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Perspectives: Past, Present, and Future Developments in Particle Science and Technology †

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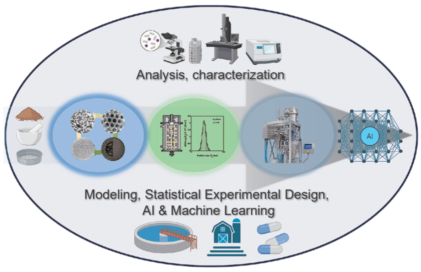
Members of the American Editorial Board of the *KONA Powder and Particle Journal* recently convened to consider current and future perspectives in the fields of particle science and technology. This brief overview presents their observations regarding current and emerging areas of interest in selected domains of particle and powder technologies. The major areas of practical significance identified were particle characterization, milling, granular material handling, scale-up considerations, and particle design strategies for environmental and pharmaceutical applications. An attempt has been made to highlight the role of artificial intelligence (AI)/machine learning (ML) in generating robust modeling and simulations for designing particle and powder systems for future process and product innovations.

Keywords: particle handling, modeling, environment, pharmaceutics, AI/ML, scale-up



1. Introduction

Particle or powder science and technology has a long history (Fayed and Otten, 1997; Higashitani et al., 2019) and has seen extensive technological advancements over the years, significantly impacting diverse industries such as pharmaceuticals, agriculture, food, environment, mining, ceramics, cement, semiconductors, and energy. With the advent of artificial intelligence (AI), particle science and technology are poised for explosive growth in the future.

This review presents observations from the American Editorial Board of the *KONA Powder and Particle Journal* on emerging areas of interest in select fields, with the prospect of influencing future research and development directions.

Specifically, we have structured the paper to cover the important issues of particle characterization, milling, granular material handling, scale-up, and manufacturing, concluding with environmental and pharmaceutical applications. These topics were identified by the group as both currently prominent and of emerging significance.

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2. Particle characterization

Understanding the fundamental nature of materials, especially as particles, has driven advancement in various fields since the beginning of scientific investigation. The characterization of particles is essential for fostering creativity and innovation in fields such as materials science, nanotechnology, and medicine. What began in the 1950s with mechanical separation methods has evolved into a complex environment in which quantum physics and AI reveal the complex atomic-level secrets of matter (Betz et al., 2023; Gao et al., 2024). This evolution not only marks significant technological advancements but also highlights a more refined and profound comprehension of the intricate nature of materials. In the past, particle observation and isolation were performed manually. With the advent of AI, however, a new age has begun in which enormous datasets can be examined with astounding speed and precision. These powerful computational tools allow us to predict particle behavior and interactions with a level of sophistication that was once thought impossible (Vora et al., 2023). This capacity to process and analyze information has revolutionized material characterization. In addition, quantum mechanics has introduced entirely new methodologies for probing the very fabric of materials, enabling us to visualize and manipulate particles with unprecedented precision. At the quantum level, particles behave in ways that defy classical understanding, and the tools emerging from this field allow for insights into material properties that were once beyond our reach (Faye, 2024). The ability to observe quantum states and their interactions opens new possibilities for altering the structures and properties of materials, enhancing their functionality in unimaginable ways. A new world of possibilities has been made possible by the capacity to alter materials at the nanoscale. From precise drug delivery systems targeting specific cells or tissues to developing cutting-edge materials with completely novel qualities like ultra-strength, distinct electrical conductivity, and self-healing capabilities, the potential applications are numerous and revolutionary (Chehelgerdi et al., 2023). These innovations not only improve current technology but also open doors to new sectors and offer solutions to some of the most important problems facing the globe today, such as energy storage, environmental clean-up, and medical diagnostics and treatment. This section explores how particle characterization has changed over time, from conventional separation techniques to cutting-edge quantum sensors, and discusses upcoming innovations that will drive further progress in this field.

2.1 A century of discovery: the road to precision

The past century's journey in particle characterization is a reflection of science's unrelenting quest for accuracy and comprehension. The foundation for contemporary particle analysis was established in the early 20th century with the introduction of crude but fundamental methods that would develop into the advanced approaches we use today. Basic techniques for classifying particles according to size and density were offered by these early techniques, which included sieving and sedimentation (e.g., Andreasen pipette). Although these methods worked well for larger particles, they lacked the precision and resolution required to meet the expanding needs of fine particle applications (Jillavenkatesa et al., 2001). Optical microscopy provided the first glimpse into the morphology, but its diffraction limit (~200 nm) left much of the sub-micron world hidden (Balasubramanian et al., 2023).

Finer resolution in particle-size analysis was made possible by the development of laser diffraction and dynamic light scattering (DLS) in the 1970s, which was a significant leap for industries requiring precise control over material properties. Laser diffraction enabled the measurement of particle-size distributions with greater accuracy, whereas DLS provided insights into the dynamic behavior of particles in suspension, including aggregation and dispersion (Caputo et al., 2019). The momentum of innovation continued into the 1980s with breakthroughs in transmission electron microscopy (TEM) and scanning electron microscopy (SEM), which expanded analytical capabilities to the nanoscale. SEM provided detailed images of surface structures, whereas TEM enabled researchers to investigate internal features at the atomic level (Golding et al., 2016).

By the 1990s, the field had advanced further with the introduction of atomic force microscopy (AFM) and X-ray diffraction (XRD) technologies. AFM provided researchers with comprehensive knowledge about surface structures, mechanical properties, and interaction force measurements by enabling them to visualize and even manipulate individual particle properties at the atomic scale (Goksu et al., 2009). XRD, on the other hand, became a potent technique for examining the crystallographic composition of materials, exposing their atomic configurations, and distinguishing between various phases (Ali et al., 2022). These methods enabled a more thorough understanding of particle behavior by bridging the gap between imaging and material analysis.

2.2 Quantum leap: future of particle characterization

Real-time AI-driven analysis, portable *in situ* monitoring, and quantum-based sensing are expected to transform the next frontier of particle characterization. These developments promise to provide previously unheard-of levels of accuracy, speed, and adaptability while overcoming the drawbacks of traditional techniques in various sectors, including minerals and materials processing, environmental science, and biomedical technologies.

