# Supplementary material
# Signal focusing through active transport

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In this Supplemental Material we summarize the calculations and full results for active transport coupled to reversible binding to a target. We also discuss the scenario, where the receptor can bind a molecule in the active phase and estimate the bounds to the effect of the prefactor, which is not captured by the fluctuation-dissipation theory.

## LINEARIZED AND FOURIER-LAPLACE TRANSFORMED EQUATIONS

The Fourier transformed linearized Eqs. (2) and (3) read

$$\begin{aligned} -i\omega\delta\tilde{n}(\omega) &= -\tau_c^{-1}\delta\tilde{n}(\omega) + k_{\rm on}(1-\langle n\rangle)\delta\tilde{c_p}(\mathbf{r}_0,\omega) + k_{\rm off}\langle n\rangle\beta\delta\tilde{F}(\omega) \\ -i\omega\delta\tilde{c_a}(\mathbf{k},\Omega,\omega) &= -(i\mathbf{v}(\Omega)\cdot\mathbf{k}+\tau_a^{-1})\delta\tilde{c_a}(\mathbf{k},\Omega,\omega) + (4\pi\tau_p)^{-1}\delta\tilde{c_p}(\mathbf{k},\omega) \\ -i\omega\delta\tilde{c_p}(\mathbf{k},\omega) &= -(Dk^2+\tau_p^{-1})\delta\tilde{c_p}(\mathbf{k},\omega) + \tau_a^{-1}\int\delta\tilde{c_a}(\mathbf{k},\Omega,\omega)d\Omega + i\omega\delta\tilde{n}(\omega)e^{-i\mathbf{k}\cdot\mathbf{r}_0} \end{aligned} \tag{S1}$$

where we have used the constraint imposed by detailed balance $\delta k_{\rm on}/k_{\rm on} - \delta k_{\rm off}/k_{\rm off} = \delta F/(k_BT)$ when linearizing Eq. (2) in the main text.

## VARIANCE OF THE TOTAL CONCENTRATION ESTIMATE

If we assume that the total concentration follows immediately from the measured receptor occupancy that the error in measuring $c_{\rm tot}$ in the transport controlled regime is given by

$$\delta c_{\rm tot}^2 = \left[1+\frac{k_{\rm on}c_{\rm tot}}{k_{\rm off}}(1+\tau_a/\tau_p)\right]^2\left(\frac{1}{1+\tau_a/\tau_p}\right)^2\delta n^2, \tag{S2}$$

which corresponds to the precision ratio in Eq. (17) in the main text.

## RECEPTOR RECOGNITION IN THE ACTIVE PHASE

In this section we discuss the sensing precision in the situation, where molecules can bind to the receptor also in the active phase. In this case Eq. (3) need to be modified such that the flux to the target equals $-\frac{1}{2}\delta(\mathbf{r}-\mathbf{r}_0)\frac{dn(t)}{dt}$ in both phases and we consider the fluctuation dynamics of $c(\mathbf{r},t) = c_p(\mathbf{r},t) + \int c_a(\mathbf{r},\Omega,t)d\Omega$. The end result is Eq. (1) but with $D_{eff}$ instead of $D$. Focusing again on the transport-controlled sensing (*i.e.*, second term of Eq. (1) we find

$$\frac{\overline{\delta c^2}}{\langle c\rangle^2} = \frac{1+\dfrac{\tau_a}{\tau_p}}{1+\dfrac{(v\tau_a)^2}{3D\tau_p}} \tag{S3}$$

which depends on $x_a/x_p$ and on $\frac{D}{va}$. The numerical results of Eq. (S3) are shown in Figure 1.

In contrast to the situation with passive receptor recognition Fig. 1 shows the approach towards absolute sensing precision, when active excursions become exceedingly larger than passive ones. It should be noted, however, that the finite size of a cell does set a bound to sensing precision.

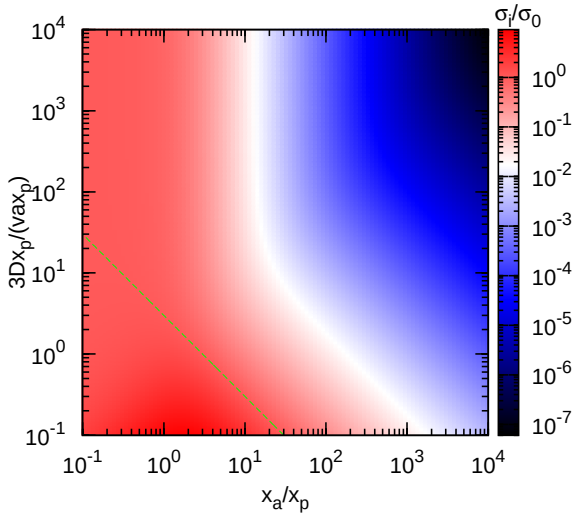


FIG. 1: Numerical results of Eq. (S3) depicting an approach towards infinite precision as $x_a/x_p \gg 1$. The green contour denotes $\sigma_i/\sigma_0 = 1$.

