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Enzyme clustering can induce metabolic channeling

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Direct channeling of intermediates via a physical tunnel between enzyme active sites is an established mechanism to improve metabolic efficiency. In this talk, I will present a theoretical model that demonstrates that coclustering multiple enzymes into proximity can yield the full efficiency benefits of direct channeling. The model predicts the separation and size of coclusters that maximize metabolic efficiency, and this prediction is in agreement with the spacing between coclusters in yeast and mammalian cells. The model also predicts that enzyme agglomerates can regulate steady–state flux division at metabolic branch points: we experimentally test this prediction for a fundamental branch point in *Escherichia coli*, and the results confirm that enzyme colocalization within an agglomerate can accelerate the processing of a shared intermediate by one branch. Our studies establish a quantitative framework to understand coclustering-mediated metabolic channeling and its application to both efficiency improvement and metabolic regulation.