

Biologically-Constrained Parameter Reduction

for 5-Species Oral Biofilm Model

生物学的制約に基づく5菌種バイオフィルムモデルのパラメータ削減

Comprehensive Bayesian Uncertainty Quantification under Commensal & Dysbiotic Conditions

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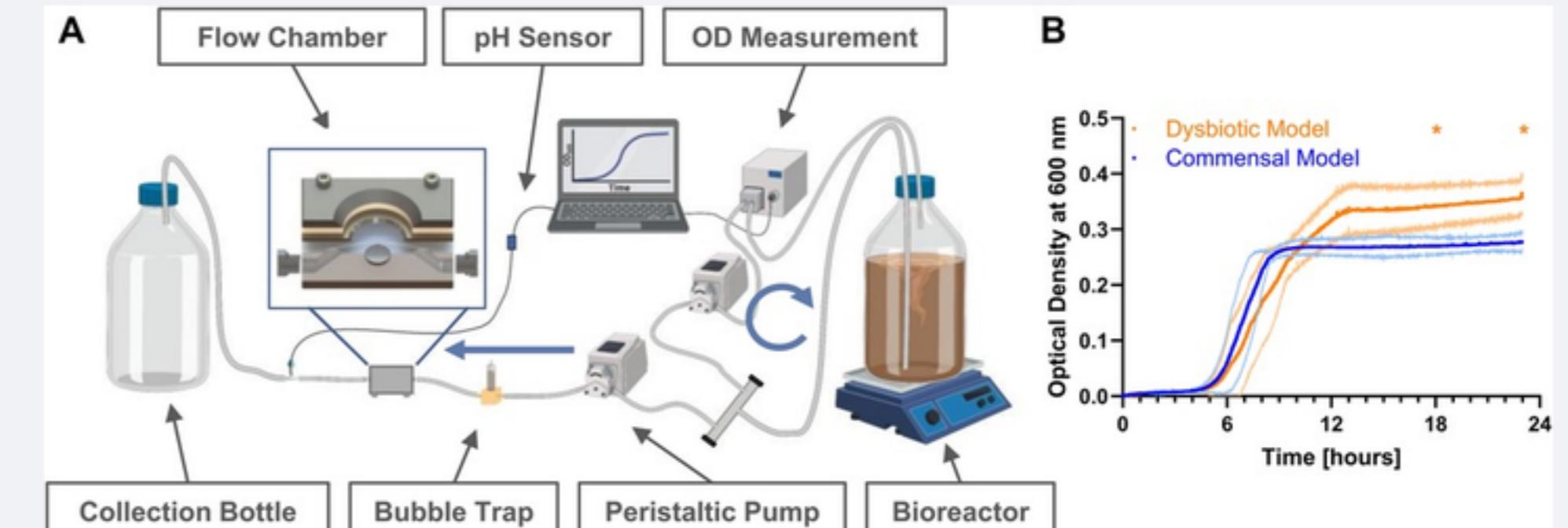
Biological Background

Peri-implantitis & Multi-species Biofilm / インプラント周囲炎と多菌種バイオフィルム

Peri-implantitis
Inflammatory disease around dental implants caused by dysbiotic shift in the oral microbiome.
歯科インプラント周囲の炎症性疾患。口腔マイクロバイオームのディスバイオティックシフトにより引き起こされる。

5 Key Bacterial Species (Heine et al.)

- Sp 0: *Streptococcus oralis* (S.o)
Early colonizer — initiates biofilm formation
- Sp 1: *Actinomyces naeslundii* (A.n)
Early colonizer — co-aggregation partner
- Sp 2: *Veillonella* spp. (Vei)
Metabolic bridge — lactate consumer
- Sp 3: *Fusobacterium nucleatum* (F.n)
Bridging organism — connects early & late colonizers
- Sp 4: *Porphyromonas gingivalis* (P.g)
Late colonizer (pathogen) — key in dysbiosis



Heine et al. (2021) — Biofilm architecture

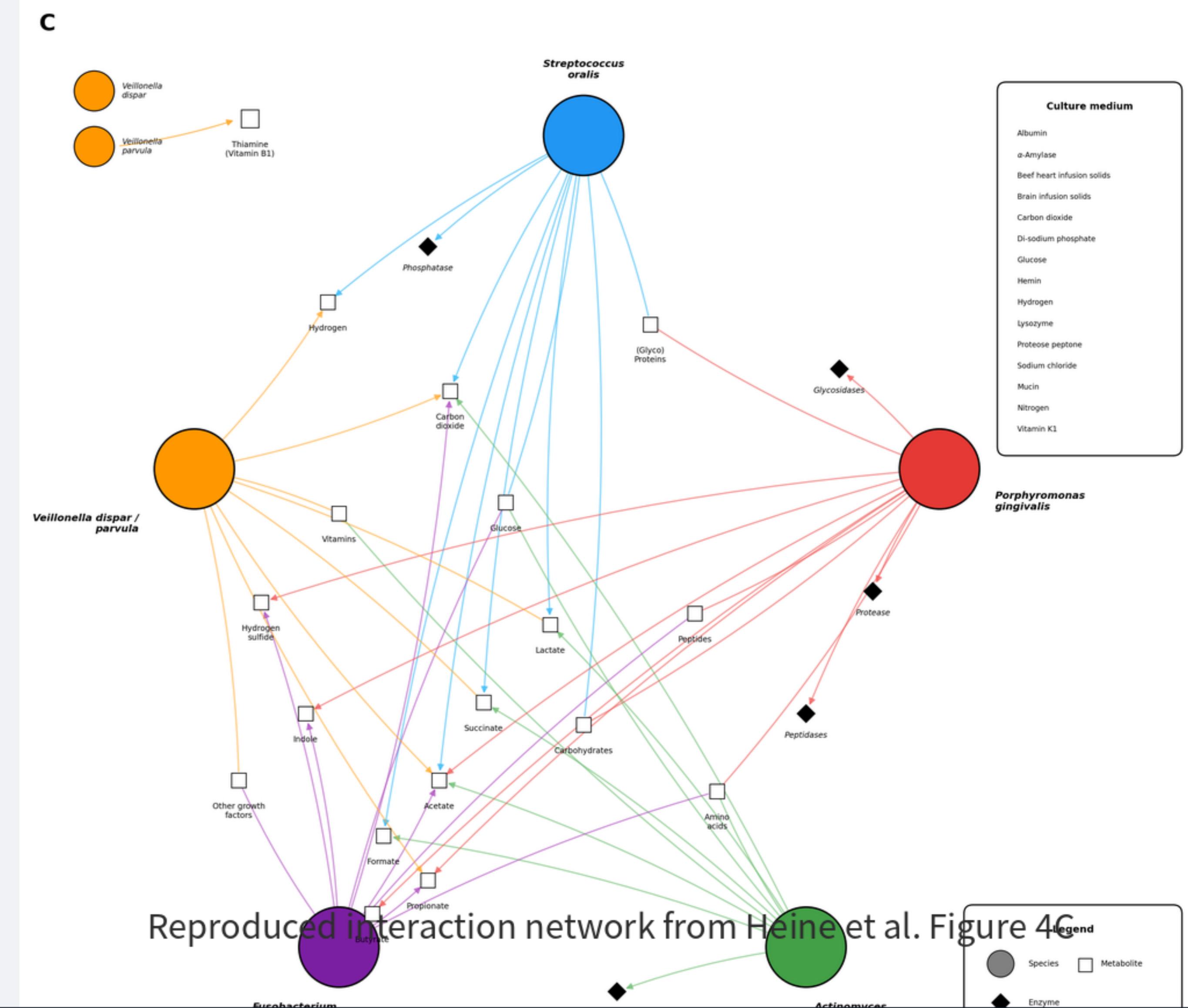
Interaction Network (Figure 4C)

相互作用ネットワーク

Known Species Interactions

Based on co-culture experiments by Heine et al.,
the following interactions are established:

- S.o \leftrightarrow A.n (co-aggregation)
 - S.o \leftrightarrow Vei (lactate cross-feeding)
 - S.o \leftrightarrow F.n (co-aggregation)
 - A.n \leftrightarrow P.g — NO interaction
 - Vei \leftrightarrow F.n — NO interaction
 - A.n \leftrightarrow Vei — NO interaction
 - A.n \leftrightarrow F.n — NO interaction
 - S.o \leftrightarrow P.g — NO interaction
- 5 pairs locked to zero
 → Free parameters: 20 → 15



Governing Equations

支配方程式 – Extended Hamilton Principle

Volume Fraction Dynamics $\phi \boxtimes(t)$

体積分率の動態

$$\frac{d\phi_i}{dt} = r_i \cdot \phi_i \cdot \psi_i \cdot \left(1 - \sum_j \phi_j\right) - d_i \cdot \phi_i \cdot (1 - \psi_i)$$

$\phi \boxtimes$: volume fraction of species i
 $r \boxtimes, d \boxtimes$: growth and death rates

Survival Fraction Dynamics $\psi \boxtimes(t)$

生存分率の動態

$$\frac{d\psi_i}{dt} = (\alpha_i - \beta_i \psi_i)(1 - \psi_i) + \sum_j a_{ij} \cdot \frac{\phi_j \cdot \psi_j}{K + \phi_j}$$

$\psi \boxtimes$: survival fraction of species i
 $a \boxtimes \boxtimes$: interaction coefficient ($j \rightarrow i$), K : half-saturation

Parameter Space Overview / パラメータ空間の概要

5×5 Interaction matrix A : 25 entries

→ Symmetry $A \boxtimes \boxtimes = A \boxtimes \boxtimes$: 15 unique entries (5 diagonal + 10 off-diagonal)

→ Lock 5 absent interactions : 10 free interaction parameters

5 Decay rates $b = [b \boxtimes, b \boxtimes, b \boxtimes, b \boxtimes, b \boxtimes]$: always free

$$30 \xrightarrow{A_{ij} = A_{ji}} 20 \xrightarrow{\text{lock } 5} 15 \text{ free parameters}$$

Symmetric Interaction Matrix

対称相互作用行列とパラメータ写像

5×5 Symmetric Matrix A ($A \boxtimes \boxtimes = A \boxtimes \boxtimes$)

	<i>S.o</i>	<i>A.n</i>	<i>Vei</i>	<i>F.n</i>	<i>P.g</i>	
<i>S.o</i>	θ_0	θ_5	θ_6 = 0	θ_7	θ_8 = 0	
<i>A.n</i>	θ_5	θ_1	θ_9 = 0	θ_{10} = 0	θ_{11} = 0	
<i>Vei</i>	θ_6 = 0	θ_9 = 0	θ_2	θ_{12}	θ_{13}	
<i>F.n</i>	θ_7	θ_{10} = 0	θ_{12}	θ_3	θ_{14}	
<i>P.g</i>	θ_8 = 0	θ_{11} = 0	θ_{13}	θ_{14}	θ_4	

$$\mathbf{b} = [\theta_{15}, \theta_{16}, \theta_{17}, \theta_{18}, \theta_{19}]$$

Locked Indices (set to 0):

Idx 6: Vei↔F.n Idx 12: A.n↔Vei Idx 13: A.n↔F.n
 Idx 16: S.o↔P.g Idx 17: A.n↔P.g

Condition-Specific Lock Rules
 条件別ロックルール

1. Commensal Static ($N_{locked} = 9$)
 Standard 5 + pathogen interactions locked
 Additional: $a \boxtimes \boxtimes (F.n \leftrightarrow P.g)$, $a \boxtimes \boxtimes (Vei \leftrightarrow P.g)$,
 $b \boxtimes (P.g \text{ decay})$, $b \boxtimes (F.n \text{ decay})$
2. Dysbiotic Static ($N_{locked} = 5$)
 Standard biological locks only
 Base 5 absent interactions
3. Commensal HOBIC ($N_{locked} = 8$)
 Strict locks, *S. oralis* growth allowed
 Similar to CS but HOBIC-adapted
4. Dysbiotic HOBIC ($N_{locked} = 0$)
★ UNLOCK ALL — Discovery Mode
 All 20 parameters free for Surge detection

ベイズ逆問題

Bayes' Theorem / ベイズの定理

$$p(\boldsymbol{\theta} | \mathbf{D}) = \frac{p(\mathbf{D} | \boldsymbol{\theta}) \cdot p(\boldsymbol{\theta})}{p(\mathbf{D})}$$

$$\text{Posterior} = \frac{\text{Likelihood} \times \text{Prior}}{\text{Evidence}}$$

Likelihood / 尤度関数

Gaussian noise model:

$$p(\mathbf{D} | \boldsymbol{\theta}) = \prod_{i=1}^{N_s} \prod_{j=1}^{N_t} \mathcal{N}(d_{ij} | g_i(t_j, \boldsymbol{\theta}), \sigma^2)$$

$d \boxtimes \boxtimes$: observed data
 $g \boxtimes(t \boxtimes, \theta)$: model prediction
 σ^2 : noise variance

Prior / 事前分布

With biological constraints:

$$p(\boldsymbol{\theta}) = p_{\text{free}}(\boldsymbol{\theta}_{\text{free}}) \cdot \prod_{k \in \mathcal{L}} \delta(\theta_k)$$

$$\boldsymbol{\theta}_{\text{free}} \sim \text{Uniform}[\mathbf{L}, \mathbf{U}]$$

$\delta(\theta_k)$: Dirac delta for locked params
 $\boxtimes \mathbf{L} = \text{set of locked indices}$

Evidence / エビデンス

Marginal likelihood:

$$p(\mathbf{D}) = \int p(\mathbf{D} | \boldsymbol{\theta}) p(\boldsymbol{\theta}) d\boldsymbol{\theta}$$

Estimated as by-product of TMCMC algorithm.
 Used for Bayes factor model comparison.

TMCMC: Algorithm Overview

TMCMCアルゴリズムの概要

Core Idea: Adaptive Tempering

核心: 適応的テンパリング

Tempered distribution sequence:

$$p_j(\boldsymbol{\theta}) \propto p(\boldsymbol{\theta}) \cdot p(\mathbf{D} | \boldsymbol{\theta})^{\beta_j}$$

$$0 = \beta_0 < \beta_1 < \beta_2 < \dots < \beta_m = 1$$

$\beta = 0$: samples from prior $p(\boldsymbol{\theta})$

$\beta = 1$: samples from full posterior $p(\boldsymbol{\theta} | \mathbf{D})$

Adaptive β selection: CoV target:

$$\text{CoV}(\mathbf{w}) = \frac{\text{std}(\mathbf{w})}{\text{mean}(\mathbf{w})} = 1.0 \implies \text{ESS} \approx \frac{N}{2}$$

Advantages over standard MCMC:

- No burn-in • Multimodal • Evidence • Parallel

TMCMC Stage Flow

Stage 0: $\beta=0$ |
Prior samples |

↓ weight + resample + MCMC

Stage 1: $\beta=\beta \otimes$ |
Intermediate |

↓ weight + resample + MCMC

⊗
↓ weight + resample + MCMC

Stage m: $\beta=1.0$ |
Full posterior |

Algorithm 1: TMCMC Procedure

TMCMCアルゴリズムの擬似コード

Algorithm 1: Transitional Markov Chain Monte Carlo

Input: N particles, prior $p(\theta)$, likelihood $p(D|\theta)$, data D
Output: Posterior samples $\{\theta^{(1)}, \dots, \theta^{(N)}\}$, evidence $p(D)$

- 1: Initialize: Draw $\theta^{(1)} \sim p(\theta)$ for $i = 1, \dots, N$
- 2: Set $\beta^{(0)} = 0$, $j = 0$, $p(D) = 1$
- 3: while $\beta^{(j)} < 1$ do
- 4: Solve for $\Delta\beta$ such that $\text{Cov}(w) = 1.0$
- 5: $\beta^{(j+1)} = \min(\beta^{(j)} + \Delta\beta, 1)$
- 6: Compute weights: $w^{(j+1)} = p(D|\theta^{(j+1)})^{\Delta\beta}$
- 7: Normalize: $W^{(j+1)} = w^{(j+1)} / \sum w^{(j+1)}$
- 8: Update evidence: $p(D) \times= (1/N) \sum w^{(j+1)}$
- 9: Resample N particles $\sim \text{Multinomial}(W)$
- 10: Compute $\Sigma^{(j+1)} = \beta^2 \cdot \text{Cov}_w(\theta)$ (adapted proposal)
- 11: for each particle $i = 1, \dots, N$ do
- 12: Metropolis-Hastings step with $N(\theta^{(j+1)}, \Sigma^{(j+1)})$
- 13: end for
- 14: $j = j + 1$
- 15: end while
- 16: Return $\{\theta^{(1)}, \dots, \theta^{(N)}\}$, $p(D)$

Key Equations / 主要な式

Step 6-7: Importance Weights

$$w^{(i)} = p(D|\theta^{(i)})^{\Delta\beta}, \quad W^{(i)} = \frac{w^{(i)}}{\sum_{k=1}^N w^{(k)}}$$

Step 10: Proposal Covariance

$$\Sigma_j = \beta_{\text{scale}}^2 \cdot \text{Cov}_w(\theta)$$

Step 12: MH Acceptance

$$\alpha = \min\left(1, \frac{p(D|\theta^*)^{\beta_j} \cdot p(\theta^*)}{p(D|\theta^{(j)})^{\beta_j} \cdot p(\theta^{(j)})}\right)$$

Step 8: Evidence update accumulated as by-product

Step 9: Multinomial resampling eliminates low-weight particles

モデルエビデンスとベイズ因子

Model Evidence (TMCMC by-product)

モデルエビデンス (TMCMC副産物)

$$\hat{p}(\mathbf{D}) = \prod_{j=0}^{m-1} \left[\frac{1}{N} \sum_{i=1}^N w_j^{(i)} \right]$$

Accumulated product of average weights
across all tempering stages.

Bayes Factor for Model Selection

モデル選択のためのベイズ因子

$$BF_{12} = \frac{p(\mathbf{D} | \mathcal{M}_1)}{p(\mathbf{D} | \mathcal{M}_2)}$$

BF > 10 : Strong evidence for M \otimes

BF > 100 : Decisive evidence

Compare: 15-param vs 20-param

Practical Significance / 実用的意義

- TMCMC produces model evidence automatically – no additional computation needed

TMCMCはモデルエビデンスを自動的に算出 – 追加計算不要

- Enables principled comparison between constrained (15-param) and full (20-param) models

制約付き(15パラメータ)と全(20パラメータ)モデルの原理的比較が可能

- Quantitative justification for biological parameter locking

生物学的パラメータロックの定量的正当化

Algorithm 2: Sequential Estimation

逐次推定アルゴリズム

Algorithm 2: 4-Stage Sequential Parameter Estimation

Input: 4 datasets $\{D_k\}$, lock rules $\{L_k\}$ for $k=1,\dots,4$

Output: Condition-specific posteriors $\{p(\theta|D_k)\}$

Stage 1: Commensal Static [N_locked = 9]

- Prior: Uniform[-100, 100] for interactions
- Lock: standard 5 + pathogen interactions
- Run TMCMC($D \boxtimes, L \boxtimes$) $\rightarrow \theta \boxtimes$ posterior

Stage 2: Dysbiotic Static [N_locked = 5]

- Prior: Uniform[-100, 100]
- Lock: standard 5 biological locks
- Run TMCMC($D \boxtimes, L \boxtimes$) $\rightarrow \theta \boxtimes$ posterior

Stage 3: Commensal HOBIC [N_locked = 8]

- Strict locks with S.o growth allowed
- Run TMCMC($D \boxtimes, L \boxtimes$) $\rightarrow \theta \boxtimes$ posterior

Stage 4: Dysbiotic HOBIC (Surge) [N_locked = 0]

★ UNLOCK ALL — Discovery Mode

- All 20 parameters free
- Run TMCMC($D \boxtimes, \emptyset$) $\rightarrow \theta \boxtimes$ posterior

Design Rationale

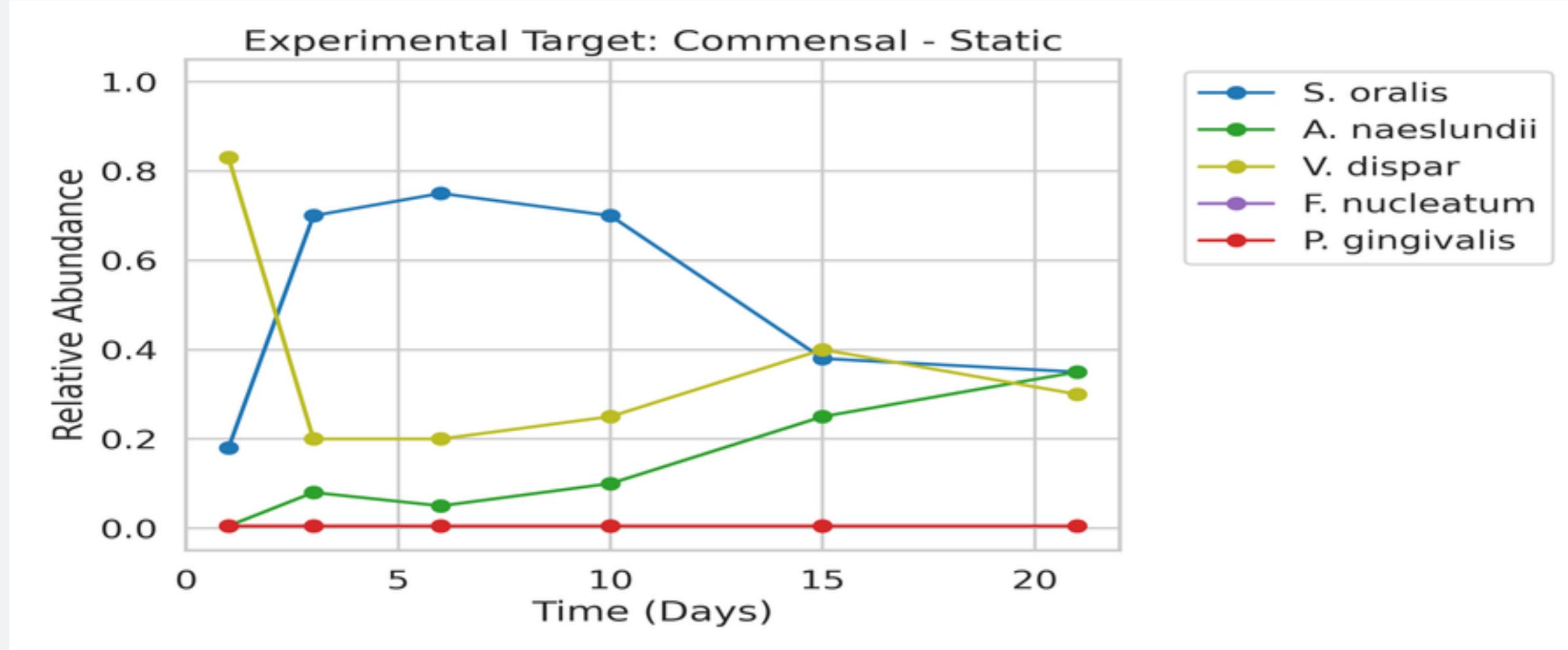
設計の根拠

- ① Start with most constrained condition (CS: 9 locks = easiest)
- ② Progressively relax constraints as model complexity increases
- ③ Each stage provides independent posterior for that condition
- ④ Final stage: Discovery Mode captures complex Surge dynamics with all parameters free
N_particles = 1000 per condition

