

Taking inspiration from nature: computational transition state analogue design

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Kuano is a hybrid biotech / AI company looking to develop better drugs by using state of the art technologies to accelerate and refine an methodology known as transition state analogue design. This approach is based on the concept that the quantum chemistry of enzymes makes use of incredibly tightly bound states (Transition States) to accelerate chemistry - with the speed of the reaction depending on the strength of the binding. Each enzyme is shaped by evolution within a particular environment leading them to use unique Transition States. Most drugs targeting enzymes block their function by binding to the same site as the input chemicals meaning that this configuration can be used as a template for drugs with incredible strength and specificity. As 40% of all marketed drugs target enzymes this is a highly attractive method to design new therapeutics. We use quantum simulations to model the enzyme reactions and AI approaches to generate stable chemicals that mimic the Transition State.

We face three main challenges in taking this approach; 1) accurately capturing the quantum mechanism of enzymes, 2) enabling compute intensive simulations in an affordable and efficient manner and 3) obtaining druglike molecules that match the transition state from AI approaches. In this talk we describe how we have tackled these issues in our first internal project - which targets a metalloprotease. This project brings together hybrid quantum-classical (QMMM) simulations with our in-house generative AI, and has even inspired us to experiment with cutting edge quantum computing inspired approaches.