SUPPORTING MATERIAL

Analysis of the linearized dynamics

In Fourier space (where $\widehat{a}(\omega)$ denotes the Fourier transform of $a(t)$) the dynamics defined in Eq. (5) of the Main Text takes the form

$$
\begin{aligned}
i\omega\widehat{x_i} &= -d_i\widehat{x_i} + \widehat{b_i^o} - k_i^+([\mu]\widehat{x_i} + [m_i]\widehat{y}) + k_i^-\widehat{z_i} \\
i\omega\widehat{y} &= -\delta\widehat{y} + \widehat{\beta_o} - \sum_i k_i^+([\mu]\widehat{x_i} + [m_i]\widehat{y}) + \sum_i (k_i^- + \kappa_i)\widehat{z_i} \\
i\omega\widehat{z_i} &= -(\sigma_i + k_i^- + \kappa_i)\widehat{z_i} + k_i^+([\mu]\widehat{x_i} + [m_i]\widehat{y}) \quad ,
\end{aligned}
\tag{1}
$$

and leads to the following equations:

$$
\begin{aligned}
\widehat{x_i}(\omega) &= \frac{\widehat{b_i^o} - k_i^+\Gamma_i(\omega)[m_i]\widehat{y}}{\mathrm{i}\omega + d_i + k_i^+[\mu]\Gamma_i(\omega)} \\
\widehat{y}(\omega) &= \frac{\widehat{\beta_o} - [\mu]\sum_i k_i^+\Lambda_i(\omega)\widehat{b_i^o}}{\Delta(\omega)} \\
\widehat{z_i}(\omega) &= \frac{k_i^+([\mu]\widehat{x_i} + [m_i]\widehat{y})}{\mathrm{i}\omega + \kappa_i + \sigma_i + k_i^-} \quad ,
\end{aligned}
\tag{2}
$$

where

$$
\begin{aligned}
\Gamma_i(\omega) &= 1 - \frac{k_i^-}{\mathrm{i}\omega + \sigma_i + \kappa_i + k_i^-} = \frac{\tau_{2,i}(1 + \mathrm{i}\omega\tau_{3,i})}{\tau_{3,i}(1 + \mathrm{i}\omega\tau_{2,i})} \\
\Delta(\omega) &= \mathrm{i}\omega + \delta + \sum_i k_i^+[m_i]\left(1 + \frac{[\mu]}{\mu_{0,i}Z_i(\omega)}\right)^{-1}
\end{aligned}
\tag{3}
$$

$$
\Lambda_i(\omega) = \frac{\sigma_i}{d_i(k_i^- + \kappa_i + \sigma_i)}\frac{1 + \mathrm{i}\omega\tau_{4,i}}{(1 + \mathrm{i}\omega\tau_{1,i})(1 + \mathrm{i}\omega\tau_{2,i})}\left(1 + \frac{[\mu]}{\mu_{0,i}Z_i(\omega)}\right)^{-1} \quad ,
$$

and we have used the time scales $\tau_{k,i}$ ($k = 1, \ldots, 4$, see Main Text) as well as the function

$$
Z_i(\omega) = \frac{(1 + \mathrm{i}\omega\tau_{1,i})(1 + \mathrm{i}\omega\tau_{2,i})}{1 + \mathrm{i}\omega\tau_{3,i}} \quad . \tag{4}
$$

The dynamical response may be quantified through the susceptibility

$$
\widehat{\chi_{ij}}(\omega) = \frac{\partial\widehat{x_i}}{\partial\widehat{b_j^o}} \quad . \tag{5}
$$

We note that

$$\widehat{\chi_{ij}}(\omega) = \frac{\partial \widehat{x_i}}{\partial \widehat{y}} \frac{\partial \widehat{y}}{\partial \widehat{b_j^o}} \equiv g_{i\mu}(\omega) g_{\mu j}(\omega) \ , \tag{6}$$

where we have introduced the frequency-dependent gains

$$g_{i\mu}(\omega) \equiv \frac{\partial \widehat{x_i}}{\partial \widehat{y}} = -\frac{[m_i]}{[\mu]} \left(1 + \frac{\mu_{0,i}}{[\mu]} Z_i(\omega)\right)^{-1} \tag{7}$$

