Petri Nets as a Unifying Tool to Link Physiologically Based Toxicokinetic (PBTK) Models to Adverse Outcome Pathways (AOPs)

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Physiologically Based ToxicoKinetic (PBTK) Models and Adverse Outcome Pathways (AOPs) are common tools used in predictive and computational toxicology. PBTK models are used to predict internal tissue concentrations of a contaminant in an organism from various exposures. AOPs, on the other hand, describe a pathway leading from a molecular initiating event to an adverse outcome, ie. inhibited growth. While these tools are complementary, there has yet to be a unifying tool to link the two. PBTKs are generally written as a system of ordinary differential equations (ODEs), while AOPs may consist of various underlying models. We present Petri Nets (PN) as a way to quantitatively link PBTKs to AOPs, providing a complete exposure to outcome model. As an example, we quantify waterborne antidepressant exposure in hybrid striped bass (HSB) and the resulting inhibition of time to capture prey.