

# Network Analysis of Oral Microbiome Interactions in Early and Advanced Periodontitis

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## Abstract

Periodontitis is a dysbiosis-driven disease in which disruptions to the oral microbiome’s interconnected community alter microbial interactions. Given that the microbiome operates as a network of interacting taxa, network analysis offers a powerful framework to reveal features linked to community resilience. Here, we determine how oral microbiome network structure and the influence of key taxa differ between individuals with early and advanced periodontitis. Using National Health and Nutrition Examination Survey (NHANES) 2009–2010 data, we constructed correlation-based networks at the phylum level using FastSpar and applied spectral graph theory and network metrics to characterize groups. We then simulated phylum removal through perturbation experiments to assess their effect on network integrity. We found that in early periodontitis, Fusobacteria removal enhanced stability, while Spirochaetes supported local clustering; in advanced periodontitis, Fusobacteria loss weakened the network. These findings show how network-based approaches can identify vulnerabilities in the oral microbiome, informing precision-targeted interventions for periodontitis.

## Background

### Periodontitis and Oral Dysbiosis

- Periodontitis is a chronic inflammatory gum disease, the leading cause of tooth loss. It is driven by a shift from a balanced to a pathogenic oral microbiome.<sup>3, 7</sup>
- Overgrowth of anaerobic bacteria in oxygen-depleted pockets causes inflammation, tissue destruction, and bone loss; linked to systemic diseases (e.g., cardiovascular disease, diabetes, Alzheimer’s).<sup>2</sup>
- Keystone Pathogen Hypothesis: low-abundance species like *Porphyromonas gingivalis* (Bacteroidetes) can disproportionately disrupt community structure.<sup>1</sup>
- Periodontitis-associated microbiomes are enriched in Bacteroidetes, Firmicutes, Fusobacteria, Spirochaetes, and Synergistetes phyla; Actinobacteria are more abundant in health.<sup>4</sup>

### Network Analysis in Microbiome Studies

- Goes beyond abundance, revealing positive/negative microbial associations, specific interaction patterns, keystone taxa, network stability, and structural vulnerabilities that may drive dysbiosis.

## Acknowledgement

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## References

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## Data / Method

### Data:

- NHANES Data (2009-2010)
- Group Classification based on American Academy of Periodontology (AAP) thresholds for Probing Pocket Depth and Interdental Clinical Attachment Loss
  - 558 samples with early-stage periodontitis (I-II)
  - 3,194 samples with advanced-stage periodontitis (III-IV)

### 1. Construct Phylum-Level Networks Using FastSpar



### 2. Calculate Global-level Metrics for Group Comparison (With Bootstrap Test)



### 3. Perturbation Analysis for Node-Level Importance (With Permutation Test)



### 4. Dimensionality Reduction Using Uniform Manifold Approximation and Projection (UMAP)

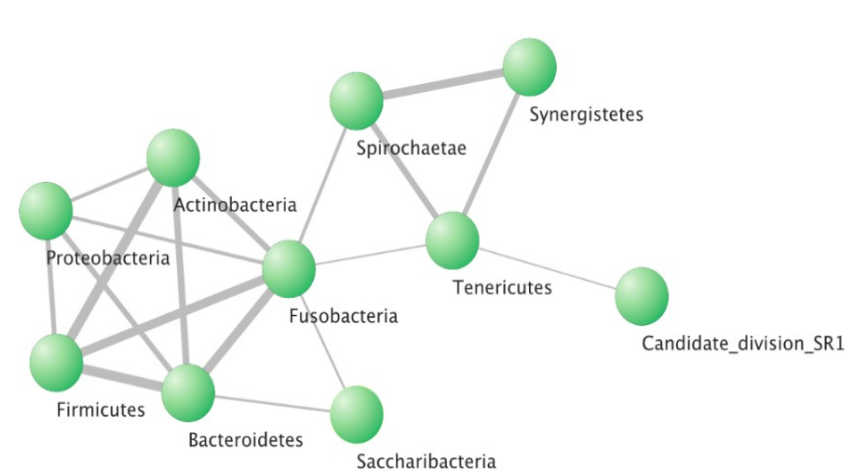
Metric	Description
Network Density	Proportion of realized to possible connections; high = tightly knit, low = fragmented
Average Degree	Average number of connections per node; higher = more interaction
Average Degree Centrality	Mean connectivity across network; high = many direct links per node
Average Closeness Centrality	Average network reachability; high = efficient spread of influence
Average Eigenvector Centrality	Overall network influence; high = centralized network
Average Clustering Coefficient	Likelihood neighbors are also connected; high = tight-knit groups
Fiedler Value	Connectivity robustness; high = resilient, low = prone to fragmentation
Largest Eigenvalue	Influences network dynamics (spreading or synchronization)
Number of Zero Eigenvalues	Indicates disconnected components; more zeros = more separate sub-networks.
Graph Diameter	Longest shortest path between any two nodes; smaller = more compact network
Average Path Length	Mean shortest distance between nodes; smaller = faster interactions

