Dose-Dependent Bioactivity Disruptions and SPARFlow: From a Conceptual Challenge to a Methodological Tool

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Abstract

Biological activity is not solely structure-dependent and, beyond classical dose–response behavior, can exhibit dose-driven disruptions—abrupt, nonlinear changes in potency or even in the type of biological activity. This phenomenon constitutes an inherent blind spot in conventional structure–activity modeling. Our recent work formalizes this concept and examines its implications for predictive modeling, emphasizing the need to integrate dose–response context into cheminformatics [1]. In parallel, we developed SPARFlow, a transparent workflow designed to ensure reproducibility and standardization in model construction [2]. Although the conceptual and methodological foundations are established, progress toward quantitative implementation remains limited by the scarcity of harmonized multi-dose datasets—a community-level challenge that must be addressed to achieve truly dose-aware predictive modeling.