## TWO MEAN FIELD THEORIES AND ACTIVE FOCUSING

The difference between the two mean field approaches of Refs. [1] and [2], which effectively start from the same level of description, is the treatment of correlations between two mean field variables, the probability of receptor occupancy and the probability of finding a molecule at the receptor site. The approach of Bialek and Setayeshgar follows a perturbative route and linearizes the fluctuations to first order [1]. Conversely, Kaizu and coworkers [2] keep the correlation term but approximate it in a non-perturbative fashion by assuming that the molecule binds to the receptor in a non-steady state distribution of molecules, whereas the distribution is uniform when it unbinds. They present empirical support for their assumption and show that their result agrees with Green's Function Reaction Dynamics simulations—involving piece-wise Smoluchowski dynamics for decoupled pairs of particles and hence generically neglect fluctuation effects. The difference of both theories lies in the cross-fluctuations of mean fields and results in a prefactor

$$\frac{1}{2(1-\langle n\rangle)}, \tag{S4}$$

which leads to a large discrepancy as $\langle n\rangle \to 1$, where the theory of Bialek and Setayeshgar predicts a finite variance whereas Ref. [2] would lead to a divergence.

Comparison of the prefactor with respect to the present problem of active sensing precision shows that it is in fact well within the anticipated accuracy of any mean field theory. The *factor* $1-\langle n\rangle$ stands for the probability that the receptor will on average be found empty and is missing in [1]. Since we are considering relative precisions of active with respect to passive sensing it the will exactly cancel out in the presence of receptor recognition in both $a$ and $p$ phases as well as when considering precision at passive recognition but at equal $\langle c_p\rangle$. For the case of passive receptor recognition the difference between the theories of Refs. [1, 2] will be

$$\frac{1-\langle n\rangle_0}{1-\langle n\rangle_a} \tag{S5}$$

where $\langle n\rangle_0 = (\frac{k_{\rm off}}{k_{\rm on}c_{\rm tot}} - 1)$ and $\langle n\rangle_a = (\frac{k_{\rm off}}{k_{\rm on}\langle c_p\rangle} - 1)$ with $\langle c_p\rangle$ given in Eq. (14). In any reasonable biological signaling system the affinity for the receptor must be much larger than to one for the molecular motor and hence $\frac{k_{\rm off}}{k_{\rm on}} \lesssim \frac{\tau_p}{\tau_a}$ such that the value of Eq. (S5) will always be set by the partitioning between $a$ and $p$ phases. Moreover, there is no unique value for $c_{\rm tot}$ but the receptor response to concentration changes is largest near $\langle n\rangle \simeq 0.5$. In Fig. 2 we consider $c_{\rm tot}$ corresponding to an interval where the sensitivity to detect concentration changes is reasonable. The corresponding

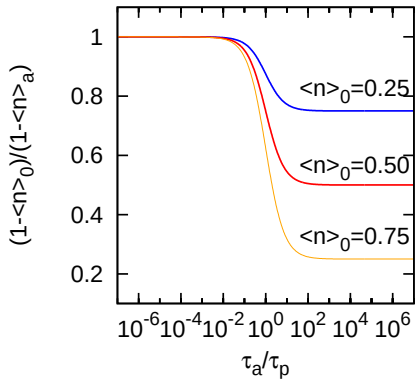


FIG. 2: Ratio of 'missing' factors for passive recognition at constant $c_{\rm tot}$. The different curves represent different $c_{\rm tot}$ corresponding to the listed $\langle n\rangle$ values. The value of the dissociation constant $k_{\rm off}/k_{\rm on}$ for receptor binding is not important as the affinity to the receptor must be larger than the one for the molecular motor. Here we use $k_{\rm off}/k_{\rm on} = 10^{-7}$M corresponding to moderately strong affinity. Smaller values do not produce observable differences.

values of $\langle n\rangle_a$ will be slightly smaller than the one for $\langle n\rangle_0$. The values for the improvement of the sensing precision we obtain are thus only a factor between 1.3 and 4 below those using the theory of Ref. [2].

[1] W. Bialek & S. Setayeshgar, Proc. Natl. Acad. Sci. USA **102**, 10040 (2005).
[2] C. Kaizu et al., Biophys. J. **106**, 976 (2014).