**Table 1: Description of Global Network Metrics**

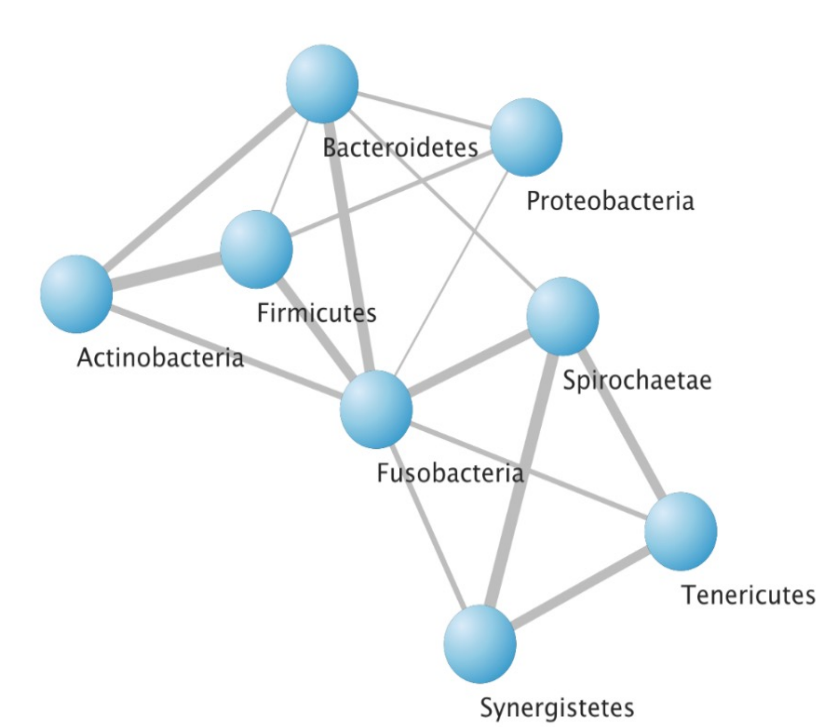
\*Spectral Properties: Eigenvector centrality, Fiedler Value, Largest Eigenvalue\*<sup>5, 6</sup>

## Results: Network Visualization

### Early Periodontitis



### Advanced Periodontitis



**Figure 1: Cytoscape Visualizations of Early and Advanced Periodontitis Networks**

## Results: Network Metrics

Metric	Early Periodontitis	Advanced Periodontitis	Comparison P-value
Number of Nodes	10.0	8.0	NA
Number of Edges	18.0	16.0	NA
Network Density	0.40	0.57	NA
Average Degree	3.60	4.00	NA
Average Clustering	0.51	0.57	NA
Graph Diameter	3.00	2.00	NA
Average Path Length	1.82	1.43	NA
Fiedler Value	0.19	0.62	4.27E-34
Largest Eigenvalue	3.94	4.00	4.27E-34
Number of Zero Eigenvalues	1.00	1.00	NA
Average Degree Centrality	0.40	0.57	NA
Average Closeness Centrality	0.57	0.71	NA
Average Eigenvector Centrality	0.28	0.34	NA