2.2.1 Quantum-based sensing and imaging

Researchers are pushing beyond the boundaries of classical limitations by leveraging the principles of quantum mechanics. Innovations, such as quantum entanglement and squeezed-light technologies, have paved the way for imaging resolutions that approach the atomic scale. These advancements enable scientists to observe molecular bonds and atomic interactions with extraordinary precision (Lin et al., 2020). Quantum-enhanced imaging could revolutionize diagnostics by enabling real-time visualization of protein folding, viral structures, and bacterial membrane dynamics. Such imaging techniques could lead to breakthroughs in the understanding of diseases at the molecular level and the development of targeted therapies (Walling et al., 2009). In addition to imaging, quantum sensors represent another transformative application. These ultrasensitive instruments are expected to detect minute variations in mass, force, and electromagnetic field parameters that are critical to the design and testing of next-generation materials, such as high-temperature superconductors, metamaterials, and photonic crystals. However, the scalability limitations of transitioning quantum technologies from laboratory to industrial applications remain a significant challenge (Crawford et al., 2021). Nevertheless, the immense potential of quantum technologies continues to drive substantial research and investment, signaling a future where quantum-enhanced tools could dominate both industrial innovation and scientific discovery.

2.2.2 AI-driven real-time analysis

With the advent of deep learning and AI, the characterization of particles is moving toward instantaneous data interpretation. Predictive modeling and automation can enable researchers to track particle behavior in real-time, whether in drug delivery systems or environmental monitoring (Vora et al., 2023). Despite these promising capabilities, several challenges limit the widespread implementation of AI-driven analysis. A lack of robust datasets and poor-quality inputs can lead to inaccurate predictions using AI models. Furthermore, the "black box" nature of some AI algorithms makes it difficult to interpret results, which raises reliability concerns. Another significant hurdle is the computational power required for AI-driven analysis. Advanced AI models often require substantial data processing capabilities, which may not be accessible to all researchers or institutions.

2.2.3 *In situ* monitoring

On-site particle analysis is possible with small, lab-on-a-chip systems of the future. This enables real-time quality monitoring without the need for elaborate laboratory facilities. As advanced detection techniques like electrochemical sensors and Raman spectroscopy are integrated into lab-on-a-chip platforms, productivity can be improved by enabling real-time quality control throughout production processes (Luka et al., 2015). In the biomedical realm, these devices can monitor drug particle uptake in tissues in real time, providing crucial insights into the therapeutic efficacy and safety of drugs. Such *in situ* monitoring could lead to more personalized and adaptive treatment strategies. These portable sensors embedded with lab-on-a-chip technology can track aerosol particles, allergens, and pollutants in real time, making them invaluable tools for air quality surveillance and climate-related research (Tovar-Lopez, 2023).

However, the main drawbacks of miniaturized systems are sensitivity, precision, and durability. Variables such as temperature, humidity, and mechanical stress can significantly impact the performance of these devices, raising questions concerning calibration stability and long-term durability.

2.2.4 Advanced computational simulations

The combination of quantum simulations with high-performance computing (HPC) is revolutionizing the way researchers model atomic-level particle interactions. These advanced computational tools significantly reduce the reliance on costly and time-consuming experimental trials, enabling faster and more efficient material development (Bauer et al., 2023). In the energy sector, computational models will guide the development of next-generation energy storage systems. Advanced batteries and fuel cells, crucial for sustainable energy solutions, can be fine-tuned for improved charge capacity, stability, and longevity through predictive simulations (Gao and Lu, 2021). In nanomedicine, molecular dynamics simulations can be used to predict how nanoparticles interact with biological systems, thereby accelerating the development of nanotherapeutics (Zhang et al., 2021). Despite their transformative potential, high-performance computing and quantum simulations face significant challenges, including the need for high computational power and the validation of simulation results. Addressing these challenges will require continued advancements in algorithm efficiency and error correction for quantum computing and improved integration of experimental validation with computational models.

In summary, the evolution of particle characterization has been a remarkable journey from rudimentary mechanical separation techniques to cutting-edge quantum-based methodologies, which are anticipated in the coming years. However, this transformation does not come without challenges. The stability of quantum systems is threatened by environmental noise, scalability is still a major barrier to introducing lab-based advances to industrial settings, and the high computing costs of quantum simulations necessitate additional improvements in hardware and algorithm efficiency. As these techniques mature, they have the potential to revolutionize drug discovery and disease diagnostics and enable next-generation materials with extraordinary properties. The quantum leap in characterization is set to shape the future of particle science and technology in ways we are only beginning to imagine.

In addition to particle characterization, particle processing and handling are also critical. The following sections provide a brief overview of the technologies for mechanical milling and bulk material handling.

3. Emerging trends in milling and its computational modeling

Mechanical milling is the most important top-down process of particle formation. It is also extensively studied in the synthesis of different types of non-equilibrium alloys within mechanical alloying (Suryanarayana, 2022) and solvent-free synthesis of compounds as part of mechanochemistry (Baláž et al., 2014).

The scale of milling operations varies dramatically in different industries. In the minerals and cement industries, this process is performed in machines that continuously process up to hundreds or thousands of tons of solids per hour. In the ceramic, chemical, and food industries, the scale of operations is typically moderate, whereas the pharmaceutical industry uses milling technologies to process batches as small as a few kilograms or even less using significantly smaller machines. The characteristics of the materials also dramatically vary, explaining the numerous milling technologies available.

3.1 Past and present

From the pestle and mortar of the Stone Age (Lynch and Rowland, 2005) to the several mill types used today, grinding technologies have evolved tremendously over several millennia.

The tumbling media mill, developed in the later part of the 19th century (Lynch and Rowland, 2005) and responsible for the largest installed power in the industry among all size reduction machines, nearly became the standard in the minerals and cement industries. It has been widely used for size reduction in intermediate and fine size ranges, even when dealing with coarse (+100 mm) rocks in autogenous and semi-autogenous mills. The simplicity of its design, availability in a wide range of diameters (up to 12.8 m) and powers (up to 28 MW of installed power), and flexibility, partially associated with the large variety of grinding media options, explain the enormous popularity of this technology. However, its notably low energy efficiency (Fuerstenau and Abouzeid, 2002) and low power density have opened the path for alternative milling technologies.

