Predicting Particle Properties of Organic Materials using Surface Descriptors

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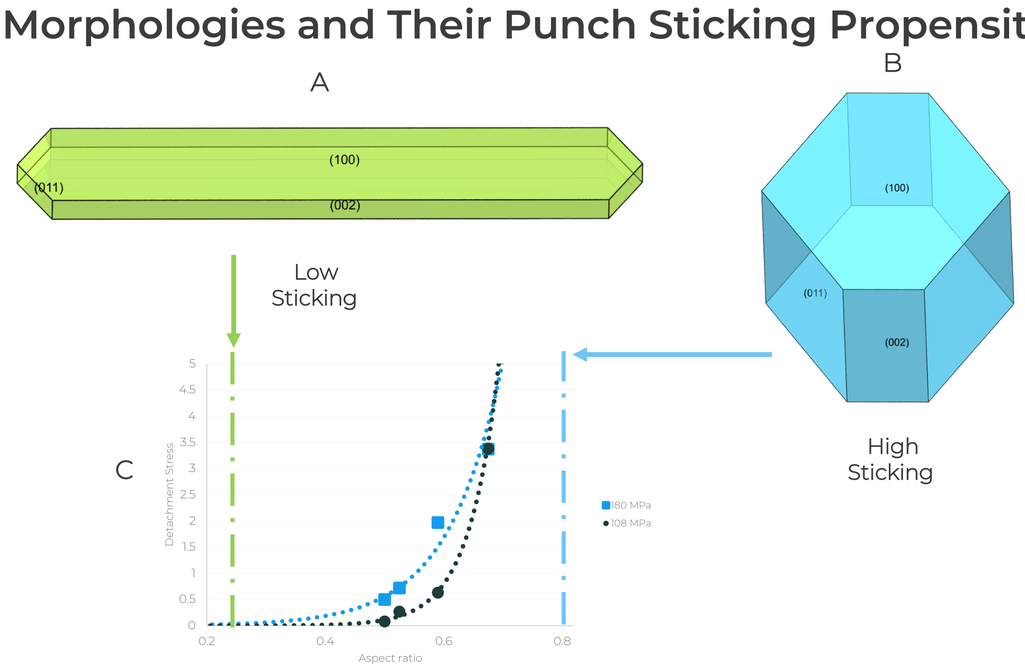
Introduction

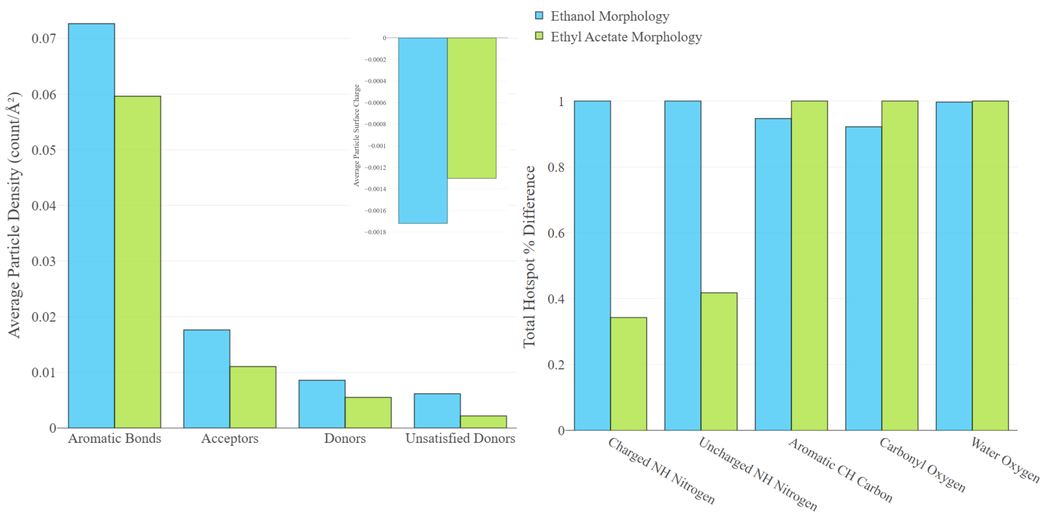
Particle properties are responsible for a large number of manufacturing and product performance issues within the formulated product industries, such as fast-moving consumer goods, pharmaceuticals, agrochemicals, and dyes[1]. The surface chemistry and roughness of particulates can influence processing qualities such as flow, hygroscopicity, packing, and sticking. Understanding these particle properties plays a crucial role in formulation decisions and typically requires extensive trial and error studies with a high material cost. Here we show new tools for calculating and visualising surface properties, including the chemistry, roughness and potential interactions preferences. We then aggregate the facet descriptors to describe experimentally observed particles and their propensity to stick to punch presses during tabletting.

Morphologies and Their Punch Sticking Propensity



Morphology representations based on facet growth data from Cano *et al.*[2] for particles grown from ethyl acetate (A) and ethanol (B). Punch sticking propensity plotted against the aspect ratio of Ibuprofen (C) reported by Hooper *et al.*[3], the more regular block shape was measured to stick more to a punch press.