**Table 2: Network Calculations for Early and Advanced Periodontitis**

\*Highlighted = Significant Metrics between groups (Bootstrap)\*

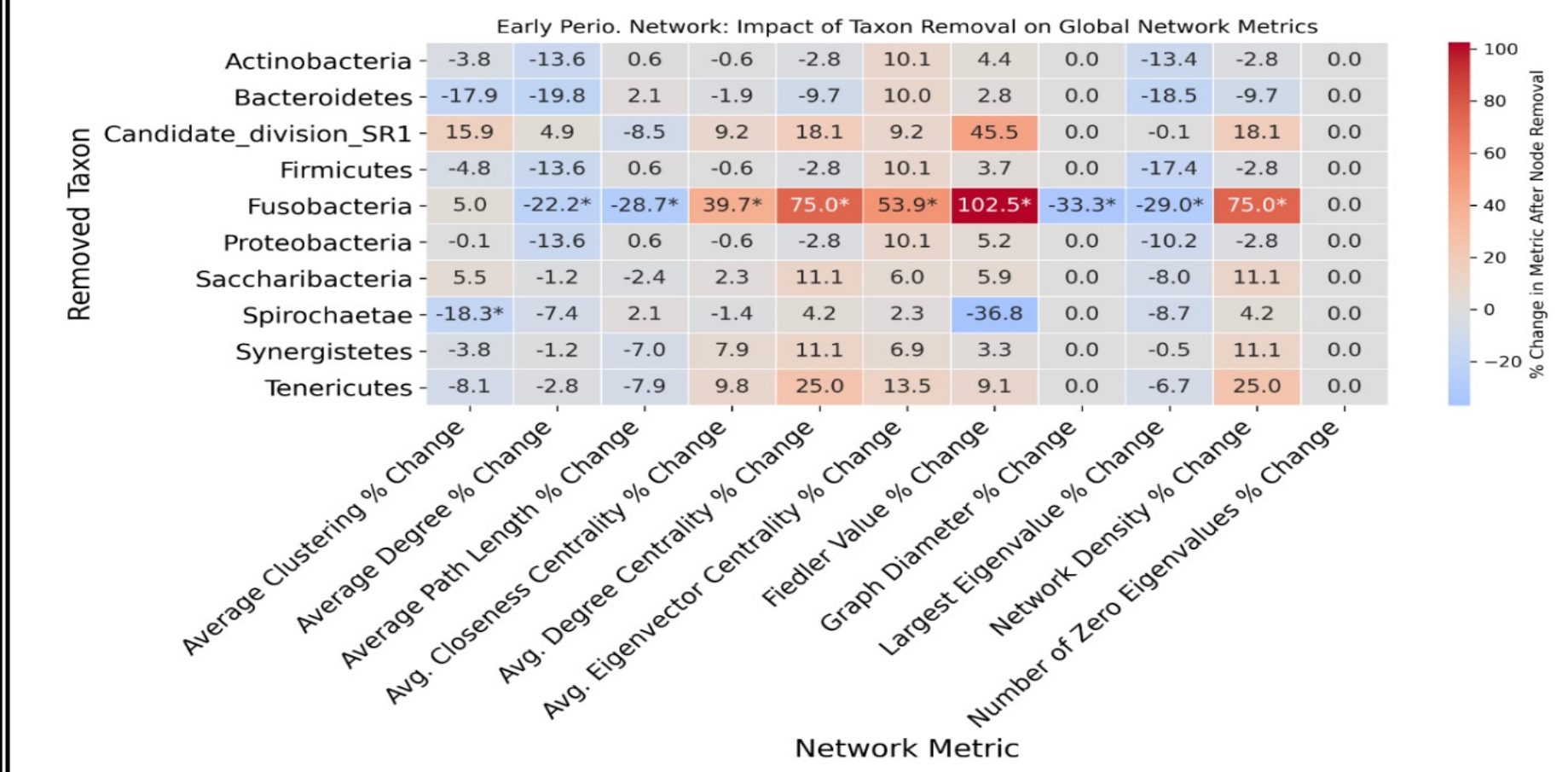
### Early Periodontitis:

- More nodes/edges but lower density; longer paths suggest a looser, less connected structure.
- Lower Fiedler Value and Largest Eigenvalue → weaker stability and hub influence.

