

CoRa —An approach for quantifying feedback control in biomolecular systems

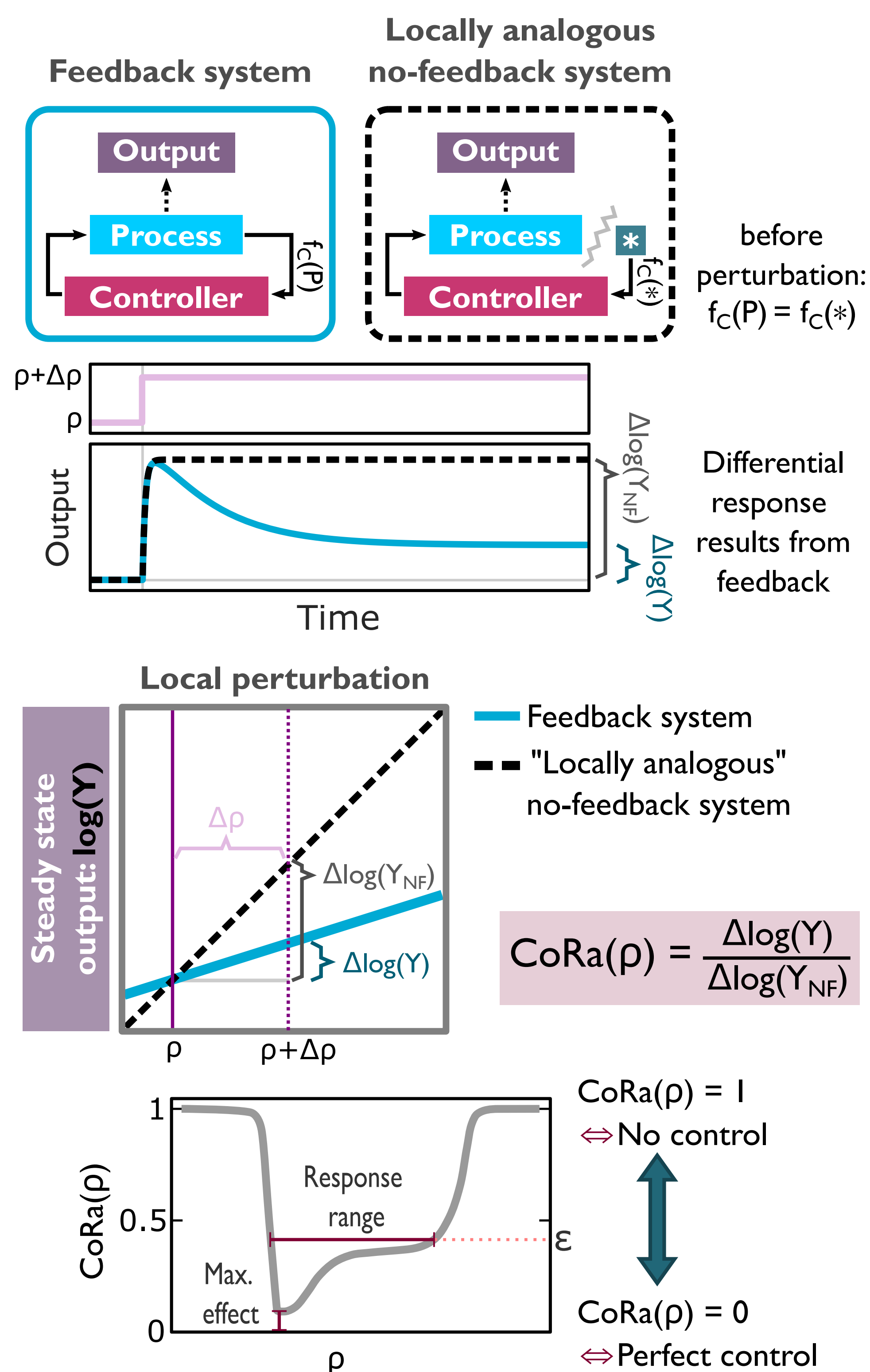
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Abstract

Feedback control is ubiquitous in biomolecular networks, being the mechanism behind homeostasis and biochemical adaptation. The ability to rigorously evaluate the contribution and limitations of feedback control mechanisms is a critical step to meaningfully understand and ultimately design feedback control systems in biomolecular contexts. Here, we introduce **CoRa** –or **Control Ratio**–, a metric that quantifies the advantage of a feedback control system compared to a series of “locally analogous” systems without feedback, such that the internal states of the two systems with and without control are identical without perturbations. CoRa is then computed by perturbing both systems and scoring the difference in their behaviors. In this way, CoRa effectively isolates and measures the contribution of the feedback control, while considering the impact of all the intrinsic biomolecular constraints of the system. We demonstrate through examples that CoRa is a powerful tool to characterize, compare, and design controllers in biomolecular contexts.

