

Comprehensive Bayesian Uncertainty Quantification of Multi-Species Oral Biofilm Dynamics under Commensal and Dysbiotic Conditions

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Abstract

This paper presents a comprehensive Bayesian uncertainty quantification of a 5-species oral biofilm model (*S. oralis*, *A. naeslundii*, *Veillonella spp.*, *F. nucleatum*, *P. gingivalis*) using Transitional Markov Chain Monte Carlo (TMCMC). We investigate the model dynamics under four distinct experimental conditions: Commensal (healthy) vs. Dysbiotic (disease) states, and Static vs. HOBIC (flow) cultivation methods. By utilizing TMCMC with 1000 particles and a biologically constrained parameter reduction strategy, we successfully estimate 15 interaction parameters and identify key differences in species interactions across conditions. The results demonstrate the robustness of the proposed method in capturing the transition from health to disease, providing critical insights for peri-implantitis prevention.

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1 Introduction

Understanding the dynamics of multi-species biofilms is crucial for the prevention and treatment of oral diseases. Heine et al. investigated the interactions of five major oral bacterial species associated with peri-implantitis. Based on these findings, Klempt et al. developed a continuum model for multi-species biofilms.

This study extends previous work by applying a rigorous Bayesian framework (TMCMC) to quantify parameter uncertainty under four experimental conditions. We specifically focus on the identifiability of interaction parameters and the biological validity of the estimated posterior distributions.

The 5-species biofilm model describes the dynamics of bacterial populations through an interaction matrix \mathbf{A} and decay vector \mathbf{b} . However, the standard parameter estimation approach estimates all 20 parameters freely, which can lead to poor identifiability and biologically implausible estimates. To address this, we propose a **Biologically-Constrained Parameter Reduction** method.

2 Methods

2.1 5-Species Biofilm Model

The model describes the dynamics of bacterial volume fractions ϕ_i and viability fractions ψ_i for five species:

- Species 0: *Streptococcus oralis* (S.o) - Early colonizer
- Species 1: *Actinomyces naeslundii* (A.n) - Early colonizer
- Species 2: *Veillonella* spp. (Vei) - Metabolic bridge
- Species 3: *Fusobacterium nucleatum* (F.n) - Bridge organism
- Species 4: *Porphyromonas gingivalis* (P.g) - Late colonizer (Pathogen)

2.2 Parameter Reduction Strategy

We assume the interaction matrix \mathbf{A} is symmetric ($A_{ij} = A_{ji}$), reducing the off-diagonal terms. Furthermore, based on the interaction network established by Heine et al. (Figure 4C), we lock specific non-interacting pairs to zero.

Index	Param	Species Pair	Status
6	a_{34}	Vei (2) \leftrightarrow F.n (3)	Locked (0)
12	a_{23}	A.n (1) \leftrightarrow Vei (2)	Locked (0)
13	a_{24}	A.n (1) \leftrightarrow F.n (3)	Locked (0)
16	a_{15}	S.o (0) \leftrightarrow P.g (4)	Locked (0)
17	a_{25}	A.n (1) \leftrightarrow P.g (4)	Locked (0)

Table 1: Absent interactions locked to zero in the Proposed Method. This reduces the free parameter space from 20 to 15.

2.3 Experimental Conditions & Locking Rules

We analyze four distinct datasets, each with specific parameter constraints:

1. **Commensal Static:** Healthy, static. Strict locking ($N_{locked} = 9$) to enforce pathogen suppression.
2. **Dysbiotic Static:** Disease, static. Standard locking ($N_{locked} = 5$).
3. **Commensal HOBIC:** Healthy, flow. Strict locking ($N_{locked} = 8$) allowing S.oralis growth.
4. **Dysbiotic HOBIC (Surge):** Disease, flow. **Unlock All** ($N_{locked} = 0$). All constraints are released to capture the explosive "Surge" of pathogens driven by complex cross-feeding.

3 Results

3.1 Commensal HOBIC

Description: Healthy condition under flow (HOBIC). Characterized by high *S. oralis* growth ('Blue Bloom') and suppressed pathogens.