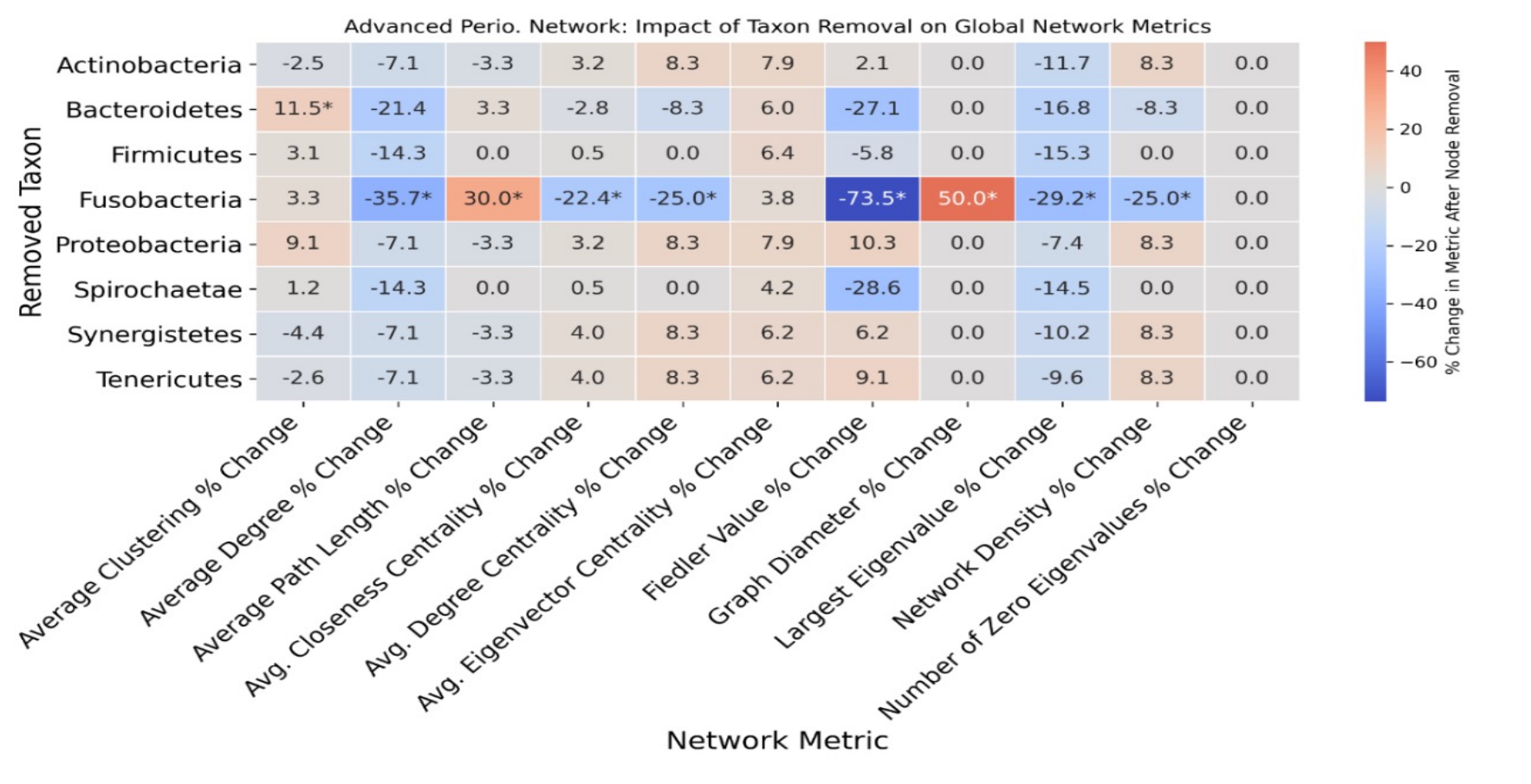
### Advanced Periodontitis:

- Fewer nodes/edges but higher density; shorter paths indicate a tighter, more connected network.
- Higher Fiedler Value and Largest Eigenvalue → greater stability and hub dominance.

