Information transmission by receptors correlated through ligand diffusion

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***Short Abstract* — Receptors on a cell surface capture external ligand molecules to estimate their concentrations. Such receptors have positive correlations among themselves (due to extrinsic fluctuations in the ligand concentrations), as well as negative correlations (due to intrinsic fluctuations caused by the fact that a single molecule can only be absorbed by one receptor). This structure of extrinsic and intrinsic correlations is widely expected to increase the information that the receptors measure about the ligand. Here we argue analytically and numerically that these correlations have only a small effect on the information, and the information is, in fact, decreased by the correlations, contrary to the established intuition.**

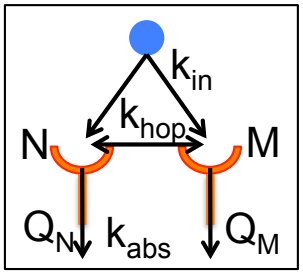
***Keywords* —mutual information, correlated receptors, cell signaling**

I. Motivation

CELLS measure the concentration of external ligands by capturing ligand molecules with receptors on the cell surface. Generally, the number of molecules each receptor captures is proportional to the external ligand concentration. Thus variations of the concentration, extrinsic to the cell, introduce ligand-induced positive correlations between the receptor activities. In addition, ligand molecules and the receptors themselves are discrete, resulting in an intrinsic stochasticity in the receptor dynamics. Since a molecule captured by one receptor cannot be captured by another, these correlations among the intrinsic fluctuations in different receptors should be negative. Importantly, in the context of neural information processing, it has been firmly established that pairs of neurons with stimulus-induced and intrinsic correlations of opposite signs carry more mutual information (MI) about the signal than do independent neurons [1]. We ask if the same may be true in cellular information processing; that is, if receptors on a cell surface coupled through a diffusing ligand carry more information about the ligand concentration than independent receptors.

II. Model and Methods

We consider a simplified model of two receptors that are diffusively coupled, and thus compete for the same ligand molecule (see Figure). Diffusion is modeled by ligand hopping between the receptors, and the ligand molecules can be absorbed by the receptors. We describe this system in terms of a master equation, and solve it for various correlation functions of the number of molecules absorbed at each receptor (Q_N, Q_M) analytically using the generating functional approach [2], and numerically using the stochastic simulations algorithm.



III. Results and Conclusion

If receptor-ligand binding is linear in the ligand concentration, the intrinsic noise covariance between the receptors is found to be identically zero, cov(Q_N, Q_M)=0. That is, the receptors are not coupled by ligands, and the information between the absorbed molecules and the ligand concentration is independent of the ligand hopping rate k_{hop} (or, equivalently, of the ligand diffusion). For nonlinear, saturating receptors the covariance is nonzero. And yet, in contrast to the neuroscience intuition, the variance of individual Qs changes correspondingly, such that the overall MI between the coupled receptors on the one hand, and the ligand concentration on the other is still independent of the hopping rate in the limit of long observation times. At intermediate times, interactions do not affect information in the linear noise (Gaussian) approximation, but contribute to non-Gaussian corrections, which decay as (1/time). Surprisingly, these corrections are negative, so that coupled receptors transmit less information about the ligand, again in contrast to the neuroscience intuition. Simulations confirm our analytical results. These results are a direct consequence of the noise correlations being induced by the conservation of the total number of absorbed molecules. Hence we expect them to generalize to a broad class of receptors coupled through ligand binding.

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