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Shaken not stirred: procedures in mechanochemical syntheses and how to define them

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Over the past 20 years, the chemistry community has seen the rapid advancement of mechanochemical methods for chemical and materials synthesis. In the laboratory, the most common of these today include ball and planetary milling, and twin-screw extrusion,¹ with recent reports also exploring other methods,^{2–9} such as resonant acoustic mixing,¹⁰ sonication,¹¹ or jet milling.¹² The application of these mutually very different tools has further revealed many of the unique challenges in making such syntheses broadly accessible and viable for scale up. Central to this is not only the need for understanding of the details of the techniques used for mechanical processing but,¹³ critically, for well-defined reporting methodologies that will enable not only reproducibility of results, but also advance the cross-platform designs that may be needed as we begin to envision scale-up of such approaches across diverse industrial applications.

To accomplish this, there are important elements that influence reactions that must be defined. For example, in mechanical milling, these range from the type of instrument used and the materials from which components of the milling assembly (e.g., jars and balls) are constructed, to the general operating parameters,^{14,15} such as milling ball mass,

reactor filling ratio, milling frequency, the types of reagents being milled, their particle sizes¹⁶ and their physicochemical properties, as well as the interactions of these materials with the milling assembly, including abrasion and catalysis.^{17,18} These factors (and certainly many others) control the results, from the kinetics of the reactions to their product distributions and yields. The need for detailed reporting becomes even more obvious when considering the many ways¹⁹ in which mechanochemistry and mechanical processing can be performed, with just “ball-milling” covering a wide range of designs that can affect mechanochemical reactivity: the outcomes of a process are going to be different depending on whether ball-milling is done in a vibratory, attrition, hammer, planetary, vortex or a lunar mill design²⁰ – to name just a few (Fig. 1).

In addition to these methodological protocols, guidelines are also needed for product analysis. Chemical and structural transformations (for example, crystallisation of an amorphous phase) can proceed after the input of mechanical energy has ceased,²¹ which is related to the field of mechanical activation, and means that aging of reagents in the mixed powders can influence the nature and structure of the product, as well as the reported yields. Such aging transformations²² can be facilitated by atmospheric gases, including moisture,²³ (as is

well known in fields such as pharmaceutical formulations²⁴) temperature, or organic vapors,²⁵ which makes them of interest as synthetic techniques, but also stresses the need to clearly define and report sample handling prior and during analysis. All this illustrates how the timing and execution of post-reaction analyses can be of critical importance as researchers compare their results. Here, advancements in the development of hybrid methods that enable direct visualization of reactions *in situ* offer a means to capture such chemical and structural changes. There have been exciting studies that have demonstrated how *in situ* X-ray,^{26,27} Raman,²⁸ and even NMR,²⁹ can reveal the hidden underpinnings of the reactions being studied. Work such as this, as well as advances in the design of new reactor platforms,^{30,31} and the incorporation of models of the mechanical environments during reaction,^{14,32,33} bring us ever closer to clear paradigms for mechanochemical syntheses.

While the approaches just noted often require access to special tools, the results of these studies can aid in developing protocols for analysis that can be established for more routine work that can also advance our understanding. In concert with this is the need for more detailed, cross-scale, computational studies to fully advance our fundamental understanding of mechanochemical

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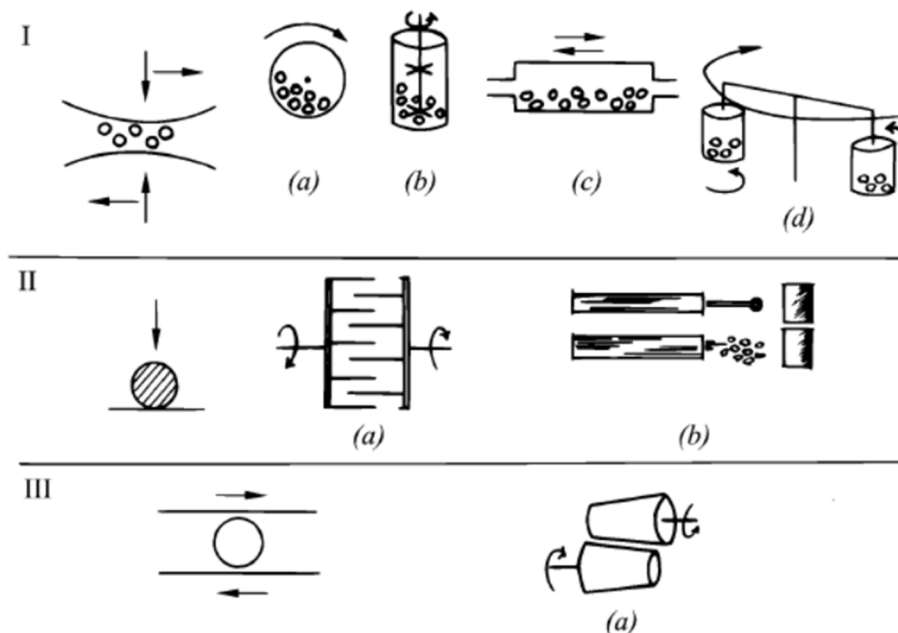


Fig. 1 Illustration of different types of mechanical treatments, adapted from Boldyreva: (I) – shear and impact: (a) roller mill, (b) attritor, (c) vibratory mill, (d) planetary mill; (II) – impact: (a) pin mill, (b) jet mill; (III) – shear: (a) rollers (used with permission from ref. 19).

reactions, and how to design them from the ground up.

To capture such efforts and to build off of them, systems must also be readily catalogued and made accessible. To this end, a Mechanochemical Reactions Database has been created.³⁴ This is a fork of the open-source Open Reactions Database (ORD), with new fields specific to mechanochemistry.^{35,36} Here, the community will be able to add their work to this open platform that will capture reaction conditions and results, with an eye toward being able to use this data to advance machine learning tools to develop and predict mechanochemical processes.

It must be highlighted that immense advances in the popularization and understanding of mechanochemical synthesis and scale-up have been accomplished through community-building societies, initiatives and consortia, such as the International Mechanochemical Association (IMA), the European Union COST Action project CA18112 (Mechanochemistry for Sustainable Industry, MechSustInd³⁷), the US National Science Foundation's Center for the Mechanical Control of Chemistry (NSF CMCC),³⁸ the European Union's Horizon Europe research and

innovation programme IMPACTIVE,³⁹ and IUPAC's Task Group focusing on mechanochemistry terminology, classifications and symbolism.⁴⁰

Now, to continue to build on the many advances we have seen, *RSC Mechanochemistry* will be reaching out to you, the mechanochemistry community, to help identify, and define the key parameters for each type of reaction platform in use. While we intend to begin with the most common ones, how such parameters cross boundaries to new techniques will also be important, as this is what fosters innovation. For example, how do the reactions carried out in a ball mill compare to those nominally the same reactions when conducted in an extruder, an acoustic mixer, or a jet mill? We have entered a rapidly evolving time in mechanochemistry, and the development of these standards will give the community a firm footing moving forward.

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