## Early Periodontitis Perturbation Results



## Advanced Periodontitis Perturbation Results



**Figure 2: Effects of Node-Removal on Network Metrics (Blue = Decrease in % Change; Red = Increase in % Change)**

\*Stars = significant changes (permutation + FDR)\*

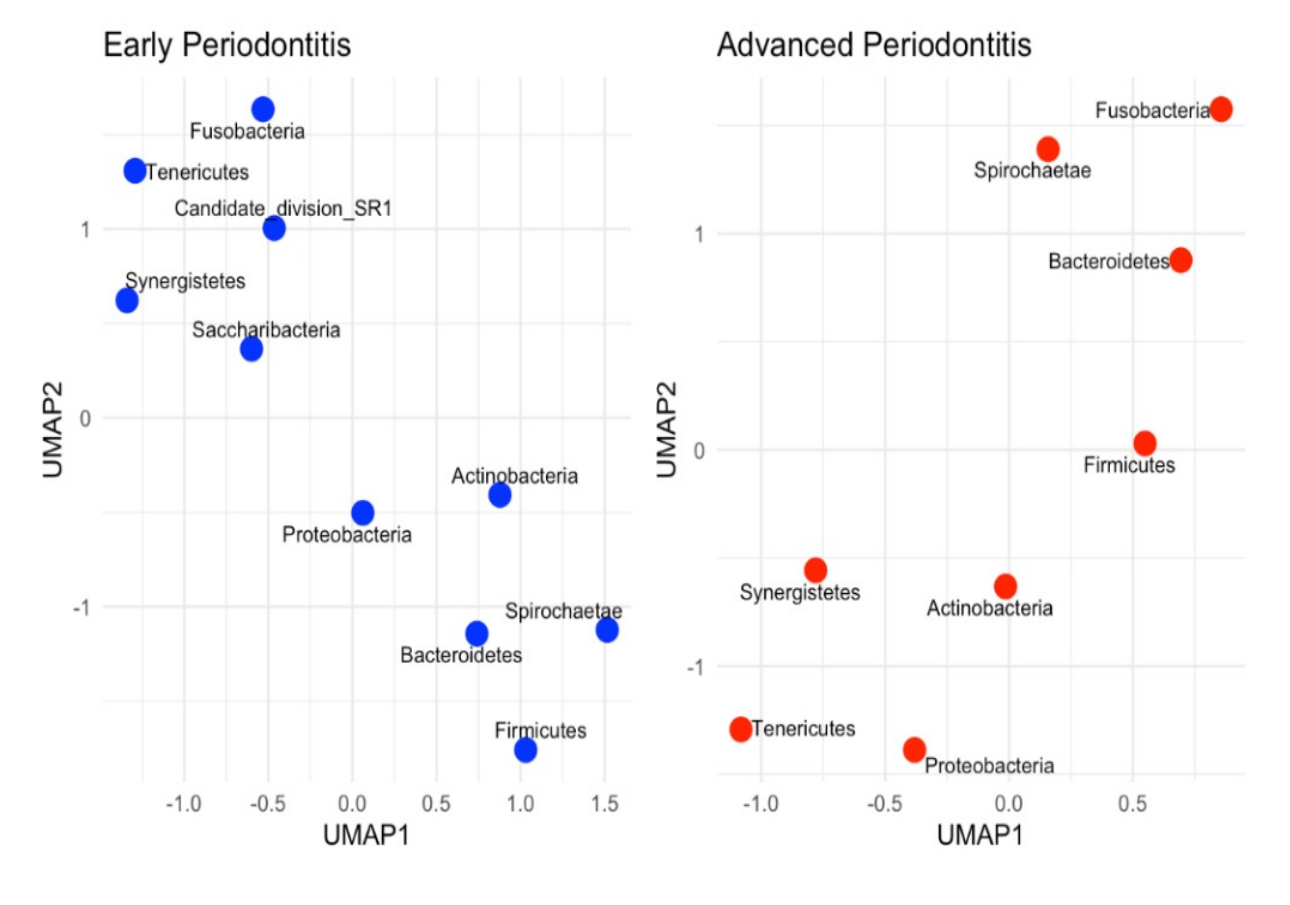
### Early Periodontitis:

- Spirochaetes – Significant drop in clustering (support local neighborhoods).
- Fusobacteria – Significant changes where removal increased nearly all metrics → destabilizing role in early periodontitis.

