Understanding and Controlling Crystallisation Across Different Length Scales

Crystallisation underpins the purification and performance of many pharmaceutical compounds, yet its outcome remains highly sensitive to molecular interactions, interfaces, and process conditions. This talk will highlight the Heng group's current activities in crystallisation research across molecular length scales, from small organic molecules to peptides. Emphasis will be placed on how crystal growth, nucleation, and process control can be better understood and manipulated through a combination of targeted experiments and enabling technologies.

Conventional process models rarely account for crystal growth following particle breakage, often leading to unrealistic predictions of crystal size and shape. We have investigated this limitation by reporting the crystal regeneration phenomenon [1], [2], in which organic crystals, such as paracetamol, restore their pre-breakage morphology when fractured along the cleavage plane. These observations reveal a strong coupling between surface energetics, solute–solvent interactions, and previously unreported growth kinetics [3], [4]. Building on this interfacial perspective, the talk will then examine strategies to control nucleation in more complex systems, specifically glycine homo-peptides, using heterogeneous templates such as silica beads [5], [6]. This approach demonstrates how rationally selected nucleants can overcome kinetic barriers to crystallisation, addressing a long-standing challenge in (bio)pharmaceutical systems [7], [8].

Finally, current efforts to translate these fundamental insights into more efficient experimental workflows with the use of fully automated and benchtop semi-automated platforms will be discussed. Overall, this talk aims to shed light on key challenges and emerging opportunities in the crystallisation of organic molecules, spanning fundamental understanding through to advances in pharmaceutical process control.

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[3] I. Bade, D. Etit, and J. Y. Y. Heng, "The effect of solvents on crystal regeneration," 2025

[4] D. Etit, I. Bade, C. T. T. Tan, and J. Y. Y. Heng, "Post-breakage Crystal Regeneration : Multiple Breakage Sites , Growth Kinetics , and Effects on Mass Production," *Cryst. Growth Des.*, vol. 25, pp. 8073–8080, 2025

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[6] M. Guo, M. J. Jones, R. Goh, V. Verma, E. Guinn, and J. Y. Y. Heng, "The Effect of Chain Length and Conformation on the Nucleation of Glycine Homopeptides during the Crystallization Process," *Cryst. Growth Des.*, 2023

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[8] U. V. Shah, C. Amberg, Y. Diao, Z. Yang, and J. Y. Y. Heng, "Heterogeneous nucleants for crystallogenesis and bioseparation," *Curr. Opin. Chem. Eng.*, vol. 8, pp. 69–75, 2015

Short biography

Isha Bade is a Postdoctoral Research Associate in the Department of Chemical Engineering at Imperial College London, UK. Her research focuses on the crystallisation of both small organic molecules and larger (bio)pharmaceutical compounds, with particular emphasis on therapeutic peptides and their fragments, using advanced seeding strategies. She completed her MEng in Chemical Engineering and her PhD at Imperial College London in 2020 and 2025, respectively. Her doctoral work investigated the post-breakage growth mechanisms in macroscopic single crystals, uncovering insights into the phenomenon of crystal 'regeneration'. Isha's contributions have been recognised through multiple awards, including the 2025 Dudley Newitt Award for Experimental Excellence at Imperial College London and the British Association of Crystal Growth (BACG) Young Scientist Award (2025).