$$g_{\mu j}(\omega) \equiv \frac{\partial \widehat{y}}{\partial \widehat{b_j^o}} = -\chi_{\mu\mu}(\omega) V_j(\omega) \tag{8}$$

with $\chi_{\mu\mu}(\omega) = \Delta(\omega)^{-1}$ and

$$V_j(\omega) = \begin{cases} \frac{\sigma_j}{\sigma_j + \kappa_j} \frac{1 + i\omega\tau_{4,j}}{1 + i\omega\tau_{3,j}} \left(1 + \frac{\mu_{0,j}}{[\mu]} Z_j(\omega)\right)^{-1} & \text{if } \sigma_j > 0 \\ \frac{i\omega\tau_{5,j}}{1 + i\omega\tau_{5,j}} \left(1 + \frac{\mu_{0,j}}{[\mu]} Z_j(\omega)\right)^{-1} & \text{if } \sigma_j = 0 \ . \end{cases} \tag{9}$$

Upon defining the filters $J_i(\omega), C_i(\omega), S_i(\omega)$ and $D(\omega)$ as in the Main Text, one may re-cast the above gains as

$$g_{i\mu}(\omega) = J_i(\omega) g_{i\mu}(0) \tag{10}$$

and

$$g_{\mu j}(\omega) = \begin{cases} -D(\omega) J_j(\omega) S_j(\omega) g_{\mu j}(0) & \text{if } \sigma_j > 0 \\ -D(\omega) J_j(\omega) C_j(\omega) \widetilde{g}_{\mu j}(0) & \text{if } \sigma_j = 0 \ , \end{cases} \tag{11}$$

where $\widetilde{g}_{\mu j}(0)$ is the steady state term for the completely stoichiometric case (obtained upon setting $\kappa_i \to 0$ and $\sigma_i \to \kappa_i$)

Putting pieces together, we find

$$\widehat{\chi_{ij}}(\omega) = \begin{cases} D(\omega) \Big[S_j(\omega) J_i(\omega) J_j(\omega) \Big] \chi_{ij}^{ss} & \text{if } \sigma_j \neq 0 \\ D(\omega) \Big[C_j(\omega) J_i(\omega) J_j(\omega) \Big] \widetilde{\chi}_{ij}^{ss} & \text{if } \sigma_j = 0 \end{cases} \tag{12}$$

where

$$\chi_{ij}^{ss} \equiv \widehat{\chi_{ij}}(0) = g_{i\mu}(0) g_{\mu i}(0) \tag{13}$$

and

$$\widetilde{\chi}_{ij}^{ss} \equiv \lim_{\sigma_j \to 0} \frac{\sigma_j + \kappa_j}{\sigma_j} \chi_{ij}^{ss} \ , \tag{14}$$

which corresponds to the steady state susceptibility of a system without recycling (i.e. with $\kappa_i \to 0$ and $\sigma_i \to \kappa_i$). Finally, the self response is given by

$$\widehat{\chi_{ii}}(\omega) \equiv \frac{\partial \widehat{x_i}}{\partial \widehat{b_i^o}} = \frac{J_i(\omega) \chi_{ii}(0)}{1 + \mathrm{i}\omega\tau_{1,i}} \tag{15}$$

Susceptibilities

Figure S1 through S4 show the dynamical susceptibility $\chi_{ij}(\omega)$ for pairs of 'free', 'susceptible' and 'bound' ceRNAs in the different limits considered in the main text.

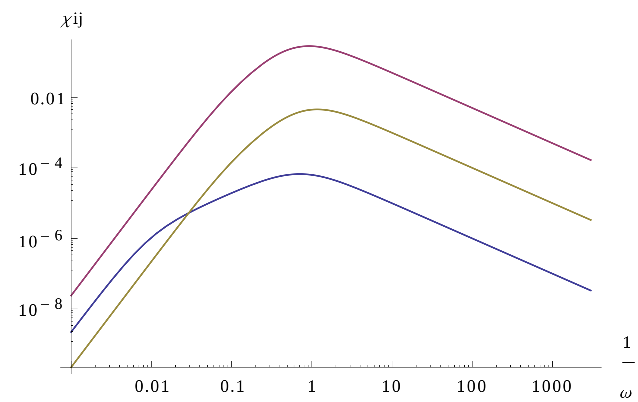

Figure S1: **Slow dissociation, fast processing** Dynamical susceptibility $\chi_{ij}(\omega)$ for slow complex dissociation in a fully catalitic system ($\sigma_i = 0, \kappa_i = 10$) for pairs of 'free' ($\rho_i = 100$, in yellow), 'susceptible' ($\rho_i = 1$, in red) and 'bound' ($\rho_i = 0.01$, in blue) ceRNAs. Remaining parameters are set as follows: $d_i = 1, k_i^- = 0, \delta = 1, b_i = 1$ for each i.

