PREDICTABLE MECHANICAL ACTIVATION IN MOLECULAR CRYSTALS

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Summary. With top-up funding from the University of Birmingham (UoB), this project will support a 3.5-year PhD studentship focused on understanding how mechanical activation in molecular crystals is governed by the strength of their non-covalent interactions. The ultimate goal is to develop a predictive strategy - based on crystal structure analysis - to assess the likelihood that a molecular crystal can be mechanically activated. The project leverages state-of-the-art experimental and computational capability of the Michalchuk group, including novel crystal bonding descriptors and advanced techniques for time-resolved in situ monitoring of mechanochemical reactions. By partnering with the Diamond Light Source and Prof Costantini (UoB), the project will deliver a unique research programme, providing significant added benefit to the project, and ensuring the PhD student receives world-leading training across a breadth of industrially relevant techniques. The project will be based in the UoB's Centre for Mechanochemistry and Mechanical Processing, providing further access to many world-leading researchers and > £2M worth of mechanochemical equipment and solid-state characterisation facilities.

Science Case The mechanical processing (milling, grinding, compaction) of solids is well known to modify both the macroscopic (particle) structure, and the local inter-atomic structure.[1,2] Understanding these deformations within the industrial setting is critical, as they can influence both the bulk powder behaviour (flowability, compressibility) as well as the physico-chemical behaviour of the powder (dissolution rates, melting temperature[3]). These effects – known as mechanical activation – are particularly pronounced in organic molecular crystals, which are typically soft and deformable as a result of the low-energy interactions that stabilise them. Although it is well established that mechanical processing affects the functional behaviour of powders, we are far from understanding the degree of activation that is achievable for any given powder under specific processing conditions. This means that industry must undergo extensive and costly trial-and-error protocol to design a mechanical processing strategy that is 'safe' for their given powder and its applications.

Current understanding,[4] Figure 1, suggests that any mechanically induced transformation of a solid arises from two processes: (1) the generation of a stress field within the solid; and (2) the relaxation of that stress field. The former is influenced by particle properties (shape, size, etc) and environmental conditions (e.g., temperature). The latter depends on the crystal's ability to dissipate stress, which is governed by the nature of its interatomic interactions. This interplay between the generation and relaxation of mechanical stress means that solids with different physical properties and bonding types, subjected to different mechanical stresses, will exhibit markedly different physical responses to mechanochemical processing.[5]

To determine *a priori* how a given solid form will respond to mechanochemical processing, we must identify routes that link heuristic descriptors of the crystal to their mechanochemical response.

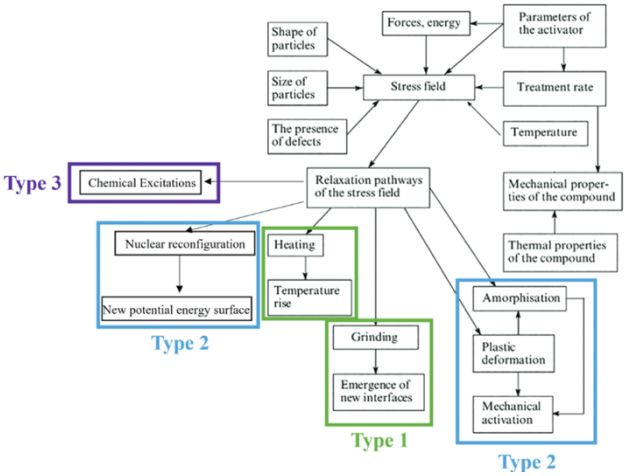


Fig 1. *The generation and flow of mechanical energy in a chemical system, underpinning different types of mechanochemical process. In Type 1, stress relaxation facilitates mixing/heating; in Type 2 (mechanical activation), stress relaxation causes a permanent change in the nuclear coordinates, changing the underlying reactivity of the materials; in Type 3, mechanical energy directly causes a chemical reaction.*

Background Research The macroscopic mechanical properties of molecular crystals (e.g., bulk or Young's modulus) are governed by the energy required to deform the crystal. Recent studies suggest that plastic deformation under mechanical force (mechanical activation) also depends on this energy requirement.[6,7] While these mechanical properties can, in principle, be tuned by altering the types and strengths of interatomic interactions in the crystal, quantitative relationships between bonding and mechanical response remains elusive.

Current frameworks to describe crystal mechanical behaviour only account for the total change in crystal energy during mechanical deformation. These frameworks do not provide insight into how individual interactions contribute. This lack of detailed insight prevents the use of well-established principles of crystal engineering to predict the mechanical properties of a given crystal *a priori*. As a result, heuristic structure-based models routinely produce errors of several orders of magnitude, and unexpected behaviours are common. [8–10]

To tackle this challenge, we are developing a (soon to be published) computational approach to quantify the individual mechanical strength of non-covalent interactions in molecular crystals, Figure 2. The method uses as input a set of vibrational frequencies for the crystal. From these vibrational frequencies, we can mathematically extract

interatomic force constants and map them onto individual non-covalent interactions. In doing so, we obtain a quantification for the mechanical strength of individual interactions. Although the approach depends on vibrational frequencies obtained from density functional theory (DFT) calculations, its accuracy can be readily validated by comparing the simulated and experimental (e.g. Raman spectroscopy) frequencies. This computational framework is the **only method capable of isolating the mechanical strength of individual non-covalent bonds** and therefore provides a unique opportunity to establish quantitative structure-property relationships between a crystal's bonding and its propensity to be mechanically deformed.