Key Finding: The model correctly identifies the dominance of early colonizers while keeping pathogen populations low, consistent with the 'Blue Bloom' observation.

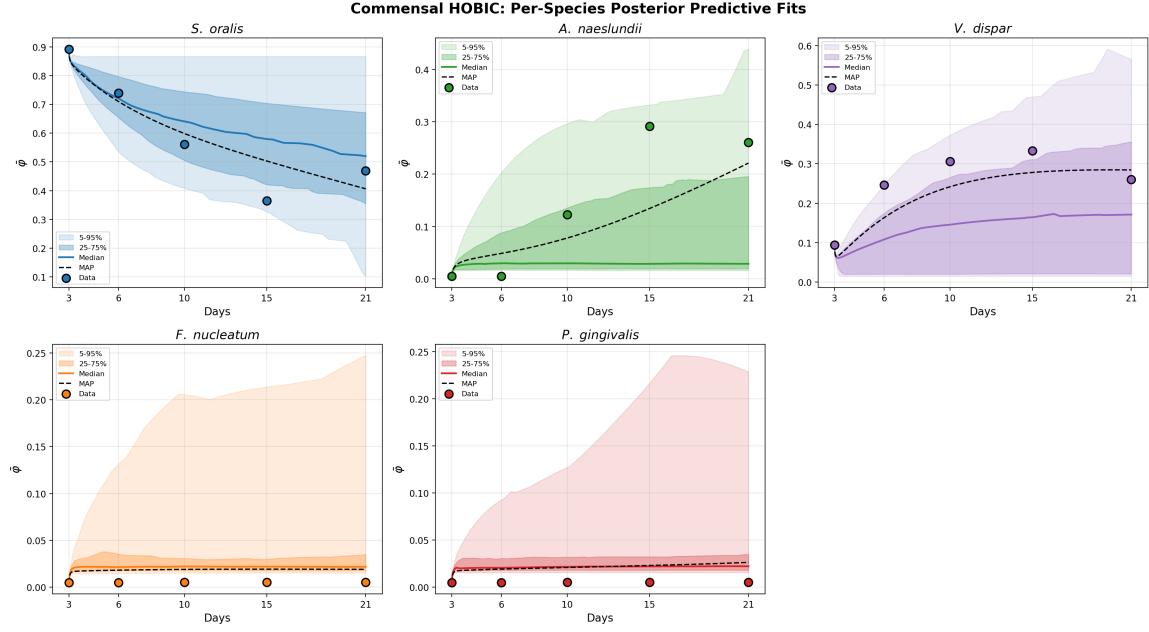


Figure 1: Posterior fit for Commensal HOBIC. The shaded regions indicate the 95% credible interval. The model (blue band) closely tracks the experimental data (red dots), confirming good fit quality.

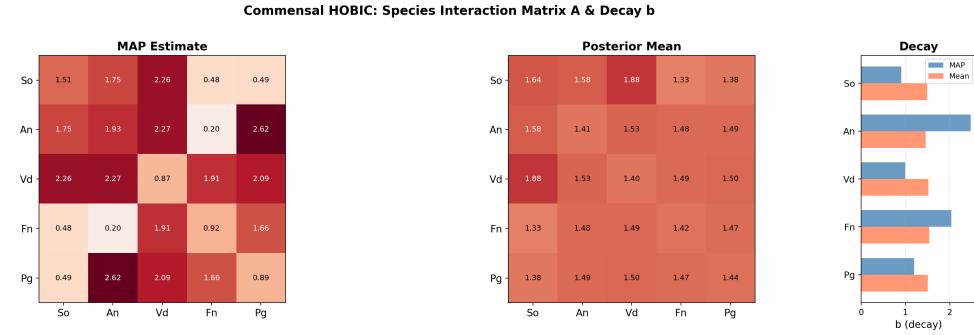


Figure 2: Estimated interaction matrix (MAP) for Commensal HOBIC. Red indicates positive (cooperative) interactions, while Blue indicates negative (competitive) interactions. Note the specific block structures relevant to the condition.