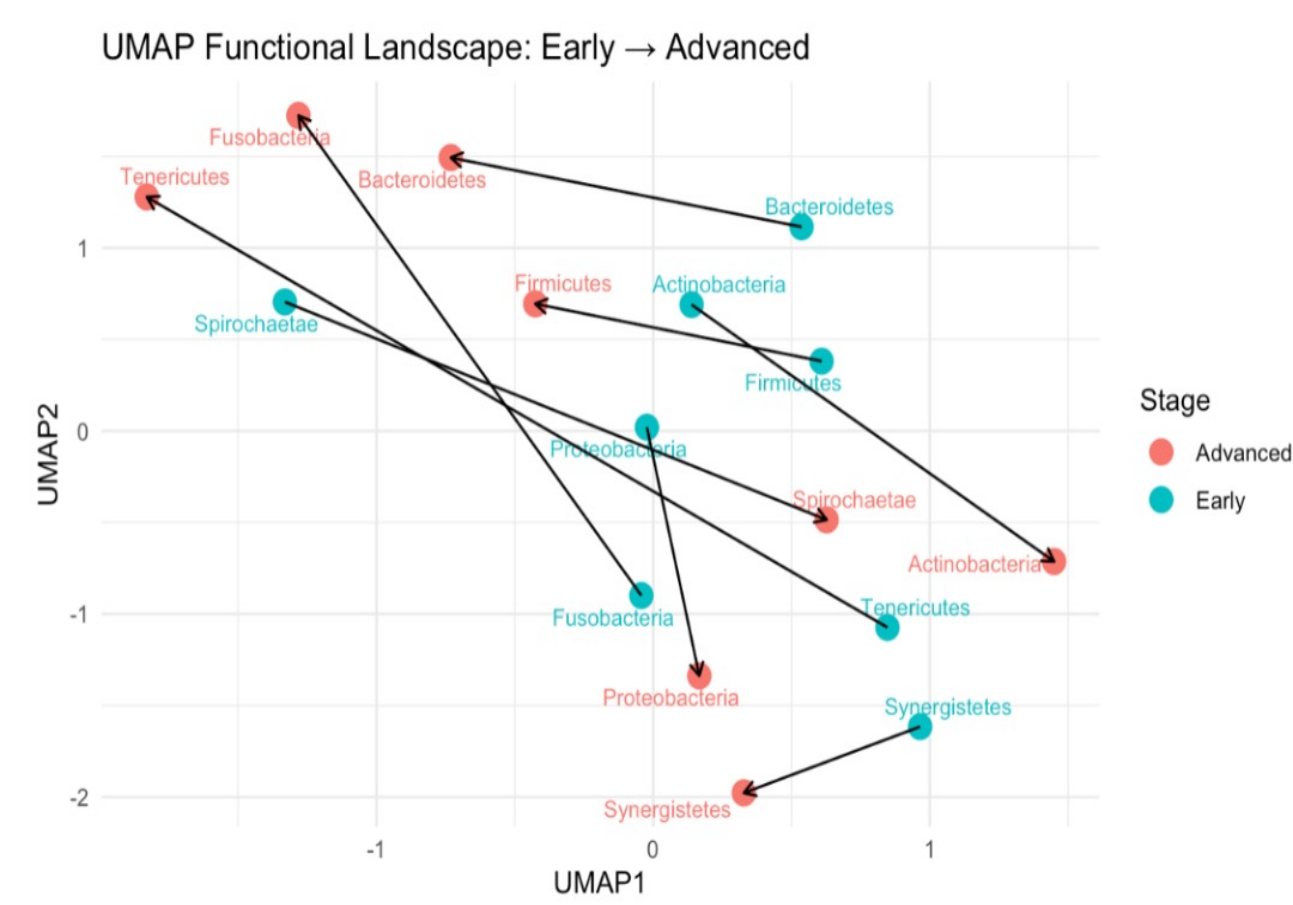
### Advanced Periodontitis:

- Bacteroidetes – Significant drop in clustering.
- Fusobacteria – Significant changes where removal decreased nearly all measures → stabilizing hub role in advanced periodontitis

## Separated UMAP (Early vs Advanced)



## Combined UMAP (with Arrows)



**Figure 3: Separated UMAP and Combined UMAP of Perturbation Results**

### Separate UMAP:

- Fusobacteria shifted nearest neighbors to Spirochaetes and Bacteroidetes, indicating functional space changes

### Combined UMAP:

- Taxa with long arrows (like Fusobacteria, Tenericutes, Bacteroidetes) have big changes in their “functional neighborhood” → possibly more sensitive to disease state.

## Discussion / Conclusion

### Discussion

- Fusobacteria, though <10% abundant in both early and advanced periodontitis, plays a disproportionate role in network stability, underscoring the value of network analysis over abundance profiling.
- Higher-resolution, metagenomic, and experimental validation will be essential for translating these insights into targeted interventions to restore microbial balance and reduce systemic risks.

### Conclusion

- Integrating network topology, perturbation effects, and functional visualization identifies group-specific keystone taxa, informing precision microbiome interventions for periodontitis.
- Therapies should be group-specific: early stages may target destabilizing taxa, while advanced stages may focus on preserving or rewiring stabilizing hubs via probiotics, bacterial interference, or metabolic disruption.