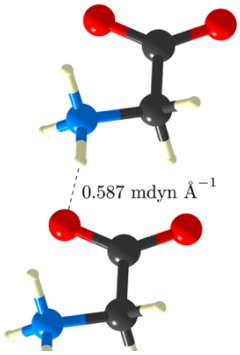


Fig 2. *Calculation of the mechanical strength of an individual hydrogen bond in crystalline glycine.*

In our initial efforts to explore the relationship between intermolecular bonding and the mechanochemical reactivity of molecular crystals, we launched a research program using atomic force microscopy (AFM) to probe the stability of crystal surfaces under mechanical deformation.[11] Specifically, we scratched (mechanically activated) the surfaces of molecular crystals and monitored their ability to self-heal. Remarkably, we found that crystals with more highly 'dynamic' surfaces (i.e. those capable of rapid self-healing) were generally less mechanochemically reactive. We tried to establish structure–property relationships for this self-healing behaviour, but at the time only had access to total crystal energy analysis (energy framework calculations) and heuristic packing analysis. However, even this simplified approach revealed a strong qualitative correlation between mechanochemical reactivity and crystal bonding. Importantly, this preliminary study highlights that combining AFM with more robust computational bonding analysis, like our local mechanical strength descriptors, could become **a powerful strategy for developing predictive models of mechanical activation and reactivity in molecular crystals**.

While a molecular- or nano-scale view of mechanical activation is fundamentally important, **understanding how this behaviour translates to the activation of bulk powders is critical for process efficiency and material safety in industrial settings**. For example, mechanically activated powders are often more soluble than non-activated powders[12] and may exhibit different thermally induced decomposition pathways.[13] We have also recently demonstrated[14] that mechanical activation can dramatically influence the rates of ball milling reactions, Figure 3, a quickly growing technique for sustainable chemical and materials manufacturing.

A major challenge in linking mechanochemical processing to bulk powder activation is the inherent instability of the activated state in many molecular crystals, as observed at the molecular scale in AFM studies.[11] When mechanical activation is studied using *ex situ* analyses, the powder's activated state not only reflects the processes of mechanical excitation and relaxation (Figure 1), but also includes the additional influences of aging. This can severely complicate efforts to establish clear links between the input mechanical energy, crystal properties (e.g., bonding), and the degree or nature of the mechanical activation that is achieved.

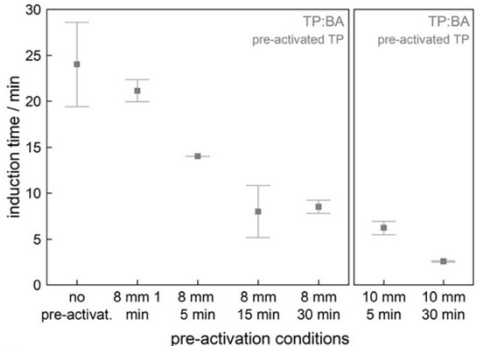


Fig 3. *The effect of mechanically activating reagents on the kinetics of a ball milling cocrystallisation reaction.*

To address this challenge, we have pioneered the use of time-resolved in situ (TRIS) techniques to study mechanochemical transformations in molecular solids, including TRIS X-ray powder diffraction (PXRD), TRIS X-ray absorption spectroscopy, [15,16] and TRIS pairwise distribution function (PDF) analysis. We have recently developed new data collection and analysis algorithms that allow us to move beyond monitoring phase composition alone; we can now track, in real time, how both crystallite size and strain evolve in molecular crystals *during* mechanochemical treatment, Figure 4.[17,18] This is to say that **we can track, in real time, the mechanical activation of molecular crystals inside ball mills.** This capability has only recently been developed and, while its potential for studying and quantifying mechanical activation in molecular solids is immense, its full strength has not yet been exploited.

