



Cite this: *Phys. Chem. Chem. Phys.*,
2024, 26, 27245

Fundamental basis of mechanochemical reactivity

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DOI: 10.1039/d4cp90153c

rsc.li/pccp

In the last decade, the scientific community has witnessed a renewed and formidable surge of interest in mechanochemistry. After revolutionizing metallurgy and materials science, respectively in the 1970s and 1990s, mechanochemistry has finally broken into inorganic and organic synthesis, hitting at the heart of chemistry. Here, the capability of mechanical force to initiate or sustain physical and chemical transformations has emerged, once again, with its many strengths.

What immediately catches the eye is the unique opportunity provided by mechanochemical methods to access entirely new chemicals that are difficult to prepare, or are even unobtainable, by any other route.¹ Notably, this can be done without the need for bulk solvent, which opens wide and largely unexplored prospects for innovation in the green chemistry paradigm. In this respect, mechanochemistry offers a

transformative route to sustainable chemical technologies,² and is already sparking serious reflection on the future strategies of the chemical and pharmaceutical industries.

These new opportunities have caused immense excitement around mechanochemistry, and this excitement is spreading across researchers from diverse backgrounds. This is giving rise to an unprecedented breadth of exciting research and discussion. However, propelled by this enthusiasm and curiosity, studies in the community have proceeded in a seemingly disparate and stochastic way, sprinkled across the field in all its flavours. The result is countless tiles cast across a table, each being pieces of the larger puzzle that, together, could reveal the nature of mechanochemistry.

This is the ironclad law of science, glorious and inescapable. Any fast progress of knowledge cannot but require, in a sort of retrospect, the careful examination of the many results that have been collected. It is only once the dust raised by the feverish activity starts to settle that the time comes to try to discern the bigger picture that lies beyond.

It is in that context that the idea of this themed collection of *Physical Chemistry Chemical Physics* (PCCP) was born, driven by the deep awareness that the wealth of experimental evidence regarding mechanochemical transformations is not counterbalanced by the

understanding of their fundamentals. This is a remarkable reality as mechanochemistry is by no means a new field.³ Even neglecting more ancient testimonies,⁴ mechanochemistry was described by W. F. Ostwald in the early 20th century as a reaction in any state of aggregation that is initiated by mechanical force.⁵ Mechanically initiated transformations have since underpinned technologies across the century, spanning mining and construction, defence, energy and metallurgy.⁶

Remarkably, despite this substantive history, very little is actually understood about how and why mechanochemical reactions happen. The present revival of mechanochemistry, and particularly its applications to green and sustainable chemical technology, make it more acutely obvious that without this fundamental understanding, we cannot hope to unlock the true potential of this chemical technology.

This PCCP themed collection aims to nucleate a discussion on this missing piece of the mechanochemical puzzle, and highlight recent new developments from across the discipline aimed at unravelling the fundamental basis of mechanochemistry. As deserved by a truly global field of the chemical sciences, the themed collection highlights contributions from across the world, spanning Asia, Europe, and both North and South America.

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The themed collection begins with a detailed review by Mu and Hu (<https://doi.org/10.1039/D3CP04160C>) summarising the state-of-the-art of polymer mechanochemistry and advances being made in designing advanced mechanically responsive polymers such as mechanophores. A second review by the Belgian Quantum Chemistry group then dives into the depths of quantum-mechanochemistry (<https://doi.org/10.1039/D3CP04907H>). This review provides an excellent introduction to how we can think about mechanical energy at the electronic structure level and how we can use this understanding to probe *in silico* the response of molecules and materials to mechanical force.

We subsequently learn of a number of molecules and materials that are only synthesizable by mechanochemical means, and read of the unique physical understanding of why this is the case. Scano and colleagues (<https://doi.org/10.1039/D3CP04213H>) demonstrate how the formation of liquid crystals under high-energy ball-milling conditions can template unique magnetically ordered mesoporous silica, and Krusenbaum *et al.* show how the physical characteristics of polymeric building blocks give rise to unique behaviour under ball-milling conditions to generate a plethora of polymer materials (<https://doi.org/10.1039/D3CP02128A>). Baláz *et al.* (<https://doi.org/10.1039/D3CP01788E>) instead show how, rather than synthesising materials, ball milling can restructure solids and lead to enhanced electronic properties. We also read from Xavier and colleagues (<https://doi.org/10.1039/D3CP05609K>) of how mechanical energy from ball milling facilitates the rapid mixing and regeneration of organic reducing agents, allowing them to be used in sub-stoichiometric quantities to synthesise metal nanoparticles.

This work on reactivity is supplemented with reports detailing innovations in controlling mechanochemical reactions. Alić and colleagues (<https://doi.org/10.1039/D3CP04364A>) demonstrate how thermally controlled ball milling can be used to control and optimise the onset of polymorphic transitions, and the paper by Félix *et al.* (<https://doi.org/10.1039/D3CP02540C>) outlines an innovative

set-up for applying heat to a mechanochemical reaction using inductive heating. In a report by Nagapudi and Nagapudi (<https://doi.org/10.1039/D3CP04713J>), the ability to control cocrystal formation using different types of mechanochemical reactors – and through the addition of liquids – is demonstrated, a concept continued in the work by Zuffa *et al.* (<https://doi.org/10.1039/D3CP04791A>) that reveals unexpected origins for liquid in the mechanochemical synthesis of an ionic cocrystal. Finally, in the work by Kenges we see how the addition of biological material can be used to enhance the reactivity of minerals, and how statistical models can help expedite the optimisation of mechanochemical reactions (<https://doi.org/10.1039/D4CP02354D>).