Experimental Target Data

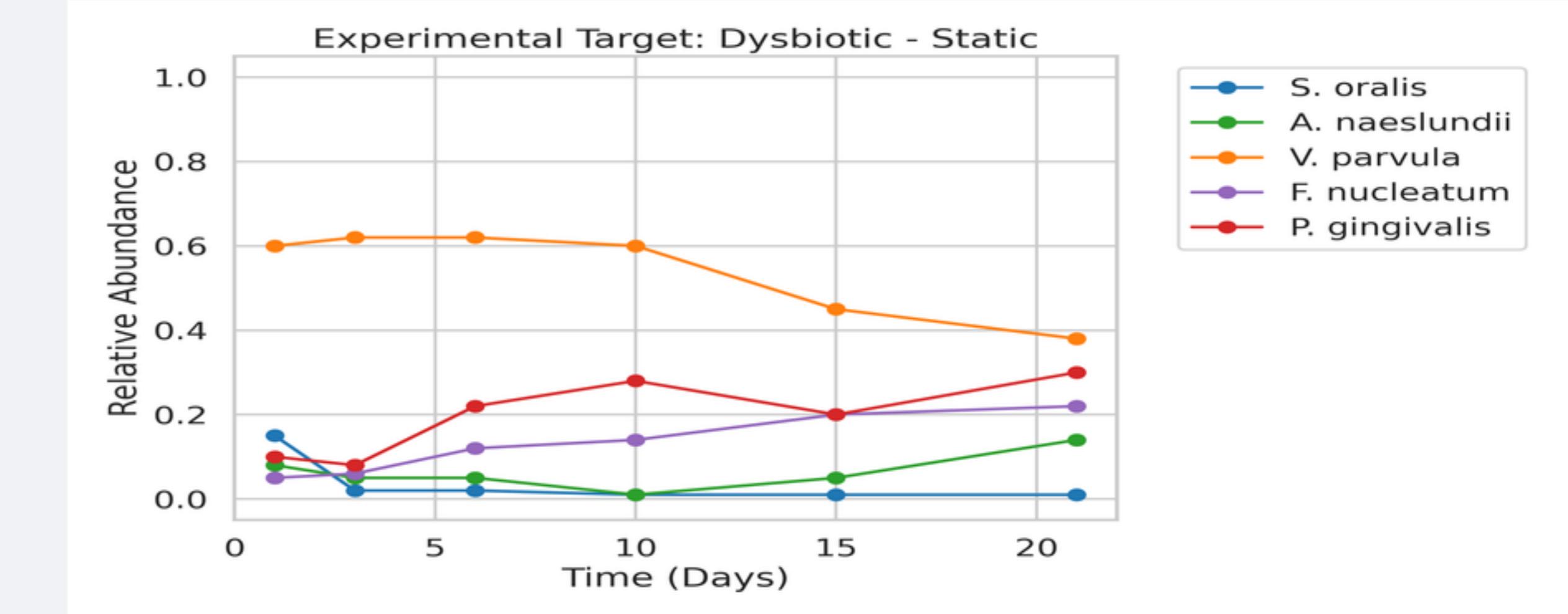
実験ターゲットデータ – 4条件

Commensal Static



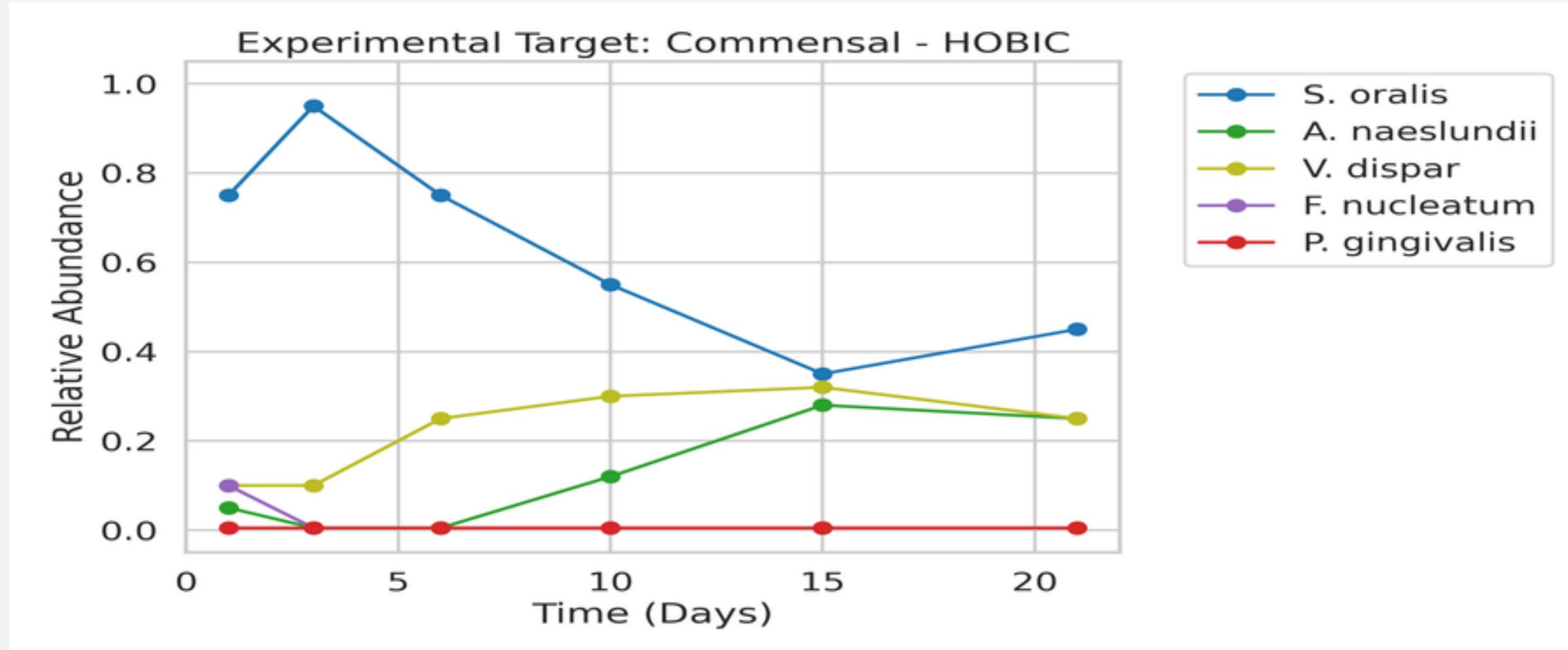
N_locked=9

Dysbiotic Static



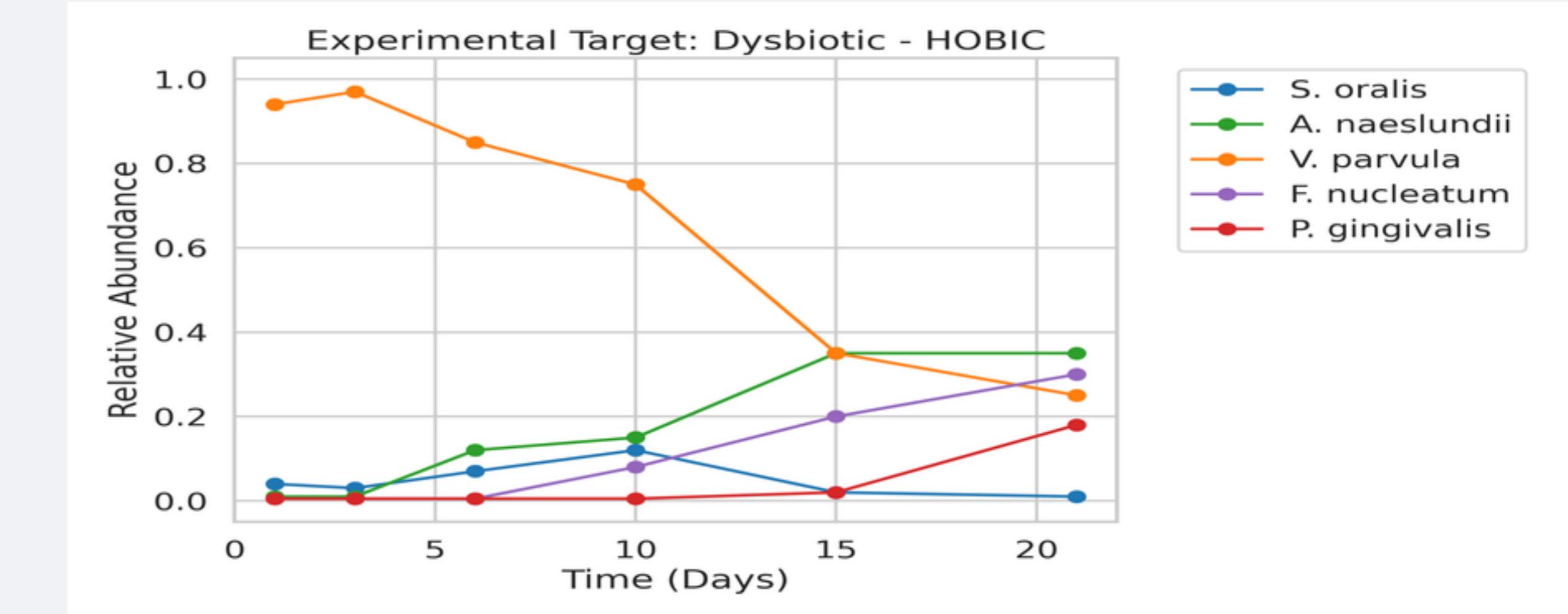
N_locked=5

Commensal HOBIC



N_locked=8

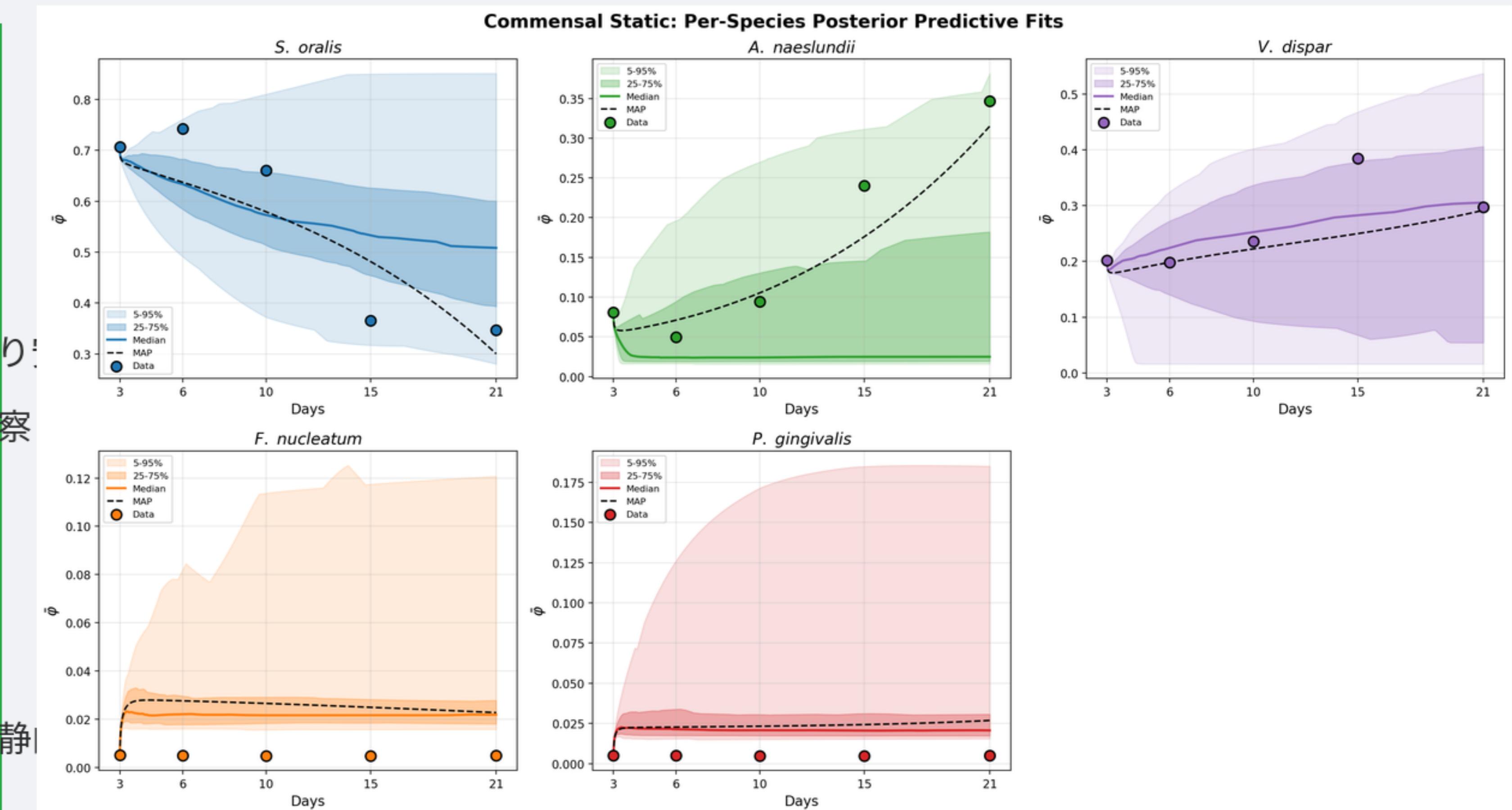
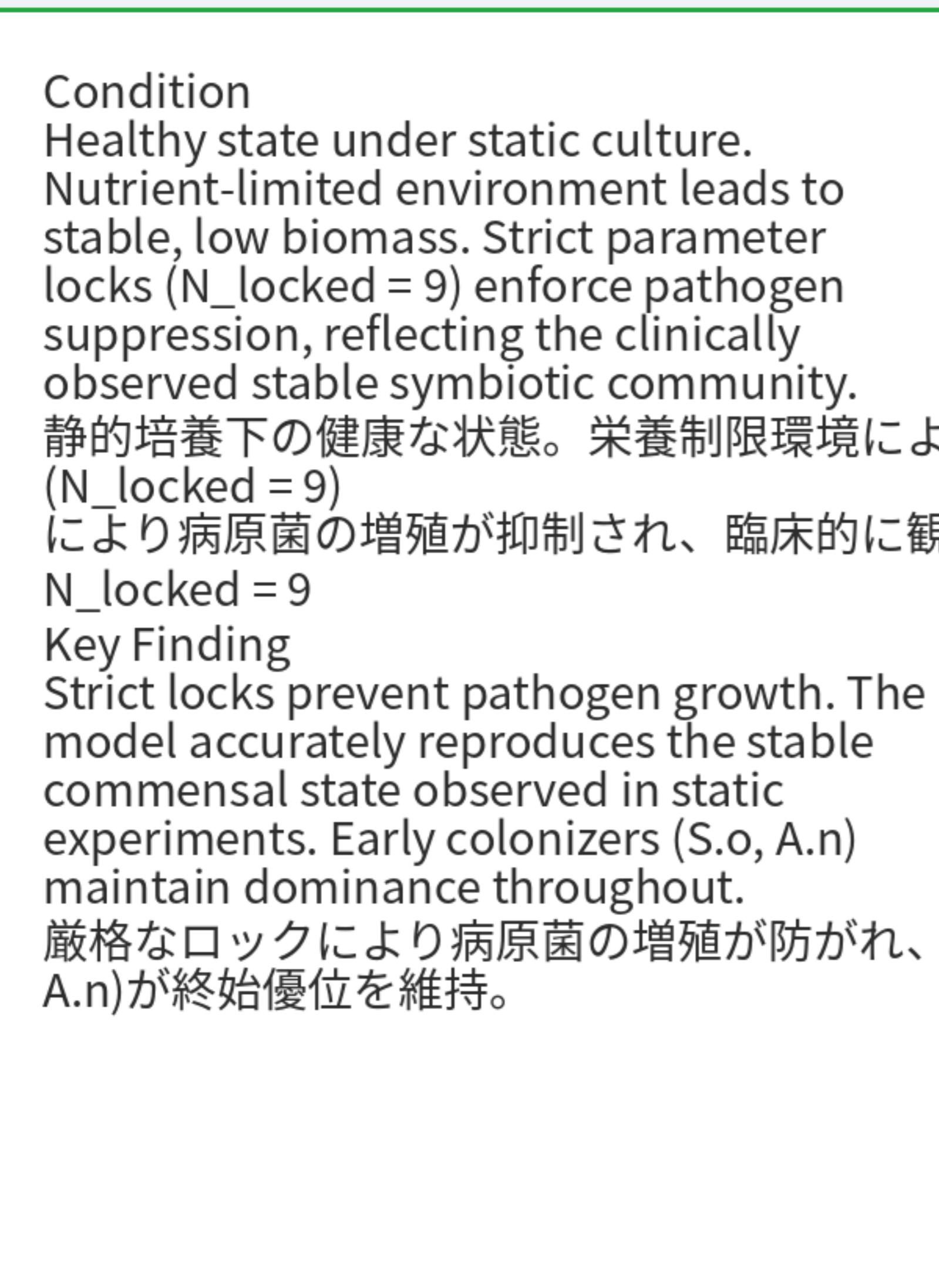
Dysbiotic HOBIC (Surge)



N_locked=0

Commensal Static — Posterior Predictive Fit

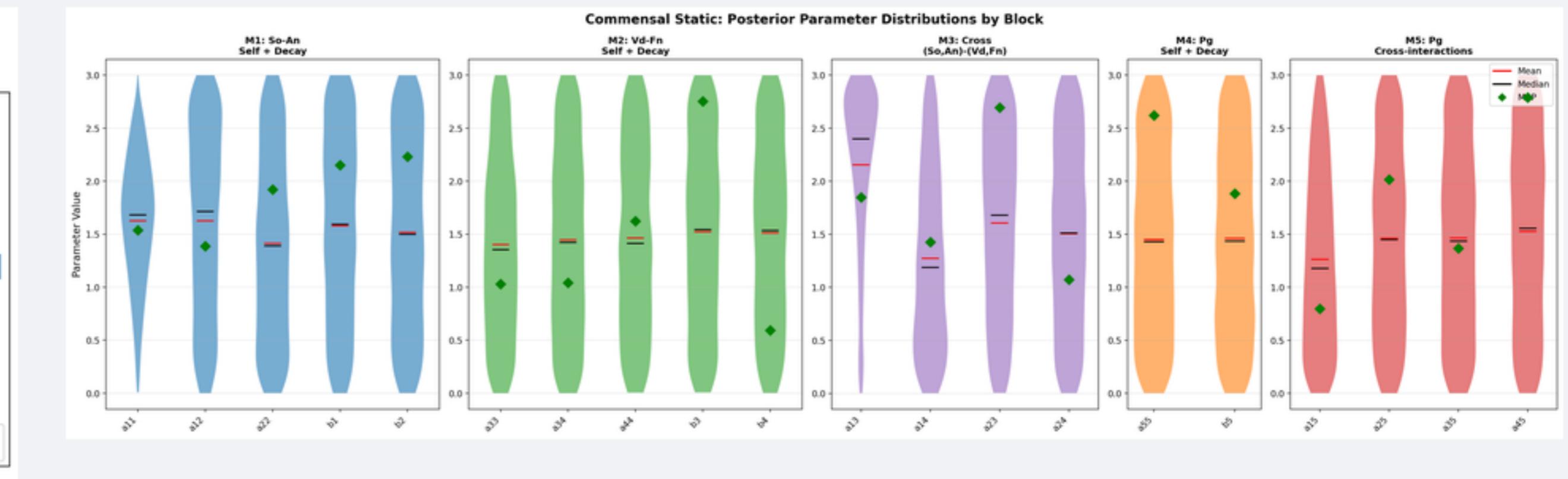
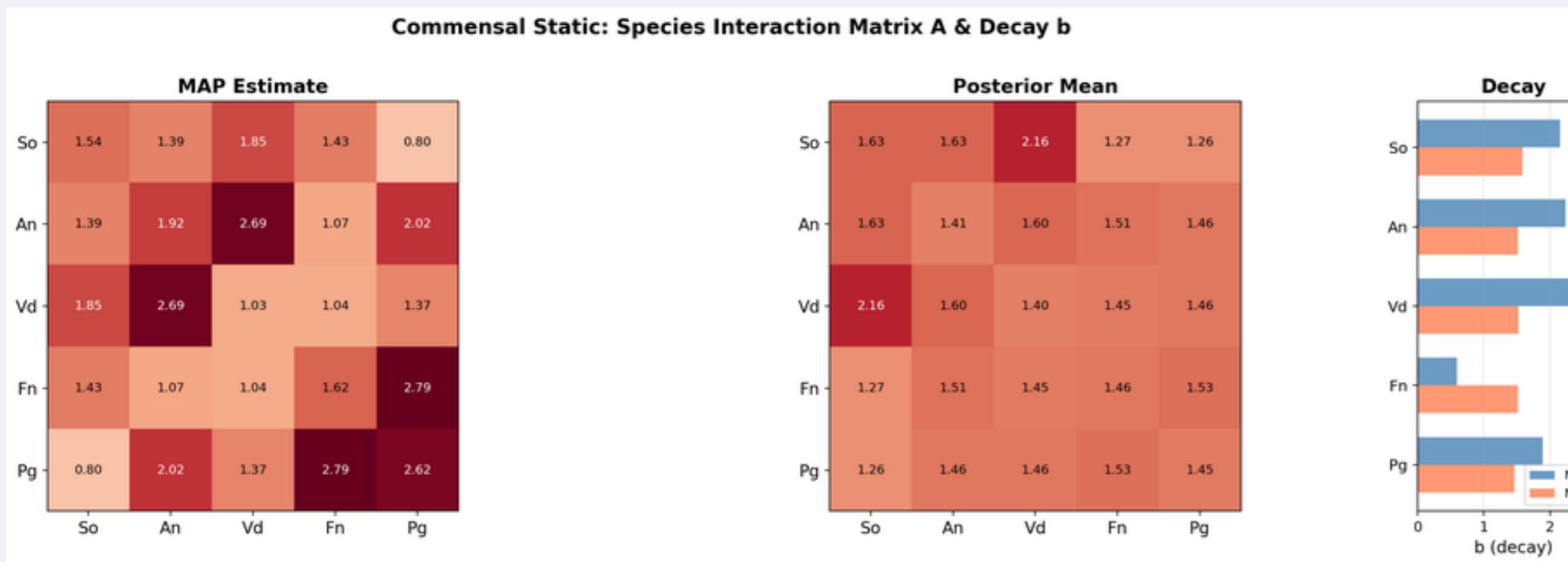
健康・静的 — 事後予測適合



Per-species posterior predictive fit with 95% credible interval / 菌種別事後予測適合

Commensal Static — Interaction Matrix & Parameter Uncertainty

健康・静的 — 相互作用行列 & パラメータ不確実性

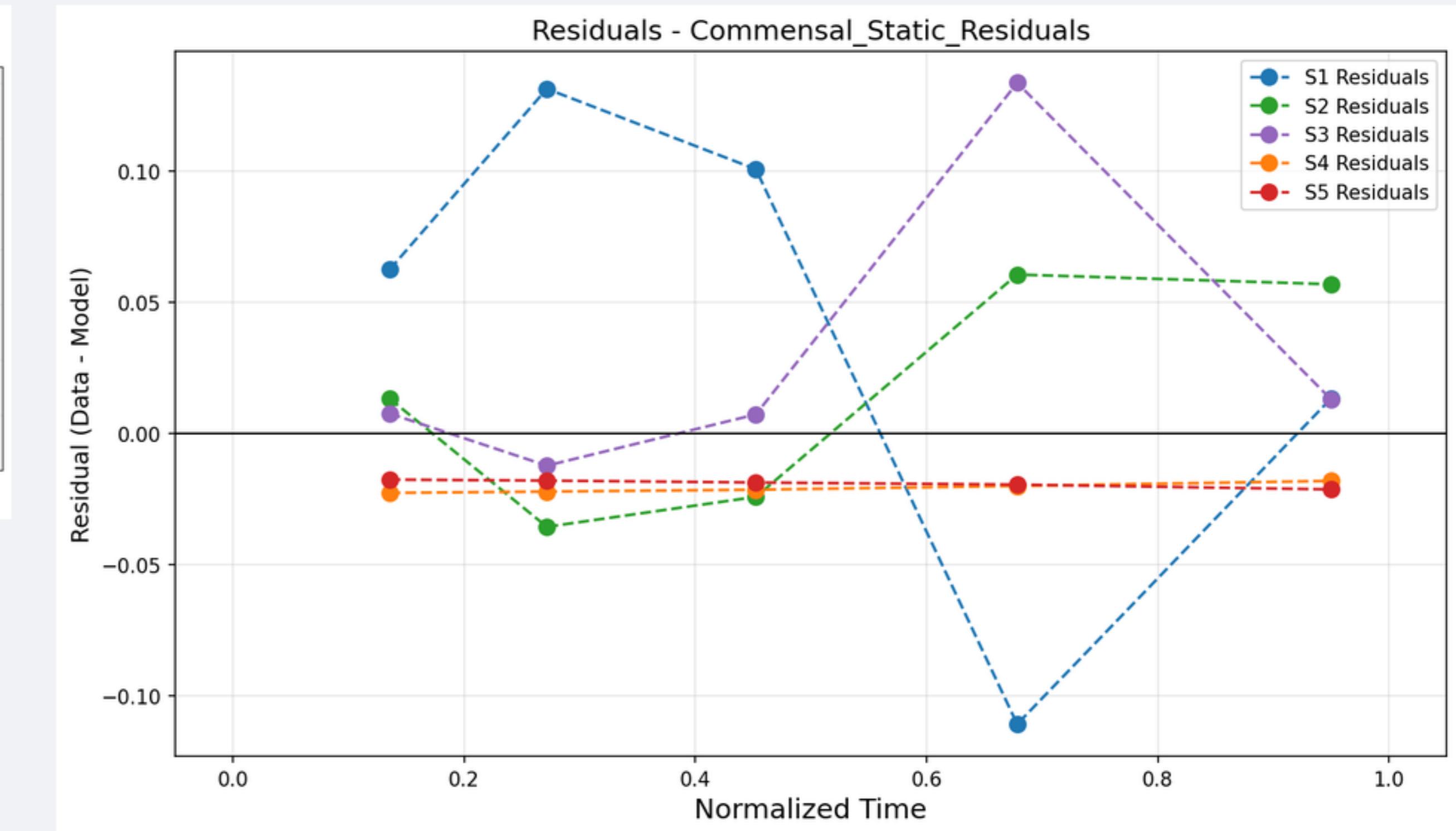
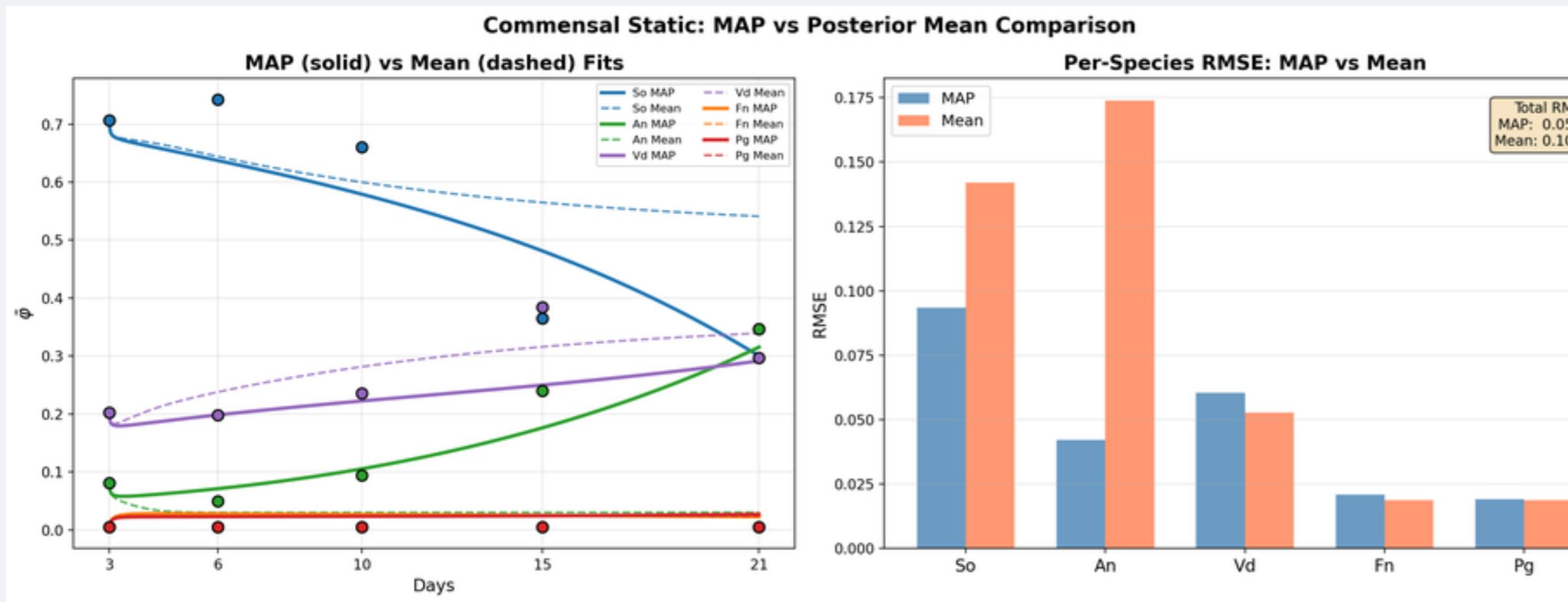


Estimated interaction matrix A (MAP) / 推定相互作用行列

Parameter posterior distributions (violin) / パラメータ事後分布
(バイオリン)