In the last few decades, the cement and minerals industries have progressively shifted to other milling technologies, with a highlight on high-pressure grinding rolls (HPGR), vertical roller mills (VRM), and stirred mills. In the case of the cement industry, the uptake of HPGRs, either fully replaced or used in hybrid circuits with ball mills, started in the 1980s (Schönert, 1988), followed by VRMs with integrated classifiers in the 2000s. More recently, dry-stirred milling technologies have been integrated into these circuits, further improving their energy efficiency (Altun et al., 2020). In the minerals industry, the transition started earlier, with the use of vertically stirred milling replacing ball mills in finer grinding (regrinding) stages, whereas the application of HPGRs started in the 1980s and grew substantially in the 1990s (Morley, 2006). Strong cases have been made for the application of VRMs in greenfield projects in the minerals industry (David et al., 2023; Segura-Salazar et al., 2021), but the uptake of the technology has been comparatively slower. More recently, a variety of stirred mill types, including those with a horizontal axis and with media fully fluidized, have been incorporated into circuits in tasks previously undertaken by ball mills. However, it is worth mentioning that the long service life, regional preferences, and characteristics of particular ores guarantee that tumbling mills will remain in operation in the foreseeable future.

A wide variety of milling technologies are employed in the chemical, ceramic, and food industries due to the diverse characteristics of feed materials and milling objectives. These materials range from food grains and pigments to active pharmaceutical ingredients (APIs), while milling tasks vary from dehulling grains to producing highly reactive nanosized particles. Commonly used mills include tumbling, hammer, rotor-stator, pin, and jet mills. One milling technology that has gained wide acceptance is stirred milling, given its ability to reach very fine sizes with comparatively lower energy demands than ball mills and with a significantly smaller footprint (Bilgili and Guner, 2021).

Major developments in mathematical modeling of milling processes have occurred in recent decades. The simple and empirical energy-size reduction relationships from the past have given way to the traditional population balance model, introduced to the field in the 1960s (Austin et al., 1984). The development of advanced mathematical models started in the 1990s, and these models now allow the simulation of breakage either explicitly or implicitly in different mill types, accounting for particle characteristics and the mechanical environment (Tavares, 2017; Weerasekara et al., 2013). These have only been possible with the development and application of discrete element method (DEM), computational fluid mechanics, smoothed particle hydrodynamics, novel advanced population balance model formulations, and detailed particle breakage models as shown in **Fig. 1** (Tavares, 2017). These have been successfully used to simulate a variety of tumbling mills (Cleary et al., 2020; de Carvalho et al., 2021), stirred mills (Bilgili and Guner, 2021; Petit et al., 2025), and other comminution machinery, including hammer mills (Chiaravalle et al., 2025) and impact mills.

3.2 Outlook for the future

In the minerals industry, pressures toward reduction of water usage and increase in energy efficiency will likely result in continuing interest in the use of dry and more efficient grinding technologies, with a focus on technologies such as HPGR, VRM, stirred mills, and novel mills following this path. In addition, various types of stirred mills have been proposed in recent years, and it is likely that novel variants will be introduced not only in the minerals industry but also in the cement industry. With the aim of reducing CO_2 emissions, alternative supplementary cementitious materials will become progressively more important in cement production, which in turn requires optimized milling solutions. Non-mechanical milling technologies, such as microwave treatment and electro-fragmentation, are anticipated to reach industrial scales. However, their use will

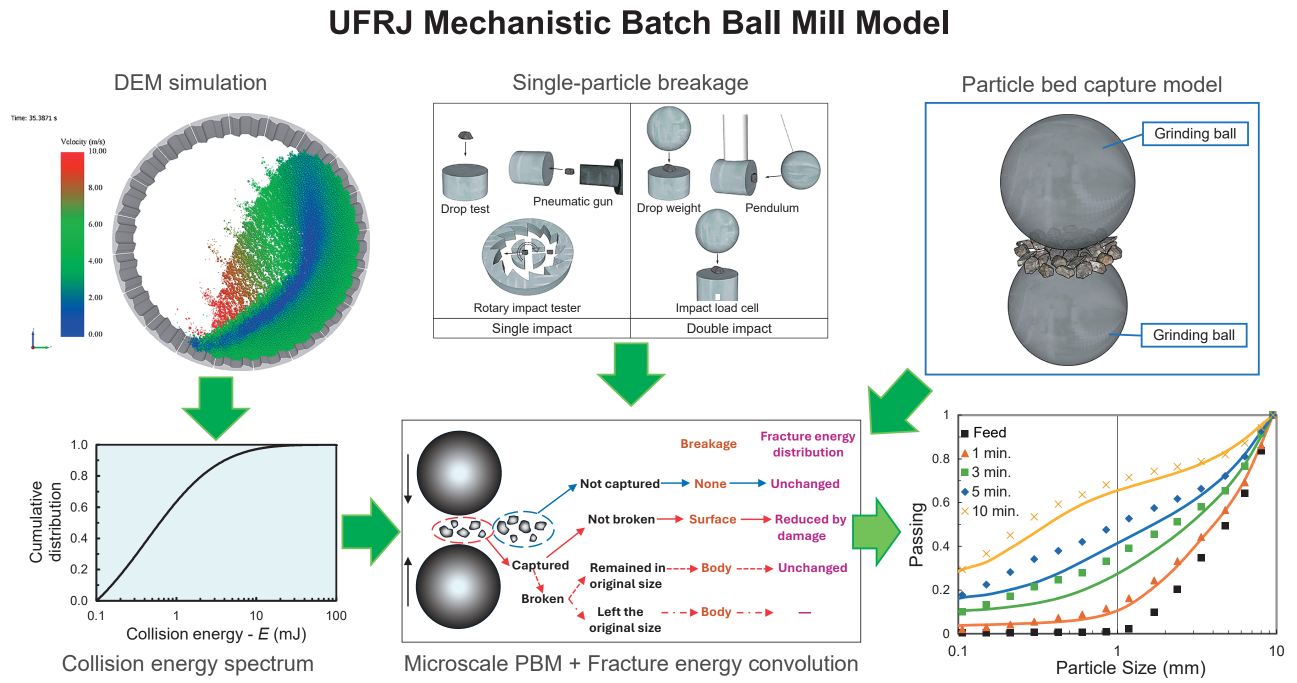

Fig. 1 Overview of the ball mill modelling. Reprinted from Ref. (Tavares, 2017) under the terms of the CC-BY 4.0 license. Copyright: (2017) The Author, published by Hosokawa Powder Technology Foundation.

likely remain limited to niche applications or as preconditioning steps before conventional mechanical milling. Similarly, mechanochemistry is expected to evolve toward highly specialized applications in the future.