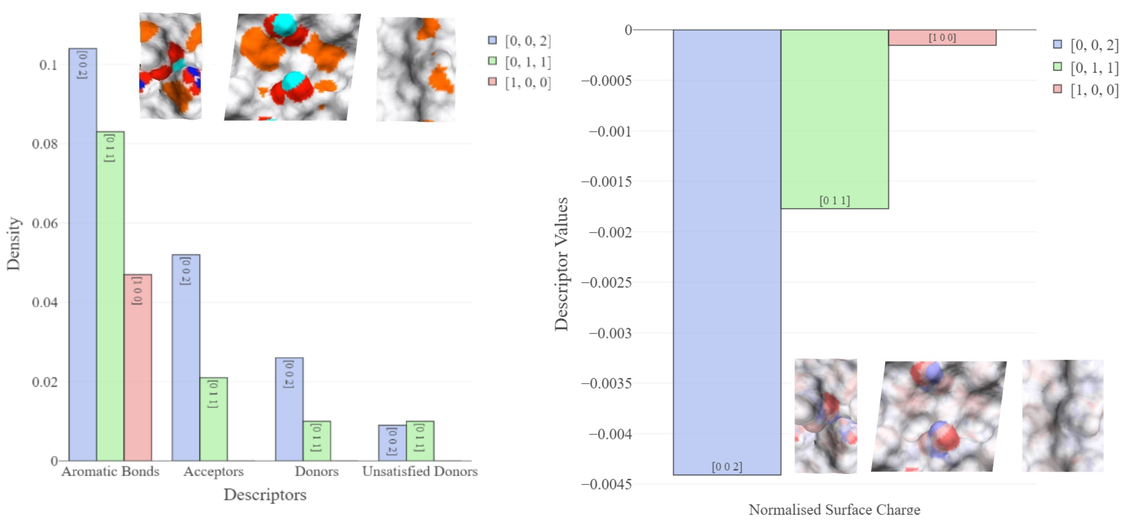
Particle Properties



Average particle properties based on the morphologies reported by Cano *et al.* [2]

- (Left) Illustrates that the ethanol-based morphology has a higher density of H-Bond donors/acceptors and more negatively charged particles.
- (Right) Donor-based probes have a probability of interacting with ethanol-based morphology, indicating an affinity towards positively charged surfaces.

Analysing All Surfaces



Surface descriptors of all facets.

- (Left) Showing that the {100} is the least chemically active.
- (Right) {002} is predicted as the most negatively charged surface.

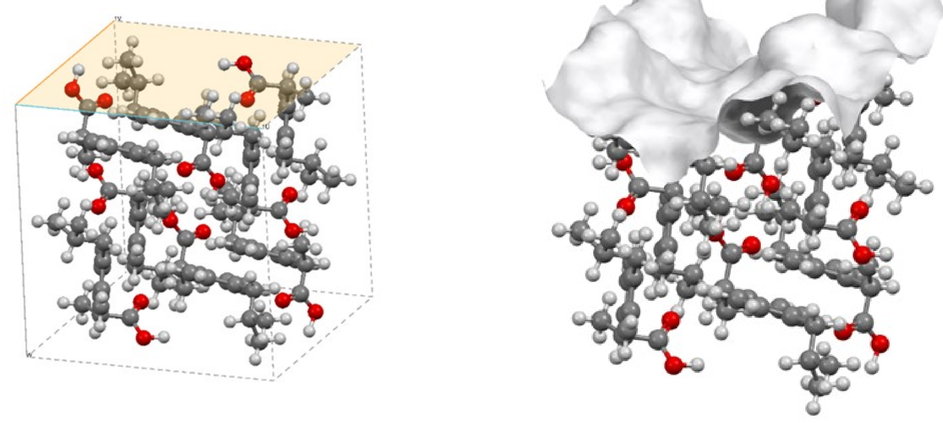
Conclusions

We present new surface analysis tools that enable the visualisation and quantification of chemical and topological information derived from crystallographic data. By utilising functional group analysis, roughness calculations, and interaction informatics, we have demonstrated how this approach can represent surfaces, allowing for straightforward comparisons between them.

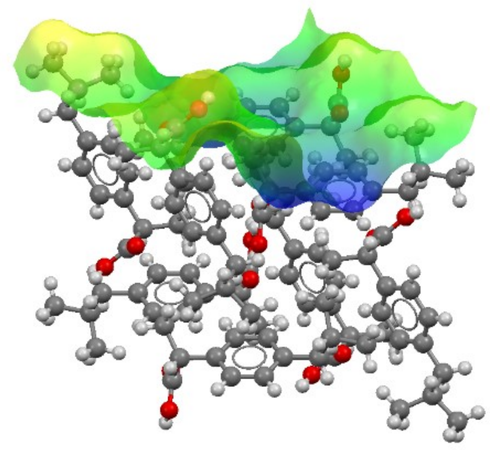
References

1. Seville JPK, Wu C-Y. Particle Technology and Engineering. **2016**.
2. Cano H, Gabas N, Canselier JP., *Journal Crystal Growth*, **2001**; 224:335–41.
3. Hooper D, Clarke FC, Docherty R, Mitchell JC, Snowden MJ. *International Journal Pharmaceuticals* **2017**;531:266–75.
4. J.F. McConnell, *Crystal Structure Communication* **1974**, No. 3, 73.