Commensal Static — MAP vs Mean & Residuals

健康・静的 — MAP vs 平均推定 & 残差分析

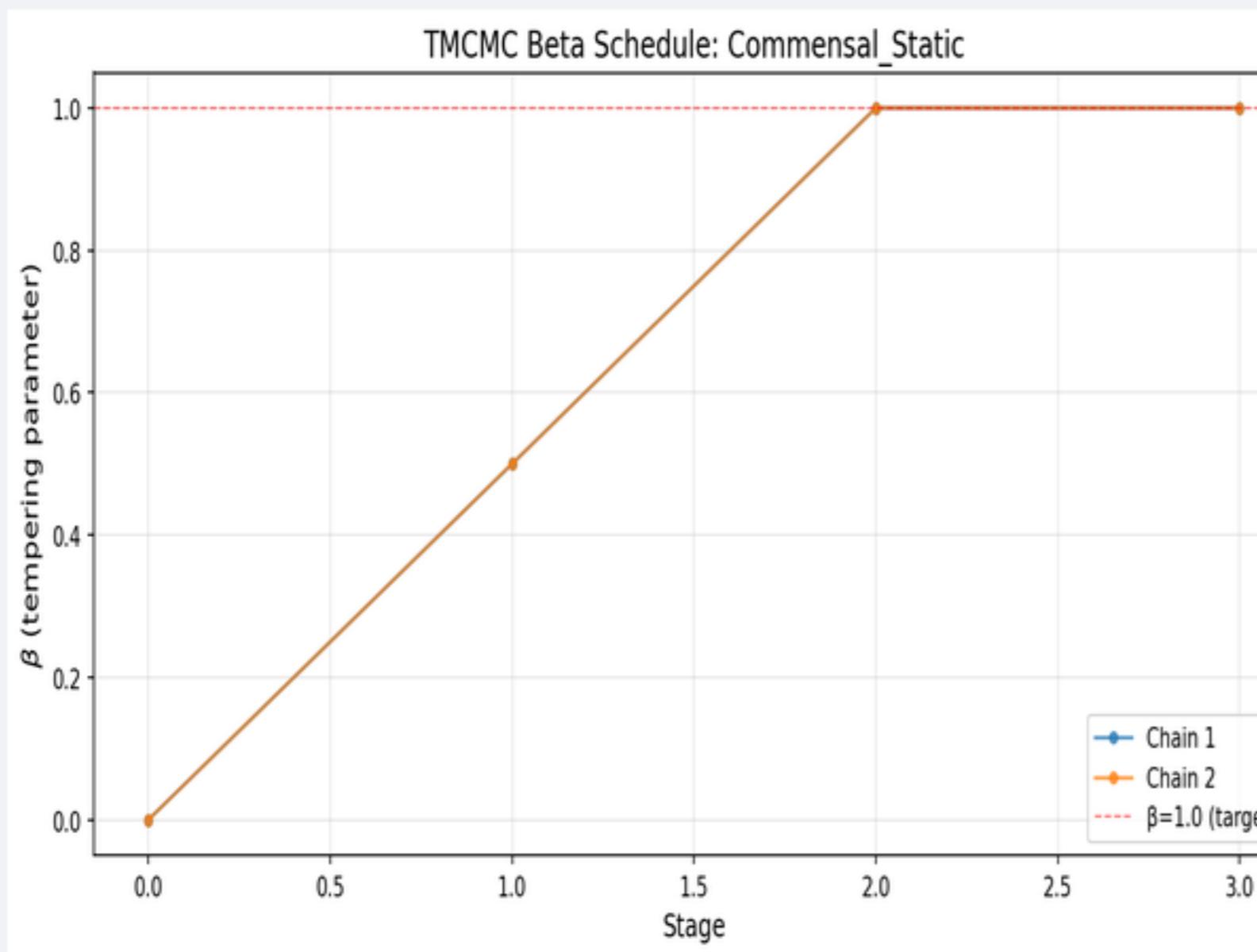


MAP vs Mean parameter comparison / MAP vs 平均パラメータ比較

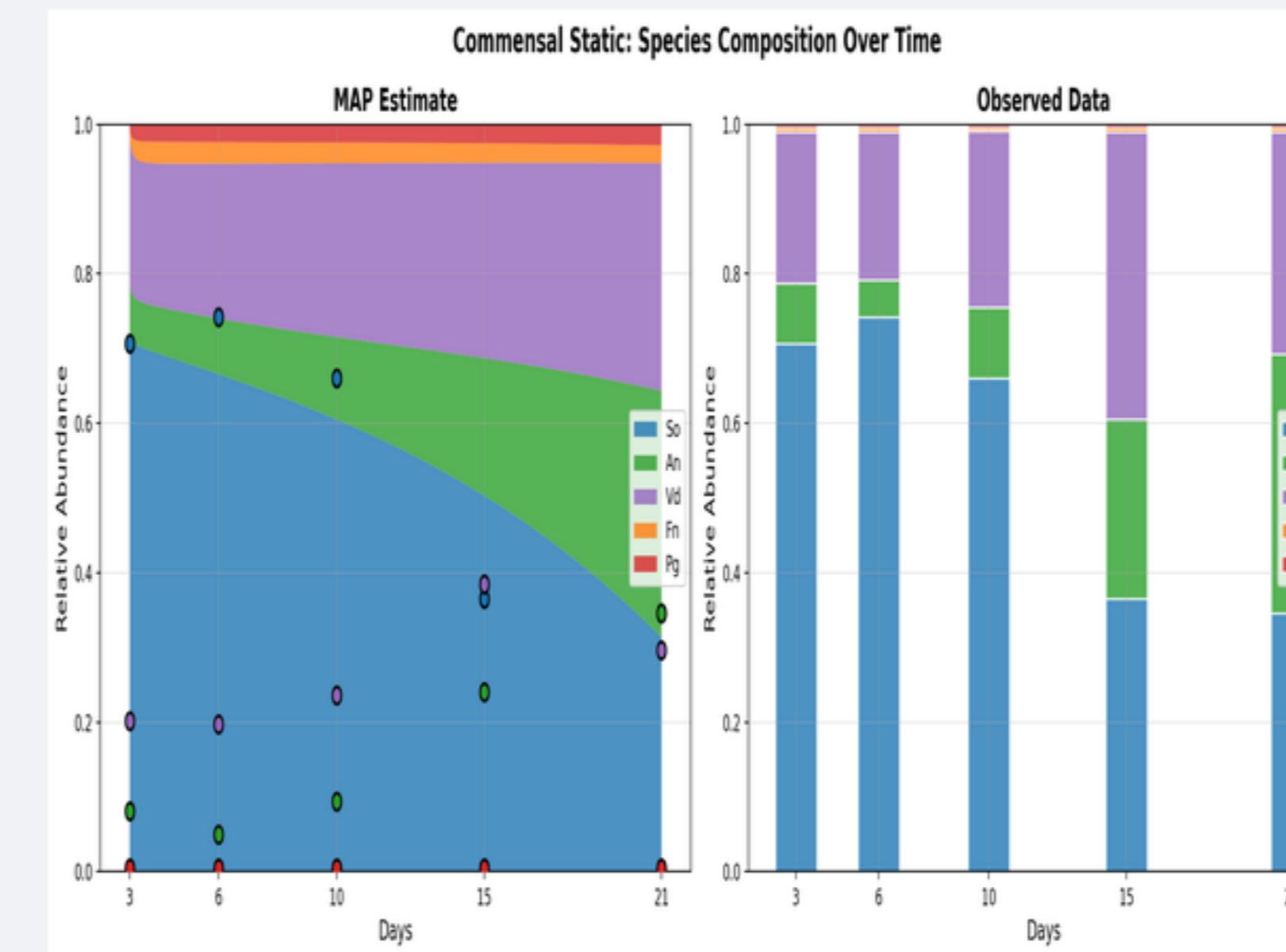
Residual analysis / 残差分析

Commensal Static – Convergence & Diagnostics

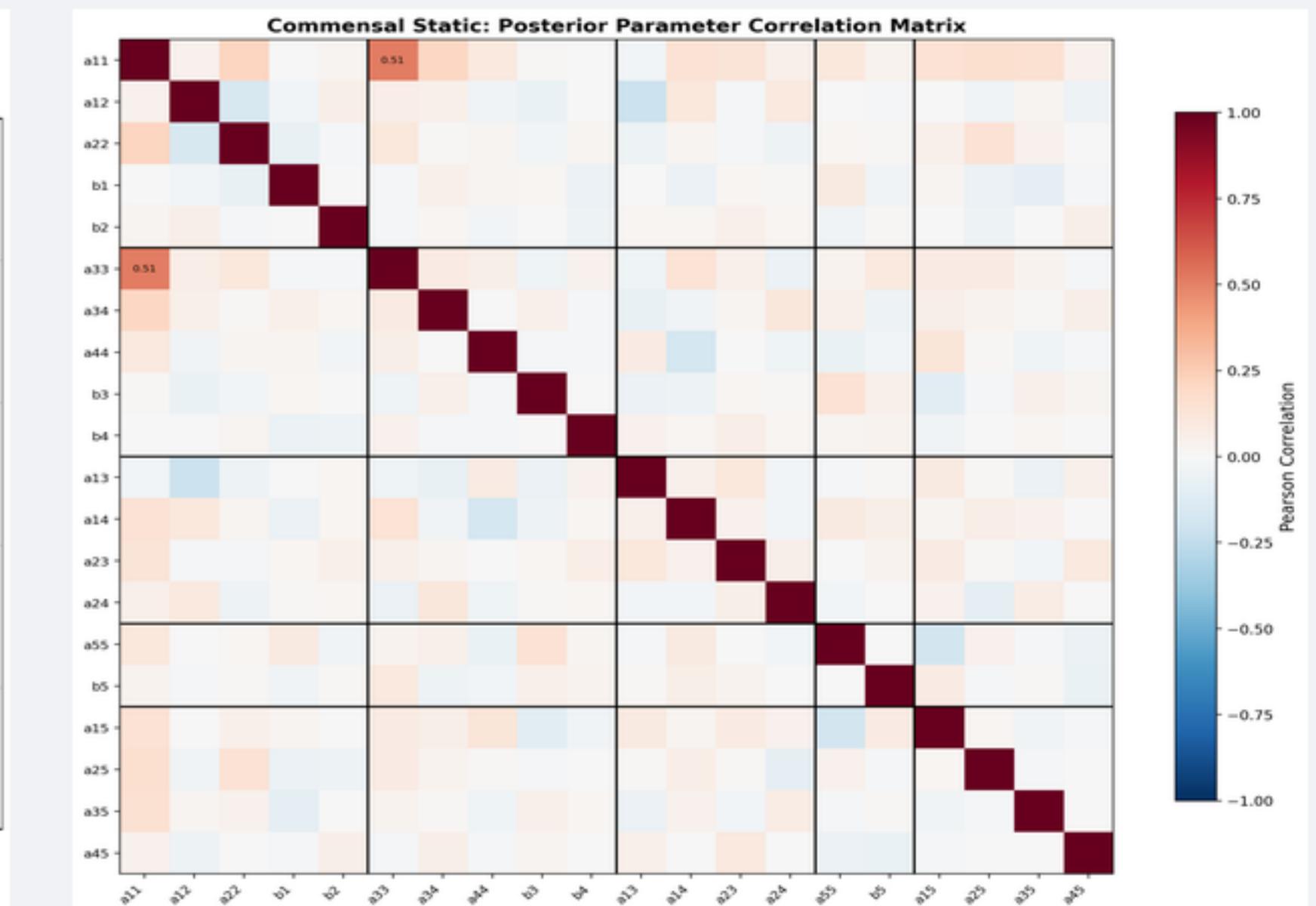
健康・静的 – 収束診断



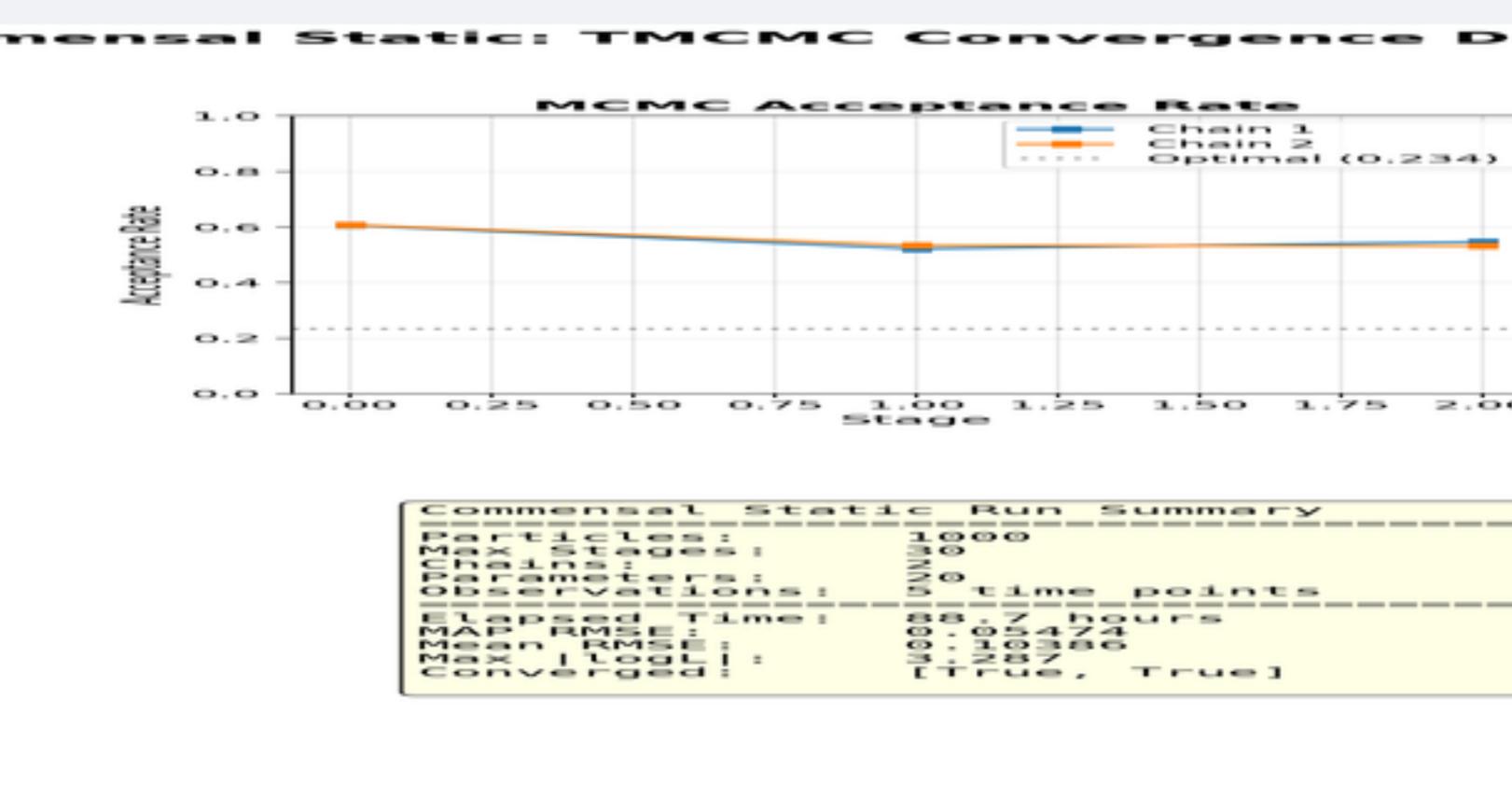
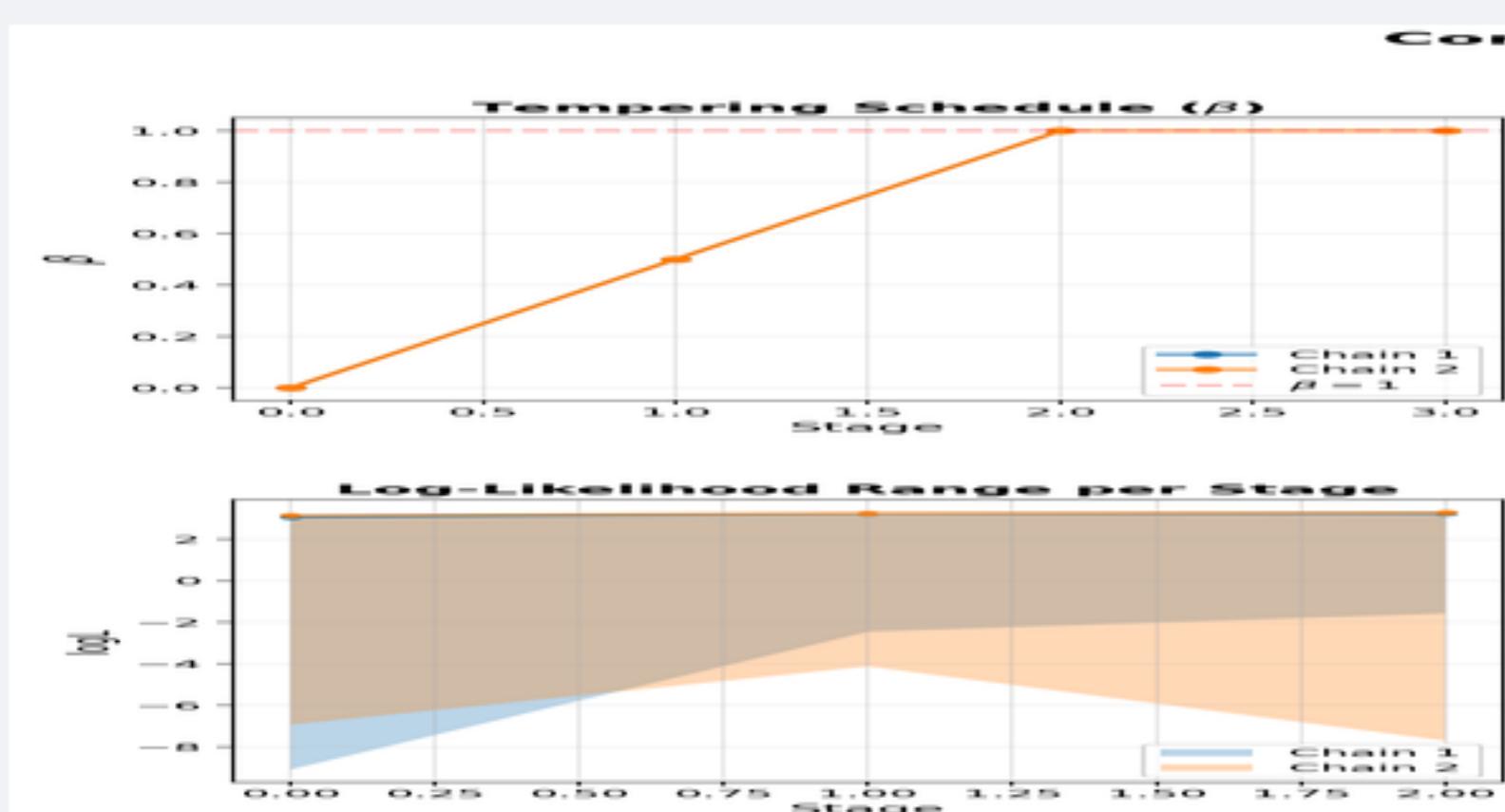
TMCMC β schedule



Species composition / 菌種構成



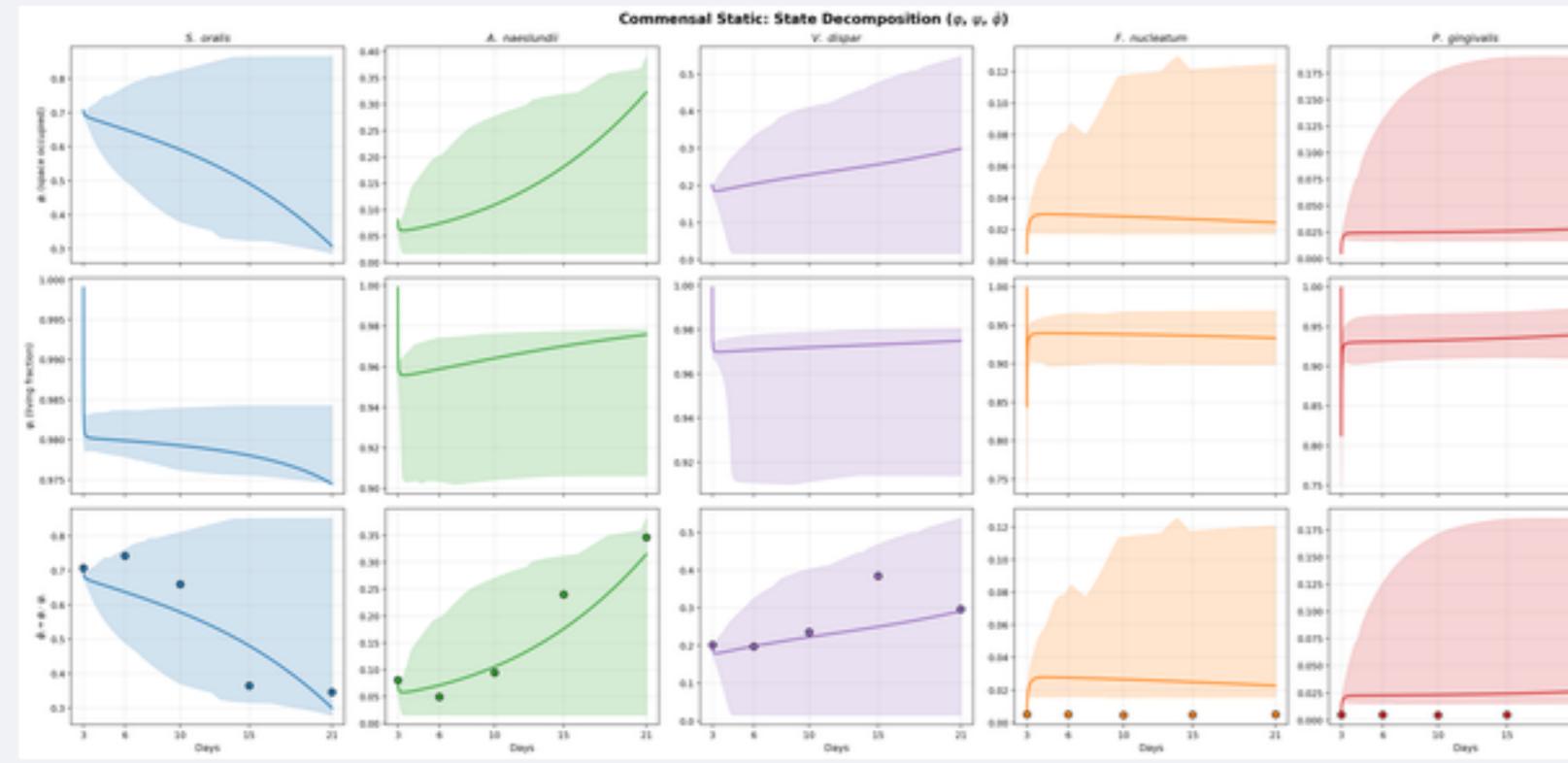
Parameter correlation / パラメータ相関



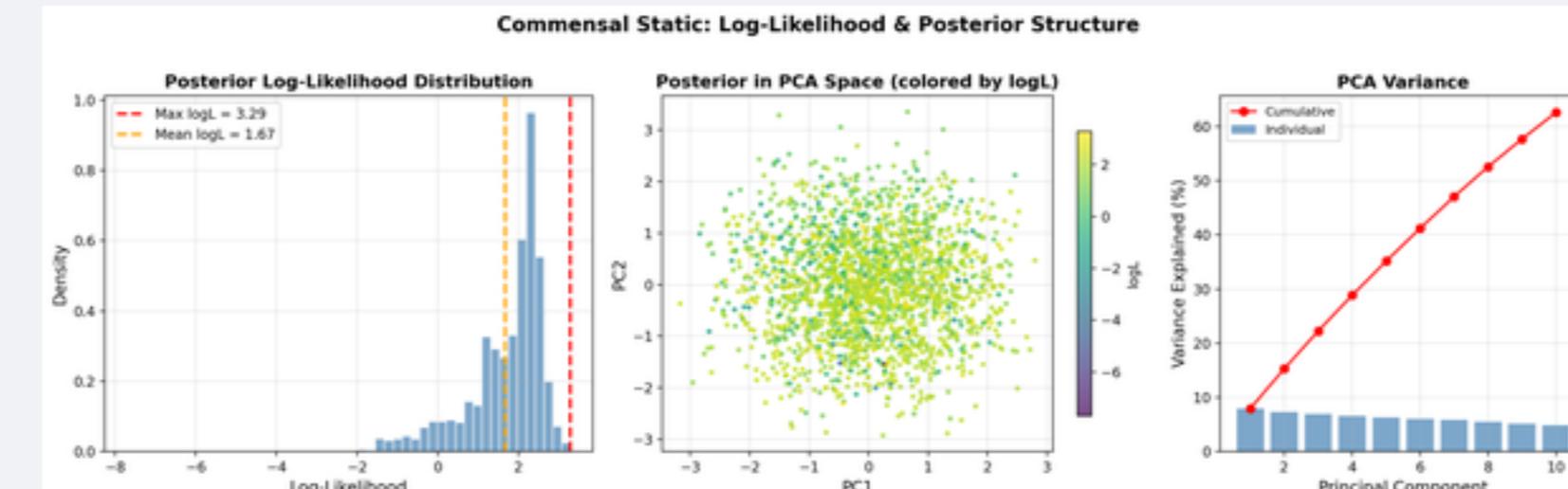
Convergence dashboard / 収束ダッシュボード

Commensal Static – Additional Diagnostics

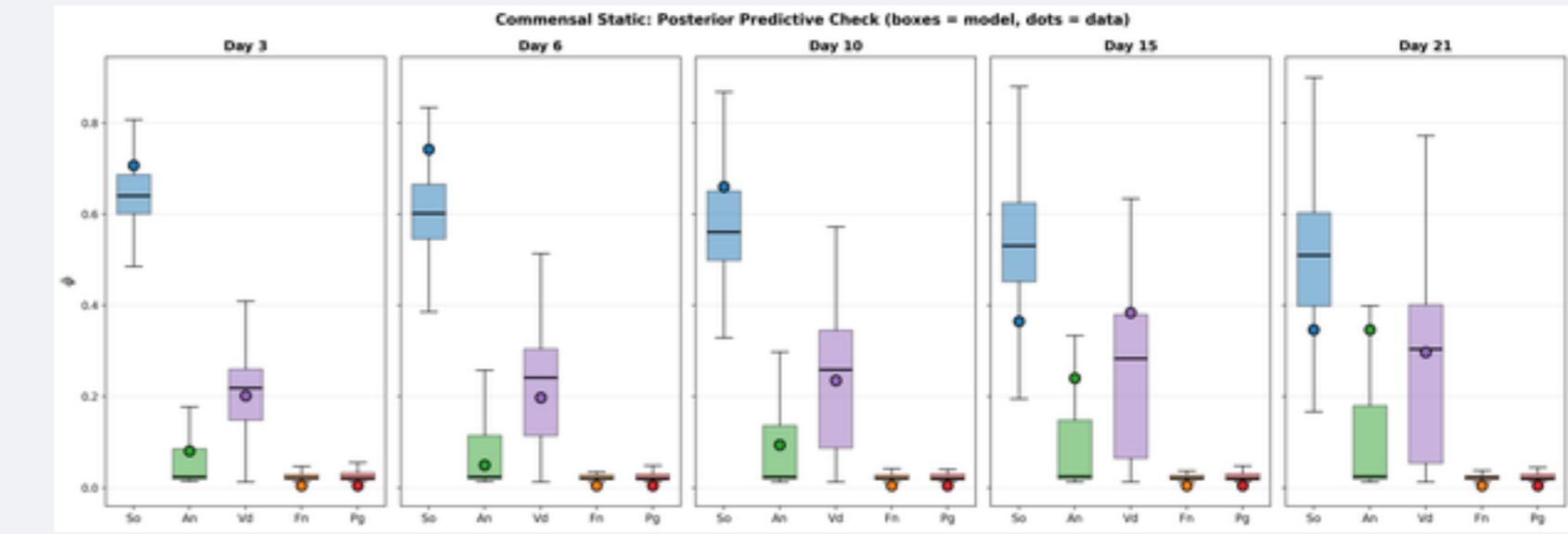
健康・静的 – 追加診断



State decomposition (ϕ, ψ) / 状態分解



Log-likelihood landscape / 対数尤度



Posterior predictive check / 事後予測チェック

Dysbiotic Static – Posterior Predictive Fit

疾患・静的 – 事後予測適合

Condition

Disease state under static culture.
Pathogens are present but limited by metabolite accumulation. Standard biological locks ($N_{locked} = 5$) are applied.