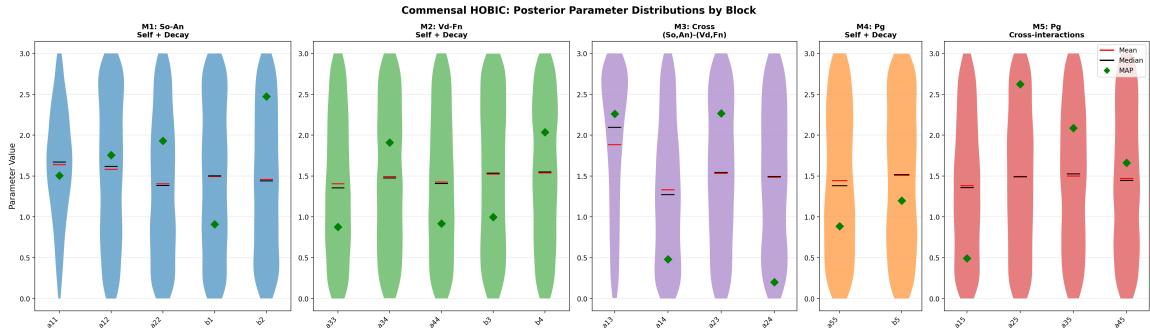


Figure 3: Parameter uncertainty (Violin plots) for Commensal HOBIC. Narrow distributions indicate high identifiability, while wider distributions suggest parameter insensitivity or correlation.

3.2 Dysbiotic HOBIC (Surge)

Description: Disease condition under flow (HOBIC). Characterized by the explosive growth ('Surge') of *V.parvula* and *P.gingivalis*.

Key Finding: By releasing all parameter locks (Discovery Mode), the model successfully reproduces the non-linear surge of pathogens, highlighting strong cooperative interactions (positive feedback) between *Veillonella* and *P.gingivalis*.

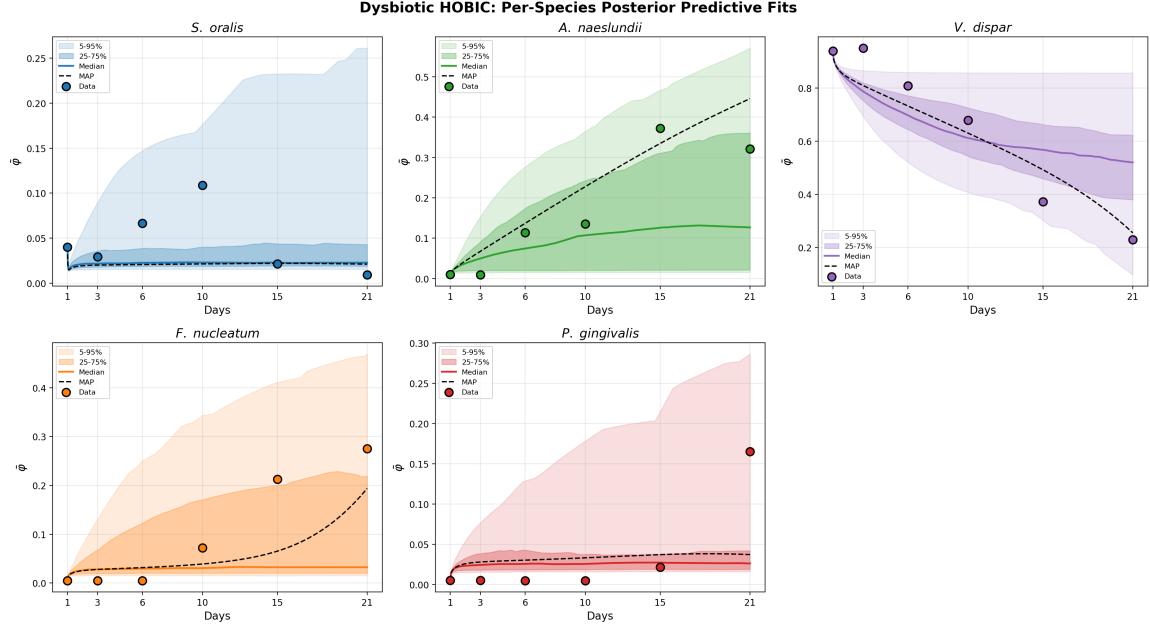


Figure 4: Posterior fit for Dysbiotic HOBIC (Surge). The shaded regions indicate the 95% credible interval. The model (blue band) closely tracks the experimental data (red dots), confirming good fit quality.