As a recurring theme in the collection, we are taught about the importance of kinetic modelling and its role in extracting mechanistic insight about mechanochemical reactions. By modelling the kinetics of a self-propagating reaction, Carta *et al.* (<https://doi.org/10.1039/D3CP05401B>) reveal how the microstructuring of powder mixtures is essential for the propagation of the reaction front. In a second contribution Carta *et al.* (<https://doi.org/10.1039/D3CP06147G>) use time-resolved *in situ* (TRIS) Raman spectroscopy, coupled with analytical kinetic models, to investigate ball-milling-induced isotope exchange in benzoic acid. In this study the authors again show the importance of interfaces in mechanochemical reactivity, showing that the reaction is kinetically dominated by the formation of new interfaces. Casali *et al.* (<https://doi.org/10.1039/D4CP01457J>) instead use powder X-ray diffraction (PXRD), also coupled to analytical kinetic models, to show how mechanically driven melting at particle-particle interfaces is responsible for the mechanochemical co-crystallisation of ibuprofen with nicotinamide. Scheurrell and colleagues (<https://doi.org/10.1039/D3CP02883F>) use a similar TRIS-PXRD approach to then identify the role of solvent polarity for controlling liquid-assisted grinding reactions. Highlighting new directions for kinetic studies in mechanochemistry, Cvetnić *et al.*

(<https://doi.org/10.1039/D3CP03933A>) show how carefully designed TRIS calorimetric studies can help quantify the thermodynamics of mechanochemical reactions, while Leger *et al.* (<https://doi.org/10.1039/D3CP05555H>) demonstrate a new protocol for studying mechanochemical kinetics by nuclear magnetic resonance spectroscopy, used to follow the formation of metal-organic frameworks (MOFs).

A strong theme in the collection is the importance of computational modelling for fundamental mechanochemical research. The synergies of computational modelling with experiment are first shown by Gómez *et al.* (<https://doi.org/10.1039/D3CP04201D>) in their study on the role of intermediates in mechanochemical cyclorhodation reactions. Galleas and colleagues subsequently show how *ab initio* simulations can provide important inputs to microkinetic simulations and help rationalise mechanochemical reactions (<https://doi.org/10.1039/D4CP01613K>). We are also shown how modelling can help rationalise the selective mechanochemical formation of multi-component halogen-bonded cocrystals in a paper by Kumar and colleagues (<https://doi.org/10.1039/D3CP04358D>). Innovations in the computational modelling of mechanochemical reactions at surfaces by Ogbomo *et al.* (<https://doi.org/10.1039/D3CP05320B>) allow us to see at the atomic level how and why molecules decompose under mechanical strain, beyond the insight possible from existing experimental techniques. We additionally learn through advanced molecular dynamics simulations performed by Ferguson and Friščić (<https://doi.org/10.1039/D3CP05475F>) what happens when two particles impact, and how such impacts can facilitate mixing and the onset of physico-chemical transformations. Further computational studies report exciting advances in understanding how to selectively manipulate molecules to enhance reactivity, both through direct mechanical force, as shown by Sakai and colleagues (<https://doi.org/10.1039/D3CP04465C>), and when in combination with externally applied electric fields, as shown by Scheele and Neudecker (<https://doi.org/10.1039/D3CP03965J>).

This themed collection also reminds us of the complexity of characterising the force conditions that occur within conventional mechanochemical reactors, and the important insights into mechanochemistry that can be obtained through model reactors. In a high-pressure study, Montisci *et al.* (<https://doi.org/10.1039/D3CP04220K>) study, using a diamond anvil cell, how controlled mechanical force can induce the dimerization of the organic semi-conductor (TTF-BTD)₂I₃. We also see the design of a new ball-milling device by Nwoye *et al.* (<https://doi.org/10.1039/D3CP02549G>) that allows for the controlled application of impact energies, and a demonstration of how such devices facilitate the quantification of energy needed to induce a mechanochemical reaction.

In short, this *PCCP* themed collection highlights the intense global efforts cur-

rently underway aiming to understand at a fundamental level how mechanochemical transformations occur. These efforts are broad, spanning both experiment and theory, and crossing the traditional boundaries of physics, chemistry, and engineering. Even with these efforts, this themed collection highlights how the challenges faced with studying mechanochemical reactivity are in many cases beyond the scope of existing methodology. There is still a need to develop new theoretical and experimental approaches to disentangle the complexity of these transformations and dig deep into the core of their mechanisms.

It is our hope that the collection compiled here will shine light on the importance of the challenges raised by mechanochemistry and inspire researchers to continue to push the boundaries of this transformative area of the chemical sciences.

Conflicts of interest

There are no conflicts to declare.

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