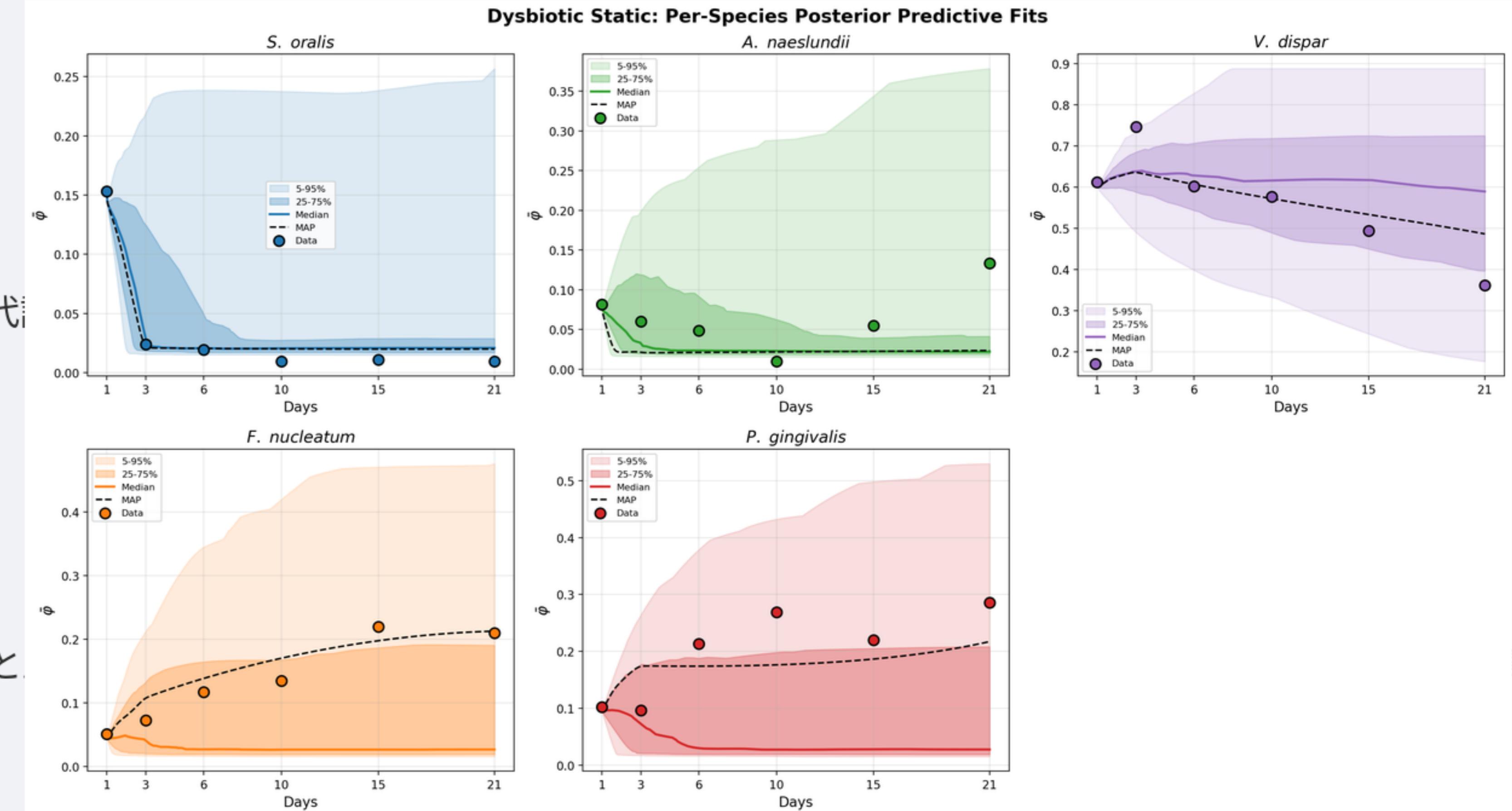
静的培養下の疾患状態。病原菌は存在するが代謝物質蓄積により活性化が抑制される(N_{locked} = 5)を適用。

$N_{locked} = 5$

Key Finding

Pathogen interactions are estimated but their magnitude is smaller compared to HOBIC conditions. This confirms that saliva flow is essential for full dysbiosis progression.

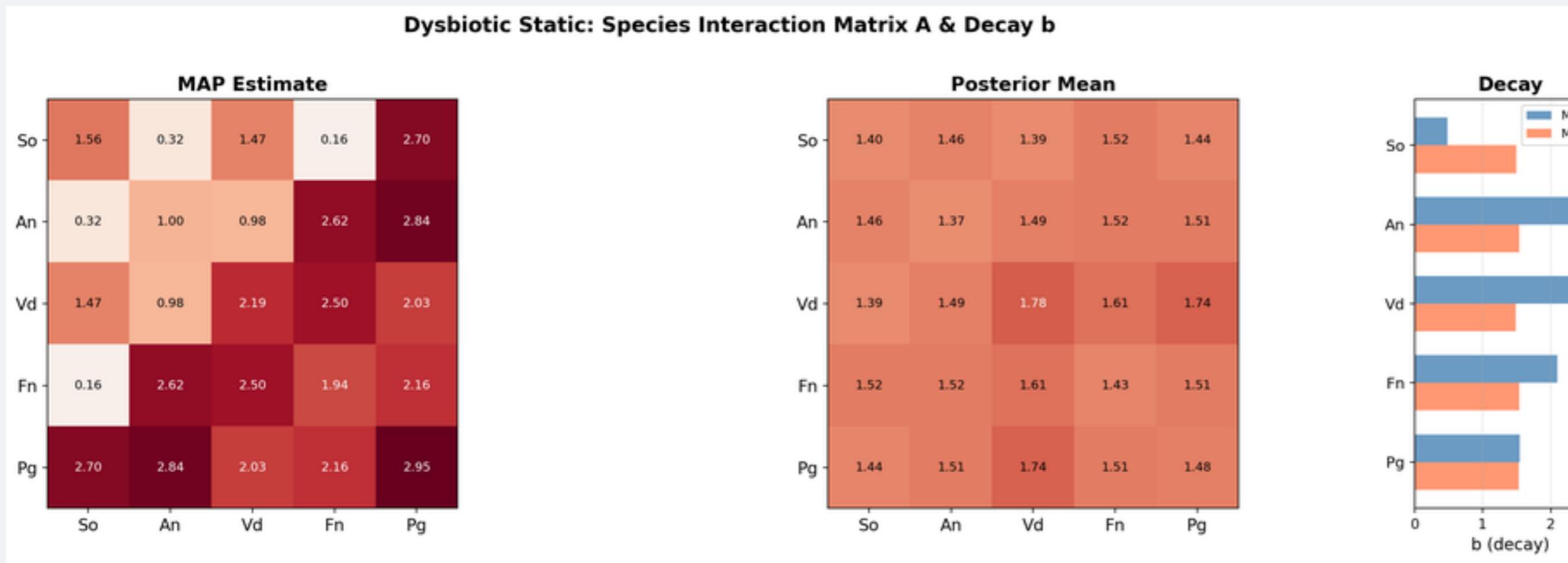
病原菌の相互作用は推定されたがHOBIC条件と比べて弱い。



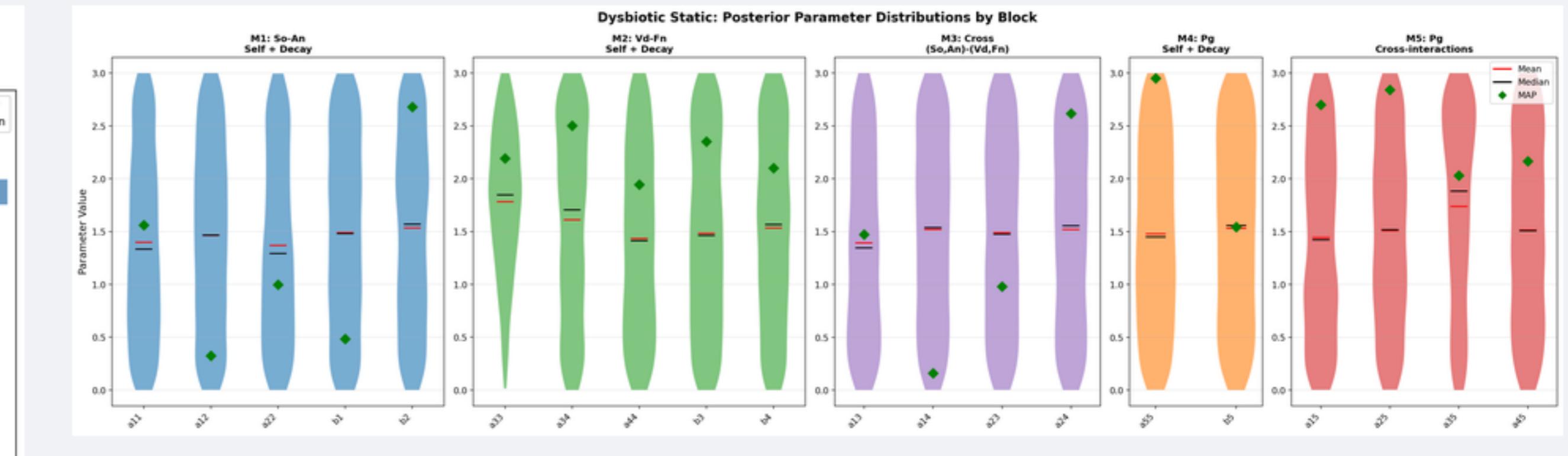
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Dysbiotic Static – Interaction Matrix & Parameter Uncertainty

疾患・静的 – 相互作用行列 & パラメータ不確実性



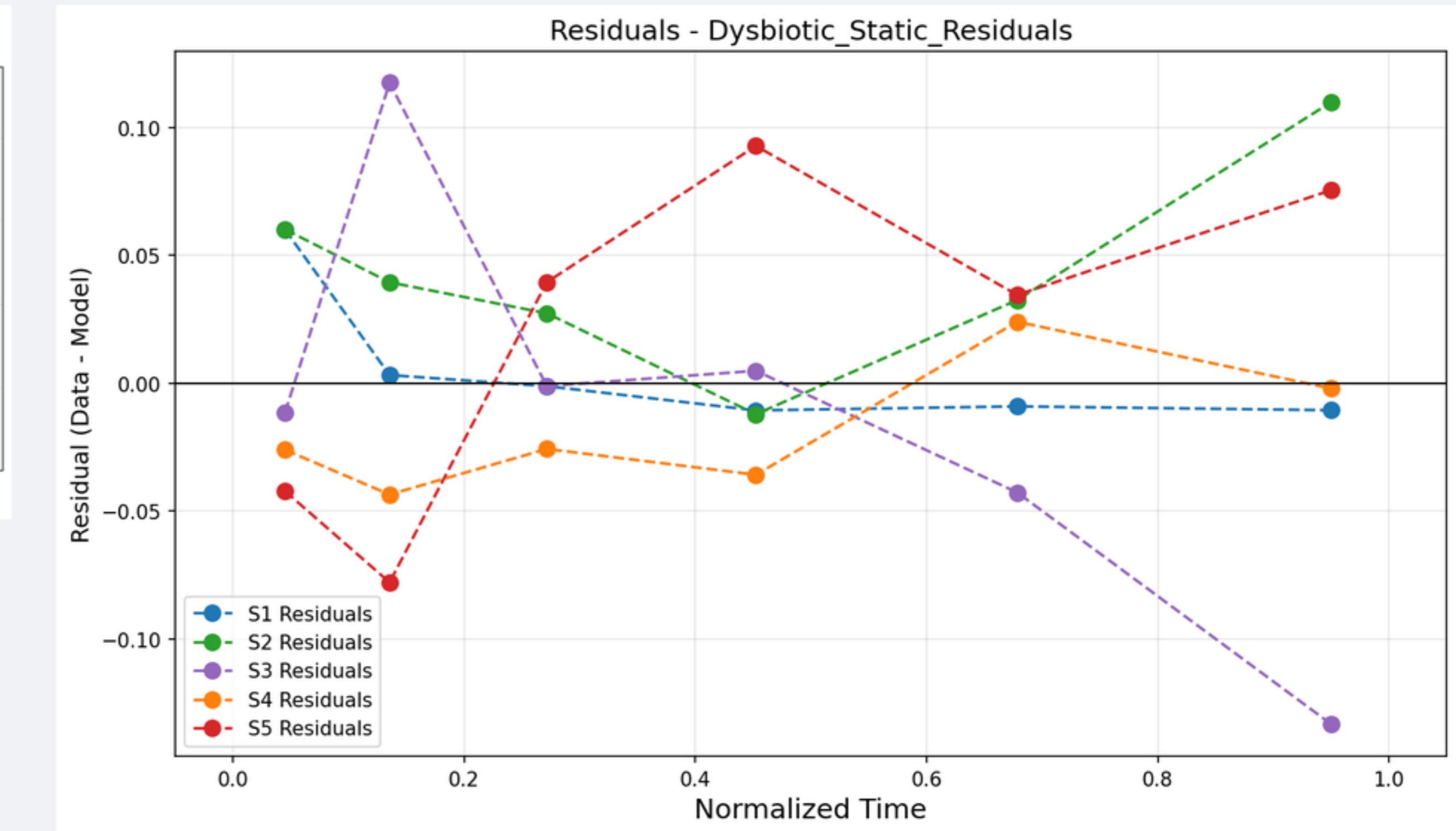
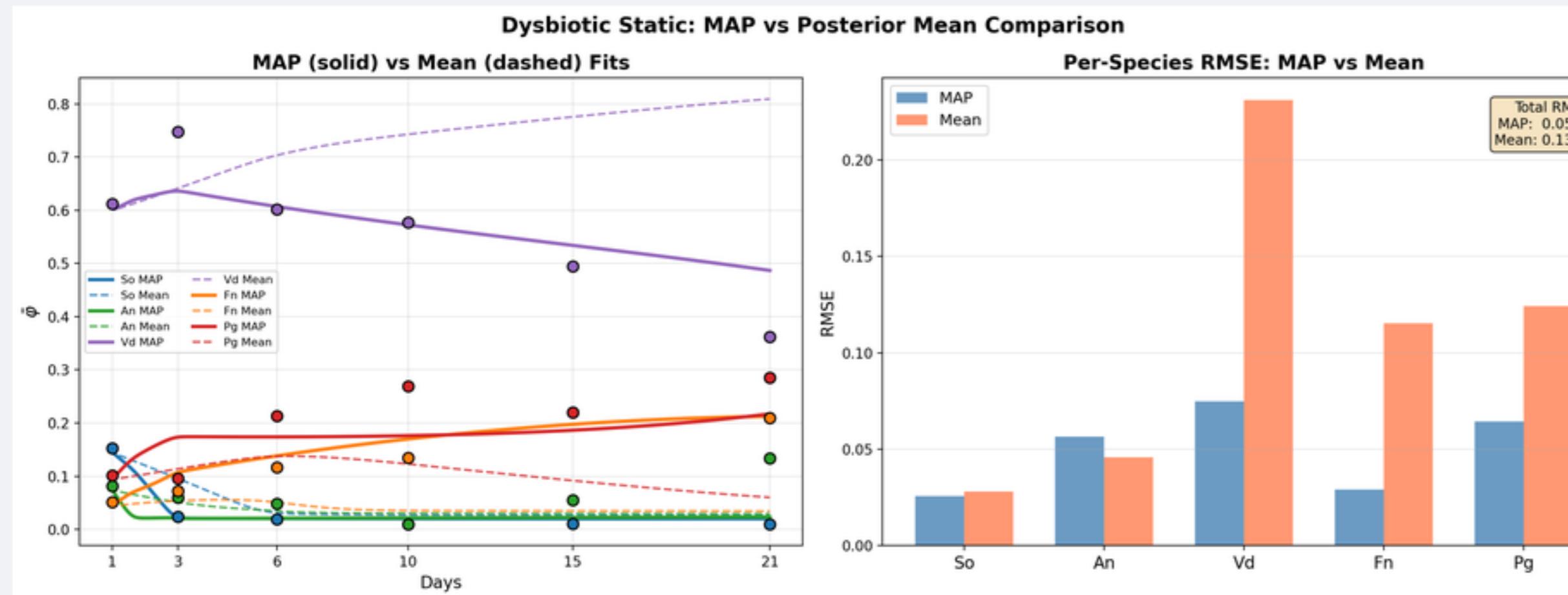
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Dysbiotic Static – MAP vs Mean & Residuals

