An Information Theoretic Model of Engineered Cell-Cell Communication

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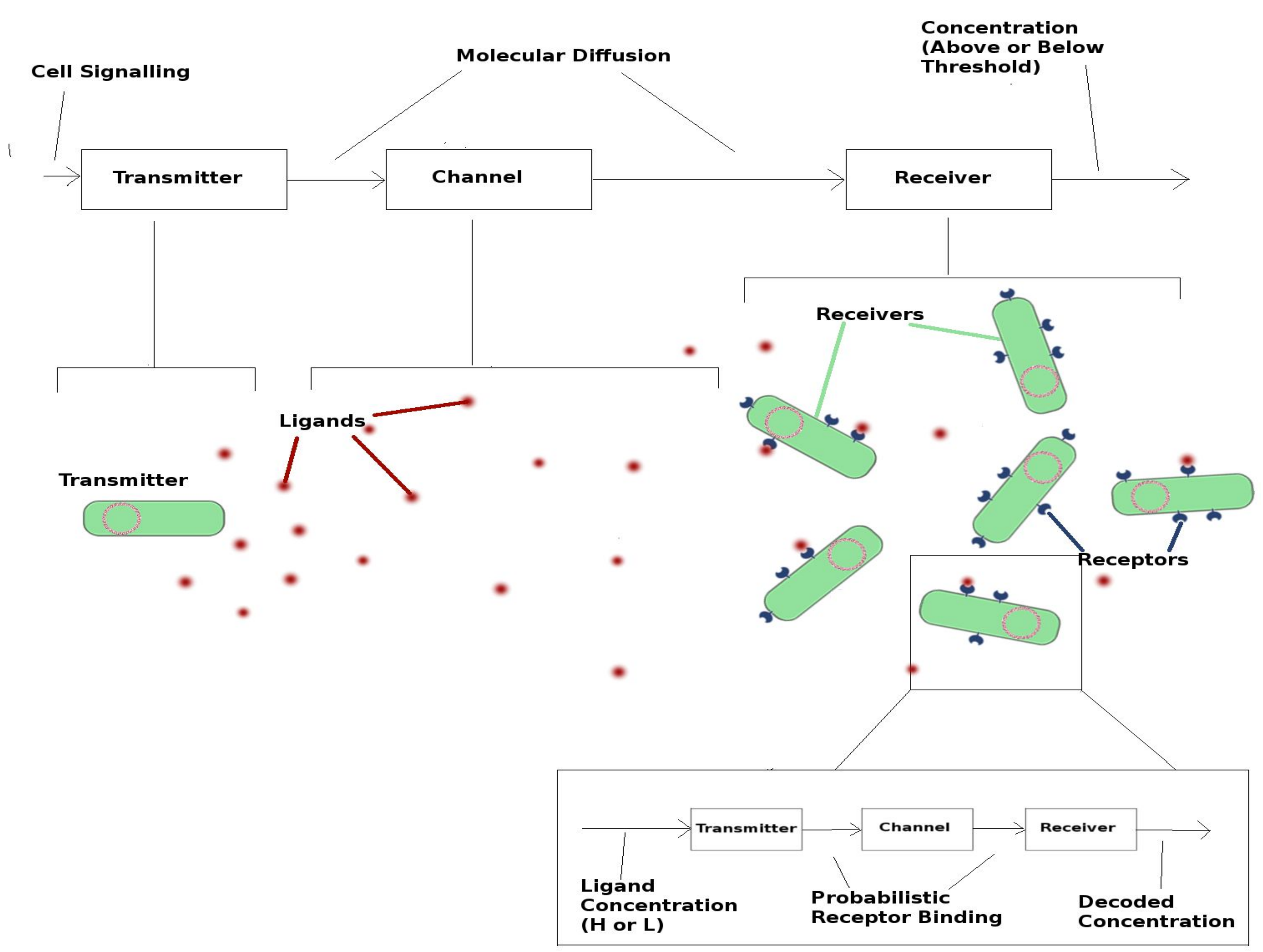
1. Introduction

- The engineering of communicating biological cell swarms is limited by a lack of theoretical design principles
- We develop an information-theoretic model of cell-cell communication to:
  - Determine the information capacity of groups of communicating cells
  - Understand bottlenecks in cellular communication
  - Derive general design principles