The various techniques under the umbrella of AI will continue to gain momentum in the field of milling, partially owing to the large availability of data from online measurements progressively more available in industrial operations. However, rather than replacing the phenomenological understanding that has been gathered over more than a century of the application of milling technologies in the industry, it is anticipated that their successful application will result from the coupling of AI with phenomenological understanding. Indeed, the recent growth in the understanding of milling from the microscale level through advanced milling simulations using DEM coupled with other techniques, the increase in reliability in online sensor data, and the novel AI tools will likely create conditions for deploying at a much larger scale the so-called digital twins of milling machines and entire milling circuits. These techniques will enable the advancement of fully autonomous operation and optimal performance of milling operations in the industry.

The maturity of advanced mill simulation models will likely create conditions for the development of novel milling machines through virtual prototyping (Morrison and Cleary, 2008). This will have the benefit of substantially reducing time, cost, and risk in the development of novel milling technologies required to meet future demands.

4. Particle technology in bulk material handling

In addition to milling, this section summarizes the advancement of particle technology for modeling granular material mechanical behavior and segregation. Several key parameters and strategies are briefly discussed.

4.1 Modeling the mechanical behavior of granular materials

4.1.1 Constitutive behavior

Constitutive modeling of granular materials is key to understanding their mechanical behavior, as well as to simulating and predicting their response. Knowledge of the mechanical behavior of granular (particulate) materials is crucial for designing systems for processing and storing bulk materials in many industries, such as chemical, pharmaceutical, and food processing industries. However, given the discontinuous nature of granular materials, constitutive modeling is extremely challenging. Many constitutive models are based on the principles of classical Cauchy formulation of continuum mechanics, which treat granular materials as continua. While these continuum models may reveal some general behavioral patterns or specific characteristics of granular materials, the fundamental characteristics of granular materials cannot be accurately modeled by classical continuum approaches. External stresses imposed on a granular material are carried through the contacts between particles, and macroscopic deformations result from interparticle movements (slip and rotation) and particle deformations. Accurate modeling of the constitutive behavior of particulate materials should be

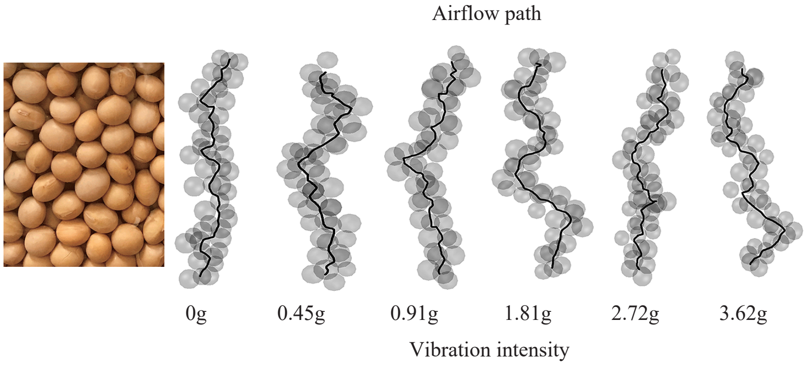

Fig. 2 Typical simulated airflow paths (as a series of associated tetrahedron units) for different vibration intensities. Reprinted from Ref. (Yue and Zhang, 2017) under the terms of the CC-BY 4.0 license. Copyright: (2017) The Authors, published by Hosokawa Powder Technology Foundation.

based on the microscopic structures (at the particle level) and the mechanisms that connect the microscopic behavior to the macroscopic behavior, leading to generalized continuum models as discussed, for example, in Misra et al. (2022), which provide a powerful method for discovering new phenomena (Yilmaz et al., 2024; Misra and Placidi, 2025). The models should incorporate the fundamental properties of granular materials. These include particle characteristics (size and shape), mechanical properties (rigidity and strength), interparticle interactions (contact stiffness, friction, and restitution coefficient), and system parameters (coordination number and porosity). The complexity of modeling granular materials makes it extremely difficult, if not impossible, to develop closed-form or even numerical models. With the rapid advancement of AI, "machine learning has emerged as an alternative paradigm to revolutionize the constitutive modeling of granular materials" (Qu et al., 2023). The AI-based constitutive models can be integrated into numerical models, such as finite element models, to simulate large-scale systems of granular materials. A significant challenge in using AI models is the lack of data for model training.

4.1.2 Pore structure

A granular material consists of solid particles and pores filled with fluids (gas or liquid). The pore structure of a granular material is affected by many factors, including particle size and shape, the formation process of the granular bed (packing), and ambient conditions, such as temperature, humidity, and ground vibration. The two important elements of pore structure are: i) the proportion of pore volume in a material (commonly measured as porosity or void ratio); and ii) pore interconnectivity. The pore structure affects not only the constitutive behavior of granular materials but also heat and mass transfer within the material, such as gas diffusion. A traditional method of studying pore structures is to use liquids (such as mercury) to fill pores in the material under increasing pressure and measure the volume of liquid that penetrates the sample as a function of pressure to determine the pore volume and size. The pore-filling method results in limited information on the pore structure and misses important information, such as the pore shape and interconnectivity. The traditional pore-filling method can be combined with computer image processing to overcome some limitations. For example, color wax was used to fill the pores in a granular material, and the sample was then sliced after the wax solidified (Nwaizu et al., 2022). The researchers took 2D images of the sliced samples and used image analysis techniques to reconstruct detailed 3D pore structures within the granular material. Furthermore, modern imaging techniques, such as CT (computed tomography), have provided a powerful tool to explore the details of pore structures of granular materials (Neethirajan and Jayas, 2008). The combination of other techniques, such as TEM and FIB/SEM, will further increase our ability to "see" the inside of granular materials without disturbing the materials (Gaboreau et al., 2016).

The DEM has been widely used to simulate granular material behavior. DEM simulations produce data on the location (coordinates) and size of each particle in a granular mass, from which the pore structure can be constructed and quantified numerically (Roozbahani et al., 2017; Yue and Zhang, 2017) as shown in **Fig. 2**. Some challenges in using DEM include the high computational power demand and the lack of material property information. Because of their high computational intensity, current DEM models can only handle a limited number of particles in simulations, and are therefore unable to simulate large-scale systems.

