Crystal breeding factory uncovered

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A breakthrough in understanding the way in which crystals develop will have a major impact for the pharmaceutical, chemical and food industries.

Lancaster University chemists in collaboration with international colleagues have uncovered a 'Crystal Nuclei Breeding Factory' which, they say, will lead to a more effective and efficient development of quality chemical products.

"Industrial crystallisation is a big, expensive business," explains Professor Jamshed Anwar, from Lancaster University's Chemistry Department.

"Crystal 'seeds' (very small crystals) are added to the process to act as a 'template' to ensure more of the same shape and size of crystals are produced."

"The rule of the garden is…if you sow a single seed you should get a single plant. However with crystals, a single seed causes thousands of new crystals to form, almost as if 'breeding' is taking place. How this happens has never been understood. It's been a big question and it's fundamental."

Previous experiments to understand the issue have been inconsequential as microscopes are just not strong enough to determine what the molecules are actually doing.

Professor Anwar and his colleagues, Dr Shahzeb Khan, of Malakand University, Pakistan, and Professor Lennart Lindfors, of AstraZeneca, Sweden, have 'mapped out' in diagram format the actual movements made by chemical molecules on their breeding journey using computer simulations.

The simulations rely on understanding the 'forces' between the atoms from which they compute what the molecules do, rather like predicting by calculation how a billiard ball is likely to make a break.

The journey involves the chemical molecules in solution forming clusters which, on attaching to the crystal seed surface, form new nanocrystals that are loosely attached to the seed surface.

Fluids, used in the process, shear the weakly tethered new crystals from the seed crystal surface allowing the surfaces to be further available for a repeat process and the new crystals to go on to act as seed crystals themselves.

"This is a big step forward," adds Professor Anwar. "It means that one can intervene in the crystallisation process and actually engineer the shape, size and type of crystals to design.

"For some drugs, having the correct 'handedness' is essential as you need the right key in the lock to make the drugs work. The 'seeding' methodology allows you to separate correct molecules from rogue ones and to do this efficiently."

The breakthrough also sheds light on the long-standing question of how the distinct 'handedness' of molecules of life might have arisen.

Molecules of life exist in pairs that are mirror images of each other. Life forms appear to have selected molecules of only one of these mirror images (known as handedness) – and how this happened has challenged scientists for a long time.

"Something happened early on in life so that one of the molecule mirror images dominated and the whole of life was built on that," says Professor Anwar.

Current ideas are that molecules of one of the mirror images came together and led to a chance formation of a mirror crystal which, subsequently, induced massive crystallisation of the same image.

"Thanks to this study, we now know how such a single crystal seed could have amplified its effect and given rise to thousands of new crystals of the same image," adds Professor Anwar.

More information: "Secondary Crystal Nucleation: Nuclei Breeding Factory Uncovered." *Angew. Chem. Int. Ed.*. DOI: 10.1002/anie.201501216

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