

Effect of biphasic interactions on integral feedback control motif response

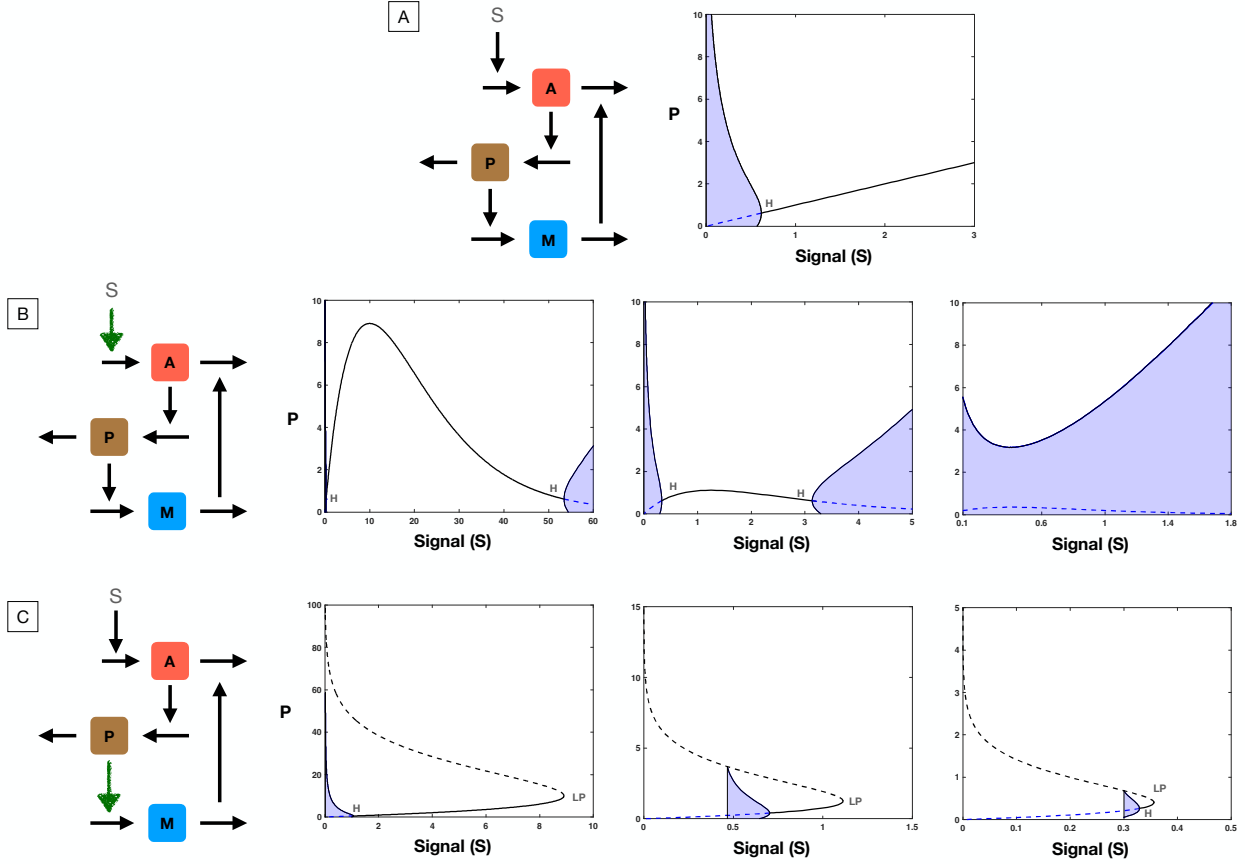


Figure 3 – figure supplement 2: **Effect of biphasic response in interactions within integral feedback control motif:** perturbation of expected homeostatic response. The simple integral feedback control motif is capable of exact homeostasis in the substrate form M , as signal (S) and substrate forms P and A change (see plot A, M not shown). The lower regions of signal activation are unstable for the system and oscillate. There exists a threshold of signal above which the single steady state is stable and there is steady exact homeostasis in M . In plots B and C we show how expected response from the motif can be affected by 1. biphasic signal regulation (B), 2. biphasic response in an interaction within the motif (C)). B shows how upstream biphasic signal regulation can diminish the range over which stable steady state homeostatic response is seen (in concentration of M - not shown), by making the system unstable through a hopf bifurcation leading to oscillations, for both low signal and high signal ranges. Depending on the nature and strength of the biphasic signal regulation (manipulated here by changing parameter values associated with the signal regulation), the stable steady state regime in signal can diminish and for a sufficiently strong biphasic signal regulation, the system can be completely unstable, completely undermining the exact homeostasis expected in M from the motif. C shows how biphasic responses in an interaction within the motif (indicated in the adjacent schematic with a brown arrow) can further arrest the expected biphasic response by ‘capping’ the signal range over which the motif can function (due to the saturating effect from the biphasic response - see text). Further, the steady state of the system can lose stability even for lower signal ranges (on the existing stable branch), due to oscillations. Thus, biphasic interactions within even a robust homeostatic motif such as integral feedback control can fundamentally subvert expected motif response. [Brown arrows in the network schematics represent biphasic interactions. LP: saddle node bifurcation. H: Hopf point bifurcation. Solid lines and dotted lines denote steady and unstable steady states respectively. Regions shaded in blue represent oscillations.]