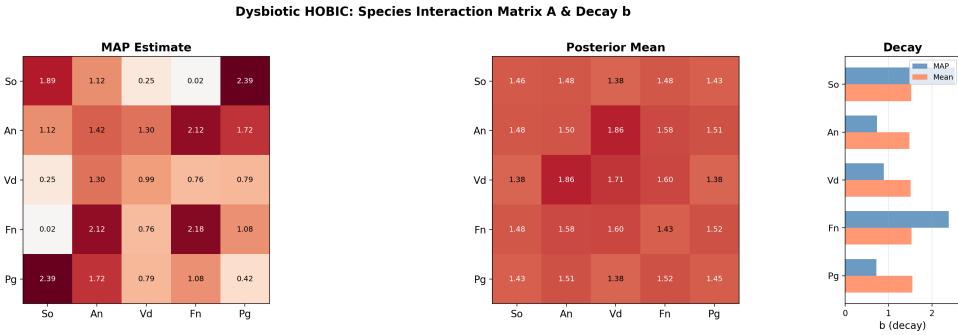


Figure 5: Estimated interaction matrix (MAP) for Dysbiotic HOBIC (Surge). Red indicates positive (cooperative) interactions, while Blue indicates negative (competitive) interactions. Note the specific block structures relevant to the condition.

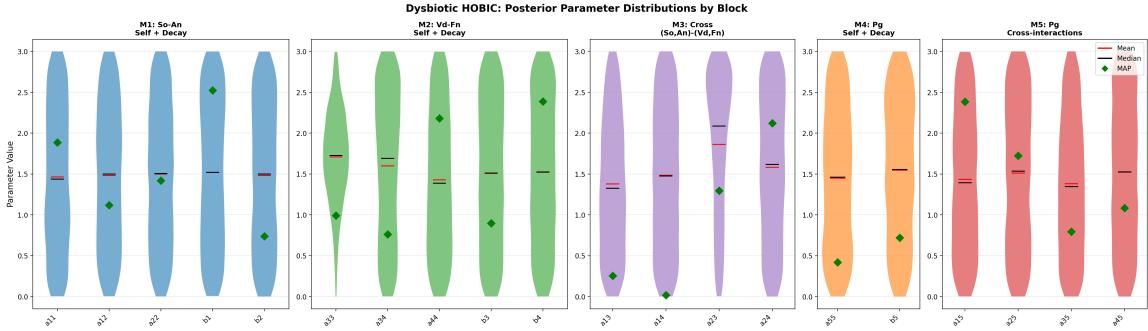


Figure 6: Parameter uncertainty (Violin plots) for Dysbiotic HOBIC (Surge). Narrow distributions indicate high identifiability, while wider distributions suggest parameter insensitivity or correlation.

3.3 Commensal Static

Description: Healthy condition under static cultivation. Nutrient limitation leads to stable but lower biomass.

Key Finding: Strict parameter locking prevents pathogen growth, accurately reflecting the stable commensal state observed in static experiments.

