Opinion

Revolutionizing pharmaceutical manufacturing: fast, non-invasive particle size distribution using imaging and machine learning

Abstract

The pharmaceutical manufacturing industry has long faced the challenge of monitoring drying mixtures—a crucial step in the production of medications and chemical compounds. Traditional methods for evaluating particle size distribution (PSD) are often time-consuming. Recent advances have introduced a novel, non-invasive approach using scattered light and machine learning to estimate PSD from a single speckle image. This technique promises increased efficiency, accuracy, and product quality in manufacturing, while reducing waste and the incidence of batch failures.

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Introduction

In pharmaceutical manufacturing, the drying process is a critical phase where particle characteristics significantly influence the final product's quality and efficacy. Accurate monitoring of PSD during drying is essential to ensure uniformity, optimize process parameters, and prevent defects that could lead to batch failures.[1]

Traditionally, PSD analysis involves imaging samples to count individual particles or using scattered light to estimate PSD. Imaging methods are often labor-intensive, time-consuming, and can increase material waste due to the invasive nature of sample collection. While scattered light techniques are non-invasive, they have historically required multiple images and extensive computational resources, limiting real-time applicability.[2]

The need for a fast, accurate, and non-invasive PSD monitoring tool has driven research into optical methods that can be integrated into existing manufacturing processes without major disruptions or costs.[3]

Background

Speckle patterns arise when coherent light, such as laser light, scatters off an irregular surface or a collection of particles. The resulting interference pattern contains information about the surface or particle characteristics. Analyzing these speckle patterns can reveal details about particle sizes and distributions without direct contact.[4,5]

Previous methods that used speckle analysis to estimate PSD generally required capturing multiple images and performing complex calculations to smooth out noise and obtain accurate measurements. Processing times for these methods could extend beyond 15 seconds, making them impractical for fast processes like drying in pharmaceutical manufacturing.[6]

Innovative approach by MIT researchers

A team of scientists led by Professor George Barbastathis from MIT's Department of Mechanical Engineering developed a new PSD estimation method addressing these limitations. The approach is detailed in the paper titled *"Non-invasive estimation of particle size distribution from a single speckle image, published in Light: Science & Applications.[7,8]

Method principle

The new method employs pupil engineering and machine learning to extract PSD information from a single speckle image, reducing analysis time to about 0.25 seconds. Pupil engineering involves modifying the optical system's aperture to enhance specific features in the speckle pattern that provide more informative particle size data.[9]

By introducing an intensity mask in the optical setup, the researchers manipulate the scattered light distribution to amplify the side lobes of the speckle correlation function, where crucial size information resides. This enhancement allows more robust and sensitive measurements from a single image, eliminating the need for multiple images and extensive averaging.[9]

Machine learning integration

The method incorporates a machine-learning model—specifically, neural networks trained on speckle patterns associated with known PSDs. The model learns to map speckle image features to corresponding particle size distributions accurately. Once trained, the neural network can quickly process new speckle images to estimate PSD in real-time.[10]

Advantages over previous methods

Speed: Analysis time is reduced by a factor of 60, from 15 seconds to 0.25 seconds.

Non-invasive: The method does not require physical contact with the powder mixture, preserving sample integrity.

Efficiency: Single-image analysis reduces computational load and enables processing on standard CPUs without specialized hardware.

Compatibility: The compact, portable prototype can be integrated into most existing drying systems through an observation window.

Experimental Validation

The research team demonstrated the method's effectiveness through experiments that collected backscattered light from powder surfaces. They showed that their prototype could accurately estimate PSD in fast dynamic systems like those found in pharmaceutical drying processes.

By optimizing the algorithm and hardware collectively, the team achieved high-speed PSD detection, offering a platform to study and model processes such as drying and mixing in real-time.[7,8]

Implications for pharmaceutical manufacturing

Rapid, non-invasive PSD monitoring has significant implications for the pharmaceutical industry:

Product quality improvement: Real-time monitoring allows for immediate adjustments in the manufacturing process, ensuring consistent product quality.

Increased efficiency: Faster analysis reduces downtime and increases production yields.

Waste reduction: Non-invasive sampling minimizes material loss, resulting in cost savings and more sustainable practices.

Better process understanding: The method provides a new platform to study particle size evolution, aiding the development of improved process models and control strategies.

Broader applications

Although developed with pharmaceutical manufacturing in mind, the method has potential applications across various industries where particle size plays a critical role:

I. **Chemical engineering:** Monitoring of catalyst particles and reaction mixtures.

II. **Materials science:** Characterization of powders and granular materials in metallurgy and ceramics.

III. **Food industry:** Ensuring consistency in powdered food products like flour and spices.

IV. **Environmental monitoring:** Analysis of particles in air or water samples.

Collaboration and interdisciplinary effort

This work exemplifies the power of interdisciplinary collaboration. The research team includes physicists and engineers from multiple MIT departments, including Mechanical Engineering, Chemical Engineering, and Electrical Engineering & Computer Science. The project was part of the MIT-Takeda program, highlighting the importance of academia-industry partnerships in driving innovation.[7,8]

Future directions

The successful implementation of this rapid PSD estimation method paves the way for further research and development:

I. **Integration with control systems**: Development of closed-loop control systems that automatically adjust process parameters based on real-time PSD feedback.

II. **Expansion to Other particle systems:** Adapting the method to work with different types of particles and mixtures, including liquids and gels.

III. **Improved machine learning models**: Training models with broader datasets to enhance accuracy and robustness under varying conditions.

IV. **Commercialization**: Scaling the technology for widespread adoption in industrial settings, potentially leading to the development of standardized equipment and protocols.[11]

Conclusion

The advancement of non-invasive PSD estimation from a single speckle image represents a significant leap in optical measurement techniques for pharmaceutical manufacturing. By addressing the limitations of traditional methods, this innovative approach enhances efficiency, reduces waste, and improves product quality. The interdisciplinary effort underscores the value of combining physics, engineering, and machine learning to solve complex industrial challenges.

As industries continue seeking ways to optimize processes and ensure high-quality products, methods like the one developed by the MIT team are poised to make substantial contributions to manufacturing technologies and beyond.

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Conflict of interest

The author declares that there is no conflict of interest.

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