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The BMP Pathway is a Programmable Multi-Ligand Signal Processing System

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The BMP signaling pathway comprises multiple ligands and receptors that interact promiscuously and appear in combinations. This feature is often understood in the context of redundancy and tissue specificity, but it has remained unclear whether it enables specific signal processing capabilities. Here, we show that the BMP pathway performs a specific set of computations, including sums, ratios, and balance and imbalance detection, across the multi-dimensional space of ligand concentrations. These computations can arise directly from receptor-ligand interactions without requiring transcriptional regulation. Furthermore, cells can re-program the type of computation performed on specific ligands through changes in receptor expression, allowing different cell types to perceive distinct signals in the same ligand environment. Together, these results may help explain the prevalence of promiscuous ligand-receptor architectures across pathways and enable predictive understanding and control of BMP signaling.