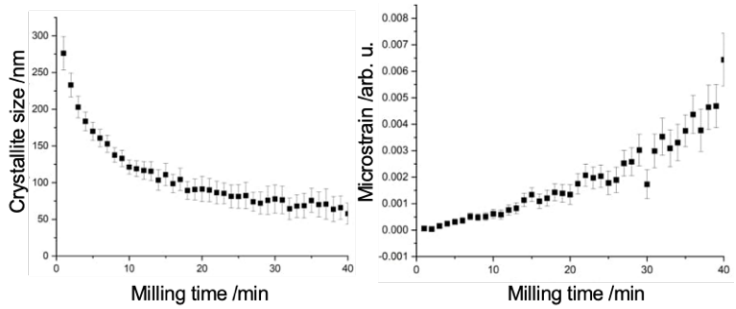


Fig 4. *The effect of ball milling on the crystallite size and microstrain, measured by TRIS PXRD.*

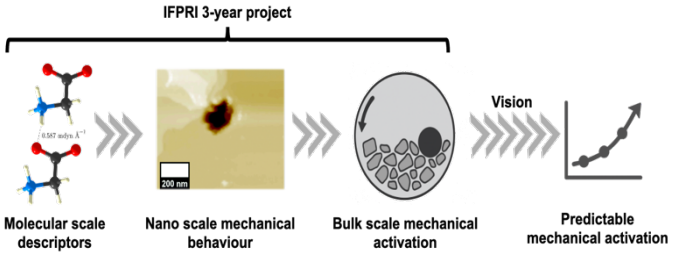
Recent advances in computational and experimental technologies provide a unique opportunity to gain unprecedented insight into the nature of mechanical activation in molecular solids. Crucially, **we now have the capability to describe and measure mechanical activation from the molecular through to the bulk scale**. It is timely to leverage these capabilities to establish, for the first time, a clear link between

molecular level properties, the nanoscopic mechanical response of crystals, and the ability to mechanically activate bulk powders. Achieving this will ultimately enable predictive models that anticipate the impact of mechanical processing on the behaviour and reactivity of molecular crystals, ensuring efficient industrial processes with reliable, predictable material outcomes.

Project and Approach There is a need to determine how to predict the impact that mechanical processing will have on the behaviour and reactivity of molecular crystals. This project takes a step towards achieving this long-term goal, by seeking to establish a tool-kit capable of predicting the propensity of hydrogen-bonded organic crystals to be mechanically activated based on analysis of the crystal structure and their bonding.

Specifically, the aim of the 3-year funding (supporting a 3.5-year PhD studentship) is to establish a definitive link between the mechanical strength of hydrogen bonding in molecular crystals and the ease with which these crystals can be prepared in a mechanically activated state.

Hydrogen bonded molecular crystals are selected in the first instance as (1) this is the most common intermolecular interaction found in molecular crystals; and (2) there are well documented variations in strength and dimensionality. While we propose to initiate studies on model hydrogen bonded systems, including amino acids and simple pharmaceuticals like paracetamol and aspirin, this aspect of the project would welcome input from IFPRI partners to ensure studies are performed on the most industrially informative systems.



Hypothesis: This project posits that there will be a direct and predictable correlation between the mechanical strength of intermolecular interactions (here, hydrogen bonding) and the ease with which one can mechanically activate a material. To validate this hypothesis, this project has three specific objectives (Ob1-3):

Ob1. Correlate the mechanical strength of hydrogen bonds to the ease of mechanically activating the crystal at the local (nano) scale.

Ob2. Correlate the ease of mechanically activating crystals at the nano scale with the ease of activating the bulk powder.

Ob3. Correlate the amount of energy needed to mechanically activate a bulk powder with the nanoscale forces needed to achieve local activation.

To achieve these objectives, the project is separated into 3 work packages (WPs), outlined in detail below. The project is planned for a 3.5-year PhD studentship at the University of Birmingham (UoB), supported by on-going research activity in the PI's group. The WPs are designed such that much of the work can take place in parallel, mitigating the risk to delays in the project.

The Project Team. The project leverages the existing expertise in the Michalchuk group (UoB), building upon ongoing activities in the team, including:

(1) the development and application of theoretical models to describe local mechanical properties of molecular crystal (a current PhD project);

(2) the development and application of novel synchrotron-based techniques to characterise local structure deformations and strain in molecular crystals during ball milling (a current PhD project and collaboration with U. Cambridge and the German Federal Institute for Materials Research and Testing (BAM));

(3) the development of models to describe how crystal size and shape affect mechanochemical reactivity (PhD project to begin Oct 2026).

The project leverages a co-supervision arrangement with beamline scientist (Dr X Liu) at the Diamond Light source. This arrangement provides essential access to world-leading synchrotron facilities to push the capabilities of time-resolved in situ powder X-ray diffraction as a tool to monitor mechanical activation in real time. Moreover, the project will collaborate with Prof G. Costantini (UoB), a world leader in the study of crystal surfaces using atomic force microscopy, providing access to unique instrumentation and expertise that is essential for the project.

WP1. A local description of mechanical activation in molecular crystals	Obj 1	M1-18
T1.3 in collaboration with Prof G Costantini (UoB)		

Aims: To establish and validate an approach to predict local mechanical properties of molecular crystals from their bonding structure, and rationalise the stability of mechanical activation.

T1.1 Growth of suitable single crystals for surface measurements| Single crystals of the model materials will be grown from solution evaporation methods. We will explore the effect of solvent choice and evaporation rates on the

morphologies of the resulting crystals. The quality of single crystals will be verified by polarised microscopy and single crystal X-ray diffraction (SCXRD), both available at UoB free of charge to the project. The morphologies of the single crystals will be characterised using SCXRD for crystal face indexing.