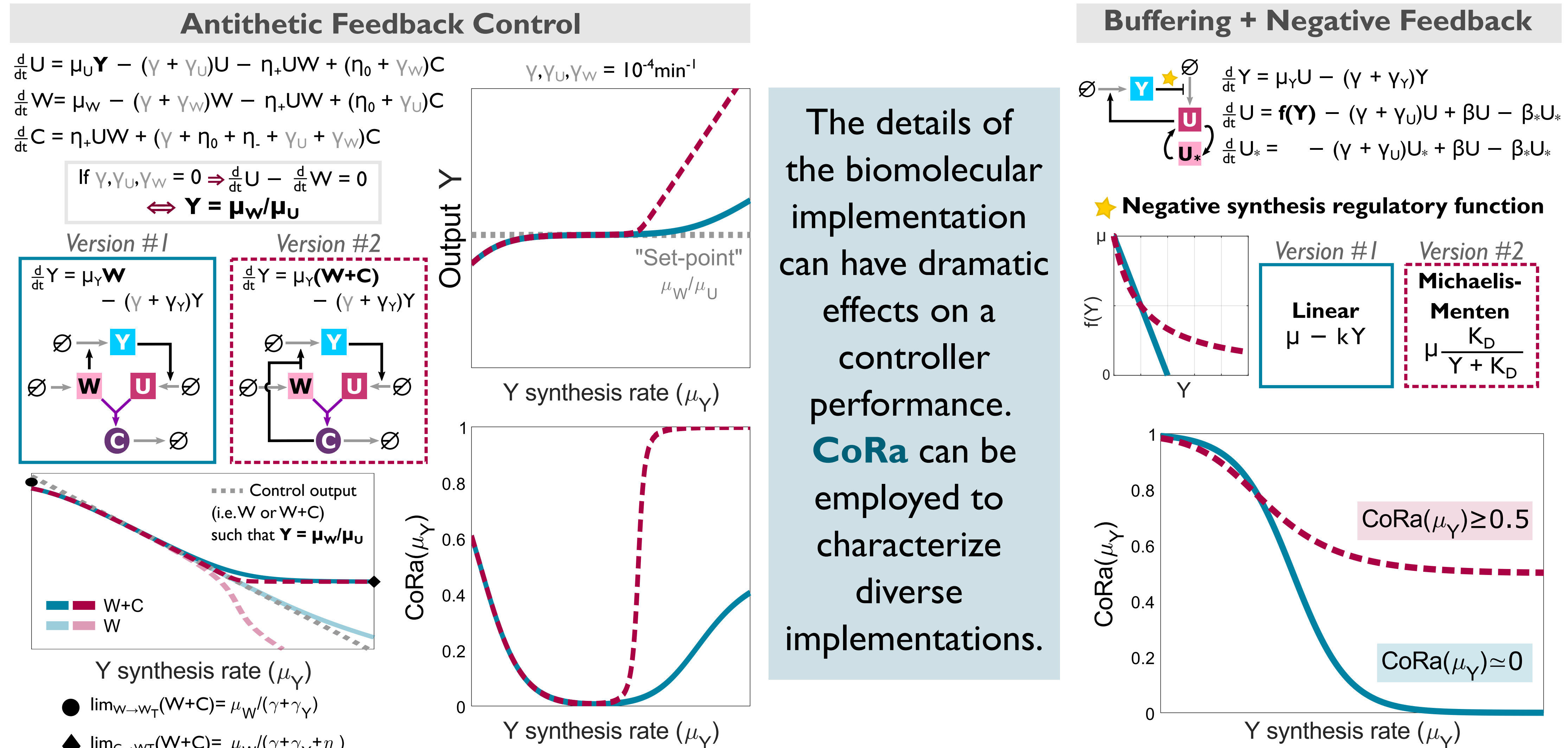
The CoRa concept



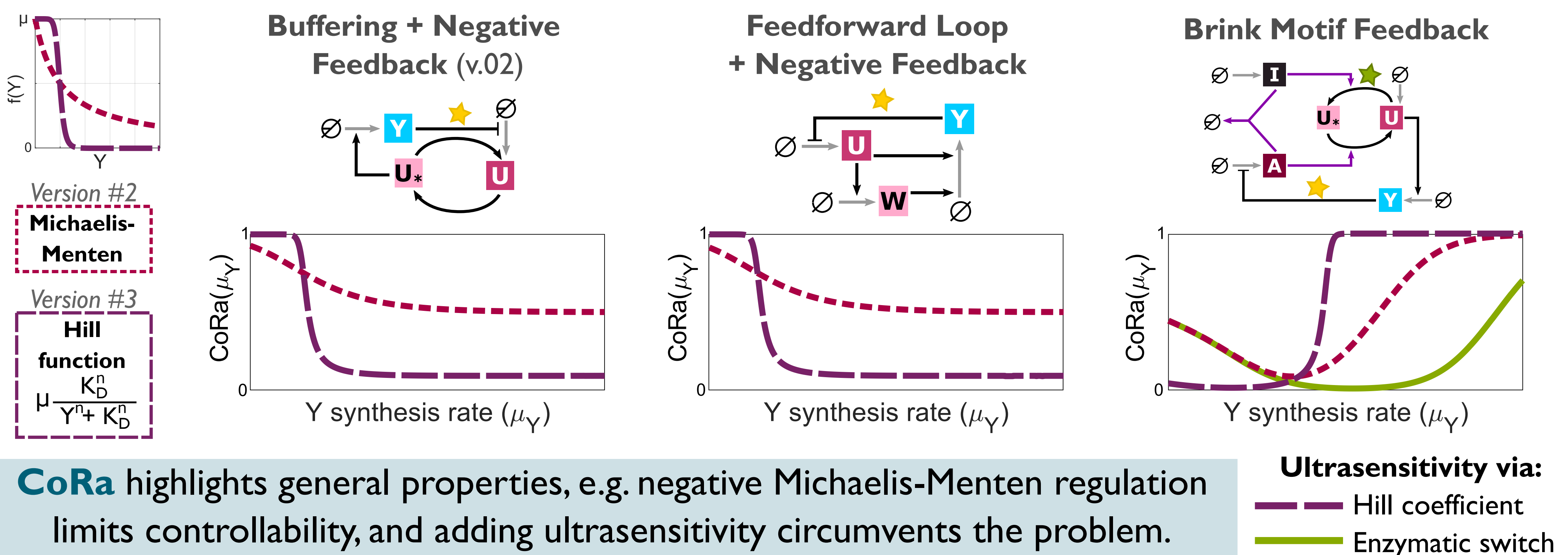
CoRa is INFORMATIVE, EASY-TO-INTERPRET, & provides a UNIFYING FRAMEWORK to quantify feedback control in biomolecular systems

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CoRa application #1: characterizing control systems