4.1.3 Segregation

In the handling and processing of bulk solids, the occurrence of segregation poses a formidable impediment to the general requisite of creating and maintaining homogeneous mixtures (Carson et al., 1986; Tang and Puri, 2004). An inability to do so can lead to serious flaws in the properties, integrity, and function of end products, with adverse economic consequences. On the other hand, segregation is advantageous when the goal is to separate constituents (e.g., see Mohabuth et al., 2007).

Its occurrence is promoted by differences in particle properties, including size, density, shape, morphology, and material behavior. Moreover, flow geometry, environmental conditions, chemical affinities, moisture content, and boundary conditions also play important roles (Desai et al., 2024; Hadi et al., 2024; Ottino and Khakhar, 2000) as shown in **Fig. 3**. Segregation is prevalent in geophysical flows, such as avalanches, landslides, pyroclastic flows, and riverbeds (Cúñez et al., 2024; Edwards et al., 2023; Jenkins and Larcher, 2023; Savage and Hutter, 1991).

The challenge in developing predictive models of segregating systems lies in the fact that the phenomenon is controlled by a coupling of different mechanisms that interact to produce generally unwanted separation of the components. Investigations have typically focused on physical experiments, simulations, and theoretical approaches that isolate factors such as particle properties and energetics. Within this context, because particle-size discrepancy is one of the primary contributors to segregation, and vibrations are typically a feature of almost all solid handling operations, many studies have focused on these factors (for example, Rosato et al., 2002; Rosato and Windows-Yule, 2020).

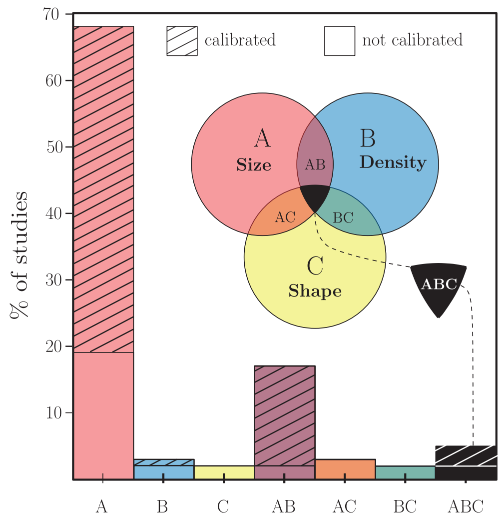

Fig. 3 Literature map of DEM modeling approaches for segregation in gravity-driven granular flows. Reprinted from Ref. (Hadi et al., 2024) under the terms of the CC-BY 4.0 license. Copyright: (2024) The Authors, published by Hosokawa Powder Technology Foundation.

Advances in non-intrusive imaging have greatly enhanced the ability to extract data in a wide variety of dense flow situations. Methods that provide detailed images of microstructure include X-ray computed tomography (Crum et al., 2019; Gustavo et al., 2025; Wang et al., 2004; Weis and Schröter, 2017) and magnetic resonance imaging. Other techniques, such as positron emission particle tracking (PEPT) (Nicusan and Windows-Yule, 2020; Parker et al., 1993; Windows-Yule et al., 2022), provide traces of individual irradiated particles at high spatial and temporal resolutions. Although the method is restricted to the use of only a few particles in the system, it has proved very useful in identifying segregation induced by particle density as shown in **Fig. 4** (Windows-Yule and Parker, 2015) and size (Habib et al., 2013) differences. Another important and useful technique is magnetic resonance imaging (MRI), which has been used successfully in a variety of different flows to construct full three-dimensional images (Caprihan et al., 1997; Stannarius, 2017; Walker et al., 2022).

Computational models are an important investigative approach in their ability to provide complete access to evolving particle positions and velocities. Consequently, these methods are often viewed as '*in silico* experiments' as they are based on the integration of the equations of motion of individual particles that interact via idealized, dissipative collision laws (Di Renzo and Di Maio, 2004; Pöschel and Schwager, 2010; Thornton, 2015). In this context, the DEM originally developed by Cundall (1974) has been

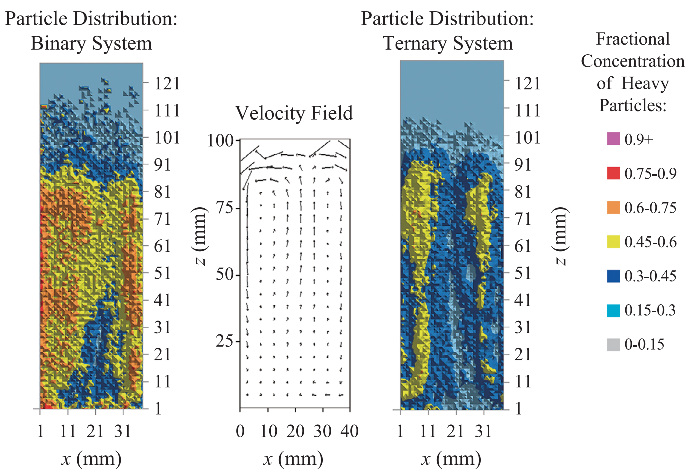

Fig. 4 Experimental and simulational study of density-driven segregation phenomena in binary and ternary granular mixtures. Reprinted from Ref. (Windows-Yule and Parker, 2015) under the terms of the CC-BY 4.0 license. Copyright: (2015) The Authors, published by Hosokawa Powder Technology Foundation.

instrumental in advancing our understanding of segregation mechanisms. The ability to dial in particle properties makes the method highly robust and useful for evaluating the effects of these properties, their distributions, boundary conditions, and energetics. While validations of simulated results rely on quantitative comparisons with physical experiments, advanced non-invasive imaging methods and improvements in hardware have rendered the DEM a more viable tool in the study of granular segregation. However, these simulations are not predictive in the sense of continuum models.