疾患・静的 – MAP vs 平均推定 & 残差分析

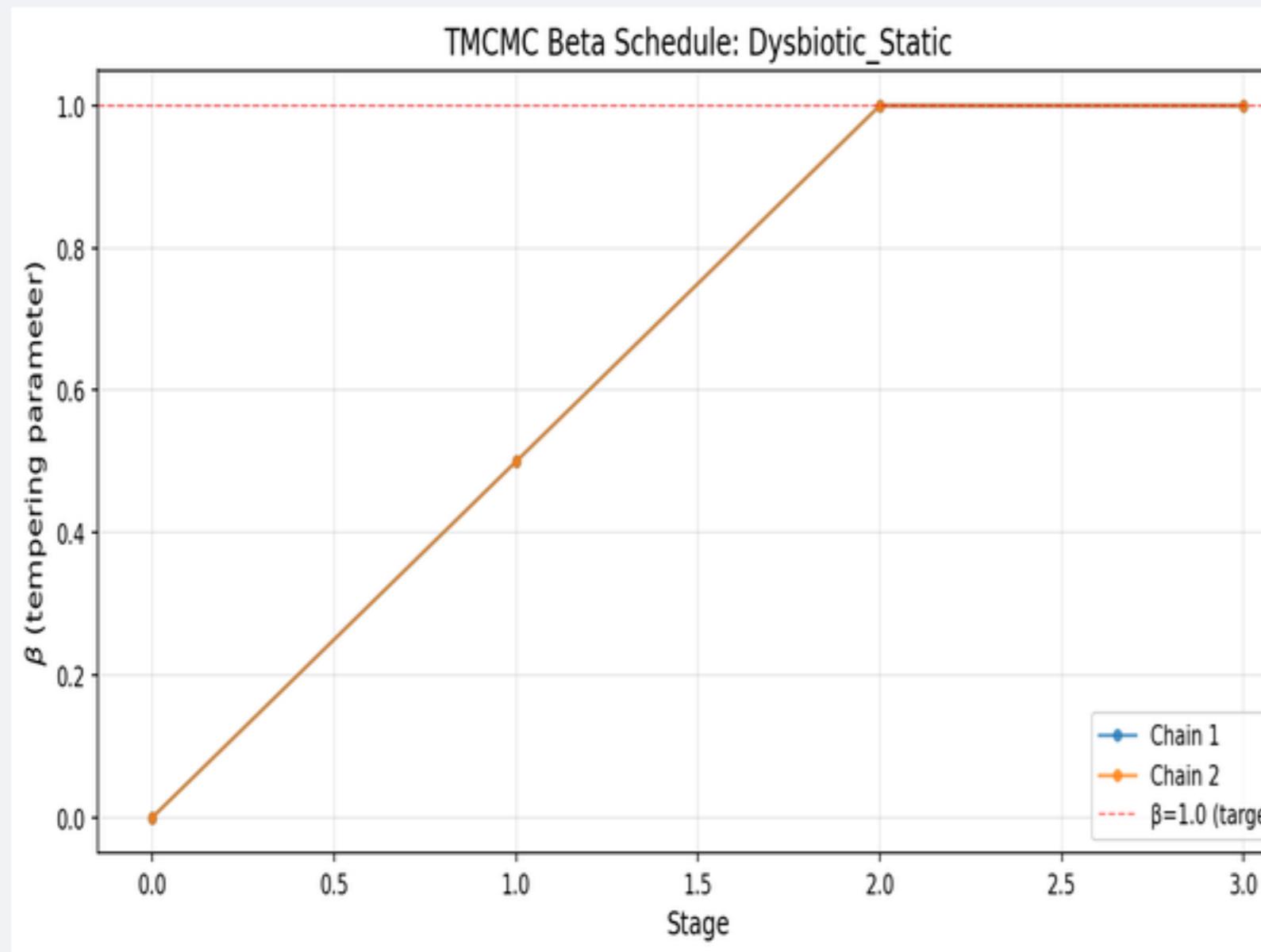


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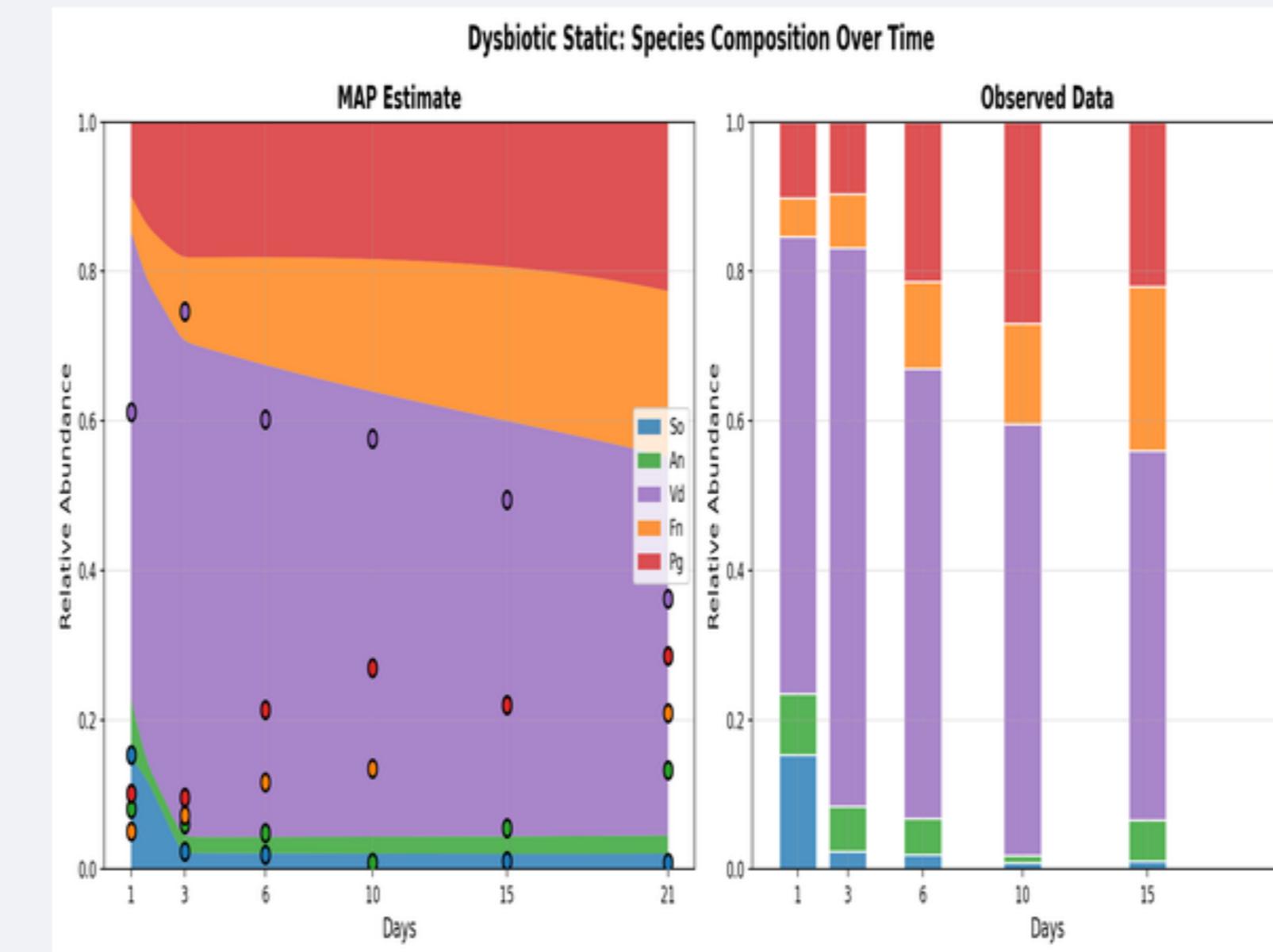
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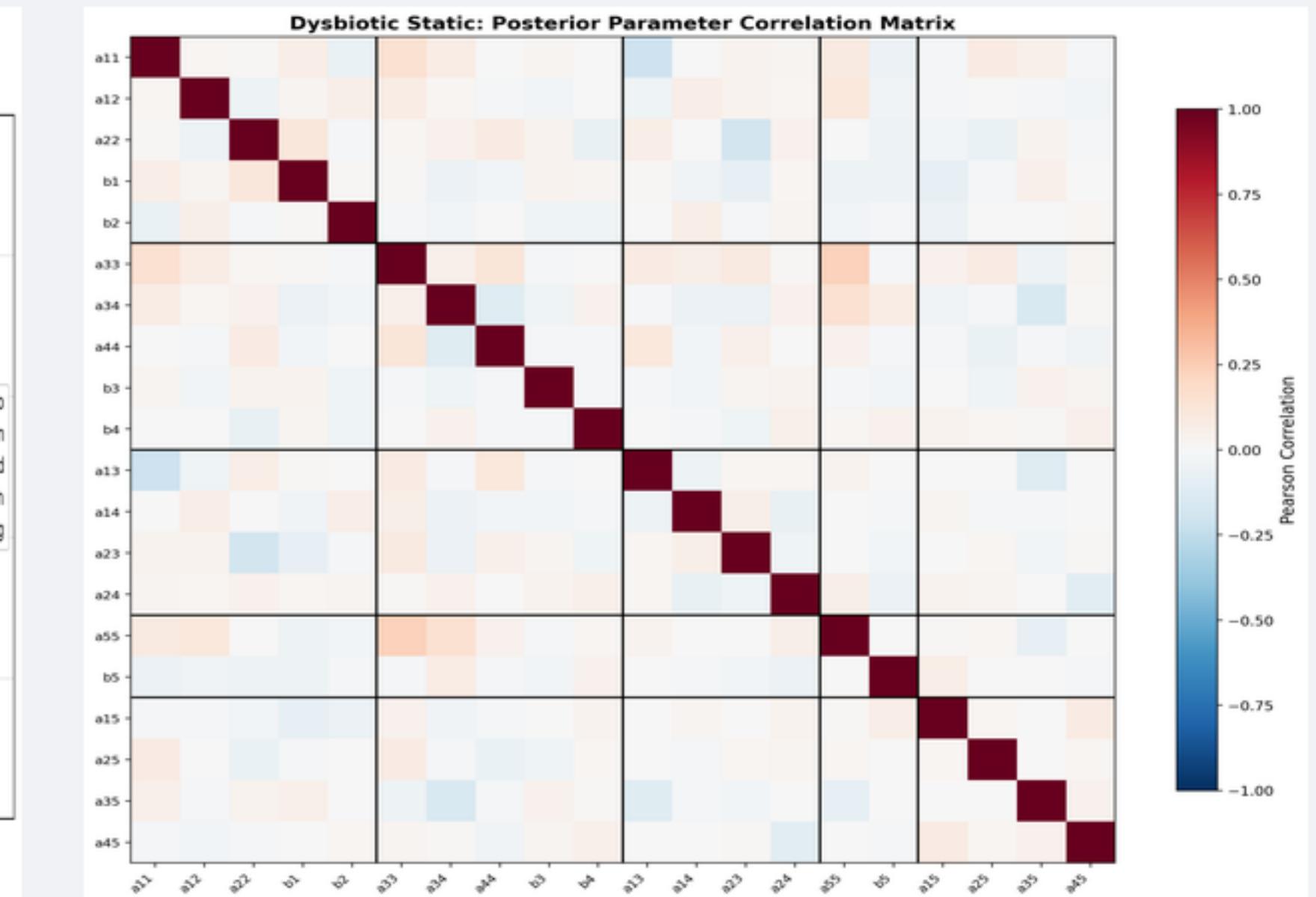
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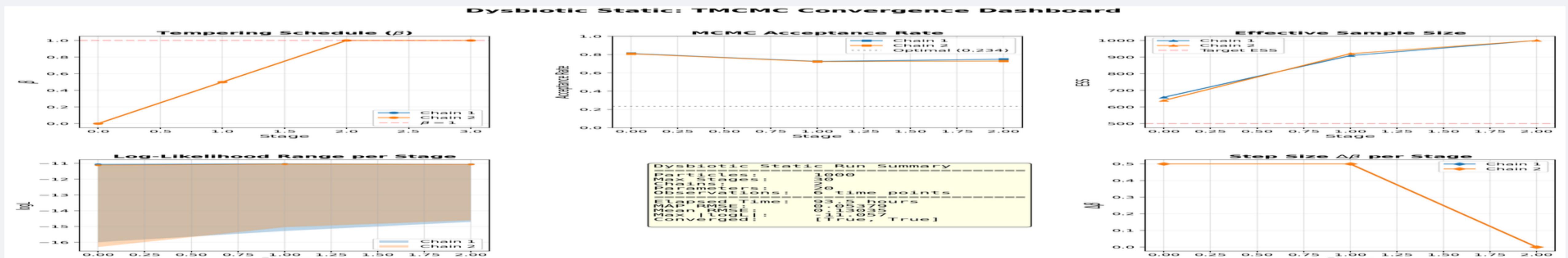
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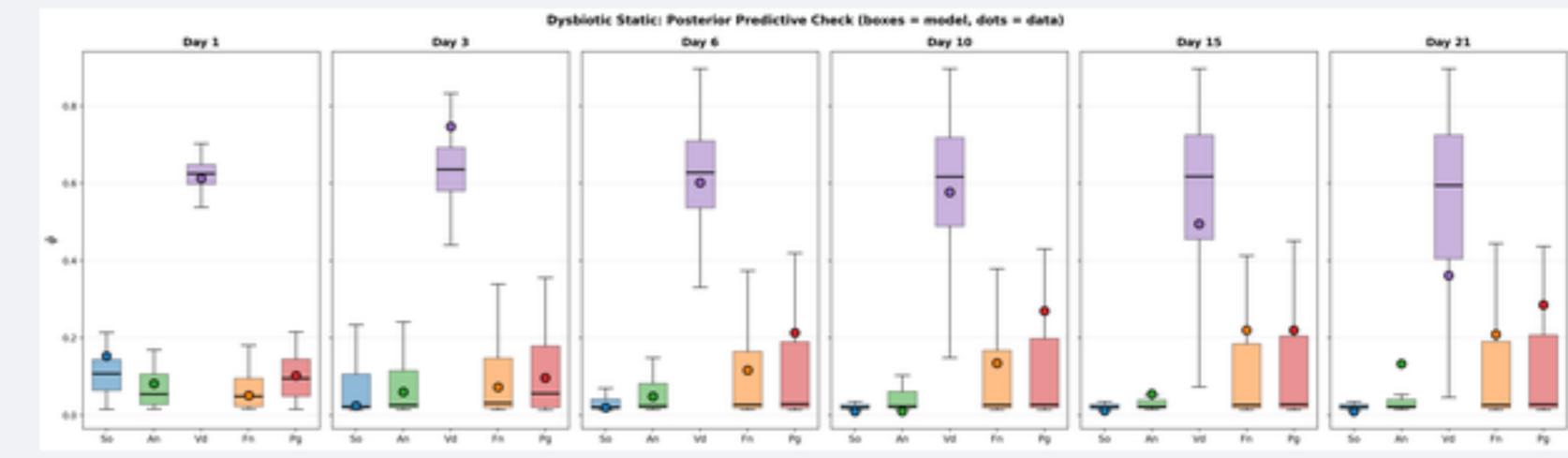
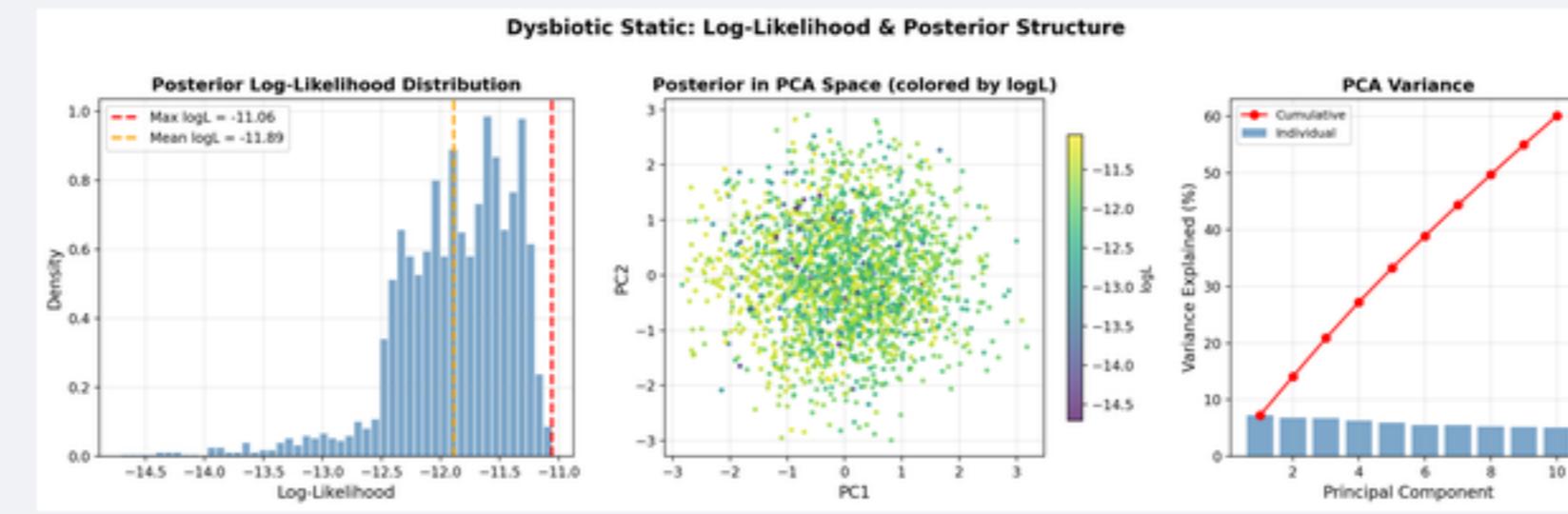
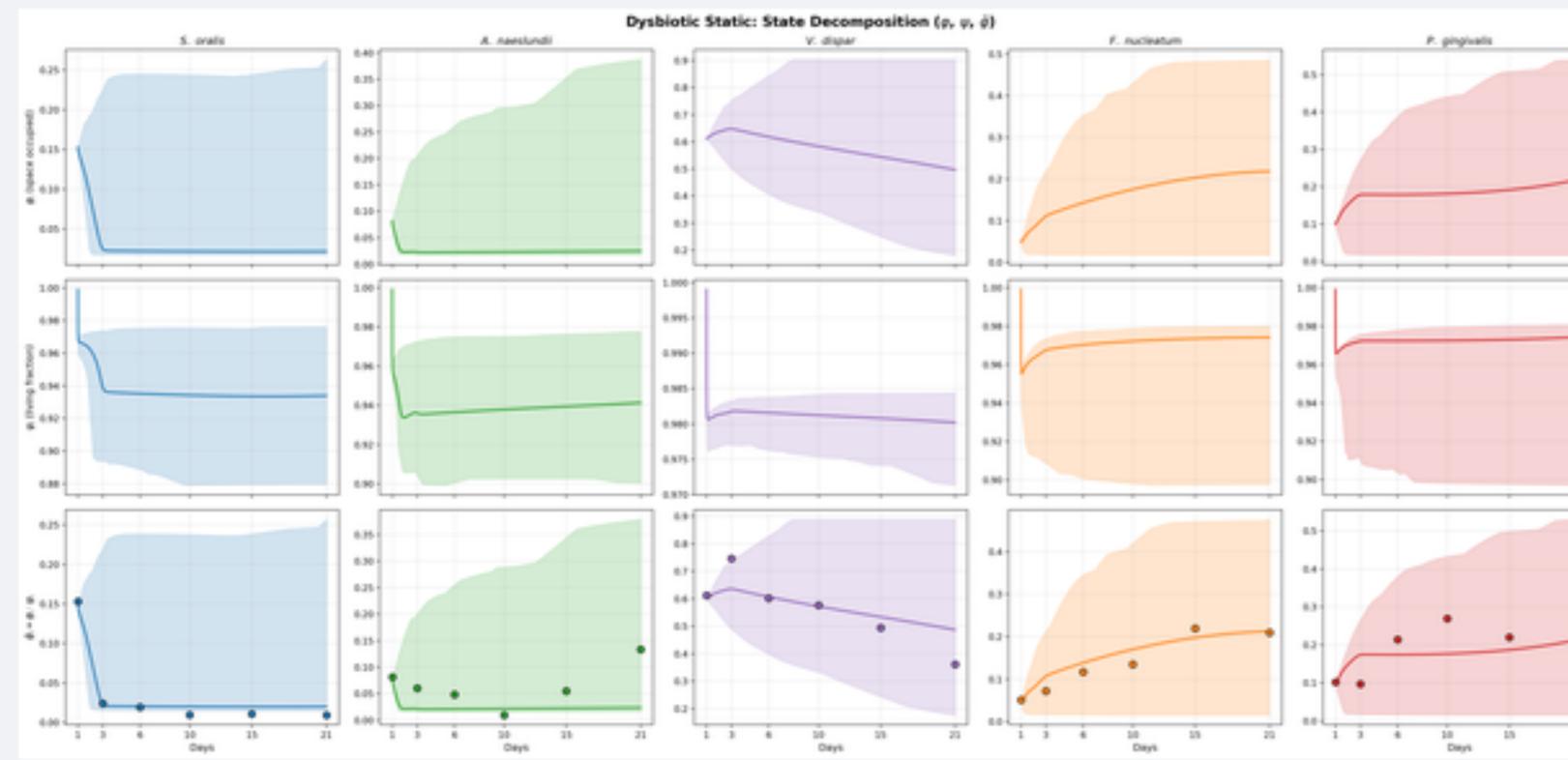
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健康・流動 (HOBIC) — 事後予測適合

Condition

Healthy state with saliva flow (HOBIC). Characterized by *S. oralis* 'Blue Bloom' — high proliferation of early colonizers under flow. Strict locks ($N_{locked} = 8$) allow *S. oralis* growth while suppressing pathogens.

流れのある健康な状態 (HOBIC)。*S. oralis*の高い増殖 ('Blue Bloom') が特徴。厳格なロック ($N_{locked} = 8$) が*S. oralis*の増殖を許容しつつ病原菌を抑制。

$N_{locked} = 8$

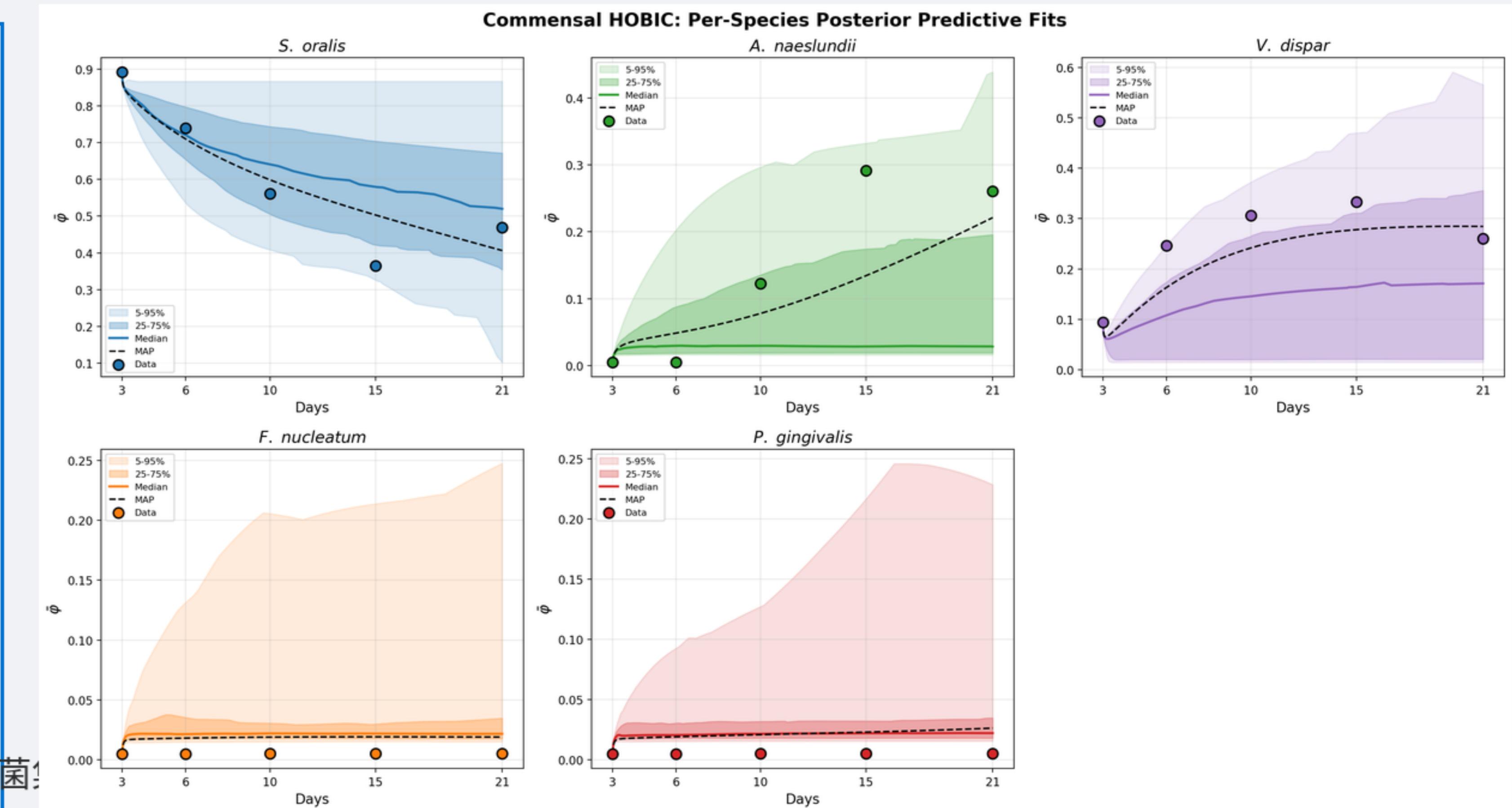
Key Finding

The model correctly identifies early colonizer dominance while suppressing pathogen populations. The 'Blue Bloom' observation is quantitatively reproduced by the MAP estimate.

初期定着菌の優位性を正しく特定しつつ病原菌

'Blue Bloom'

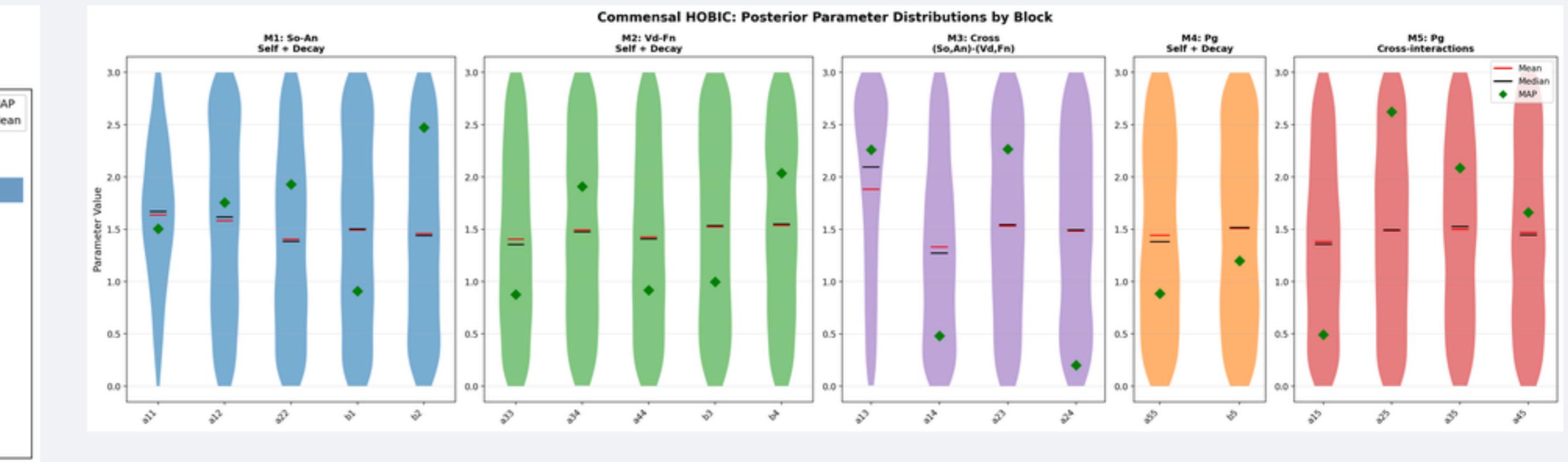
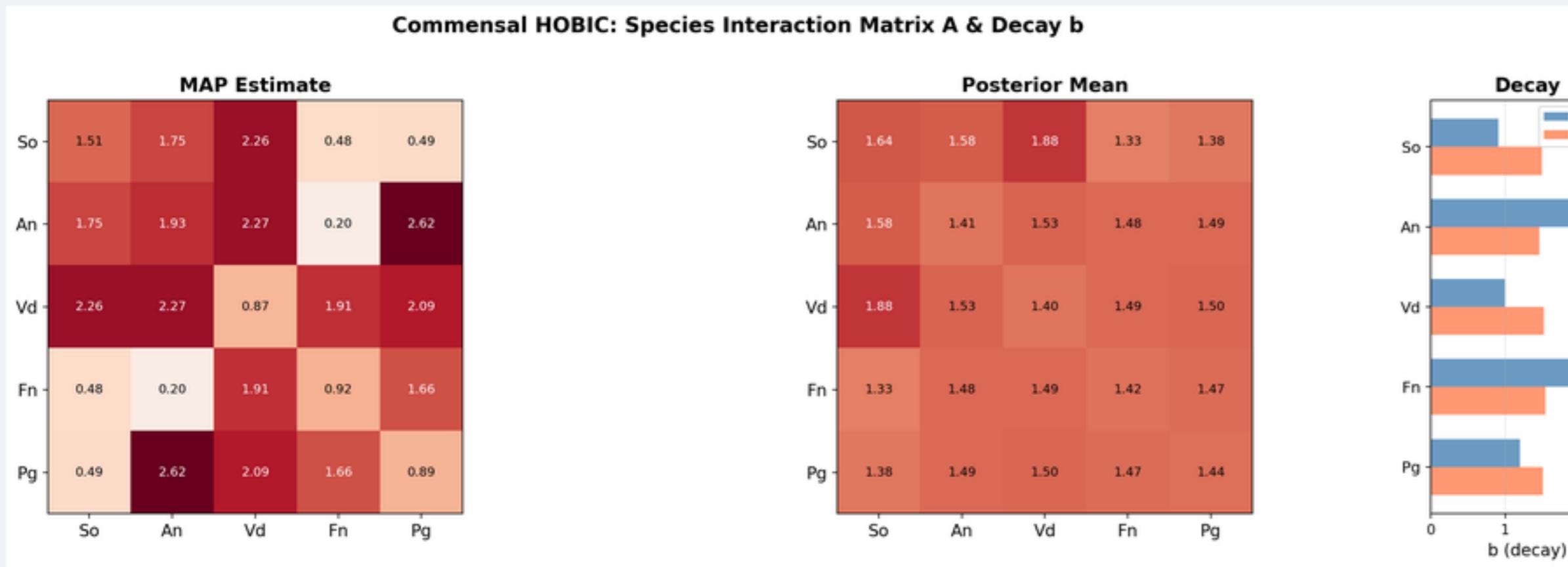
の観察結果をMAP推定値により定量的に再現。



Per-species posterior predictive fit with 95% credible interval / 菌種別事後予測適合

Commensal HOBIC – Interaction Matrix & Parameter Uncertainty

健康・流動 (HOBIC) – 相互作用行列 & パラメータ不確実性

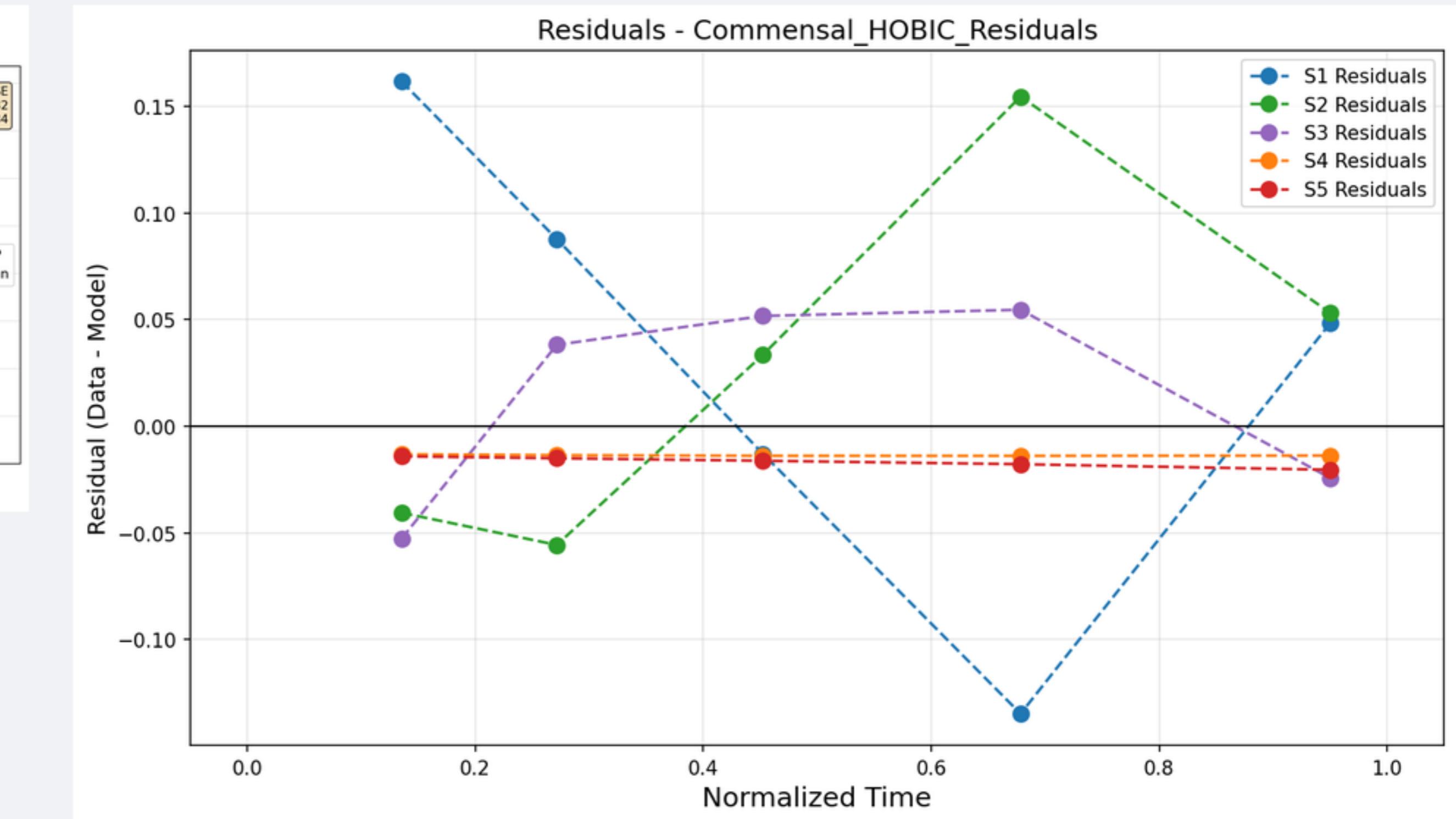
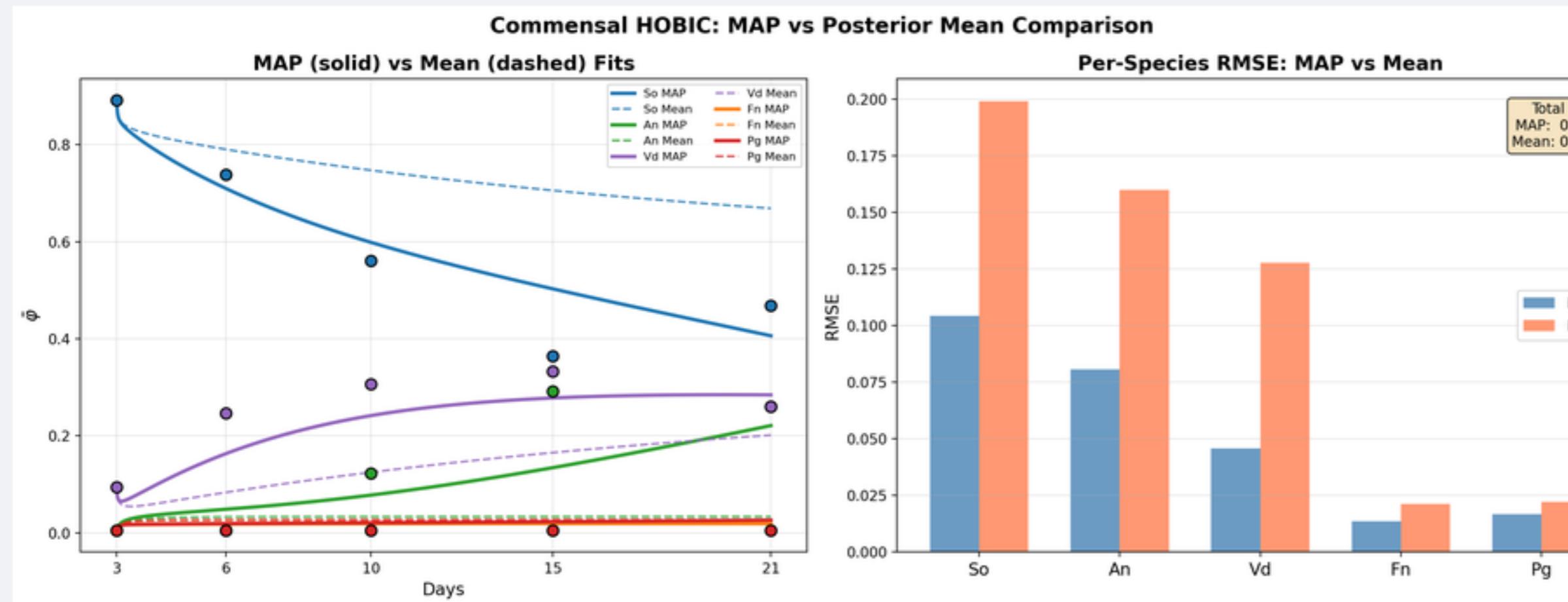


