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Sensitivity Trade-offs in Systems Biology

The stabilizing effect of negative feedback is key to biological self-regulation (homeostasis). Feedback allows a system to maintain its preferred behaviour in an unpredictable environment. The prevailing wisdom is that negative feedback typically stabilizes a system (making it less sensitive to external perturbations), while positive feedback is destabilizing (i.e. it increases sensitivity). Of course, negative feedback can also generate instability, for example in producing oscillations. However, even when acting to improve a system's robustness, negative feedback typically redistributes sensitivity within a network, rather than directly reducing it. In some cases, this redistribution is governed by an explicit constraint: a conservation of sensitivity. This talk will introduce sensitivity conservation statements commonly used in control engineering and molecular systems biology, and introduce a unifying formulation.