T1.2 Computational descriptors for local mechanical strength| We will leverage our in-house computational frameworks (see Figure 2) to calculate the strengths of individual non-covalent interactions in our model molecular crystals. Our approach requires the calculation of the crystal vibrational frequencies using density functional theory (DFT). Our group has proven expertise doing such calculations,[19,20] making use of the CASTEP DFT code and the extensive high-performance compute facilities at UoB (ca 50k CPUs; free to use for this project). Specifically, we will calculate the mechanical strength of each specific non-covalent interaction (e.g.., hydrogen bond, $\pi \ldots \pi$ interaction, etc), and project these mechanical strengths onto the crystallographic direction that corresponds to the crystal facets identified for each crystal system in T1.1. This will provide us with a descriptor for the molecular-level mechanical strength along the crystal faces that will be subsequently measured in T1.3. We note that while a local description of crystal mechanical properties has not yet been studied in this way, the conceptual framework is analogous to well established methods for calculating bulk mechanical strengths in crystals. This provides us confidence that the proposed approach will yield meaningful and useful results.

T1.3 Measure local mechanical strength and activation stability. We will study single crystals (From T1.1) using high-resolution atomic force microscopy (AFM) available in the Costantini group at UoB, Figure 5. Specifically, we will quantify local mechanical response and activation stability in molecular crystals using AFM-based nanoscale scratching. By performing controlled scratch experiments along distinct in-plane crystallographic directions, we will identify the onset loads for permanent plastic deformation and for fracture-like damage such as chipping, cracking or material removal. Concurrent recording of lateral force signals will enable direction-dependent analysis of frictional behaviour and nanoscale shear response. These experimentally derived anisotropies in plasticity, damage thresholds and shear behaviour will be directly correlated with the computational predictions developed in T1.2. Following deformation, we will monitor the scratched regions by low-load AFM imaging to track the evolution of groove depth, pile-up geometry and any fracture-like features over time. This will allow us to quantify the relaxation or self-healing of mechanically induced defects and, consequently, the stability and persistence of mechanically activated states. The combined assessment of directional mechanical response and post-activation relaxation behaviour will establish a mechanistic basis for understanding how molecular crystals sustain, dissipate or recover from local mechanical activation.

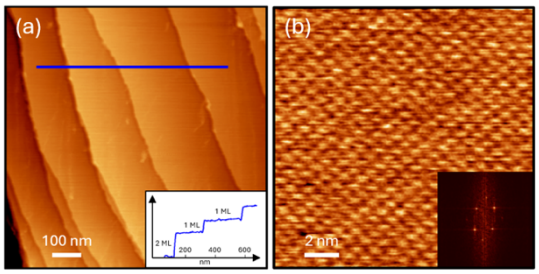


Fig 5. *AFM images of a molecular crystal acquired under ambient conditions. (a) Molecular terraces with heights corresponding to one or two monolayers (ML). (b) High-resolution of the molecular lattice. The inset shows the FFT of the image, highlighting the crystallographic periodicity.*

Principal WP Risks| [R1] Risk: Low, Impact: Low: Discover local mechanical force descriptor does not correlate to the mechanical strength of molecular crystals. Mitigate: From bulk properties, there must be *a* link between these properties. Even a partial correlation is significant improvement on current state-of-the-art. **[R2]** Risk: Low, Impact: high: Access to HPC capability is lost. Mitigation: UoB has extensive compute resource. PI is also member of UK-wide HPC consortia, offering free access to national supercomputers as necessary. **[R3]** Risk: Very low, Impact: low: Access to AFM is lows. Mitigation: Collaboration with Costantini ensures access to AFM. Worst case scenario, mechanical properties are taken unvalidated from computational simulations in T2.2.

Expected Outputs| (M1.1) Manuscript on a new theoretical framework to describe local mechanical properties in molecular crystals, validated against experiment. **(M1.2)** Manuscript on the link between intermolecular bonding and the ease of mechanically activating molecular crystals at the local scale.

Key output leading to WP2-3| Quantification of the local mechanical strength of molecular crystals, and the stability of plastic deformation in these crystals.

Connection to on-going activity in group| T1.2 will build upon on-going activity in my group (another PhD project) to develop computational descriptors for local bonding properties in molecular solids. Together these PhD projects will expand the use of our new descriptor, generating a broader scope of data with which to identify structure-property trends linking local bonding information and macroscopic crystal properties.

WP2. Kinetics of mechanical activation in bulk powders	Obj 2,3	M6-30
WP2 in collaboration with Diamond Light Source (DLS)		

Aims: Establish a link between the local mechanical properties (WP1) of crystals, and the ease of mechanically activating the bulk powder.

Systems: For WP2, we will select from WP1 ~5-10 different crystal systems which show the clearest correlations between bonding descriptors and local mechanical behaviour. We will ensure the selected systems cover a range of hydrogen bonding strengths to maximise the generality of our findings.