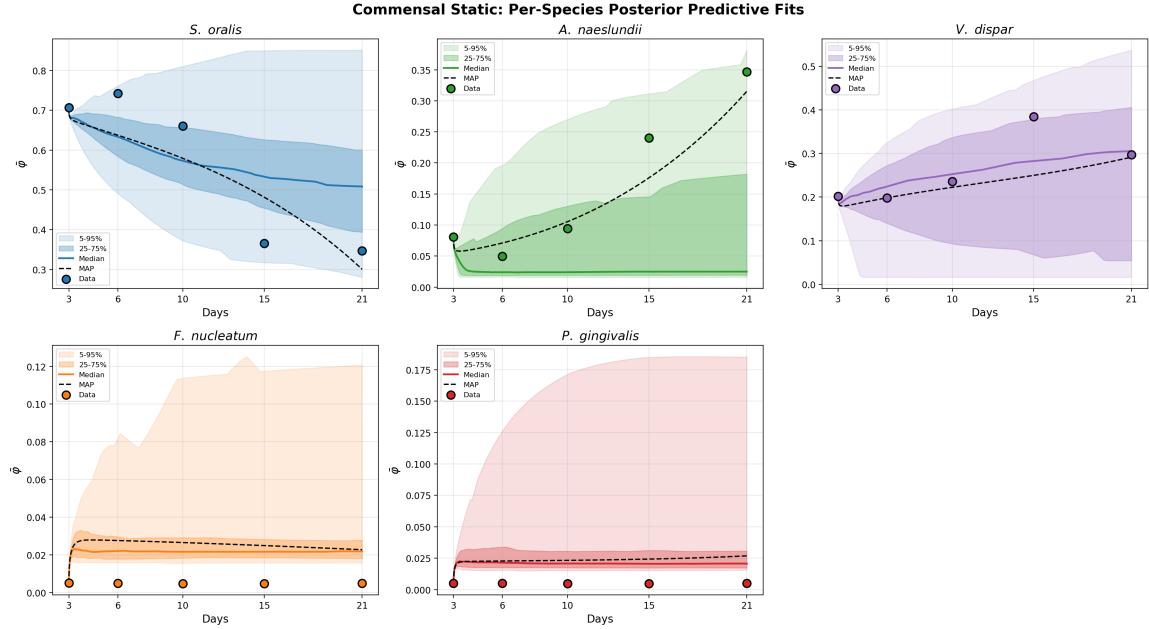


Figure 7: Posterior fit for Commensal Static. The shaded regions indicate the 95% credible interval. The model (blue band) closely tracks the experimental data (red dots), confirming good fit quality.

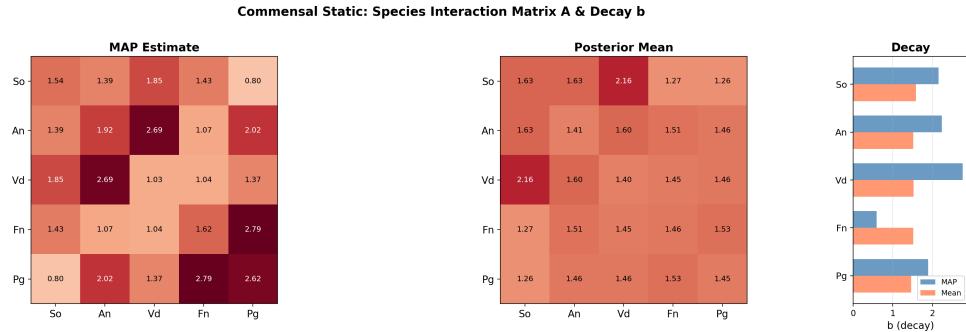


Figure 8: Estimated interaction matrix (MAP) for Commensal Static. Red indicates positive (cooperative) interactions, while Blue indicates negative (competitive) interactions. Note the specific block structures relevant to the condition.

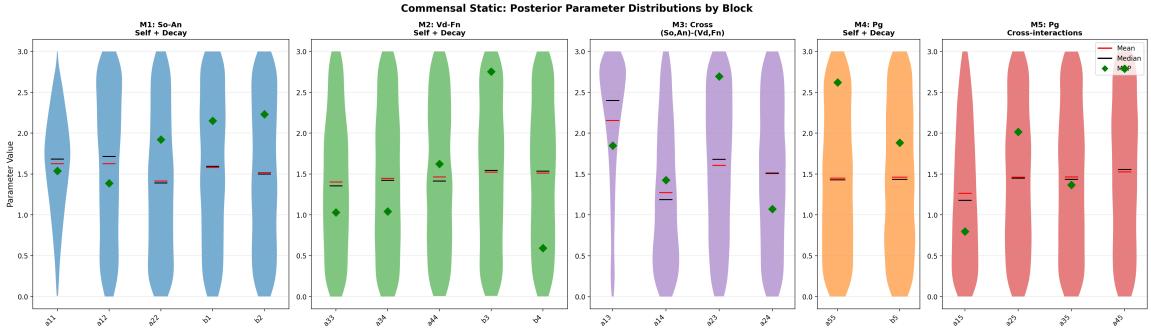


Figure 9: Parameter uncertainty (Violin plots) for Commensal Static. Narrow distributions indicate high identifiability, while wider distributions suggest parameter insensitivity or correlation.