2. Model



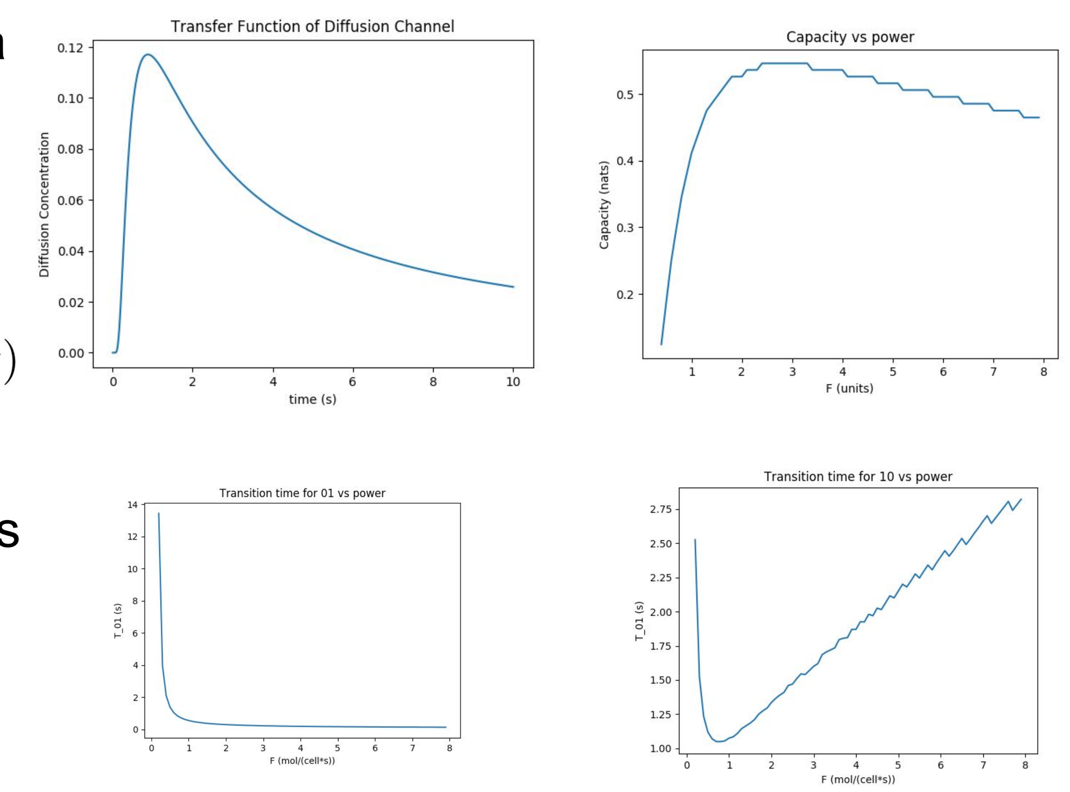
4. Analysis

Diffusion Channel

The diffusion channel is a memory-channel with a transfer function given by Fick's second law:

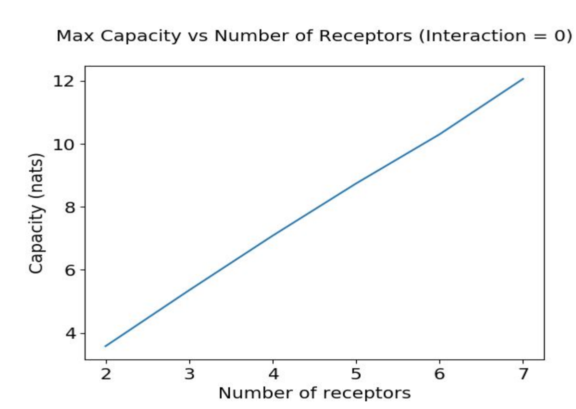
$$\frac{\partial c(x,t)}{\partial t} = D\nabla^2 c(x,t) + r(x,t)$$

The input is encoded as low or high concentrations (1 bit). Transition time is shown for 0->1 and 1->0 signal sequences [2].