T2.1 Rate of mechanical activation from time-resolved *in situ* PXRD and Raman spectroscopy. In our studies we will use crystallite size and microstrain as indicators of bulk mechanical activation. We have recently developed experimental and algorithmic methods to quantifying these parameters from time-resolved *in situ* (TRIS) PXRD data collected at synchrotron sources.[17,18] Using a Fritsch P23 ball mill we will leverage our extensive experience[14,17,21] to build a new set-up at the I15 beamline (DLS) to measure both TRIS PXRD and TRIS Raman spectroscopy data. Initial experiments will use Perspex jars, as is common for TRIS experiments in the community. Using our set-up we will study how ball milling energy – determined by milling ball size/density and milling frequency – influence the evolution of crystal size and microstrain of our model powders during ball milling. TRIS PXRD data will be complemented by tandem TRIS-Raman spectroscopy measurements to help quantify the formation of non-crystalline phases.[22] We expect that crystals most easily activated at the nanoscale (WP1) will also achieve the maximum degree of bulk activation in these TRIS studies. As jar material influences powder behaviour under ball milling,[23,24] we will also perform TRIS PXRD measurements in stainless steel jars using the high energy of the I15 beamline. This will allow us to assess the industrial relevance of results obtained in Perspex jars.

T2.2 The effect of temperature on mechanical activation rates. It is well-known that ball milling at different temperatures can influence the degree of mechanical activation.[25] This is often ascribed to the inability of defects to 'self-heal' at lower temperatures. Using our custom-built[26] temperature controller (temperature control from 0 – 80 C), Figure 6, we will study how temperature changes our ability to mechanically activate hydrogen bonded molecular crystals. For this study we will select from T2.1 a subset of systems, ensuring to include those that are most and least easily activated under ambient temperature conditions. Our priority is to quantify if temperature affects mechanical activation differently in different molecular crystals, or if activation is an intrinsic property of molecular crystals that is only fine-tuned by temperature.

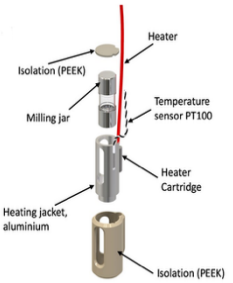


Fig 6. *Schematic of the thermal control jacket for in situ ball milling experiments using the P23 ball mill.*

T2.3 Quantify the stability of bulk mechanical activation. Following our TRIS studies of bulk mechanical activation (T2.1, T2.2), we will investigate the stability of activate powders to aging. A selection of mechanically activated powders (from T2.1) will be loaded into capillaries, and high-resolution PXRD data (either at DLS or using UoB in house diffractometers, free of charge to this project) will be recorded repeatedly over time. This will allow us to track how PXRD patterns – and hence crystallite size and microstrain – evolve as the activated state relaxes. We will additionally explore the effect of temperature on the relaxation rates, using the cryostats that are available at both DLS and on UoB diffractometers. We expect crystals most capable of nanoscale self-heal (WP1) will also exhibit the fastest and most significant recovery at the bulk scale. This study is critical for identifying which samples can be reliably studied ex situ and for understanding how relaxation dynamics influence the functional behaviour of mechanically activated powders.

Principal WP Risks| [R1] Risk: Low, Impact: high: Access to synchrotron beamtime limited. Mitigate: This is very low risk given the co-supervision of the student by DLS beamline scientist. However, Michalchuk is also a Fellow of the German Federal Institute for Materials Research (BAM), providing direct access to the BESSY-II synchrotron, which is also suitable for these measurements. **[R2]** Risk: medium, Impact: medium: We cannot identify any systems that exhibit slow relaxation effects, thereby making any ex situ analysis difficult. Mitigation: This does not make WP3 impossible, but simply reduces confidence in the findings it produces.

Expected Outputs| (M2.1) Manuscript on the relation between local mechanical properties and the ease of bulk mechanical activation. **(M2.2)** Manuscript on the stability of bulk mechanical activation in molecular crystals, and its relation to nanoscale activation stabilities.

Key output leading to WP3| Identify which systems support stable activation states and can therefore be reliably studied *ex situ*.

Connection to on-going activity in group| T2.1 and T2.2 will work within a long-standing collaboration with the Germany Federal Institute for Materials Research (BAM) and University of Cambridge (currently underpinned by a PhD student in my group) to develop technologies to probe mechanochemical reactions in situ. This will enable the current project to leverage and contribute to state-of-the-art developments in this area, enter collaboration with leading experts at DLS, U. Cambridge, and the BAM, ultimately maximising the quality of time-resolved in situ monitoring capability that is available to our wider research programme.

WP3. Quantifying mechanical activation energies	Obj 3	M24-36

Aims: Determine a quantifiable link between local mechanical properties (WP1) of crystals, and the amount of energy needed to mechanically activate the bulk powder.

Systems: For WP3, we will select from WP2 *ca* 5 different crystal systems which include those with varying ease of being mechanically activated. However, we will only select systems whose activation states (T2.3) are sufficiently stable to enable slow *ex situ* analyses.