Estimated interaction matrix A (MAP) / 推定相互作用行列

Parameter posterior distributions (violin) / パラメータ事後分布 (バイオリン)

Commensal HOBIC – MAP vs Mean & Residuals

健康・流動 (HOBIC) – MAP vs 平均推定 & 残差分析

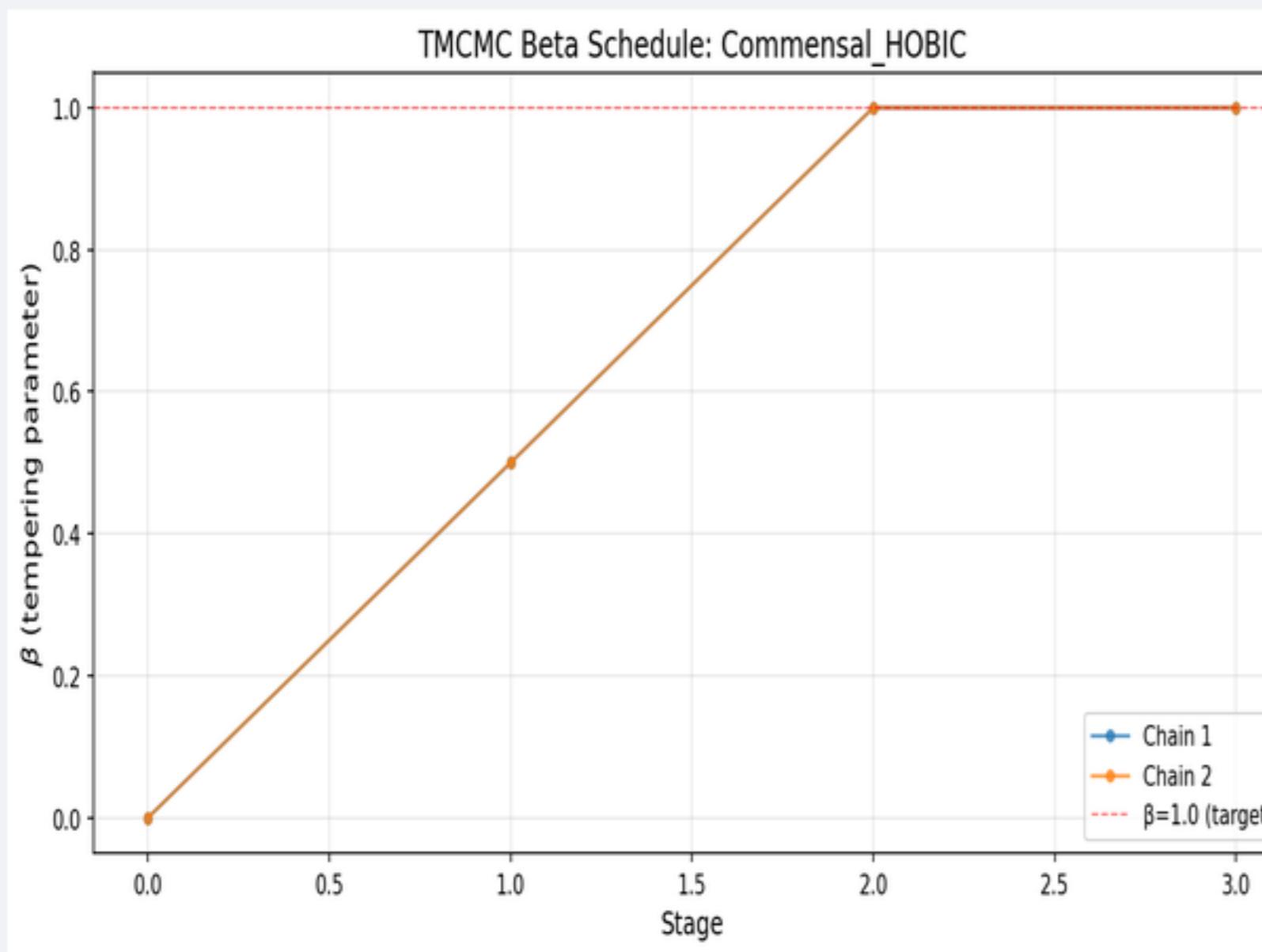


MAP vs Mean parameter comparison / MAP vs 平均パラメータ比較

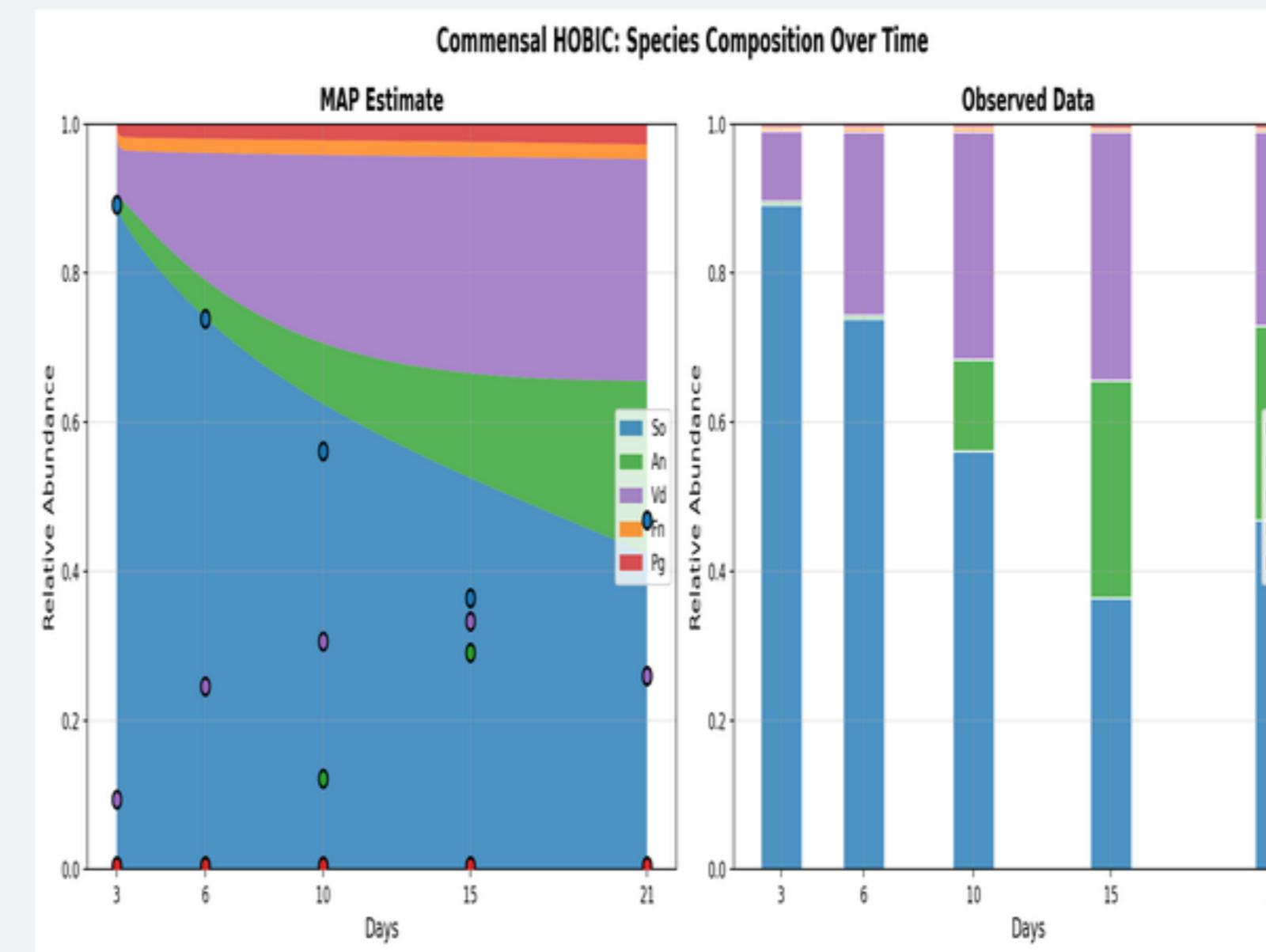
Residual analysis / 残差分析

Commensal HOBIC – Convergence & Diagnostics

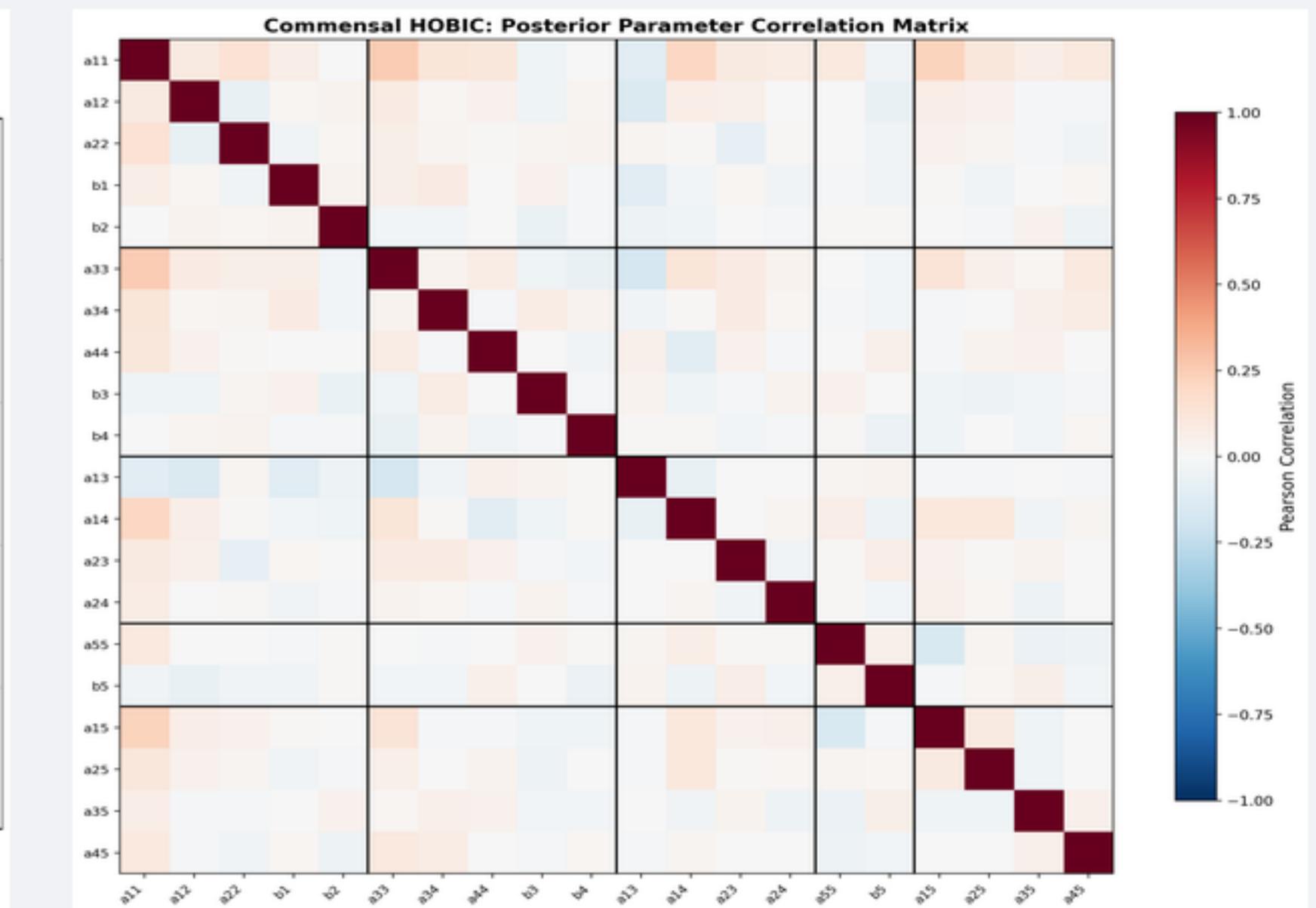
健康・流動 (HOBIC) – 収束診断



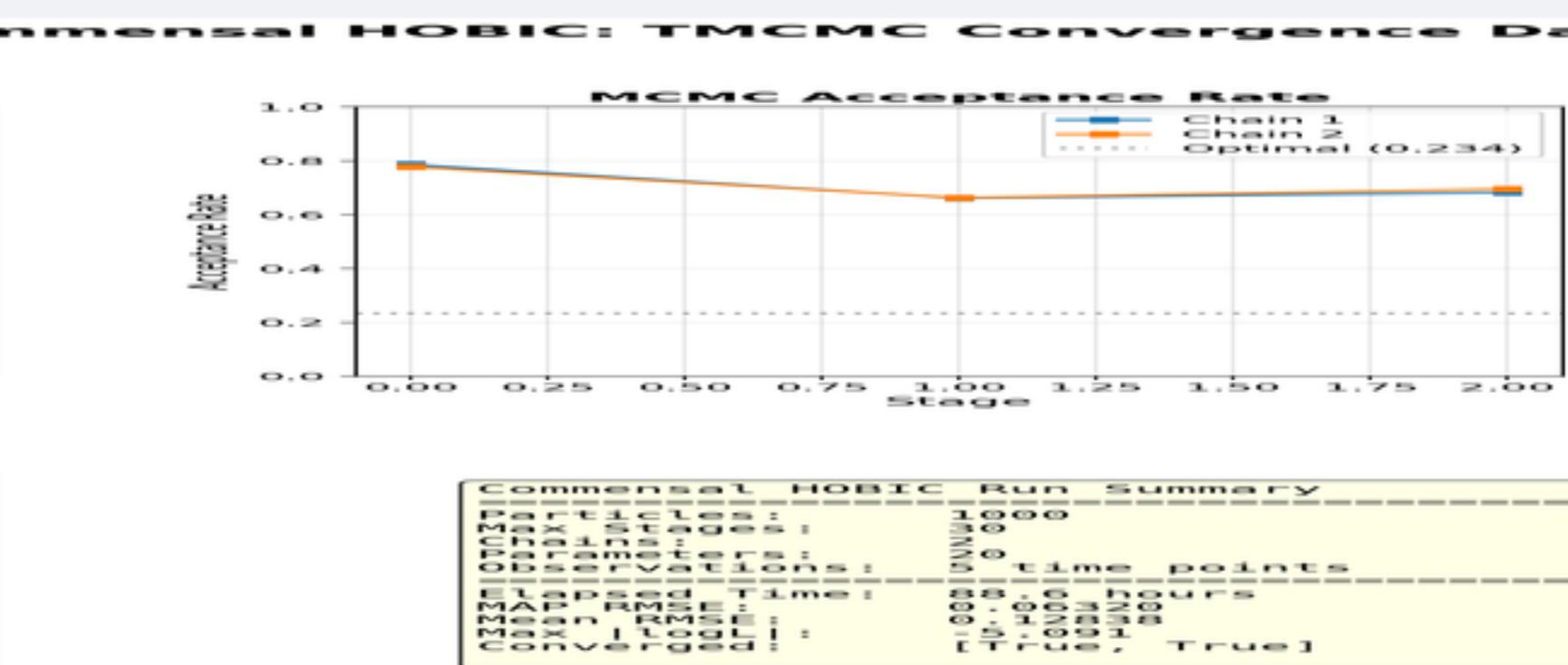
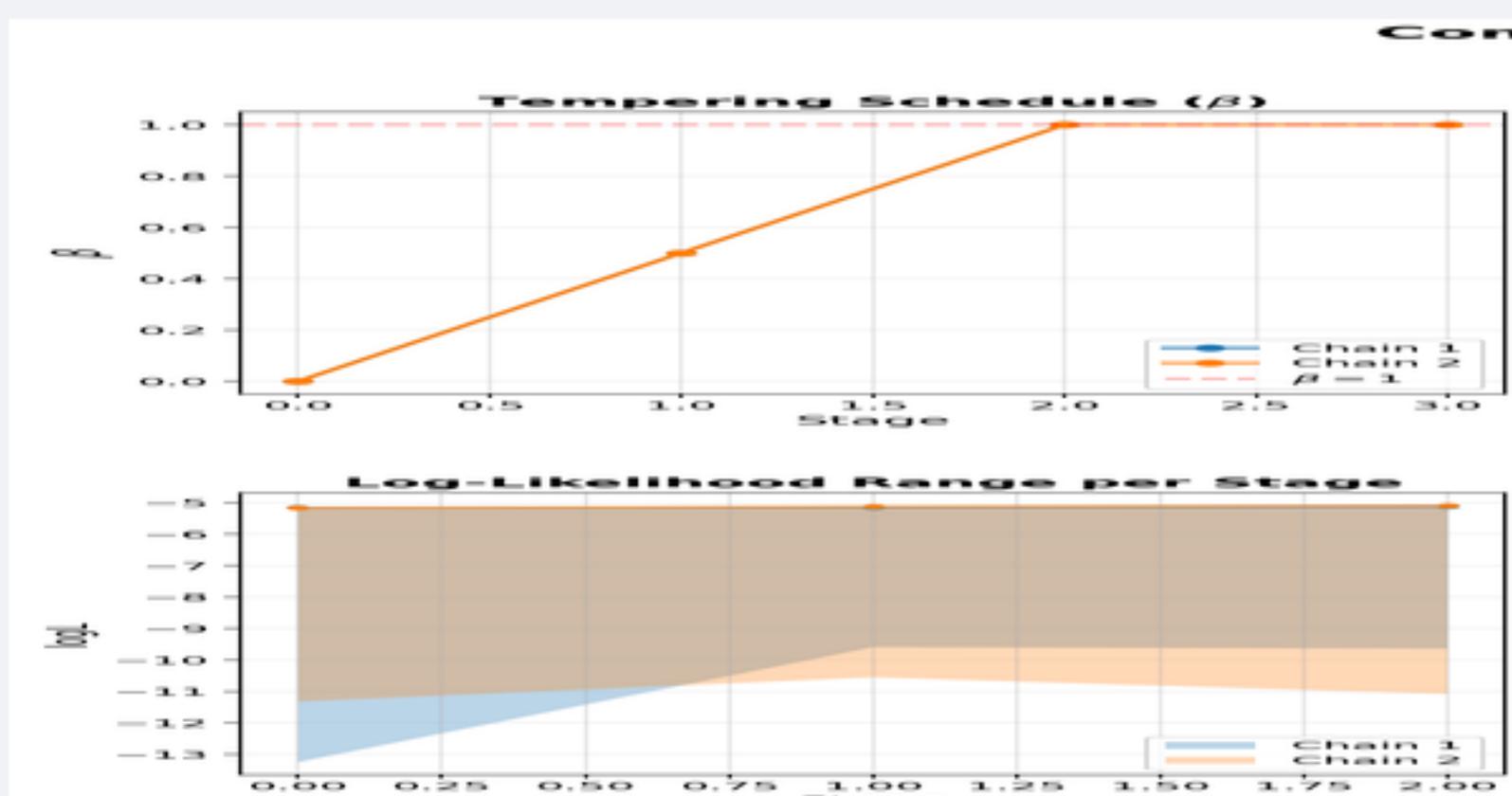
TMCMC β schedule



Species composition / 菌種構成



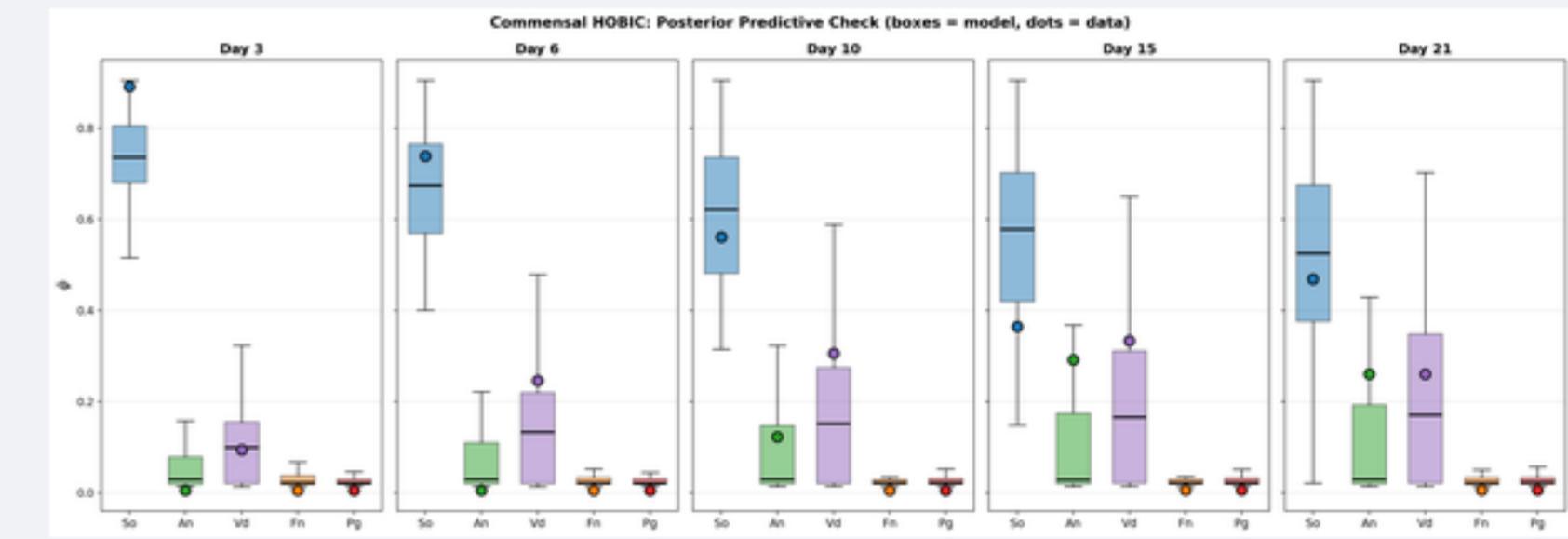
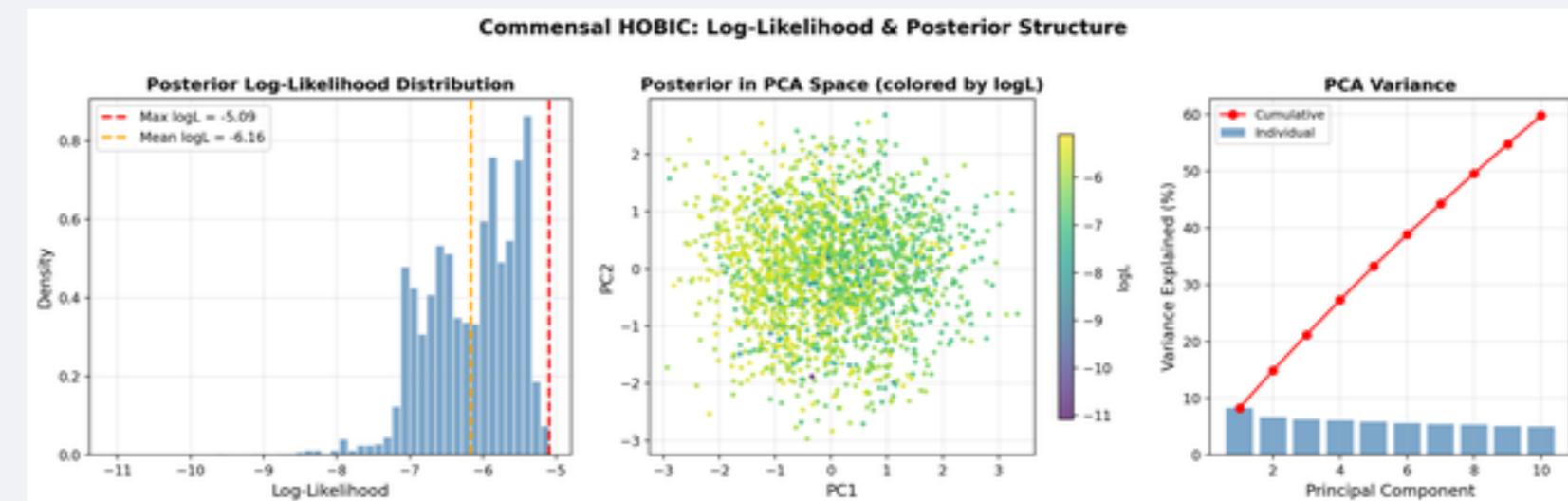
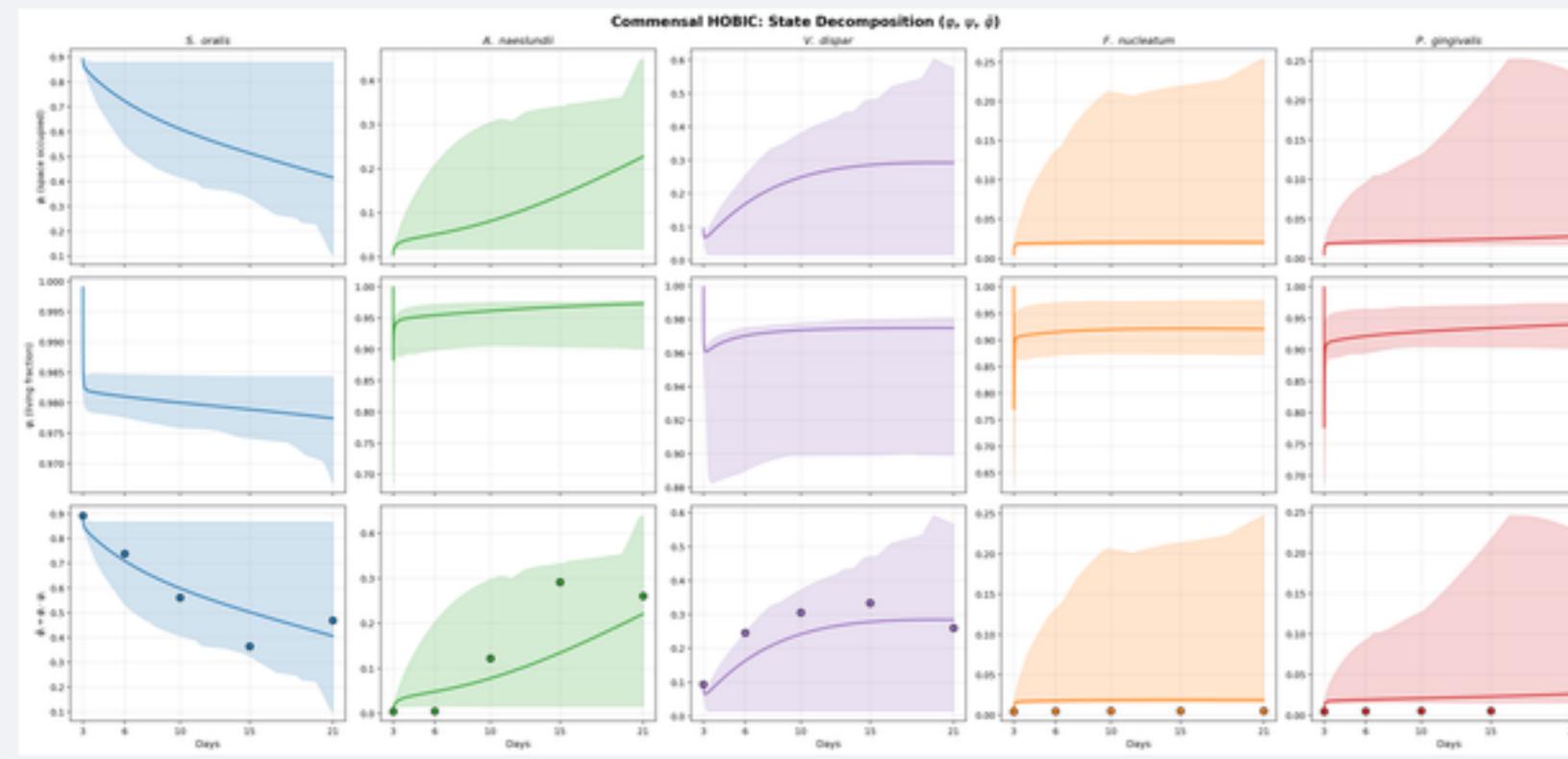
Parameter correlation / パラメータ相関



