Bridging the gap between MD and DEM:
Modeling functional particles for biotechnological applications

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Particle systems are present in many applications of biotechnology and process engineering and the physical phenomena involved therein often spread over vast scales of size and time. Depending on the scale of interest, various models have been developed. These models are typically in the DEM framework for traditional applications (>10µm) or the MD framework for nanoparticle applications (typically <100nm). However, models bridging the gap between the two regimes are rather scarce and will be addressed in this contribution. These scales are especially interesting for biological systems (e.g. enzyme structures) which can be looked at as functional particles with interesting properties concerning their interaction, structural formation, and reactive properties. Such systems have received increasing interest in recent years [1] and as they are difficult to investigate experimentally in detail [2], the need for modeling techniques on this scale is driven.

To gain insight, we develop models to transfer the essential dynamics and complex interaction from MD to DEM (see Fig. 1) in a modeling methodology termed by us the molecular discrete element method "**MDEM**". In the targeted regime between 100nm and 10µm diffusive effects are significant and interaction of particles can be anisotropic (influenced by e.g. shape, electric charge). To capture this, we developed a force-based diffusion model for DEM [3] and complex data-driven interaction models derived from MD [4-6] (both atomistic and coarse-grained) simulations. The diffusion model [3] is generally applicable to any diffusive process in DEM to enforce a canonical ensemble (i.e. constant temperature) and additionally enables a coupling to CFD. The models are parameterized "bottom-up" and validated "top-down" by comparison with experimental data, which is obtained from biolayer interferometry (BLI) and dynamic light scattering (DLS). As a model system the multi-enzyme Pyruvate Dehydrogenase Complex (PDC) is used, as it features organized self-structuring processes and a highly regulated multi-enzymatic machinery dependent upon the structure.

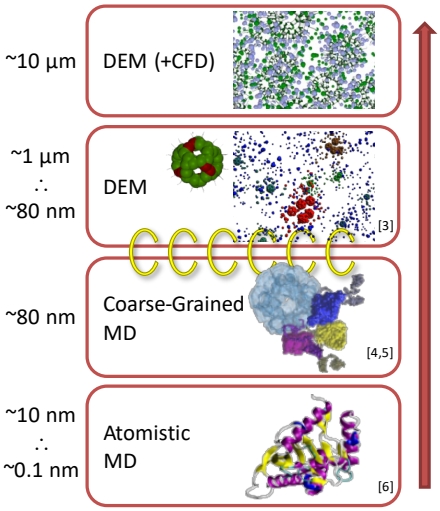

Figure 1: Multiscale modeling methodology

Obtained results for the PDC component E2 (with linker arm) show that the continuous formation and breakup of enzymatic agglomerates (typically between 50 – 70nm) can be predicted using the developed MDEM methodology [3]. This approach requires no experimental data fitting and produces accurate scale-bridging kinetics as well as agglomerate sizes matching corresponding dynamic light scattering data (75.2 nm ± 10.4%) [2].

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