T3.1 A quantifiable scale of mechanical activation. A major challenge with ball mills is that the ill-defined motion of the balls makes it difficult to quantify how much mechanical energy is in fact being injected into the powder. This makes it difficult to extrapolate quantifiable relations between crystal mechanical properties and the magnitude of mechanical energy being used to activate the system. We will overcome this issue leveraging our long-standing programmes in energetic material research. We will use our impact testing devices (e.g., ball drop) to inject quantifiable, controllable

amounts of mechanical energy into our powder samples. We will systematically inject larger amounts of mechanical energy into the powders (larger balls, higher drop heights, successive drops), and quantify the resulting degree of activation, including by PXRD analysis (crystallite size + microstrain), and from microscopy (optical, scanning electron microscopy, and transmission electron microscopy; all available at UoB with minimal charge to internal users). Our aim will be to correlate the activation process against (1) the activation kinetics observed in T2.1 and (2) the force needed to activate the crystals at the nanoscale (T1.3). (1) will allow us to provide an energy estimation for the P23 ball mill, and hence propose an 'energy-of-activation' scale for all of our TRIS measurements, which will ultimately let us generalise our findings. (2) Will let us establish direct and quantifiable links between molecular bond strengths and the propensity of a molecular crystal to be activated.

T3.2 A quantifiable scale of mechanical activation at variable temperatures. Our impact testing devices are equipped with a thermally controlled sample stage. We will use this to expand on T3.1 by exploring how sample temperature influences the degree of mechanical activation under controlled mechanical loadings. This will allow us to establish semi-quantitative scales for the variable temperature ball milling experiments performed in T2.2 and hence generalise our variable temperature data.

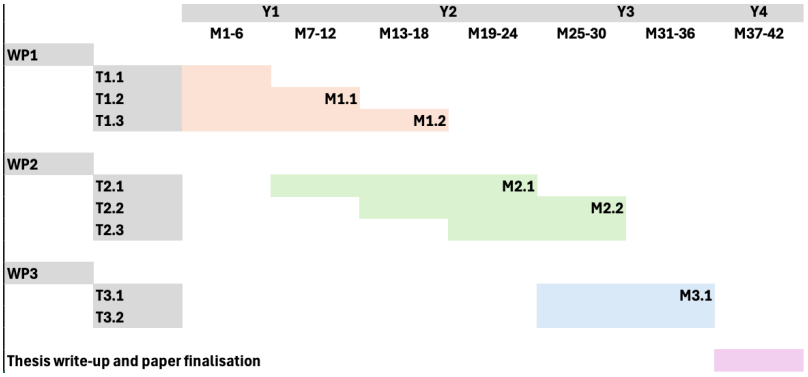
Principal WP Risks| [R1] Risk: medium, Impact: medium: Activation relaxes too quickly in all of our tested systems. Mitigation: This will reduce confidence in our findings, but not preclude our studies. Semi-quantitative correlations will still be possible. **[R2**] Risk: medium, Impact: low: We do not observe a clear relation between the strength of local mechanical descriptors in molecular crystals and the amount of energy needed to achieve mechanical activation. Mitigation: This is a valid outcome to our project hypothesis, and would indicate that much more complex phenomena are at play in determining mechanical activation than are currently understood. This would set the ground work for an entirely new research programme.

Expected Outputs| (M3.1) Manuscript detailing the quantitative link between local bond mechanical properties and the energy needed to achieve mechanical activation in model molecular crystals.

Connection to on-going activity in group| T3.1 and T3.2 will benefit from our extensive on-going activities in energetic materials mechanochemistry, our available equipment, and our expertise in impact sensitivity testing. The use of this equipment for non-energetics research will contribute significantly to our broader understanding of mechanochemical reactivity in molecular crystals, and its predictability. This will have immense impact on our developments of models for mechanochemical reactivity for enhancing industrial safety in the handling of sensitive materials.

Project Timeline

The project is expected to take place over 3 years (start Oct 2026), according to the timeline indicated in the below Gantt chart. Preparation of the manuscripts (outlined in the above WPs) are indicated in the Gantt chart as milestones M1.1-3.1, and follow completion of the appropriate task. As is customary for a UK PhD studentship, the WPs are planned to fit within a 3-year window, with the final 6 months available to mitigate against unforeseen delays in the research, and for the student to finalise work, manuscripts, and prepare their thesis.