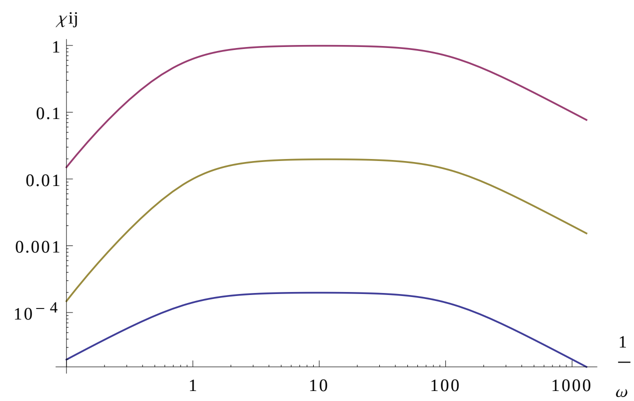

Figure S2: **Slow dissociation, slow processing** Dynamical susceptibility $\chi_{ij}(\omega)$ in a fully catalitic system ($\sigma_i = 0, \kappa_i = 0.01$) for a couple of free ceRNA ($\rho_i = 100$, in yellow), for a couple of susc ceRNA ($\rho_i = 1$, in red), for a couple of bound ceRNA ($\rho_i = 0.01$, in blue). Other parameters are set as follows: $d_i = 1, k_i^- = 0, \delta = 1, b_i = 1$ for each i.

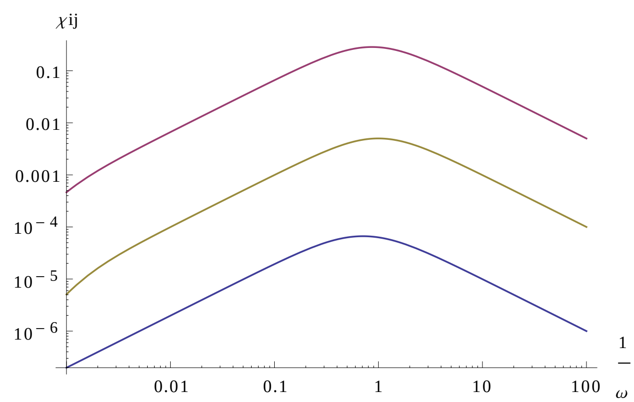

Figure S3: **Fast dissociation, fast processing** Dynamical susceptibility $\chi_{ij}(\omega)$ for fast complex dissociation in a fully catalitic system ($\sigma_i = 0, \kappa_i = 10$) for pairs of 'free' ($\rho_i = 100$, in yellow), 'susceptible' ($\rho_i = 1$, in red) and 'bound' ceRNAs ($\rho_i = 0.01$, in blue). Other parameters are set as follows: $d_i = 1, k_i^- = 1000, \delta = 1, b_i = 1$ for each i.

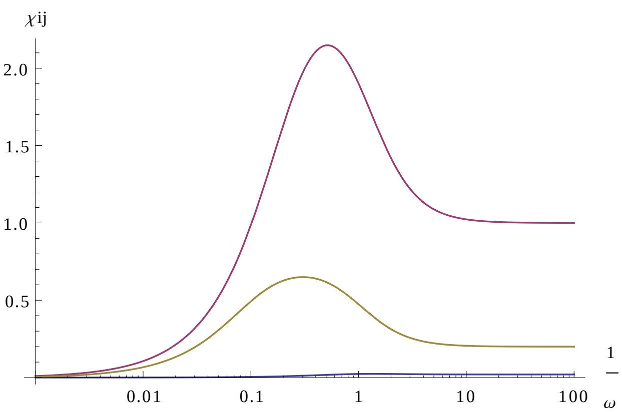

Figure S4: **Fast dissociation, slow processing** Dynamical susceptibility $\chi_{ij}(\omega)$ for fast complex dissociation in a fully stoichiometric system ($\sigma_i = 0.5, \kappa_i = 0$) for pairs of 'free' ($\rho_i = 100$, in yellow), 'susceptible' ($\rho_i = 1$, in red) and 'bound' ($\rho_i = 0.01$, in blue) ceRNAs. Other parameters are set as follows: $d_i = 1, k_i^- = 1000, \delta = 1, b_i = 1$ for each i.

