Qeios

Peer Review

Review of: "Unified Guidance for Geometry-Conditioned Molecular Generation"

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This paper introduces UniGuide, a unified framework for molecular generation by controlling unconditional diffusion models with geometric conditioning during inference . UniGuide achieves performance comparable to or better than specialized models on structure-based, fragment-based, and ligand-based drug design tasks.

While extensive experiments were done and demonstrated the effectiveness of the method, it is unclear to me how generalizable and resource efficient this method is. The authors claim “UniGuide eliminates the need for additional training”, while later in the text the authors also mentioned “UniGuide requires the unconditional model to be trained on a matching configuration space.”. From App. D, it looks like it does require separate models for SBDD/FBDD and LBDD tasks. Under what circumstances does one need separate unconditional models and when can a model be re-used? How much additional trainings can be reduced under these constraints? It would also be helpful to outline the training cost of UniGuide v.s. baseline models for individual tasks.

Additionally but non-blocking, it would be interesting if the paper could explore the impact of cross-domain data on the generation quality of the underlying unconditional model. As we all know biological domain is sparse in data, when training the underlying unconditional model, does adding additional data from other domains helps improve generation quality? It would be greatly helpful for research areas with less data, such as RNA-based drug design if this is true.

Overall interesting concept though somewhat overstating on generalizability. The authors demonstrate promising results on several tasks, suggesting the potential for broader applications in drug discovery.

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Declarations

Potential competing interests: No potential competing interests to declare.