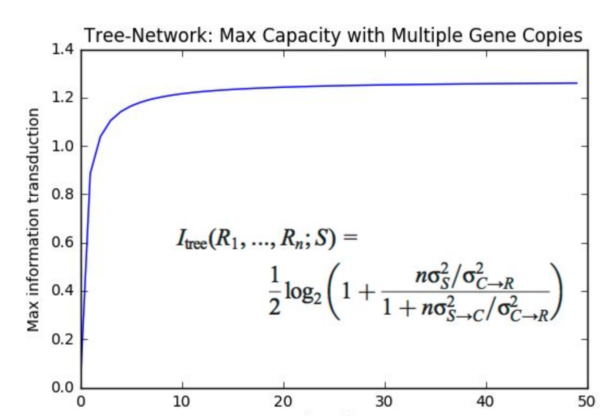
Multiple receptors

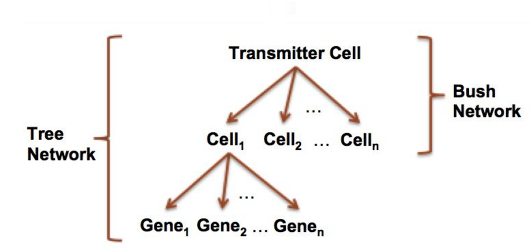
$$0 \underset{\tau\beta}{\overset{n\tau\alpha_{H/L}}{\rightleftharpoons}} 1 \underset{2\tau\beta}{\overset{(n-1)\tau\alpha_{H/L}}{\rightleftharpoons}} 2 \cdots k \underset{(k+1)\tau\beta}{\overset{(n-k)\tau\alpha_{H/L}}{\rightleftharpoons}} k+1 \cdots n-1 \underset{n\tau\beta}{\overset{\tau\alpha_{H/L}}{\rightleftharpoons}} n$$

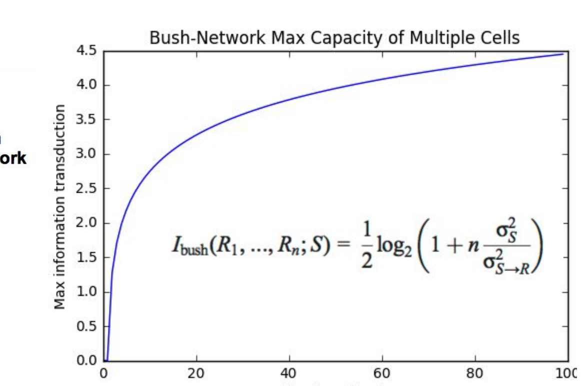


A cell with n receptors can be in any of n+1 states, where state k means any k receptors are bound. The transition diagram is shown above. Capacity for receiving cells with n independent receptors is n-times greater than cells with single receptors, and IID input maximizes capacity (left) [1].

