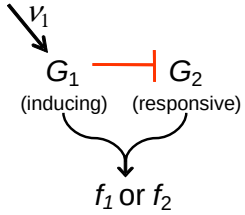
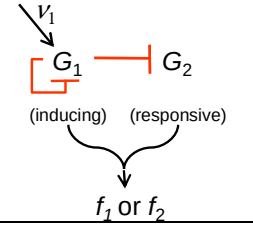
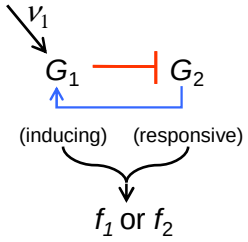
Table 3: Properties of RBCs

Motif names	**Model**	**Function I** $f_1 = G_{1st} \times G_{2st}$	**Function II** $f_2 = G_{1st} + G_{2st}$	**Susceptibility,** $\left(\frac{\nu_1}{f_2}\frac{\partial f_2}{\partial \nu_1}\right)$* * The susceptibility to fluctuations in the production rate of G_1	**Constants**
Motif I simple repression		$\nu_2 K_{12}$	$\nu_1 c_1 + \frac{1}{\nu_1} c_2$	$\frac{\nu_1^2}{\nu_1^2 + c_2} - \frac{c_2}{\nu_1^2 + c_2}$	$c_1 = 1$ $c_2 = \nu_2 K_{12}$
Motif II dampened controller		$\nu_2 K_{12}$	$\sqrt{\nu_1} c_1 + \frac{1}{\sqrt{\nu_1}} c_2$	$\frac{1}{2}\left(\frac{\nu_1}{\nu_1 + c_2^*} - \frac{c_2^*}{\nu_1 + c_2^*}\right)$	$c_1 = \sqrt{K_{11}}$, $c_2 = \nu_2 K_{12}$ $c_2^* = \frac{c_2}{c_1}$
Motif III cycled feedback		$\nu_2 K_{12}$	$\sqrt{\nu_1} c_1 + \frac{1}{\sqrt{\nu_1}} c_2$	$\frac{\nu_1}{\nu_1 + K} - \frac{K}{\nu_1 + K}$ * Simplifications: 1) $K_{12}=K_{21}=K$ 2) $G_1, G_2 >> K$	$c_1 = \sqrt{\nu_2}\sqrt{\frac{K_{12}}{K_{21}}}$ $c_2 = \sqrt{\nu_2}\sqrt{K_{12} K_{21}}$

All formulas in the table were calculated based on the simplifying assumption: K12<<G1. For detailed calculation of solutions, with and without this simplification, see supporting text.

*Analysis was exclusively limited to the three RBC circuitries that fulfill both criteria of (*i*) maintaining negative feedback and (*ii*) can be modeled with no more than two free variables.

G_1	Controller gene.	α	Degradation rate
G_2	Responsive gene	K_{IL}	Thermodynamic dissociation constant between protein 'I' and its cis-regulatory motif on gene 'L'
β	Transcription rate	$\nu \equiv \frac{\beta}{\alpha}$	maximal steady state concentration

One observation that is immediately apparent from examination of the results in table 3 is that the product of the concentrations of the two redundant proteins is insensitive to variations of the controller, G_1 (G_1x G_2 does not depend on ν_1, the maximal production rate of G_1). One important aspect of this result is its generality as it extends beyond the scope of RBCs and may hold true for complexes or heterodimers given that one monomer with these complexes negatively regulates the rest [as may be the case for some heterodimers (see HN-S/StpA, table 1)]. An interesting question stemming from this result is what are the functional advantages that are associated with this property? One attractive possibility is that this regulatory design masks the function from dosage fluctuations of the controller. In contrast to this circuits' intolerance to G_1's deletion, it is highly robust to variations in G_1's dosage (as long as it is kept above zero).