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Accelerating molecular design using deep generative models

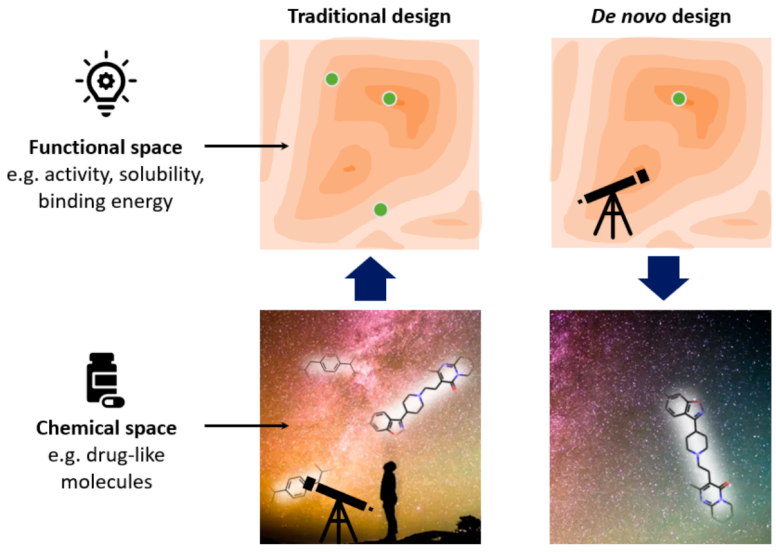
1-2 pm PST Monday August 16th, 2021
Zoom link is provided via email, or contact dyss@uw.edu

Bio

Rocío is currently a postdoc in the Molecular Artificial Intelligence team at AstraZeneca, where she has been since October 2018. Her work focuses on using deep learning methods for de novo molecular design. Before AstraZeneca, she was a PhD student in Professor Berend Smit's group at UC Berkeley and EPFL. While there, her research focused on using molecular simulations for materials discovery. Rocío received her PhD in Chemistry from UC Berkeley in August 2018. Before her PhD, she spent a few years doing undergraduate research in Professor Harry Gray's lab at Caltech, where she received her BS in Chemistry in June 2013. In August 2021, Rocío will be starting a postdoc in the MIT Department of Chemical Engineering. Her research interests lie at the intersection of chemistry and artificial intelligence for molecular discovery, with a recent focus on small molecule drug design.

Abstract

Drug discovery and development is a highly complex enterprise, where non- clinical programs such as hit discovery and lead optimization typically take up a few years in the early stages of a drug development project. Recent research at the intersection of artificial intelligence (AI) and medicinal chemistry suggests that the integration of **deep molecular generative models** in early drug development pipelines could reduce the time from target identification to market. In this talk, I will dive into the field of deep molecular generative models and show how they are promising tools for ***de novo* molecular design**. *De novo* design methods stand in contrast to high-throughout screenings, where a lot of effort is spent discovering largely inactive compounds (see figure). Instead, AI-based generative models are able to learn chemical rules and *only* generate molecules which optimize over desired constraints (e.g. high activity/low toxicity), thus concentrating the efforts on more promising compounds.
Deep molecular generative models generally leverage tools from graph theory and natural language processing to traverse the functional space in search of promising new molecules. Recently, my team and I introduced a platform for **graph-based molecular design**; this platform is called GraphINVENT and uses a tiered deep neural network architecture to probabilistically generate new molecules a single atom/bond at a time. Our graph-based models have been benchmarked and compared against other state-of-the-art models using various distribution-based metrics for molecular design, including the coverage of chemical space, and demonstrate competitive performance. Nonetheless, we are actively working to build and improve upon current deep molecular design methods. I will end my talk by comparing the advantages and disadvantages of existing models, and by discussing two major limitations many molecular generative models share (low synthetic feasibility, neglect of 3D information) and how to address them.



While the talk itself will focus on computational drug discovery, the methods I will talk about are relevant across a range of disciplines, from small molecule design, to materials design, and even polymers/protein design.