Cross-talk and information transfer in mammalian and bacterial signaling
Samante Lyons

ABSTRACT:
In both mammalian cells and bacteria, simple phosphorylation circuits play a very important role in cellular function. Bacteria have hundreds of two-component signaling systems that involve phosphotransfer between a receptor kinase and a response regulator. In mammalian cells a similar pathway is the crucial TGF-beta signaling pathway, where extracellular levels of TGF-beta family ligands lead to activation of cell surface receptors that phosphorylate Smad proteins, which in turn activate many genes. In TGF-beta signaling the multiplicity of external ligands begs the question as to how cells are able to distinguish signals coming from different extracellular ligands, but transduced through a small set of Smads. Here we use information theory with stochastic simulations of simple networks to address this question. We find that when signals are transduced through the same Smad, the cell cannot distinguish between different levels of the external ligands. Increasing the number of Smads from one to two significantly improves information transmission as well as the ability to discriminate between different external ligands. Surprisingly, both total information transmitted through the channel and the capacity to discriminate between the external ligands are quite insensitive to the cross-talk between the two Smads as long as they are not nearly identical. In sharp contrast, we find that two-component systems in bacteria show a significantly sharper decline in information transfer in the presence of cross-talk. This suggests that mammalian signal transduction can tolerate a high amount of cross-talk. This may have played a role in the evolution of new functionalities from small mutations in signaling pathways and allowed for the development of cross-regulation. Insensitivity to cross-talk also could increase robustness due to redundancy in signaling pathways. On the other hand, bacterial two component systems are much less robust against cross-talk which may provide an explanation for the lack of cross-regulation in most two component systems.