheological measurements As emulsion stability increases, droplet size and number density increase, which strengthens interactions between droplets and restricts the flow of the continuous phase. As a result, changes in rheological properties such as an increase in viscosity and the appearance of elastic components are observed. We performed viscosity measurements as the shear rate increased from 1 to 500 s^{-1}. Measurements were performed twice for each sample using a modular compact rheometer (Model MCR102e, Anton Paar).

Microscopic observations Microscopic observation allows us to directly capture microscopic changes in the dispersion structure, such as droplet size, particle size distribution, aggregation, and coalescence, which affect emulsion stability. We observed the prepared samples using a motorized upright microscope (Model Axio Imager Z2, ZEISS).

Appendix B. Raw spectrum

Fig. A.1 shows raw absorbance spectrum data. As mixing time increases, the spectral shape becomes flatter, and the wavelength dependence decreases, as can be visually observed.

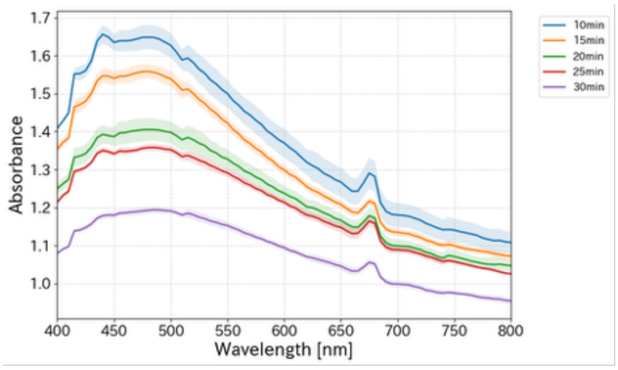

Fig. A.1: Raw absorbance spectrum in this experiment (mean ± SD, n = 3)