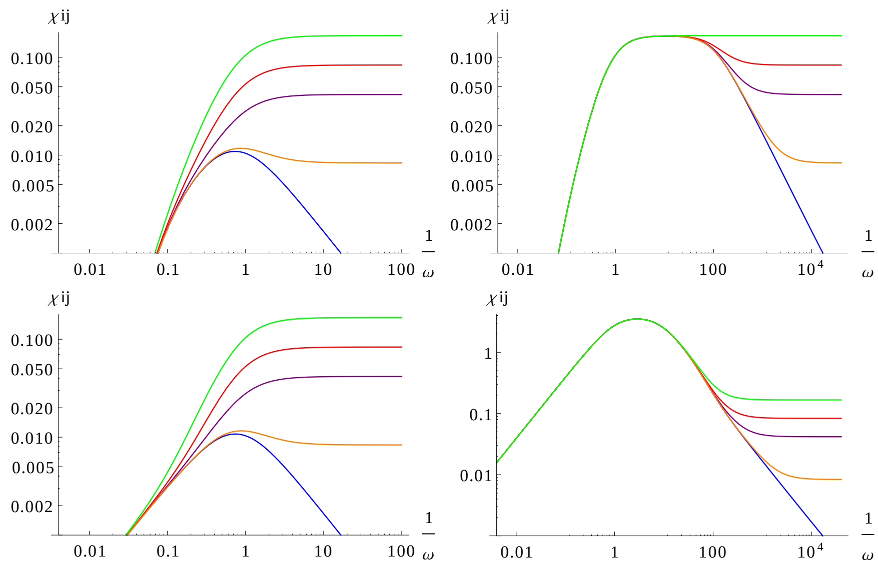

Figure S5: **Dynamical susceptibilities in case of mixed stoichiometric and catalytic complex processing** Dynamical susceptibility $\chi_{ij}(\omega)$ for pairs of 'susceptible' ($\rho_i = 1$) ceRNAs, for completely catalytic ($\sigma_i = 0$, blue line), prevalently catalytic ($\kappa_i = 20\sigma_i$, orange line), half stoichiometric/half catalytic ($\sigma_i = \kappa_i$, purple line), prevalently stoichiometric ($\sigma_i = 3\kappa_i$, red line) and completely stoichiometric ($\kappa_i = 0$, green line) systems, with fast processing and slow dissociation ($\sigma_i + \kappa_i = 10$, $k_i^- = 0$, top left), slow processing and slow dissociation ($\sigma_i + \kappa_i = 0.1$, $k_i^- = 0$, top right), fast processing and fast dissociation ($\sigma_i + \kappa_i = 10$, $k_i^- = 1000$, bottom left), and slow processing and fast dissociation ($\sigma_i + \kappa_i = 10$, $k_i^- = 1000$, bottom right). Remaining parameters have been fixed as follows: $d_i = 1, \delta = 1, b_i = 1$ for each i.

Estimate of the relaxation time following a large, saturating perturbation

In the case of a kinetically homogeneous system, where binding is irreversible and remaining kinetic parameters are the same for all ceRNAs, in particular $d_i = d$, $k_i^+ = k^+$, $k_i^- = k^- = 0$, $\kappa_i = \kappa$ (and hence $\mu_{0,i} = \mu_0 = \frac{d}{k^+}$) for all i, and assuming that ceRNAs and miRNAs reach a fast equilibrium with respect to the instantaneous values of the levels of the complexes, the following relations hold:

$$m_i(t) \simeq \frac{b_i}{d + k^+\mu(t)} \quad i = 1, ..., N \tag{16}$$

$$\mu(t) \simeq \frac{\beta + \kappa \sum_j c_j(t)}{\delta + k^+ \sum_j m_j(t)} \tag{17}$$

$$\frac{dc_i(t)}{dt} = k^+\mu(t)m_i(t) - \kappa c_i(t) \quad i = 1, ..., N \tag{18}$$

