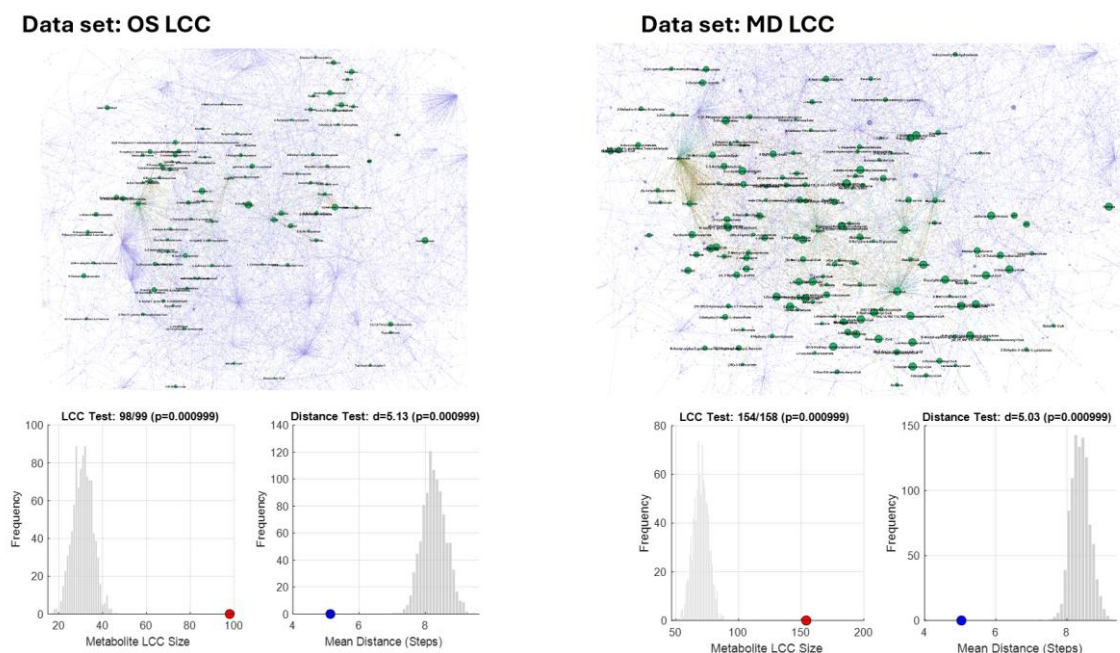


Supplementary material.

SM Figure 1. Analysis of the simulated data sets (link, OS; right, MD). To evaluate whether the spatial distribution of metabolites identified as significantly altered (Welch's t-test) reflected localized biological coordination, we implemented two complementary, degree-matched permutation tests ($n = 1000$). First, an empirical null distribution for the Largest Connected Component (LCC) was constructed by evaluating subgraphs induced strictly by reaction nodes bridging at least two target metabolites. Second, we calculated the Mean Shortest Path Distance (d_{mean}) across all unique pairs of target metabolites to assess overall spatial proximity across the network. For every permutation iteration, background node sets were selected to strictly match the exact degree distribution of the target metabolites. Metabolites highlighted in green (top row) correspond to the nodes included in the LCC of each data set.



SM Figure 2. Analysis of the real data set. To evaluate whether the spatial distribution of metabolites identified as significantly altered (Welch's t-test) reflected localized biological coordination, we implemented two complementary, degree-matched permutation tests ($n = 1000$). First, an empirical null distribution for the Largest Connected Component (LCC) was constructed by evaluating subgraphs induced strictly by reaction nodes bridging at least two target metabolites. Second, we calculated the Mean Shortest Path Distance (d_{mean}) across all unique pairs of target metabolites to assess overall spatial proximity across the network. For every permutation iteration, background node sets were selected to strictly match the exact degree distribution of the target metabolites. Metabolites highlighted in green (top row) correspond to the 15 nodes included in the LCC.