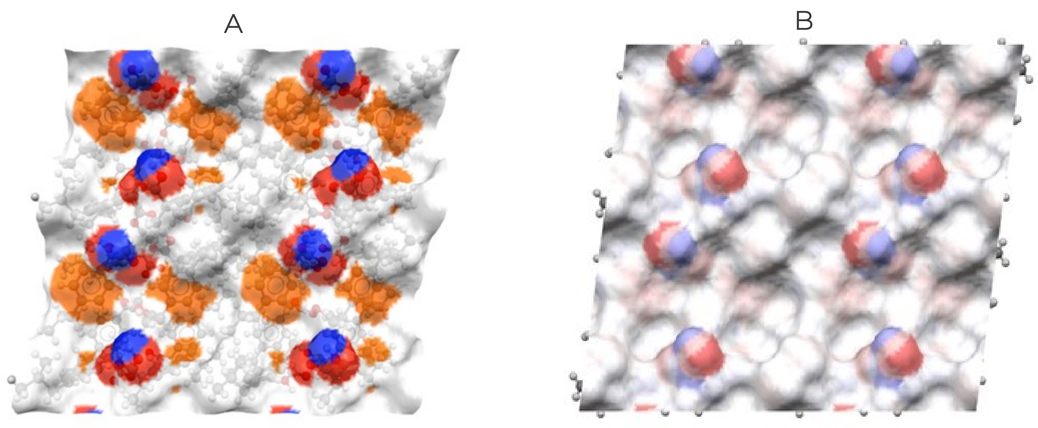
Surface Analysis – The case of {011}

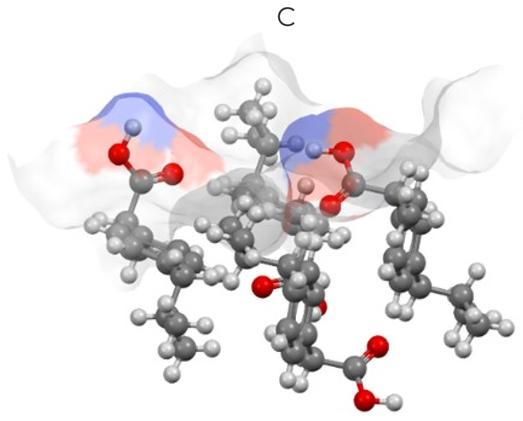


Ibuprofen[4] surface {011} (Left) The periodic boundary for surface generation. (Right) Topology representations.

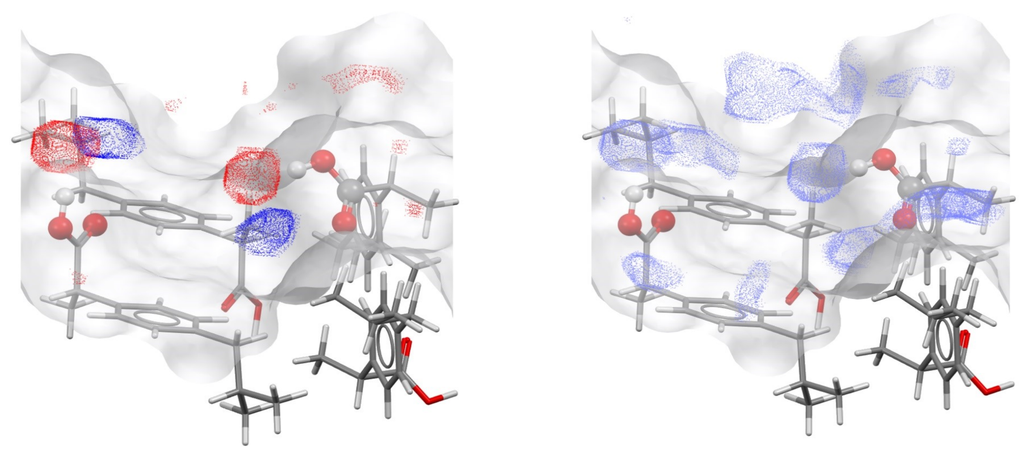


Topological representation coloured by height deviation from the mean plane.





(A) Surface chemistry of hydrogen bond donors (blue), acceptors (red), and aromatic bonds (orange). (B) Distribution of surface charge. (C) The image focuses on the carboxylic acid group with hydrogen bond donors and acceptors highlighted.



Possible interaction on the surface from derived Crystallographic Structural Database (CSD) interactions (Left) for carbonyl oxygen (red), uncharged NH (blue) probes. (Right) water oxygen probes (light blue).

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