If the perturbation is large enough, miRNAs are istantanously sequestered by the complexes and never undergo spontaneous decay, so that $k^+ \sum_j m_j \gg \delta$. In this case one finds that the overall concentration of the complexes grows at constant rate β:

$$\sum_i \dot{c}_i = \beta \tag{19}$$

It follows that

$$\mu(t) \simeq \frac{\beta + \kappa\big(\sum_j c_j(0) + \beta t\big)}{\sum_j k^+ m_j(t)} \simeq \frac{\kappa\beta t}{k^+ \sum_j m_j(t)} \tag{20}$$

for large enough t.

The relaxation time τ_{rel} can be estimated by the condition

$$\mu(\tau_{rel}) \simeq \mu_0 = \frac{\delta}{k^+} \quad , \tag{21}$$

or, accordingly,

$$m_i(\tau_{rel}) \simeq \frac{m_i^\star}{2} \quad . \tag{22}$$

Plugging (21) and (22) into (20) one gets, in the limit of large perturbations Δ_i,

$$\tau_{rel} \simeq \frac{\mu_0 k^+ \sum_j m_j}{\beta\kappa} \simeq \frac{\Delta_j b_j}{2\beta\kappa} \tag{23}$$

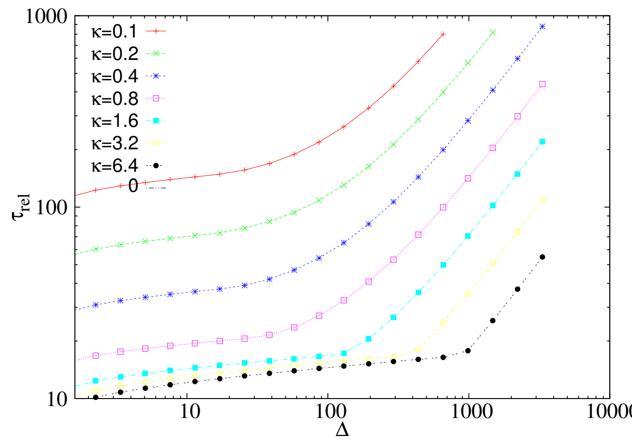

Figure S6: Relaxation time τ_{rel}, as a function of the size of the perturbation, for different values of the rate of catalytic complex processing κ. Remaining kinetic parameters are as follows: $b_1 = \beta = 1$, $b_2 = 1$, $d_1 = d_2 = \delta = 1$,$k_1^+ = k_2^+ = 100$, $k_1^- = k_2^- = 0$.

where we have used

$$\sum_i m_i(\tau_{rel}) = \sum_i \frac{m_i^\star}{2} = \frac{(\sum_i b_i) + b_j\Delta_j}{2\delta} \simeq \frac{\Delta_j b_j}{2\delta} \tag{24}$$

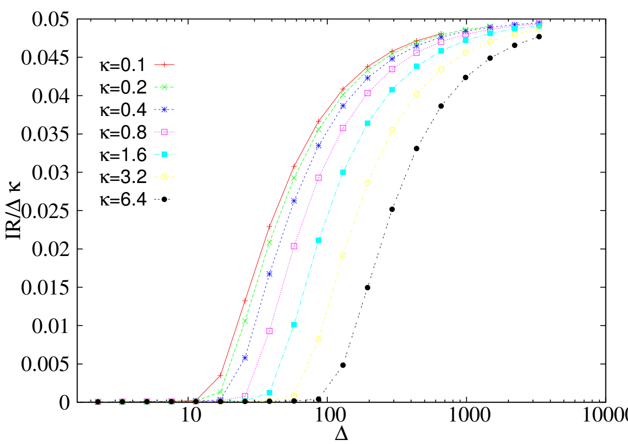

Figure S7: Integrated response IR between bound ceRNAs as a function of the perturbation size Δ, for different processing rates κ. Remaining kinetic parameters are as follows: $b_1 = b_2 = 1$, $b_2 = 1$, $\beta = 1$, $d_1 = d_2 = \delta = 1$, $k_1^- = k_2^- = 0$, $\kappa_1 = 1$, $k_2^+ = 100$