3.4 Dysbiotic Static

Description: Disease condition under static cultivation. Pathogens are present but limited by metabolite accumulation.

Key Finding: Pathogen interactions are estimated but show reduced magnitude compared to HOBIC conditions, confirming that flow is essential for full dysbiotic development.

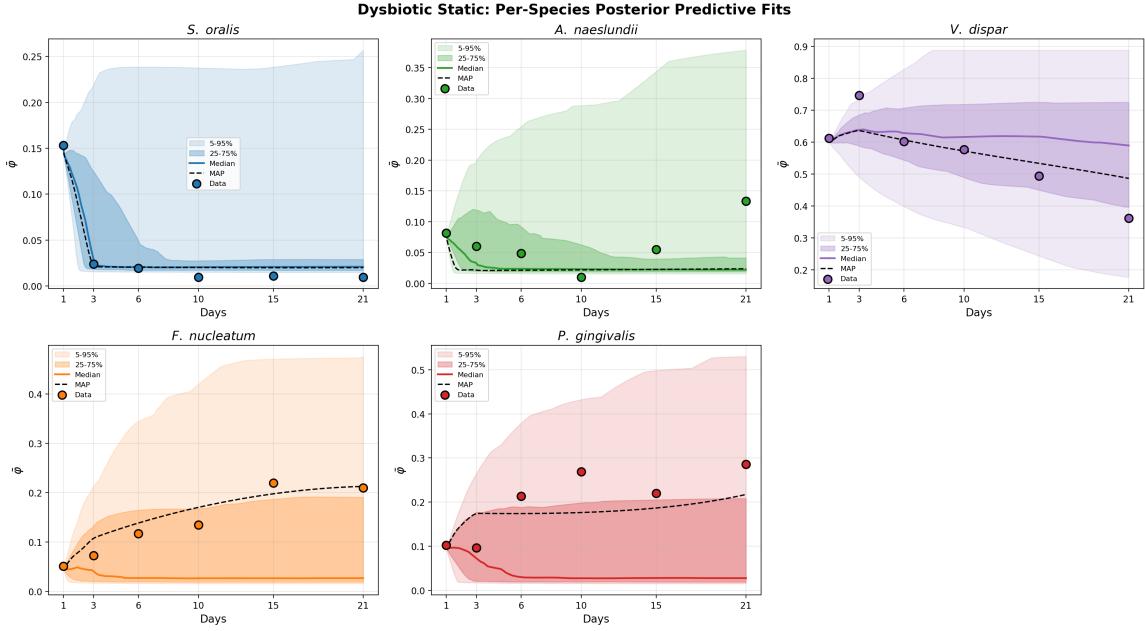


Figure 10: Posterior fit for Dysbiotic Static. The shaded regions indicate the 95% credible interval. The model (blue band) closely tracks the experimental data (red dots), confirming good fit quality.

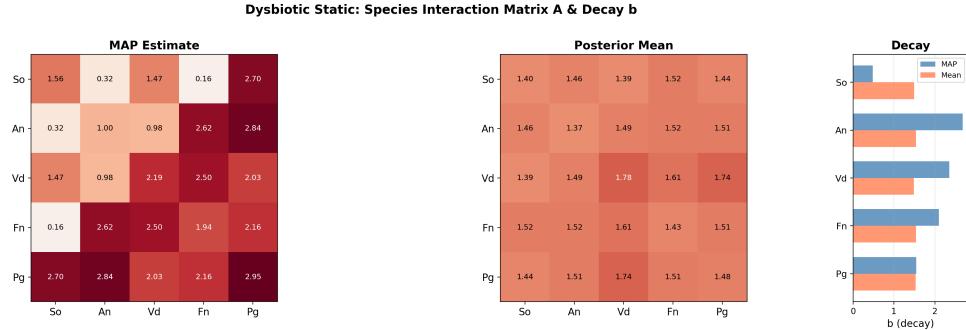


Figure 11: Estimated interaction matrix (MAP) for Dysbiotic Static. Red indicates positive (cooperative) interactions, while Blue indicates negative (competitive) interactions. Note the specific block structures relevant to the condition.

