Poster Presentation

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Solid-to-solid polymorphic transitions in amino acid crystals

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The properties of crystals are related to their structure and therefore they can be different for different polymorphs. For example, the pharmaceutical characteristics bioavailability and shelf life can depend on the formed polymorph and its stability. We aim to understand transitions between polymorphs that occur in the solid phase, with the ultimate goal to induce or inhibit these transitions. We apply Molecular Dynamics (MD) simulations as a computational microscope to study these processes at the molecular level. Our used model systems for polymorphic behavior of molecular crystals in a pharmaceutical context are amino-acid crystals, in particular DL-norleucine. The polymorphs of DL-norleucine consist of tightly packed hydrogen-bonded bilayers with straight side chains that are weakly bound through Van-der-Waals interactions. When DL-norleucine undergoes a polymorphic transition, the bilayers shift with respect to each other. In the simulations of the enantiotropically-related beta and alpha polymorph, we observe that the transformed lattice parameters and molecular properties behave identically with temperature for both polymorphs. Consequently, the polymorphs only differ in the orientation of the molecular bilayers in the a'c' and the b'c'-plane, which explains the ease of transitions between them. Moreover, in simulations of the beta polymorph at 350 K we observe partial phase transitions which we could follow with the help of specifically designed order parameters. The transitions are exclusively occurring in the b'c'-plane. This indicates a possible transformation mechanism in which first shifts of bilayers occur in this plane, followed by shifts in the a'c'-plane. Interestingly, the region of highest flexibility of the molecule shifts from the middle to the end of the carbon chain at the highest studied temperature.

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