Various segregation mechanics have been proposed, of which the most prevalent are those associated exclusively with differences in particle size. The ubiquitous nature of size segregation and its relevance to industry and geophysics is reflected in the sizeable literature on this topic (mostly notably in vibrated and rotary systems), starting with an early report by R.L. Brown (1939). Later studies, beginning in the 1960s, focused on industrial applications, as exemplified by Hoffmeister et al. (1964). A mechanism based on the probability of voids opening beneath larger particles into which smaller species can fall, consequent with larger species rising to the top, has been coined the “Brazil nut effect” (BNE) for size separation in vibrated assemblies (Rosato et al., 1987). Related to the BNE is what is known as the “reverse Brazil nut effect (RBNE)” (Hong et al., 2001), in which particle density is dominant so that much heavier species sink to the bottom. Percolation (or void-filling), as initially reported by Williams and Shields (1967), on which the BNE is based, proposes that the vibrated granular assembly acts essentially as a sieve that allows smaller species to pass through dynamically created voids. In this mechanism, as in BNE, the segregation strength increases with particle-size discrepancy. The notion of a randomly fluctuating sieve coupled with a postulated “squeeze expulsion mechanism” (due to a force imbalance on the larger species) was hypothesized by Savage and Lun (1988) to describe segregation observed in inclined chute flows. It is interesting to note that the term “kinetic sieving” was coined by G.V. Middleton (1970) to explain observations of inverse grading in sediments is essentially equivalent to the randomly fluctuating sieve concept. A deterministic model known as “arching” and based on the void-filling mechanism (Jullien et al., 1992), suggested the existence of a critical size ratio below which a large particle would not rise to the surface of a vibrated assembly. Another mechanism reported in (Knight et al., 1993) demonstrated that the upward motion of a larger particle or intruder is due to a convection stream that carries the intruder to the surface and thereafter toward the lateral boundary. It will remain there if its size is such that it is unable to be re-entrained within a narrow, downward-moving stream. At the surface near the lateral walls, smaller species can squeeze into the void space beneath larger trapped particles.

The development of kinetic theory continuum models pioneered by Jenkins and Savage (1983) over the course of several decades has greatly enhanced our current understanding of the intricate nature of particle-based systems. The very first such model of segregation accounting for non-equipartition of energy (Jenkins and Mancini, 1989) that gave rise to additional forces promoting size and density segregation was reported by Jenkins and Yoon (2002). Another approach known as granular micromechanics (Gardiner et al., 2003; Misra et al., 2022; Nejadsadeghi and Misra, 2020) derives constitutive laws by connecting particle-scale force-displacement relations to the collective behavior of the system. The proposed method has great promise for creating predictive models of segregating systems.

5. Scale-up and AI implications of process machines

In the powder processing industry, the traditional material-production development pathway follows a sequential, staged approach:

Lab-Scale Research: Initial research establishes the desired material properties and defines fundamental processing parameters.

Pilot-Scale Production: Economic viability is assessed through pilot trials to refine the process and validate scalability.

Machine Scale-up: This approach employs geometric scaling principles with careful consideration of critical process parameters that affect both product quality and production throughput.

Field Validation: The final stage involves starting up and commissioning a full-scale production process under real-world conditions.

This traditional methodology is inherently risky and time-consuming, as the success of scale-up material production remains uncertain until the full-scale machine is constructed and rigorously tested.

The application of AI and machine learning in powder processing is a rapidly evolving field, with significant implications for automation and optimization across various industries. Using its machine learning capability, AI is making an impact on applications, such as Additive Manufacturing (Talaat and Hassan, 2021) to develop 3D Printing Technology more rapidly; Surface Coating (Verma and Khanna, 2023) to control coating’s tribological, mechanical, and corrosion protection properties; and Pharmaceuticals (Takese et al., 2025) to enhance efficiency, reduce dispensing errors, and optimize medication management with automated dispensing systems and robotic aseptic preparation units. Furthermore, AI has been used to analyze data related to particle/powder characteristics and predict how those characteristics will perform in various applications, which enhances the speed and accuracy of simulations used in powder processing. This enables the faster development of new materials and processes. In summary, AI benefits the powder processing industry by increasing process efficiency, enhancing process control, and making data-driven decisions to reduce production costs by predictive maintenance and minimizing downtime and material consumption. In essence, AI is transforming powder processing by enabling greater automation, precision, and efficiency.

Regarding the integration of AI into machine design, AI-powered simulation tools are still evolving and often oversimplified, particularly in areas like powder flow prediction and multiphase flow simulation with particle/powder properties. Machine designers must prepare to leverage these tools as researchers refine simulation models. The goal is to use AI to predict design performance under various conditions, thereby reducing the reliance on physical prototypes and identifying potential issues early in the design process. This will empower engineers to create superior machines with greater speed and efficiency. Ultimately, AI is poised to revolutionize the design and scale-up of process machines that incorporate material properties for the powder processing industry.

In addition to the traditional technologies discussed above, the advancement of particle science and technology has played an invaluable role in environmental protection and pharmaceutical applications. The following sections provide a summary of these applications.

6. Particle design strategies for environmental applications

Environmental applications of particles include, but are not limited to, air pollution control, water treatment, and soil remediation through mechanisms such as filtration, adsorption/absorption, and advanced oxidation (Dai et al., 2021; Li et al., 2021; Ma et al., 2019; Pereira et al., 2021; Wang et al., 2020). Particle design for environmental applications focuses on creating particles with specific properties to improve efficacy, selectivity, and safety (Chowdhury et al., 2024; Croissant et al., 2018; He and Wang, 2019; Ling et al., 2015; Moreno-Alcántar et al., 2023). Several traditional particle design strategies are briefly described below.

6.1 Size, shape, and structure control

Size matters, especially in biological contaminant control and assessment, where nanoparticles are often good model materials because they can efficiently penetrate tissues and cells (Hoshyar et al., 2016; Xie et al., 2018). The shape of the particles can also influence their uptake by cells and distribution in tissues. For example, spherical nanoparticles are typically easier to produce and have predictable behavior; however, non-spherical shapes may exhibit improved cellular uptake and longer circulation times (Yu et al., 2024). In addition, porous and hollow particles are popular structures for adsorptive pollution remediation, where precise control of the pore size and size distribution is key.

