Do DNA Barcode networks benefit from promiscuity?

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In sequencing-based microscopy, spatial information is encoded through proximity networks, where edges represent molecular interactions. While intuitively, increased connectivity, termed here as network promiscuity, might be expected to degrade spatial reconstructions due to the presence of false edges, this study systematically examines whether promiscuity can, conversely, enhance reconstruction accuracy. By using synthetic random geometric graphs (RGGs) and experimental DNA microscopy datasets, we demonstrate that moderate network promiscuity substantially improves spatial reconstruction quality, even in the presence of noise. Our findings reveal that adding edges, contrary to conventional expectations, can reinforce true spatial signals sufficiently to offset the detrimental impact of false edges.

However, this benefit exists only up to critical connectivity thresholds (edge densities around 0.75 to 0.8), beyond which accuracy sharply declines due to excessive edge density limiting spatial resolution. Comparative analysis of reconstruction algorithms reveals distinct performance regimes: random-walk-based methods (STRND) excel in sparse, moderate-noise conditions, whereas shortest-path-based methods (MDS) outperform in densely connected, noisy environments. Additionally, experiments on real sequencing-based microscopy data confirm that controlled promiscuity enhances reconstruction robustness, aligning closely with synthetic predictions. These findings suggest a fundamental behavior governed by edge density, highlighting the practical value of intentionally designing promiscuous networks to achieve high-quality spatial reconstructions in DNA barcode network imaging.

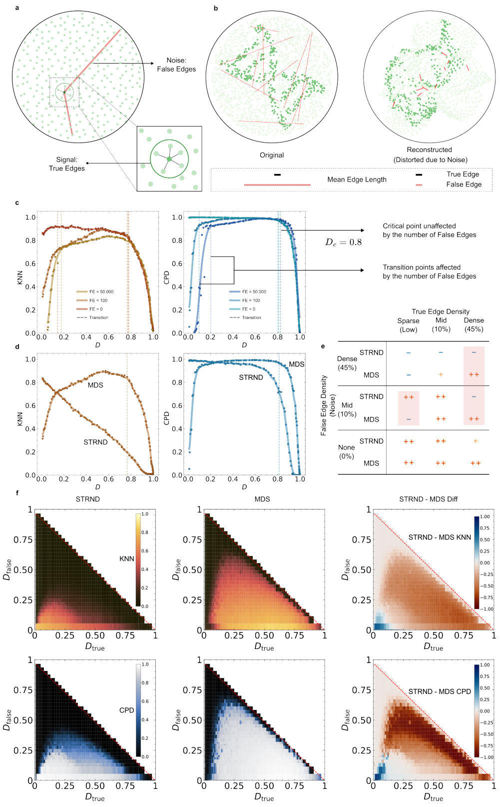

Figure 1. Otimal reconstruction algorithms under noisy conditions. a. True edges reflect actual molecular proximity; false edges are randomly created due to sequencing errors. **b.** Original and reconstructed spatial layouts illustrating distortion from even minimal (10) false edges. **c.** Local (KNN) and global (CPD) accuracy metrics showing growth–plateau–decay patterns with increasing promiscuity (edge density). Accuracy universally collapses beyond a critical density ($D_c = 0.8$). **d.** Comparative performance of STRND and MDS algorithms at fixed noise levels, highlighting superior STRND performance in sparse conditions and superior MDS performance in dense, noisy conditions. **e.** Algorithm performance summary across varying true and false edge densities. **f.** Heatmaps illustrating detailed algorithm performance differences (MDS minus STRND), confirming complementary algorithmic strengths.