Convergence dashboard / 収束ダッシュボード

Commensal HOBIC – Additional Diagnostics

健康・流動 (HOBIC) – 追加診断



State decomposition (ϕ, ψ) / 状態分解

Log-likelihood landscape / 対数尤度

Posterior predictive check / 事後予測チェック

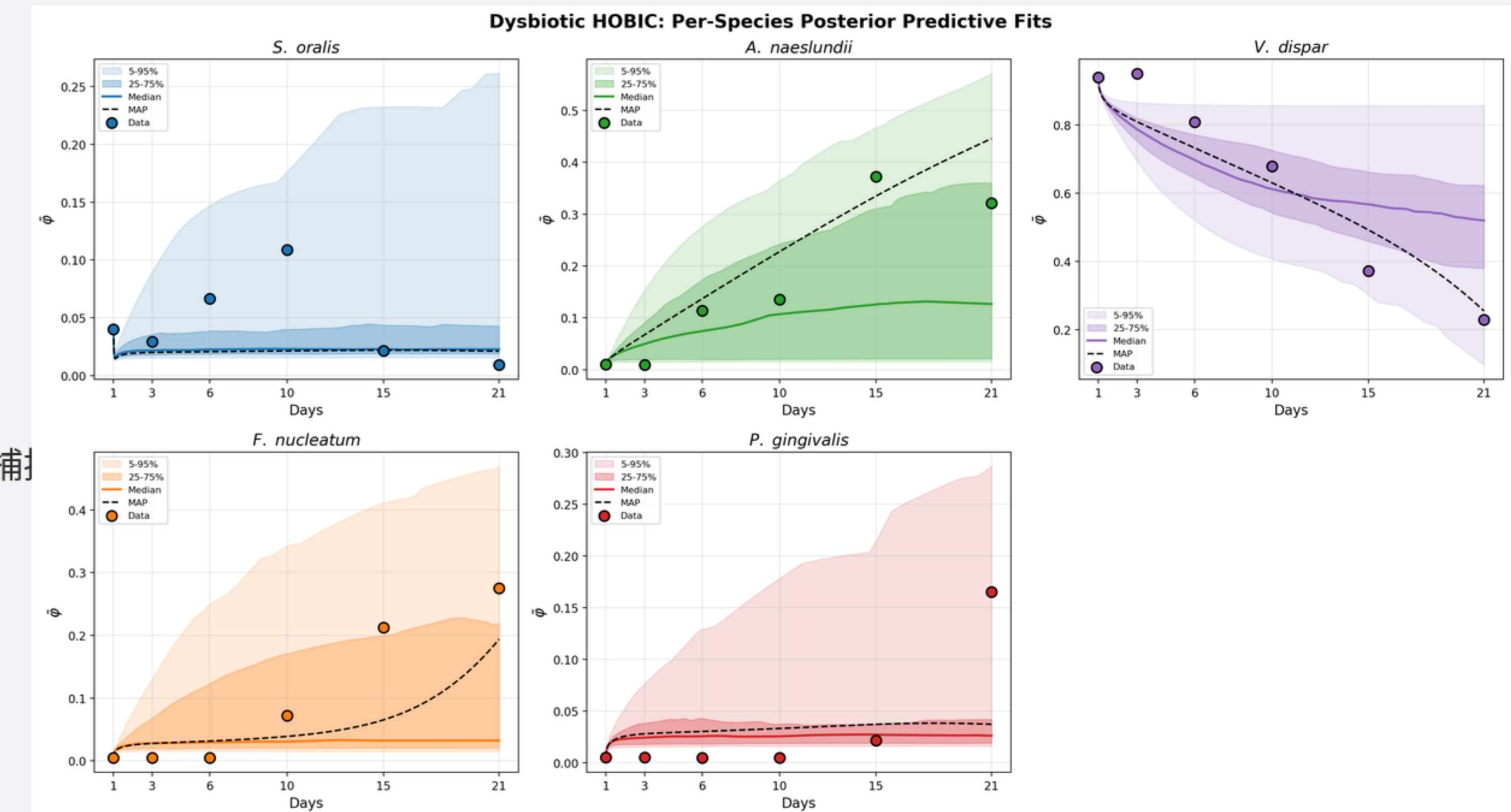
Dysbiotic HOBIC (Surge) – Posterior Predictive Fit

疾患・流動 (Surge) – 事後予測適合

Condition
 Disease state with saliva flow (HOBIC). Characterized by the explosive 'Surge' of *Veillonella* and *P. gingivalis*. All parameter locks are released ($N_{locked} = 0$, Discovery Mode) to capture complex cross-feeding dynamics.
 流れのある疾患状態 (HOBIC)。*Veillonella*と*P. gingivalis*の爆発的な 'Surge (急増)' が特徴。複雑なクロスフィーディング動態を捕らえる ($N_{locked} = 0$, Discovery Mode)。
 $N_{locked} = 0$

Key Finding
 Unlock All (Discovery Mode) successfully captures the non-linear Surge via strong Vei–P.g positive feedback. TMCMC identifies the critical cross-feeding loop (Index 18) as the driver of explosive P.g growth.

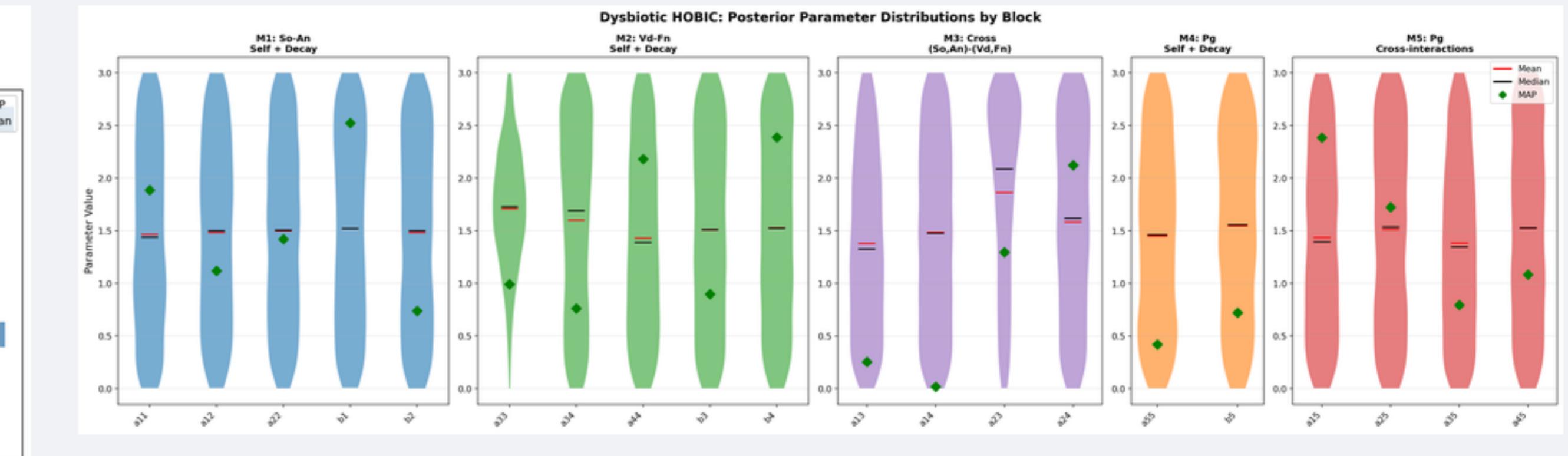
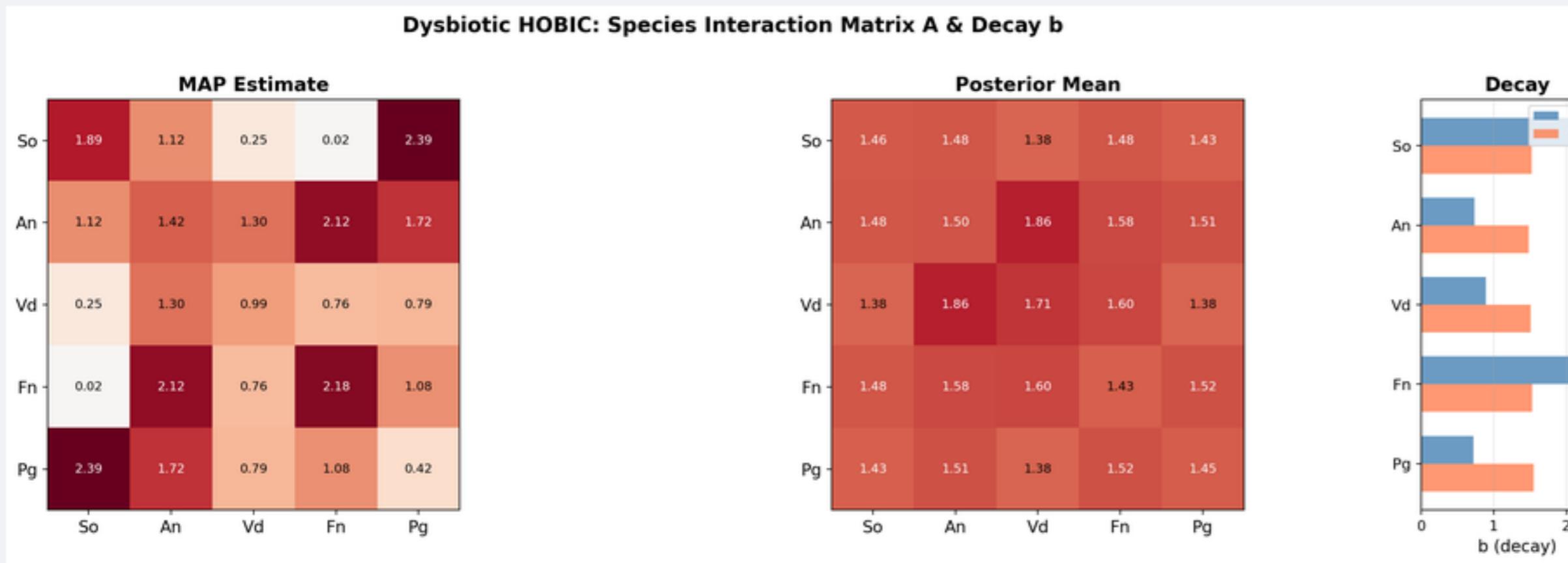
全ロック解除 (Discovery Mode)により、Vei–P.g間の強い正のフィードバックを介した非線形な急増 (Surge) を再現に成功。TMCMCがP.gの爆発的増殖の駆動因子であるクロスフィーディングループ



Per-species posterior predictive fit with 95% credible interval / 菌種別事後予測適合

Dysbiotic HOBIC (Surge) – Interaction Matrix & Parameter Uncertainty

疾患・流動 (Surge) – 相互作用行列 & パラメータ不確実性

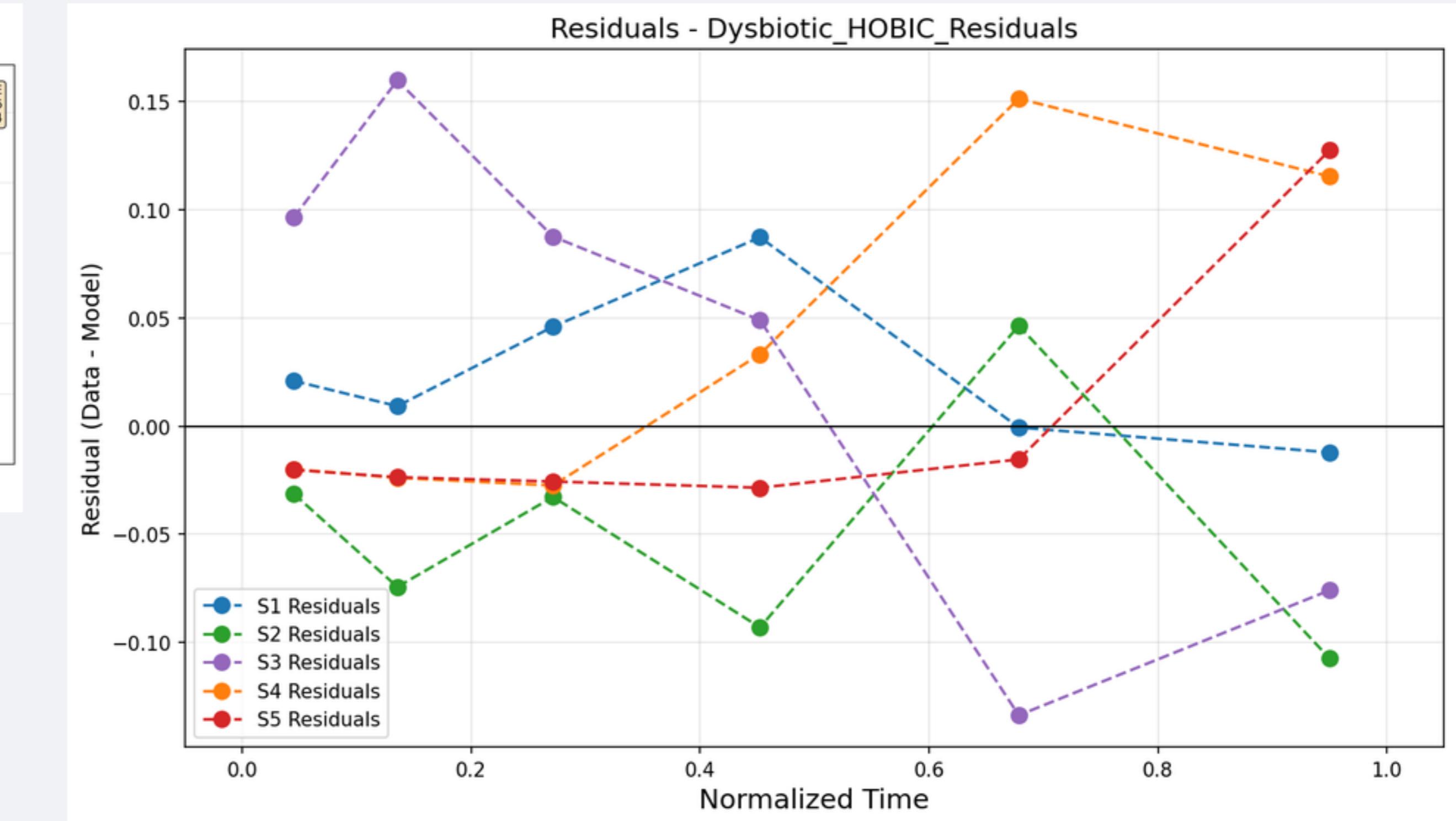
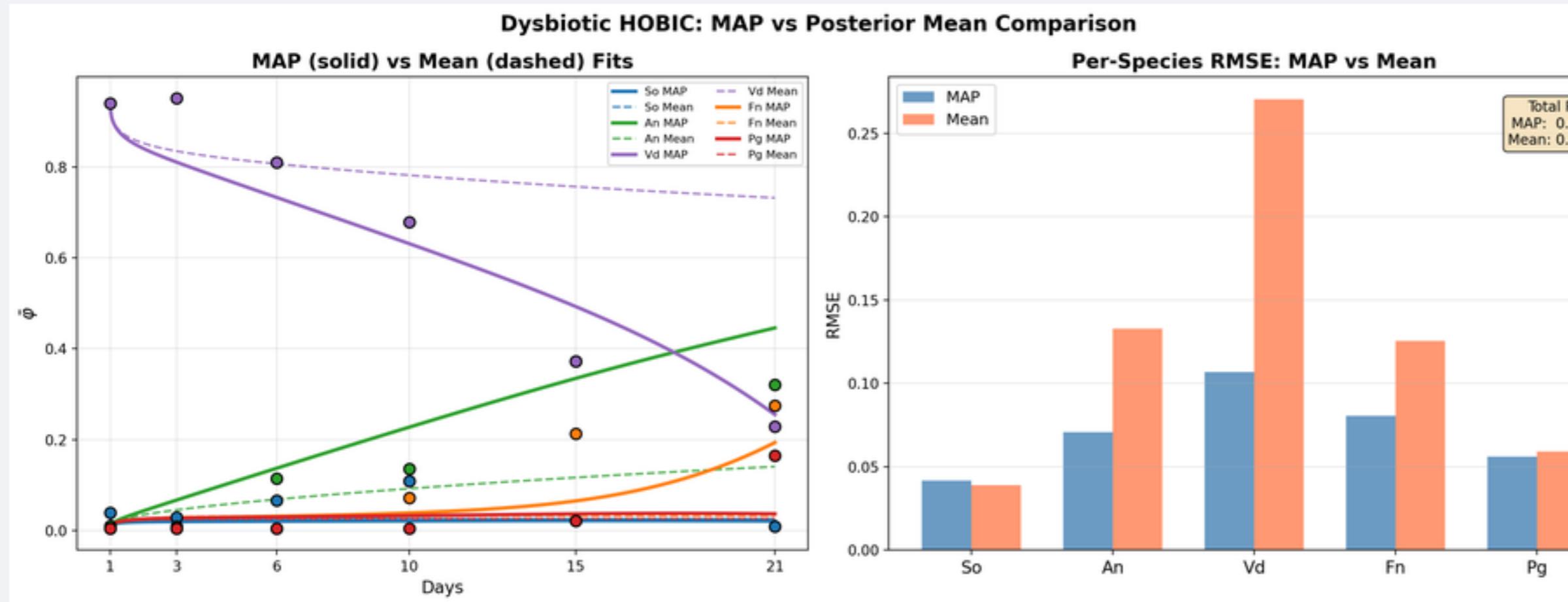


Estimated interaction matrix A (MAP) / 推定相互作用行列

Parameter posterior distributions (violin) / パラメータ事後分布 (バイオリン)