OPPORTUNITIES FOR CONTINUATION BEYOND THE 3-YEAR PROJECT

The research activity outlined above lays the foundations to continue exploring the mechanisms and processes of mechanical activation in many different directions, including:

- Quantifying the effect of temperature on mechanical activation. The mechanical properties of molecular crystals are temperature dependent. This can be quantified by variable temperature X-ray diffraction, coupled with simulation of variable temperature mechanical force constants using our local descriptors. By analysing in this way the effects of temperature on molecular crystal behaviours, it should become possible to establish structure-property correlations for the influence that temperature has on the ability to mechanically activate powders.
- We have recently shown that extremely small (μL) quantities of liquid additives can have significant influence on the crystallite size and microstrain of molecular crystals under ball milling conditions.[27] There is not, however, any detailed understanding of why liquids have such drastic effects. To tackle this, it should be possible to perform systematic studies into the effect of liquids on the mechanical activation of molecular crystals, and investigate the effects of liquids on the stability and mechanical properties of molecular crystal surfaces.
- In order to establish a tool-kit that is capable of predicting mechanical activation across the scope of molecular crystals, there will be need to perform a similar study focused on different types of non-covalent interactions. This could include halogen bonding, $\pi \ldots \pi$ interactions, etc, or focus on dimensionality of hydrogen bonding networks. One might also perform similar studies on solvates, exploring the role of solvent inclusions on the local mechanical behaviours of molecular crystals.

ENGAGEMENT WITH IFPRI MEMBERS:

Throughout the programme we would very much welcome collaborative input across the breadth of our activities, including through:

1. Defining model test materials/systems that would ensure our findings are best suited to industrial needs
2. Identifying the mechanochemical conditions typical of industrial processes, ensuring we are exploring industry-relevant conditions
3. Provide guidance on specific tests for mechanical activation that would be meaningful / useful to industrialists. This will ensure our findings and qualifications are most meaningful to industrialists.
4. Where / if possible, provide measurements or data to validate our strategies to predict/control mechanical activation on industrialist 'in-house' compounds. This would greatly broaden our scope of materials being tested beyond our own laboratory.
5. Opportunities for a PhD student to take part in an industrial experience opportunity, for example working on a real mechanical activation problem in industry, leveraging their findings and learning from the project outcomes.
6. Opportunities for the PI to interact with industrialists to gain further insight into the types of mechanical activation problems / settings that are affecting the adoption of mechanical technologies in industry.

ADDITIONAL SUPPORT FOR THE PROJECT

The University of Birmingham (UoB) has committed to provide top-up funding (~£30k) to enable this project to hire a 3.5-year PhD student. A PhD student will maximise the use of IFPRI funding, ensuring there is a dedicated researcher conducting the proposed project. In addition, Diamond Light Source (DLS), the UK's national synchrotron facility, has agreed to co-supervise the PhD student (see Letter of Support). This unique opportunity will enable the project to pioneer new equipment, algorithms, and technologies to track and characterise the mechanical activation of solids in real time, and unique training for the PhD candidate. This will be achieved through in-house commissioning time at DLS (*ca* £10k/day in kind contribution) and the student undertaking extended stays to work alongside DLS beamline scientist (Dr X Liu), who will act as a co-supervisor. The PhD student on this project will therefore be extremely well equipped with unique skills in computational chemistry, crystallography, and national facility research that will make the student a strong candidate to contribute a powerful skillset to industry.

USE OF THE IFPRI FUNDING

An IFPRI contribution of $42k (ca £31k) / year for 3 years will be allocated according to:

Year 1:

- $30k towards PhD studentship
- $4k for chemicals (e.g., powders, solvents), a student laptop, and consumables (e.g., PPE, AFM tips)
- $2k for student and PI travel / stay at Diamond Light Source or industrial visits
- $6k for a dedicated P23 ball mill, suitable for in situ studies.

Year 2:

- $30k towards PhD studentship
- $5k for chemicals (e.g., powders, solvents) and consumables (PPE; in situ milling jars for P23; AFM tips)
- $3k for student and PI travel / stay at Diamond Light Source or industrial visits
- $3k for student to attend conference (e.g., European Crystallography Meeting; European Powder Diffraction Meeting) and training opportunities (synchrotron training schools)
- $1k for speciality measurements (TEM, electron diffraction, etc) to support analysis of mechanically activated materials.

Year 3:

- $30k towards PhD studentship
- $5k for chemicals (e.g., powders, solvents) and consumables (PPE; in situ milling jars for P23, including for variable temperature studies)
- $2k for student and PI travel / stay at Diamond Light Source or industrial visits
- $3k for student to attend conference (e.g., European Crystallography Meeting; European Powder Diffraction Meeting) and training opportunities (synchrotron training schools)
- $2k for speciality measurements (TEM, electron diffraction, etc) to support analysis of mechanically activated materials.

RESEARCH ENVIRONMENT AT UNIVERSITY OF BIRMINGHAM

The project will reside within the *Birmingham Centre for Mechanochemistry and Mechanical Processing (*BCM^2*)*, which includes academics from across the School of Chemistry (Prof T Friscic, Dr D Crawford, Dr E Lu and Dr A

Michalchuk), Chemical Engineering (Prof C Windows-Yule), Mechanical Engineering (Dr J Stafford) and Materials and Metallurgical Sciences (Prof A Morris). By embedding the project in the BCM^2 it will benefit from further discussion and input from a breadth of world-leading researchers, including a current IFPRI academic, Prof C Windows-Yule, thereby enabling the cross-pollination of the institution's research activities. Moreover, by sitting within the BCM^2 centre, the project will have access to a full suite of state-of-the-art mechanochemical instrumentation. This represents approximately £1M in equipment, invested from UoB. In addition, BCM^2 contains the world's only centre for Resonant Acoustic Mixing (an additional £1.5M investment from UKRI and UoB). This will provide plenty of opportunity to explore a range of mechanochemical reactors and their impact on mechanical activation, as required by the project, at no additional charge. All facilities are free to use for academics affiliated within the BCM^2, offering the project the equivalent of approx. **£2.5M worth of access to mechanochemical infrastructure**.