6.2 Surface modification and functionalization

This method is one of the most common approaches to particle design and modification. For example, the surface of particles can be modified with specific ligands to target pollutant receptors, such as heavy metals or organic molecules (Neouze and Schubert, 2008). Polymer coatings are another popular approach to tailor surface chemistry, enhance biocompatibility, prevent aggregation, and reduce environmental contamination (Jariwala et al., 2020). Surface charge modulation is also an effective strategy for treating biological contaminants (Yuan et al., 2024; Zhu et al., 2023). For example, positively charged particles can promote cellular uptake, whereas negatively charged particles can improve biocompatibility and minimize non-specific binding. In addition, surface modification can endow particles with stimulus-responsive functionality, and this has received increasing attention in recent years. Stimulus control refers to the manipulation of particle properties by adjusting internal or external parameters such as pH, temperature, light, pressure, or electrical/magnetic fields (Wang et al., 2014). In particular, pH-responsive particles have been receiving increasing attention as drug carriers. For example, Du et al. (2010) designed a pH-responsive nanogel consisting of poly(2-aminoethyl methacrylate hydrochloride) cross-linked with diacrylate poly(ethylene glycol) and 2,4-dimethylmaleic anhydride. The nanogel is negatively charged at physiological pH (≈ 7.4) and becomes positively charged under acidic conditions (e.g., 6.5, a typical extracellular pH of tumor cells), resulting in efficient cellular uptake.

There is also an increasing need to design particles with

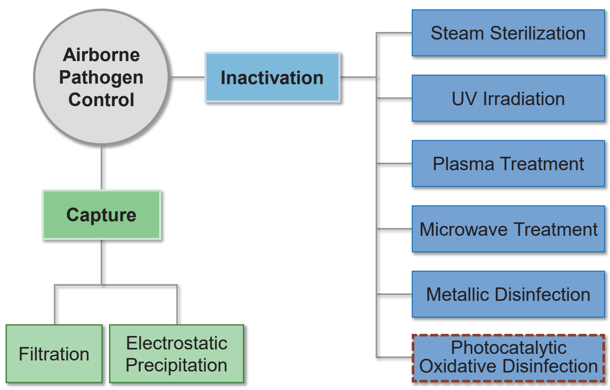

Fig. 5 Classification of various techniques for controlling airborne pathogens. Reprinted from Ref. (Chowdhury et al., 2024) under the terms of the CC-BY 4.0 license. Copyright: (2024) The Authors, published by Hosokawa Powder Technology Foundation.

multifunctionality beyond a single function. In air pollution control, there is a push to develop methods that can simultaneously capture and eliminate airborne pathogens as illustrated in **Fig. 5** (Chowdhury et al., 2024). Active air filters with bactericidal capabilities are a good example of such a design. For instance, coating positively charged polymeric quaternary ammonium compound (QAC) on traditional N95 microfiber filters could enhance both the removal and inactivation efficiencies of airborne bacteria (Zhu et al., 2021, 2023).

6.3 Unsolved challenges

Although significant progress has been made, several challenges remain. These concerns involve the long-term safety of nanoparticles in ecosystems and the scalability of production. There are also challenges in designing multifunctional particles because it is often impossible to consider all functions. In addition, communication gaps persist between scientific communities regarding the definition, use, and characterization of particles in their respective fields. For example, materials scientists often assess particle size to evaluate human health impacts, whereas environmental scientists and physicians typically focus on mass. Furthermore, while AI is transforming particle design by making the process faster, more precise, and more cost-effective, this requires high-quality, diverse datasets to train models, ensuring the generalizability of AI predictions, and addressing ethical issues surrounding data privacy and security. Ongoing research is critical for addressing these challenges and realizing the full potential of particle-based technologies in both fields.

It is also important to highlight the pressing environmental concern of micro- and nano-plastics (MNPs) (Mariano et al., 2021), which have received considerable attention in recent years due to their persistent and potentially harmful impacts on both ecosystems (Le et al., 2023) and human health (Ali et al., 2024). While the particle design strategies discussed earlier hold promise for addressing this issue, continued efforts are needed to develop more effective and practical remediation techniques, which often require interdisciplinary collaborations beyond simple particle design strategies (Kundu et al., 2021).

7. Emerging trends in pharmaceutical powder and particle science

The need to prepare drug particles and additives for inclusion in pharmaceutical dosage forms is central to disease therapy. Since the turn of the Millennium, several areas have seen disruptive progress, which is anticipated to continue into the future and warrant further research and development. For the purposes of this review, the focus can be placed on: (a) particle structure; (b) predictive tools for formulation development; (c) characterization; and (d) data collation, curation, and mining.

7.1 Particle structure

Depending on the application of the drug particles, unique properties may be required. For inhalation aerosols, the aerodynamic particle size is the dimension that is correlated with lung deposition, disposition, and efficacy. The aerodynamic diameter can be correlated with the geometric diameter through Stokes' Law in terms of the terminal settling velocity (Hinds and Zhu, 2022):

$$V_{\mathrm{TS}} = [\rho_{\mathrm{P}} D_{\mathrm{e}}^2\, gC]/[\kappa\eta] = [\rho_0 D_{\mathrm{ae}}^2\, gC]/\eta \tag{1}$$

where V_{TS} is terminal settling velocity, ρ_{P} and ρ_0 are the particle density and unit density (g/mL), D_{e} and D_{ae} are geometric (equivalent volume) and aerodynamic diameters, respectively, κ is dynamic shape factor, η is the viscosity of air (the medium in which pharmaceutical aerosols move), and C is the slip-correction factor.

For pharmaceutical aerosols, the majority of the particle-size distribution is not below 1 μm, and particles usually approach sphericity or regular polygons. Consequently, the slip-correction and shape factors can be largely ignored. Equating the geometric and aerodynamic diameters and removing these terms yields the following expression:

$$D_{\mathrm{e}} = D_{\mathrm{ae}}\sqrt{\rho_{\mathrm{P}}} \tag{2}$$

This observation may appear deceptively simple, but it revolutionized the concept of dose delivery from dry powder inhalers. Until the late 1990s, dry particle drugs for inhalation were produced in sizes suitable for inhalation by jet milling (Dobson et al., 2021). This process is highly energetic and significantly increases the specific surface area of the powder by reducing the particle size to less than 5 μm. These large, highly energetic surfaces resulted in aggregated powders that were difficult to separate into primary sizes. As a consequence, a formulation strategy was developed in which blends with large carrier particles of lactose allowed for both metering and dispersion. This formulation was an effective way to deliver highly potent drugs at low doses, which are required for treating asthma. However, the presence of large quantities of lactose limited the ability to deliver low-potency drugs at high doses, which are required for antimicrobial agents to treat infectious diseases. It has been noted that the ability to overcome the inter-particulate forces, namely intrinsic van der Waals forces and acquired surface forces (electrostatics and capillary), would lead to more effective delivery (Hickey, 2018; Hickey et al., 1994). However, the ability to change the intrinsic forces seemed beyond the existing technology. Despite technological limitations, it was clear that efforts to minimize inter-particulate forces, if successful, would promote the development of high-dose low-potency drugs and support new delivery systems. These systems are essential to address unmet medical needs.