Multiple receiver cells & gene copies

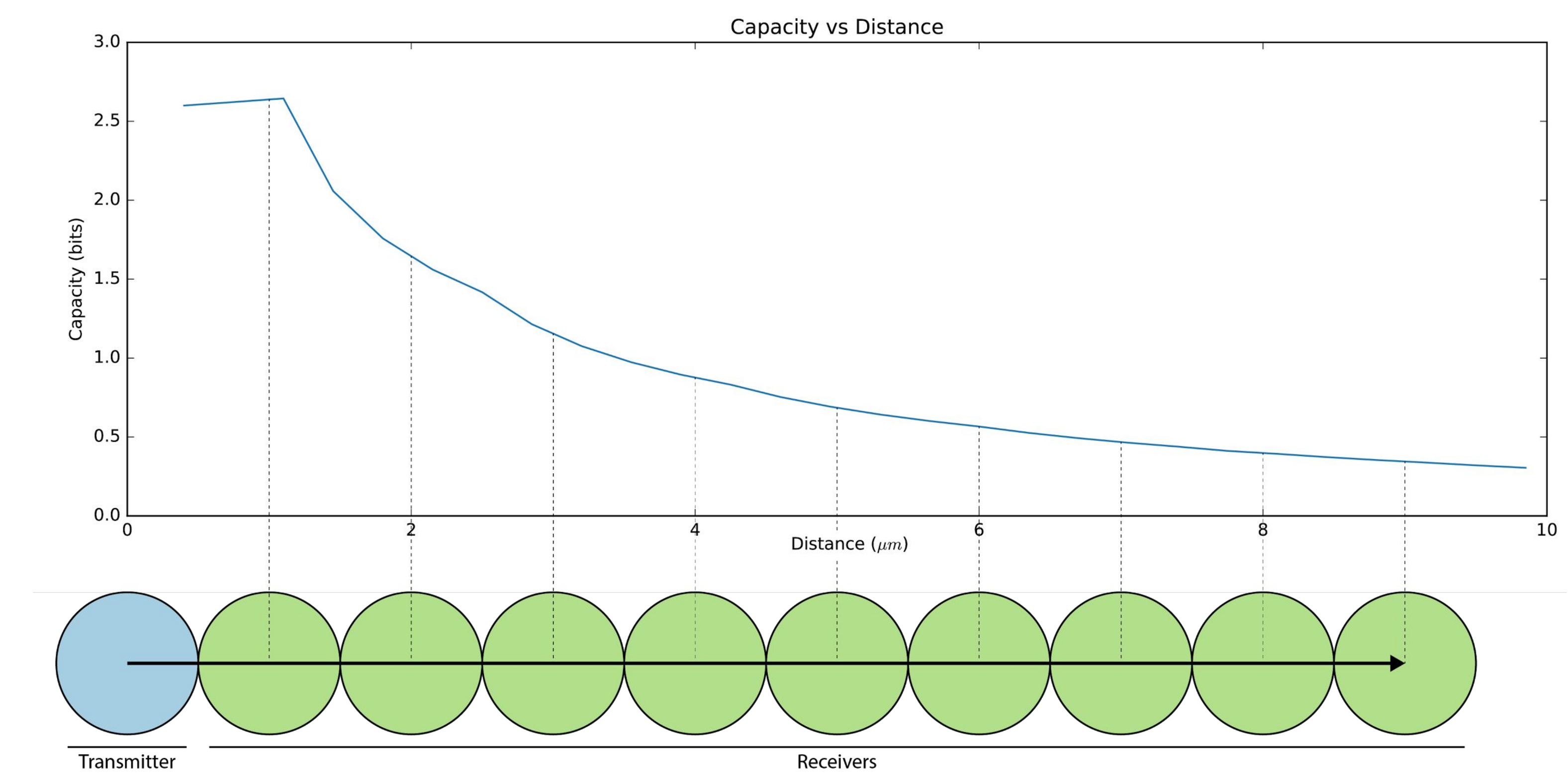




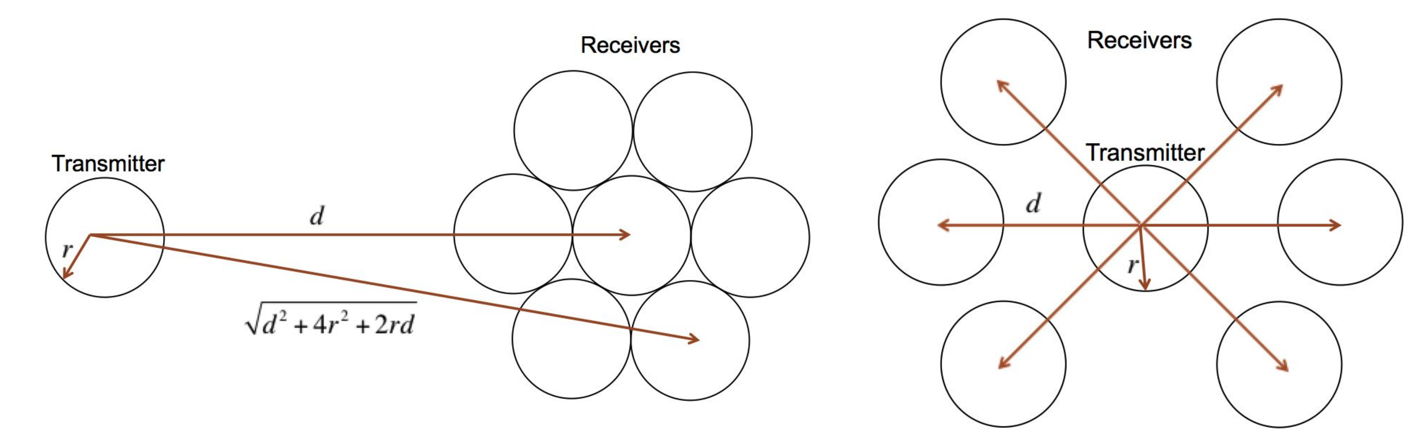


Information rate in signaling pathways such as TNF-a is limited by receiver receptors [3]. We model multiple receiving cells as a bush network to evaluate maximal improvements in capacity with multiple cells. Multiple copies of genes involved with intracellular signaling gives diminishing capacity gains because of the tree network structure.

5. Results



The capacity of receiver cells decreases with increasing distance from the transmitter. This is due to greater saturation of the memory-channel with greater distance.



We calculate the average information rate possible from one cell to a group of distant cells to be 0.88 bits/cell on average based on distance = 4μm, and from one cell to a surrounding group of six cells to be 3.9 bits total using a fixed distance of 1μm and the bush network model. We approximate the maximum possible information rate of a cell with a biologically relevant number of receptors (10,000 receptors for E. coli) to be 25,778 bits—this capacity is not limiting. Finally, we calculate the theoretical maximal information flux across a 1 mm colony of 150,000 E. coli, each cell receiving independent inputs from 6 neighbors, to be 271,103 bits. This synthesis provides a basis for designing simple cell-cell communication systems.

6. References

[1] P. J. Thomas and A. W. Eckford. Shannon Capacity of Signal Transduction for Multiple Independent Receptors. *Proc. IEEE ISIT.* 2016-April.
[2] A. Einolghozati, M. Sardari, A. Beirami, and F. Fekri. t. *Proc. IEEE ISIT.* 723-727, 2011-Aug.
[3] Cheong, Raymond, et al. "Information transduction capacity of noisy biochemical signaling networks." *science* 334.6054 (2011): 354-358.