The project will benefit from access to full suite of solid-state analytical equipment, including five powder X-ray diffractometers, two single crystal X-ray diffractometers, and thermal analysis. All facilities are free to use for PhD student researchers within the School of Chemistry. Access to scanning electron microscopy and transmission electron microscopy is available at UoB, with minimal access charge to internal users.

UoB hosts a major high performance computing infrastructure of *ca* 50k CPUs and 400 GPUs, representing over £4M investment by UoB since 2022. Based on expected computations for this project (WP1), using UKRI standard compute costs, an approximate **£500k compute** will be used (free of charge).

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25th November 2025

To whom it may concern,

RE: Support of PhD Studentship – Predictable Mechanical Activation of Molecular Solids

Subject to the final approval of a studentship agreement between the University of Birmingham ("UoB") and the Diamond Light Source Ltd ("Diamond") under its standard terms, please accept this letter as my strongest support for the proposed PhD project, submitted by Dr Adam Michalchuk.

This project aims to understand how mechanochemistry progresses in operando, providing a much-needed insight into the mechanisms underpinning this transformative and sustainable synthesis method. Whilst in situ monitoring has been performed with synchrotron radiation before (including pioneering work by Dr Michalchuk), this has typically been done using X-ray transparent plastic vessels. This is not a realistic experimental condition for real-world applications, and the use of plastic milling vessels has been shown to change mechanochemical transformations. Thus, to obtain accurate measures for mechanochemical processes with direct industrial relevance, in situ monitoring must be done using industry standard steel vessels. This is complicated as such measurements can only be done using extremely high energy radiation, which is uncommon for powder diffraction beamlines.

Diamond is the UK's national synchrotron facility and is a not-for-profit limited company funded as a joint venture by the UK Government as part of UK Research and Innovation (UKRI) through the Science & Technology Facilities Council (STFC) in collaboration with the Wellcome Trust. This studentship will see Dr Michalchuk collaborate with Dr Xiaojiao Liu of the I15 Extreme Conditions beamline at Diamond. I15 provides the high energy, focussed X-ray beams needed to study mechanochemistry under real-world conditions. Dr Liu is a talented beamline scientist with a strong background in structural characterisation at high pressure and method development – they are well placed to play a leading role in the development of new experimental capabilities for time-resolved in situ monitoring of mechanochemical transformations by synchrotron powder X-ray diffraction, and the analysis of this data from mechanically activated powders.

If successful, Dr Liu will support the proposed project by acting as a co-supervisor for the PhD student. This would enable Dr Liu to mentor and train the PhD student in synchrotron powder X-ray diffraction, facilitate access to develop and commission the experimental set-up on I15, host the PhD student for stays at Diamond to work in the development of the beamline set-up and processing of resulting data, and support the student in the preparation of manuscripts and beamtime applications for follow up studies. As such, the resulting PhD student would be extremely well trained in state-of-the-art national facility research with direct application to powder technology and mechanochemical processing, directly feeding the skills pipeline of future industrial scientists. The project is expected to start in the 26/27 academic year and run for 3.5 years, cofounded between the University of Birmingham and the International Fine Particle Research Institution.

Leveraging the specialist capabilities of Diamond's I15 beamline, part of the PhD project will aim to develop the experimental setup and data collection strategies to monitor mechanochemical transformations in real time under real world conditions. In addition, the project aims to modify the beamline's existing on-line Raman spectroscopy system to combine it with X-ray diffraction to provide complementary chemical bonding data. Not only will this lead to new directions for mechanochemical research, but it will also contribute to developing the capabilities of the I15 beamline, thereby expanding the scope of research activities our facility can support. In this respect, the proposed research project will have significant benefit both to the broad mechanochemistry community, and to the international research infrastructure available to users and industrialists at Diamond.

Dr Michalchuk and their group are highly valued users of Diamond. Dr Michalchuk has conducted internationally-competitive research using Diamond facilities via the successful award of beamtime through the peer-review system and they are currently a member of one of the Peer Review Panels which allocates beamtime for Diamond beamlines, an essential service for driving the quality of Diamond's scientific output. This project presents an exciting opportunity to strengthen the links between Diamond and Dr Michalchuk through conducting innovative fundamental research into mechanochemical synthesis while developing world-leading capabilities at the I15 beamline at Diamond. Should you have any questions, please do not hesitate to contact me.

Yours sincerely,

P.A. Chater

Dr Philip Chater, Crystallography Science Group Leader