In 1997, Edwards et al. demonstrated that spray drying produced low-density particles that consequently exhibited reduced inter-particulate forces (Edwards et al., 1997). These findings and other such observations opened the potential for high-dose delivery (Weers et al., 2007). A variety of new strategies based on modification of the particle core and surface structure have emerged (Sung et al., 2011). In this framework, additional advances have recently occurred with the preparation of unique milled particle aggregate structures (Brunaugh et al., 2022; Nair and Smyth, 2023). The range of powder doses and ease with which particles can be dispersed offer various opportunities for future product development.

7.2 Drug powder formulation

The formulation of solid dosage forms has been based on underlying chemistry, notably related to factors contributing to properties important to the dosage form, including stability, and empirical knowledge of the contribution of certain additives with respect to their prior use. A mechanistic understanding of each component of the quality and performance of the dosage form requires extensive research and the use of high-level statistical tools with respect to process control and sensitive analytical methods (Hickey and Ganderton, 2010). Recently, the application of machine learning to large data sets has allowed predictive models to direct the composition of certain dosage forms with respect to anticipated quality and performance without explicitly identifying the mechanisms responsible for these outcomes (Cern et al., 2014, 2017; Jiang et al., 2022, 2023). The advantage of this approach, when sufficient data are available, is that it allows a variety of options to be identified and enables the pharmaceutical scientist to conduct a risk assessment before conducting any experiment, thereby increasing efficiency and reducing costs. In the long run, this approach can be adapted to any formulation and aligns with the FDA's Quality by Design (QbD) principles for achieving product quality (Yu et al., 2014).

7.3 Pharmaceutical aerosol characterization

The ability to characterize particulates in a manner directly relevant to their application has long been an objective in the pharmaceutical sciences. Various approaches have been developed in the selection of molecules with respect to their potential as pharmacological agents in drug discovery (Lipinski's Rules) and with respect to their biopharmaceutical properties, related to dosage form presentation at the site of absorption or action and subsequent disposition (Biopharmaceutical classification system) (Amidon et al., 1995; Lipinski, 2000; Lipinski et al., 1997). For inhaled aerosols, the most important property for efficacy is the aerodynamic particle-size distribution, which dictates the dose deposited in the lungs (Lodge and Chan, 1986; Tougas and Mitchell, 2013). The measurement of this property is conducted by inertial impaction using a cascade method of sampling stages, each of which collects particles in a defined size range based on orifice dimensions and distance to the impaction surface at that stage.

Traditionally, impactors have been used as sizing tools, where a fixed airflow is drawn through the device, and stages are calibrated according to this airflow, corresponding to a linear velocity at the orifice. However, inspiratory airflow is not generated at a fixed rate. Rather, the inspiratory portion of the breathing cycle is a continuously variable flow characterized by acceleration and deceleration, followed by exhalation, which follows a similar (but not the same) pattern in the reverse direction. Consequently, for inertial impaction to be relevant to the lung deposition of particulates, a variable-flow system would be required in which the calibration of the device would not be valid.

Several research groups have worked to render impaction data more relevant to lung deposition, and there have been two major adaptations of impactors to accommodate this objective. The first step is to use physiologically relevant inlets to the impactor (Zhang et al., 2006). The second method is to use inspiratory flow profiles to generate and sample dry powder aerosols (Byron et al., 2010; Olsson et al., 2013).

In parallel with these efforts, an inhaled biopharmaceutical classification system (iBCS) was proposed (Hastedt et al., 2022). Similar to the gastrointestinal BCS (giBCS), the focus here is on the solubility and permeability of the drug. However, incorporated into assumptions are the aerodynamic properties of the aerosol with respect to anticipated deposition in various regions of the lungs (Bäckman et al., 2022). Applying the new approach to marketed drugs demonstrates its relevance for identifying the ease or difficulty that might be experienced in development and the need for formulation strategies to enhance the performance of the dosage form (Hastedt et al., 2024). Nevertheless, new tools may be required to generate sufficiently robust data to support this model (Forbes et al., 2025).

The ability to predict the behavior of pharmaceutical aerosol particles from first principles can allow rapid product development and regulatory review, which in turn meets the needs of patients and society for timely disease therapies.

7.4 Data mining

As the scientific literature expands exponentially, the ability to glean important information from meta-analysis of published data has been acknowledged across disciplines (Atzmueller et al., 2024). Powder and particle science is an arena in which enormous amounts of data can be curated into a database from which important new observations can be extracted. Efforts have been expended on the exploration of nanoparticles in this context. The Nanomaterial Registry was established by the National Institutes of Health in 2013 to globally extract data from the literature and curate them with respect to 12 physicochemical characteristics (PCC) intended to define the accuracy and reproducibility of the data (Tropsha et al., 2017). Since many studies did not supply all the PCC data, a qualitative label was assigned based on the number of PCCs addressed. The data were placed in gold, silver, or bronze categories, according to high, moderate, or low concordance with PCCs. Thus, users can assign confidence to interpreting their findings. An effort to curate data in cancer nanomedicine is also underway through the efforts of CaNanoLab, which is also supported by the NIH (Morris et al., 2015). Since this field is growing rapidly, the value of a searchable database to the overall R&D endeavor is self-evident. Each of these approaches, and others in a rapidly evolving field, can create the foundation for future applications of AI/ML, potentially leading to novel findings or new research directions at a speed once limited by data collation.

8. Concluding remarks

These perspectives on particle science and technology identify important aspects of understanding particle and powder systems, including characterization, bulk material processing and handling, scale-up manufacturing, and their applications in environmental protection and pharmaceuticals. The potential role of AI in the future developments of these systems is also considered, aiming to stimulate further interest in the topics discussed. However, this review does not offer a comprehensive exposition of all the exciting and emerging developments in the field, many of which are beyond its scope.

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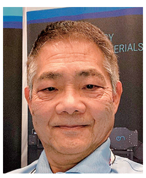

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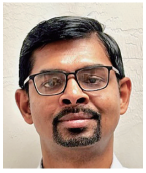

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