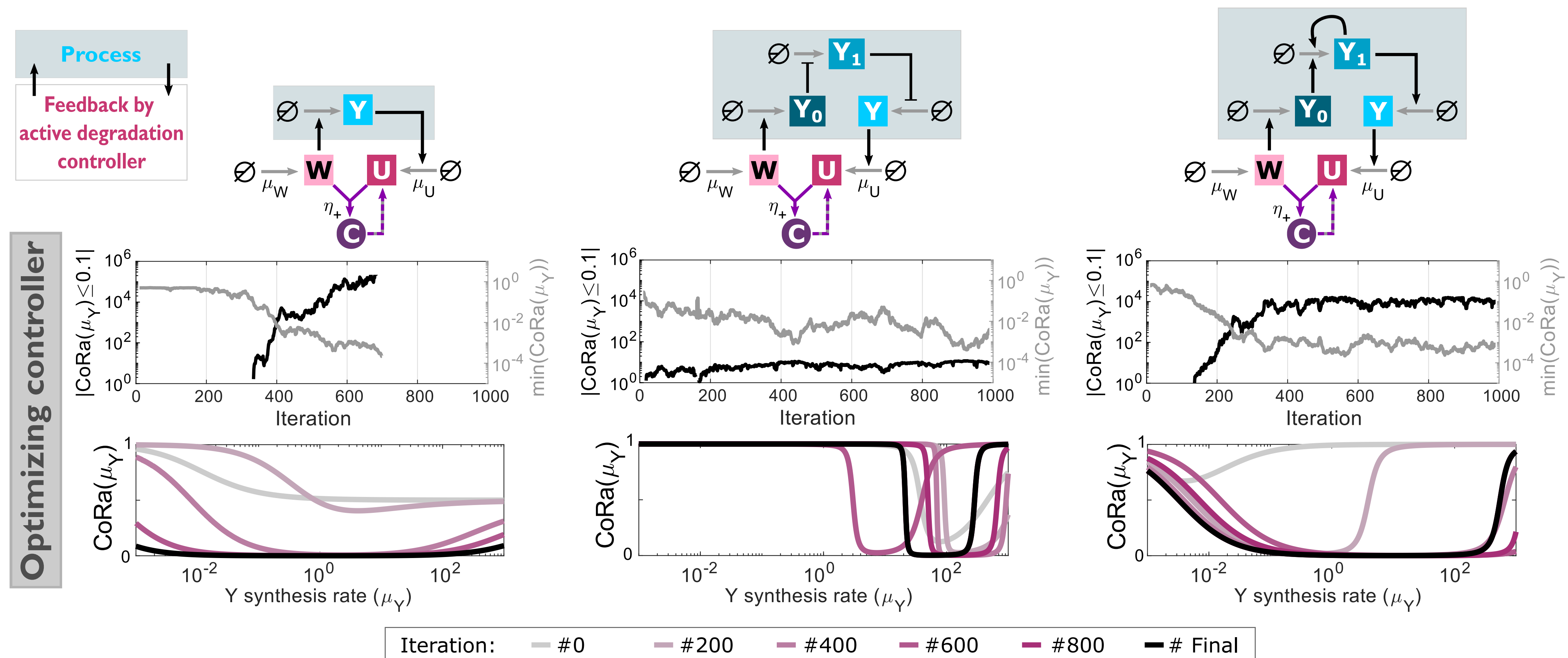


CoRa application #2: comparing controller motifs



CoRa application #3: designing biomolecular controllers

Processes of increasing complexity can be tackled with **CoRa**.



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