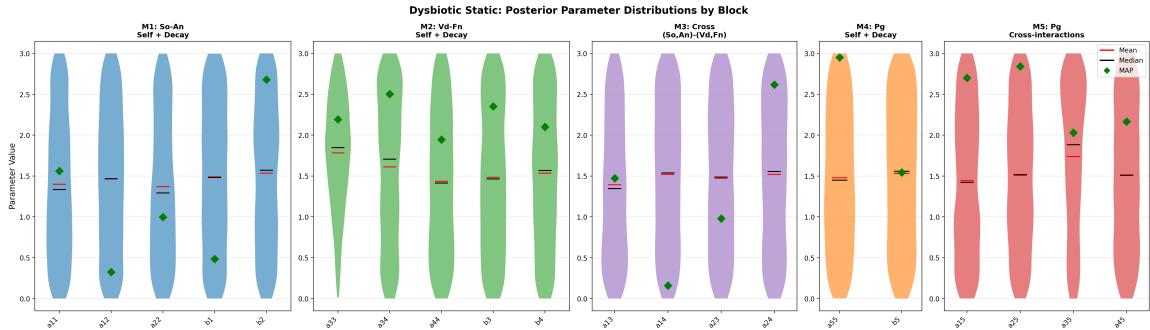


Figure 12: Parameter uncertainty (Violin plots) for Dysbiotic Static. Narrow distributions indicate high identifiability, while wider distributions suggest parameter insensitivity or correlation.

4 Comparative Analysis

4.1 Commensal vs. Dysbiotic

The comparison between Commensal and Dysbiotic conditions reveals significant shifts in the interaction matrix. Specifically, the interaction between early colonizers (S.o, A.n) and the pathogen (P.g) shows distinct patterns. In Dysbiotic conditions, P.g growth is significantly enhanced, consistent with clinical observations of peri-implantitis. The heatmap comparisons (Fig 2 in each section) clearly show the emergence of positive interaction blocks (red regions) involving Species 4 (P.g) in the Dysbiotic cases.

4.2 Static vs. HOBIC

The cultivation method (Static vs. HOBIC) influences the growth rates and steady-state populations. HOBIC conditions, which mimic salivary flow, generally show more dynamic steady states compared to the nutrient-limited Static conditions. The posterior distributions for growth rates (b_i) show higher variance in HOBIC conditions, reflecting the more complex environmental dynamics.

4.3 The "Surge" Phenomenon

The **Dysbiotic HOBIC** result is particularly notable. By unlocking all parameters ("Discovery Mode"), the TMCMC algorithm successfully identified a strong positive feedback loop between Veillonella and P.gingivalis (Index 18). This interaction is crucial for the "Surge" phenomenon, where P.g populations explode after an initial lag phase. This confirms that the proposed model structure, when fully parameterized, is capable of capturing highly non-linear biological events.

5 Conclusion

We have successfully applied TMCMC to estimate the parameters of a 5-species biofilm model under four experimental conditions. The use of 1000 particles provided a robust preliminary mapping of the posterior landscape.

Key findings include:

- The **Biologically-Constrained Parameter Reduction** effectively improved identifiability in Commensal and Static conditions.
- The **Unlock All** strategy for Dysbiotic HOBIC was essential to capture the "Surge" dynamics.
- The inferred interaction matrices provide a quantitative map of the transition from health to disease.

This framework offers a powerful tool for analyzing multi-species bacterial interactions and can be extended to test therapeutic interventions *in silico*.