Dysbiotic HOBIC (Surge) — MAP vs Mean & Residuals

疾患・流動 (Surge) — MAP vs 平均推定 & 残差分析

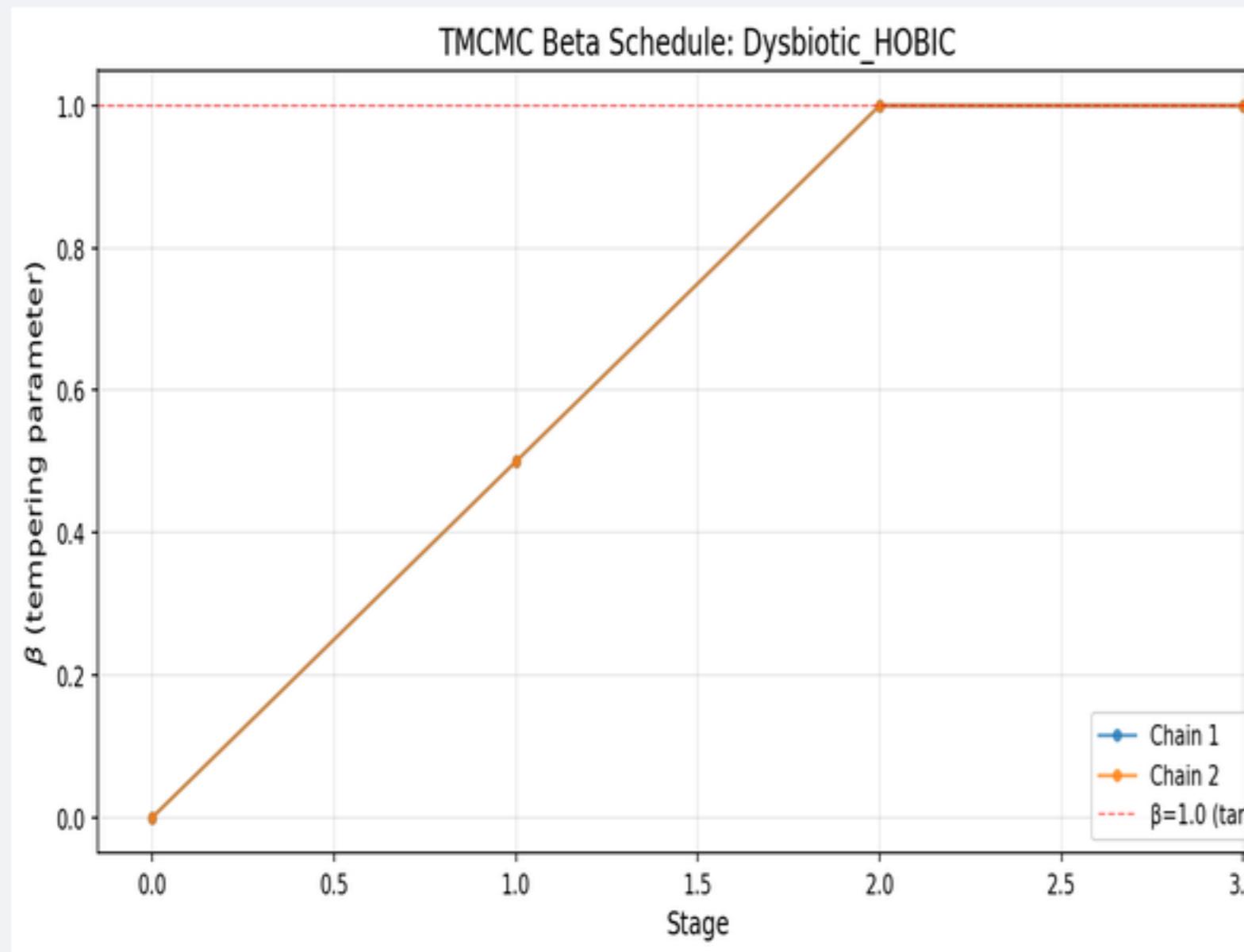


MAP vs Mean parameter comparison / MAP vs 平均パラメータ比較

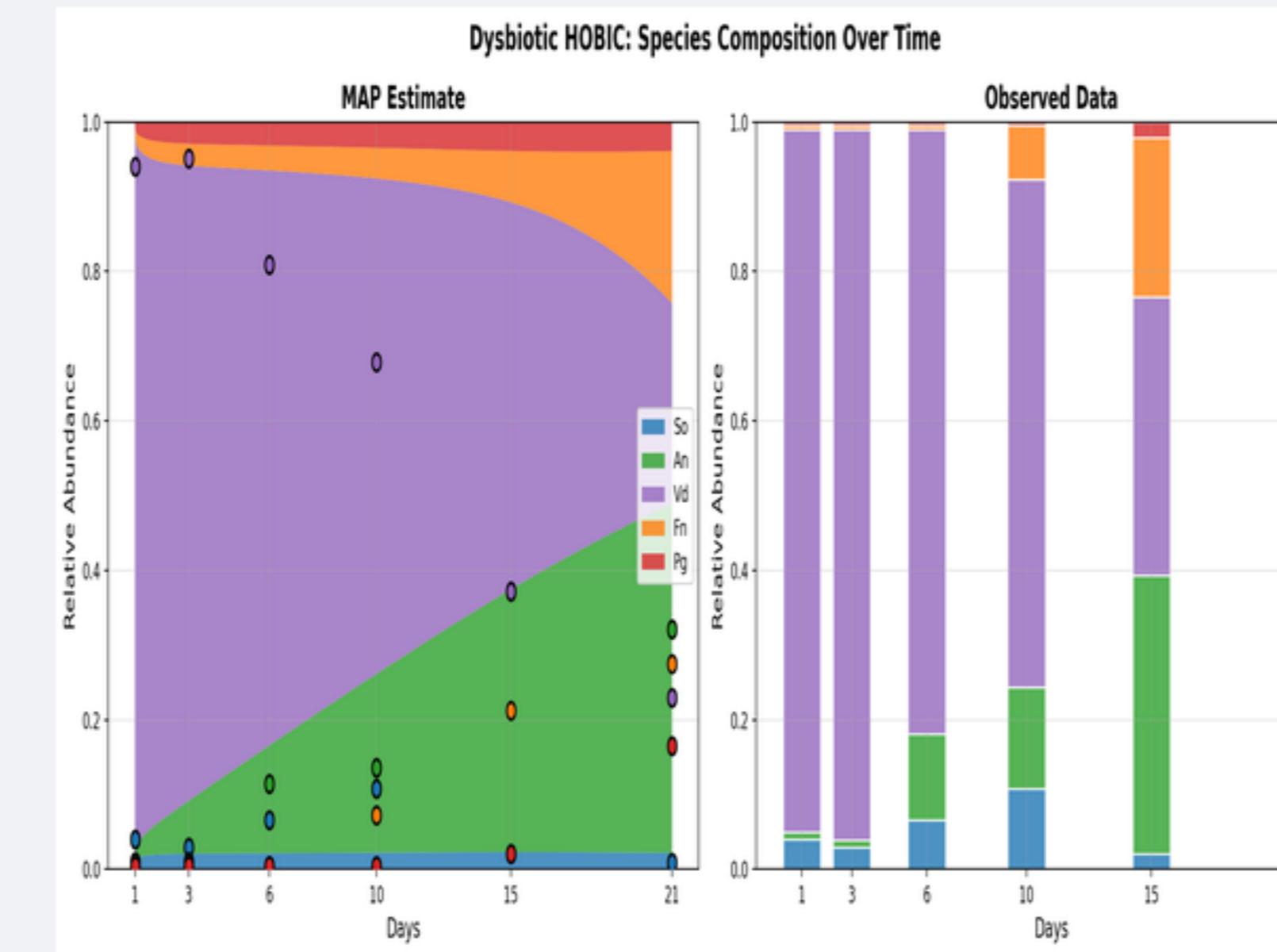
Residual analysis / 残差分析

Dysbiotic HOBIC (Surge) – Convergence & Diagnostics

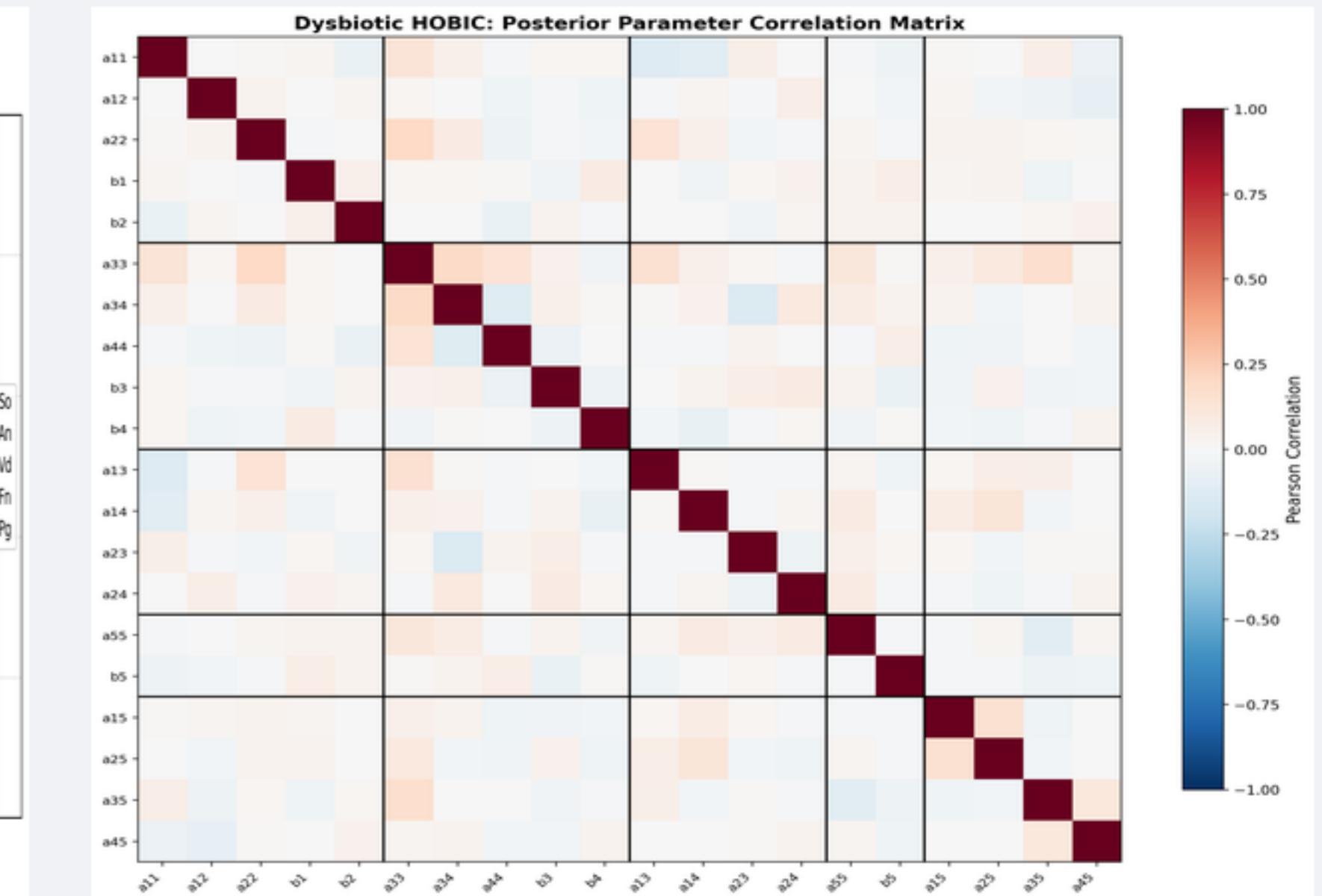
疾患・流動 (Surge) – 収束診断



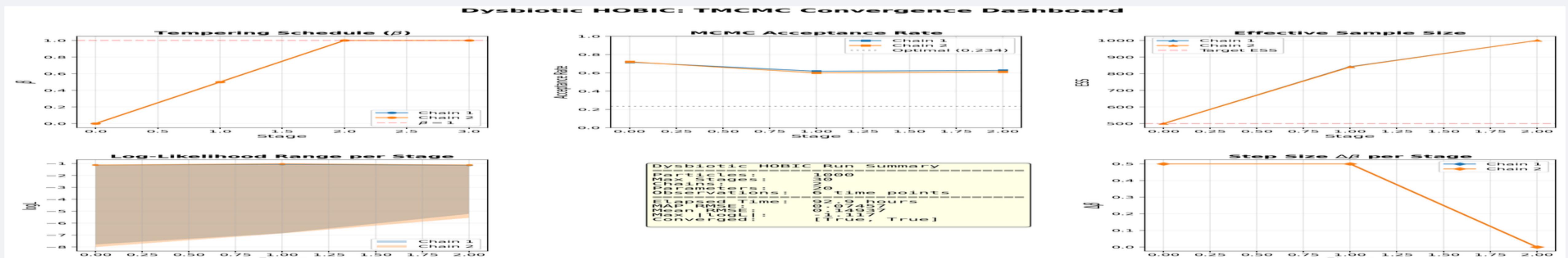
TMCMC β schedule



Species composition / 菌種構成



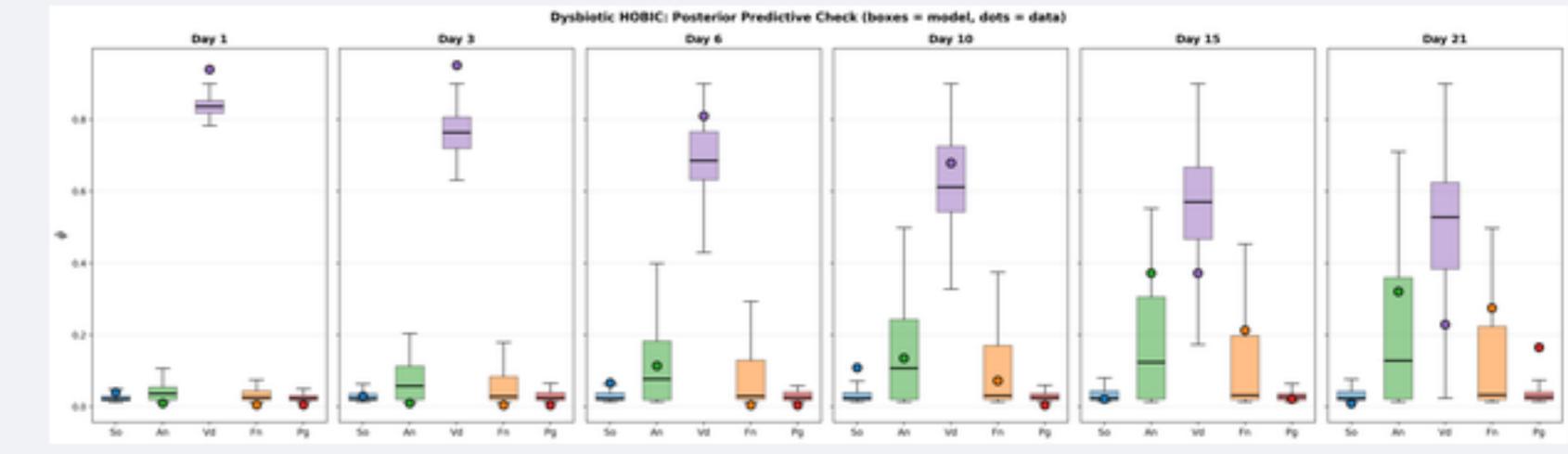
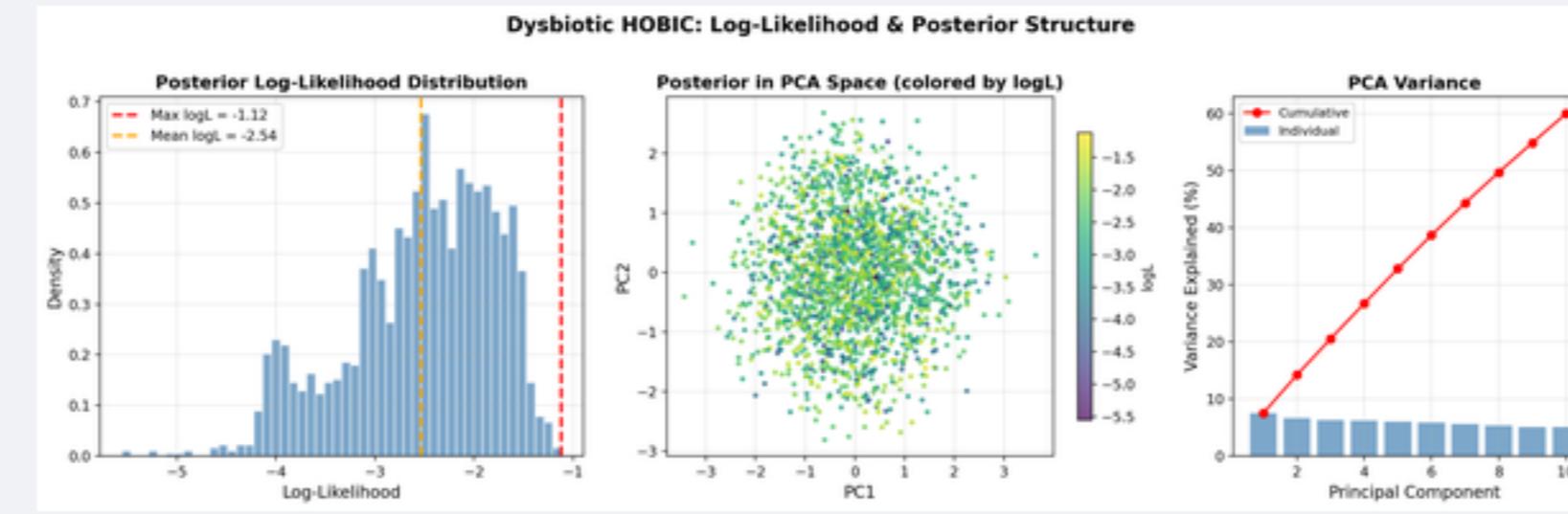
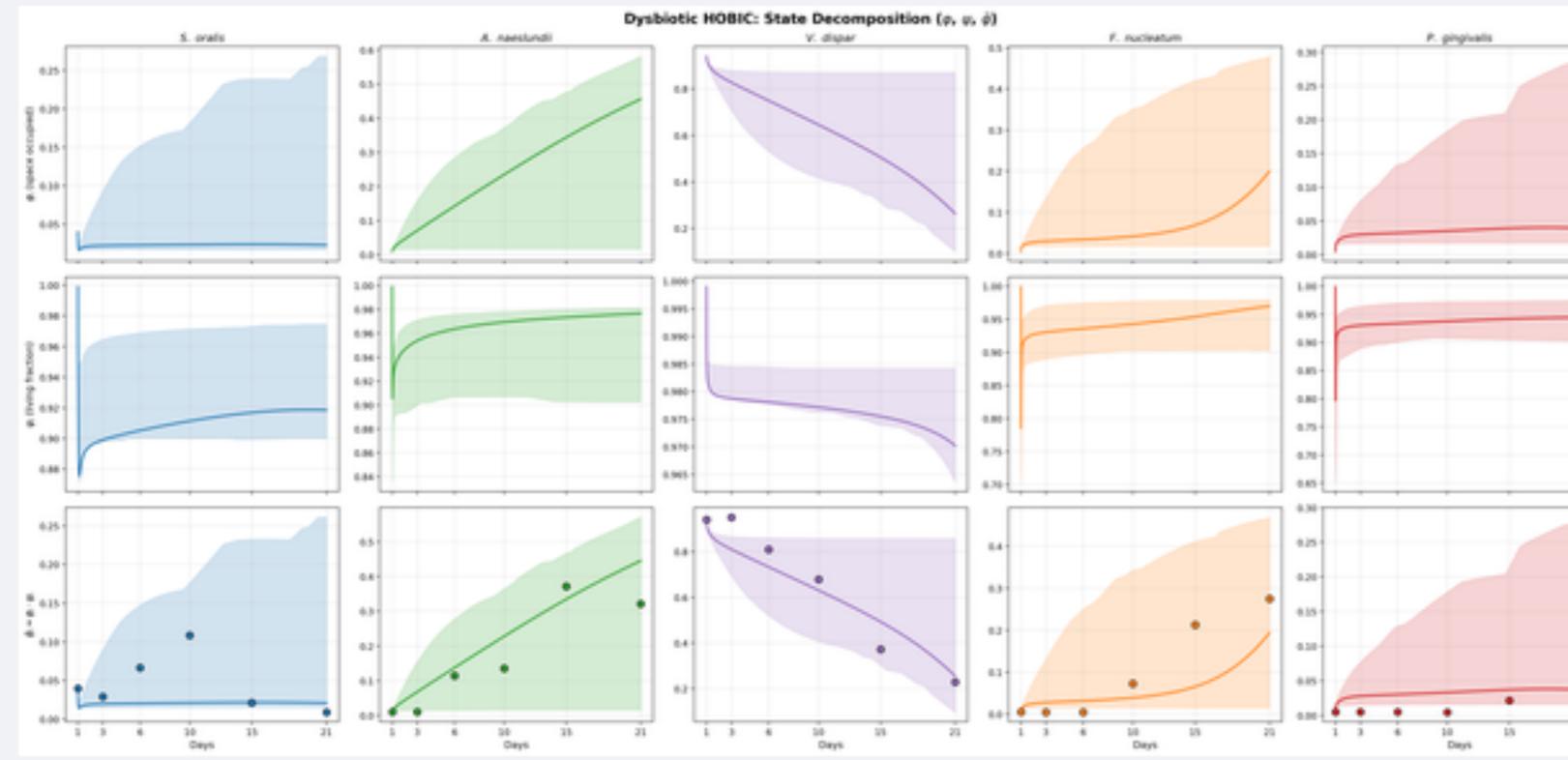
Parameter correlation / パラメータ相関



Convergence dashboard / 収束ダッシュボード

Dysbiotic HOBIC (Surge) – Additional Diagnostics

疾患・流動 (Surge) – 追加診断



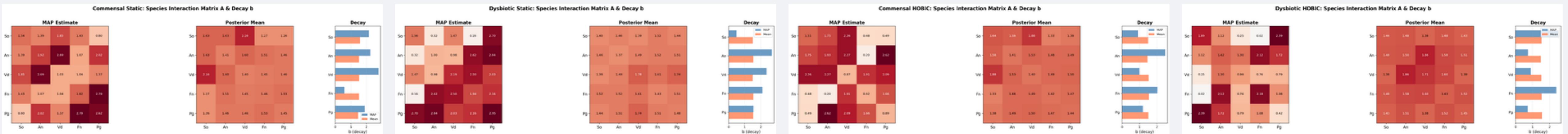
State decomposition (ϕ, ψ) / 状態分解

Log-likelihood landscape / 対数尤度

Posterior predictive check / 事後予測チェック

Interaction Matrix Comparison (All 4 Conditions)

相互作用行列の比較 – 全4条件



Commensal Static ($N_{locked}=9$)

Dysbiotic Static ($N_{locked}=5$)

Commensal HOBIC ($N_{locked}=8$)

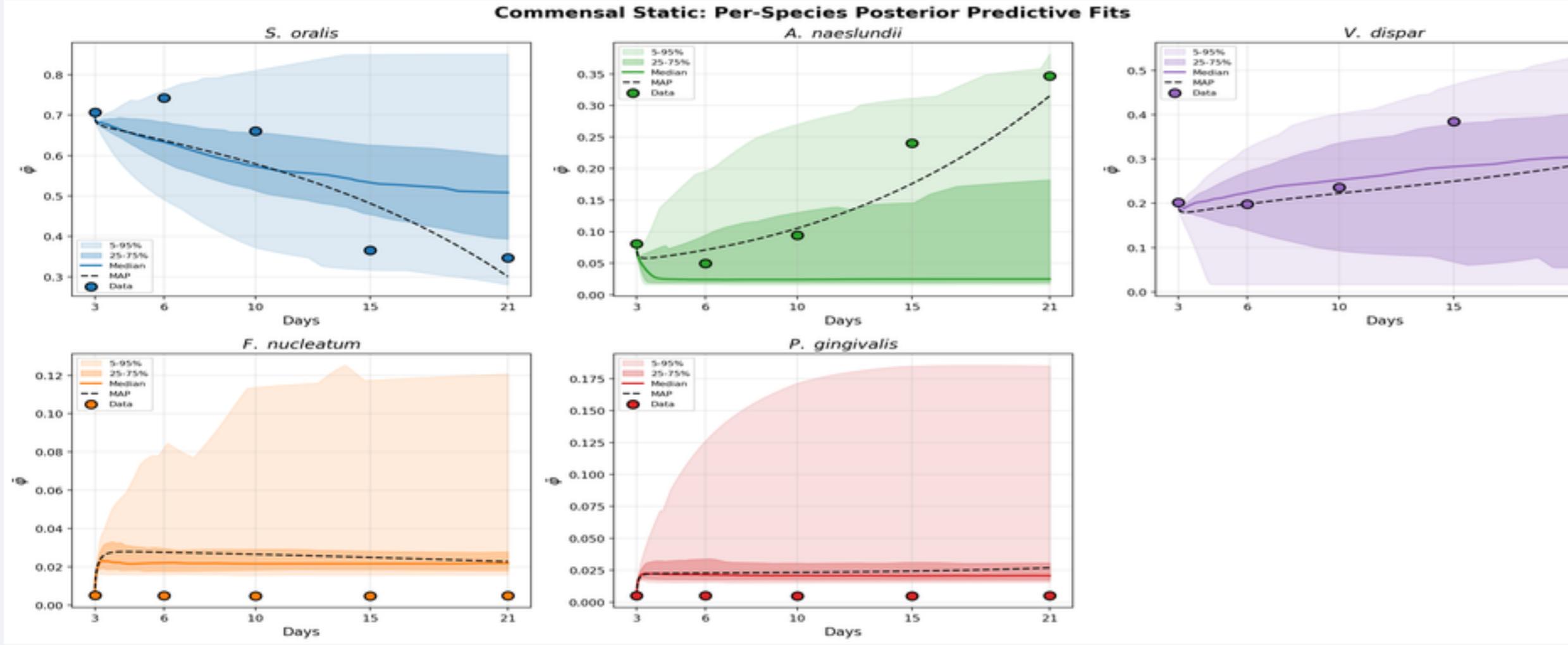
Dysbiotic HOBIC (Surge)
($N_{locked}=0$)

- Commensal: competitive (blue) blocks dominate
- Dysbiotic: cooperative (red) blocks emerge around P.g
- 健康: 競合的(青)ブロックが支配
- 疾患: P.g周辺に協力的(赤)ブロックが出現

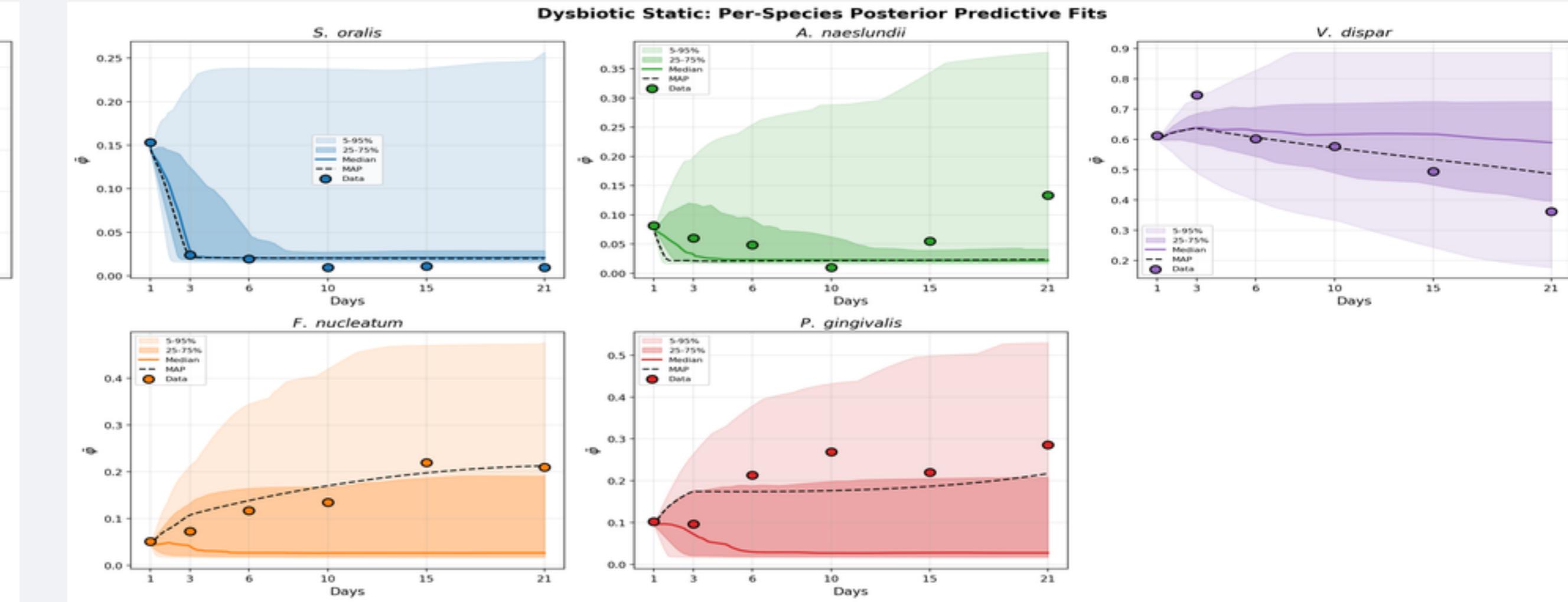
Posterior Predictive Fit Comparison (All 4 Conditions)

事後予測適合の比較 – 全4条件

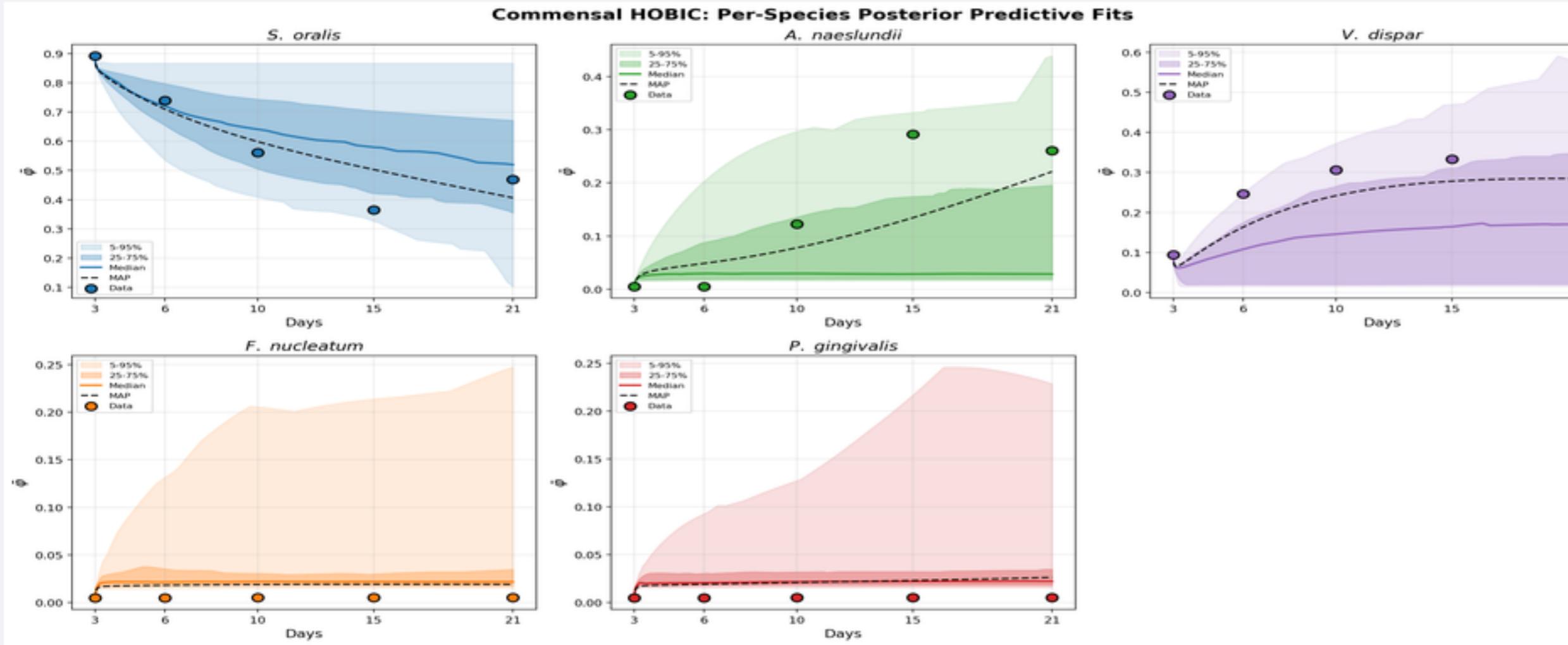
Commensal Static



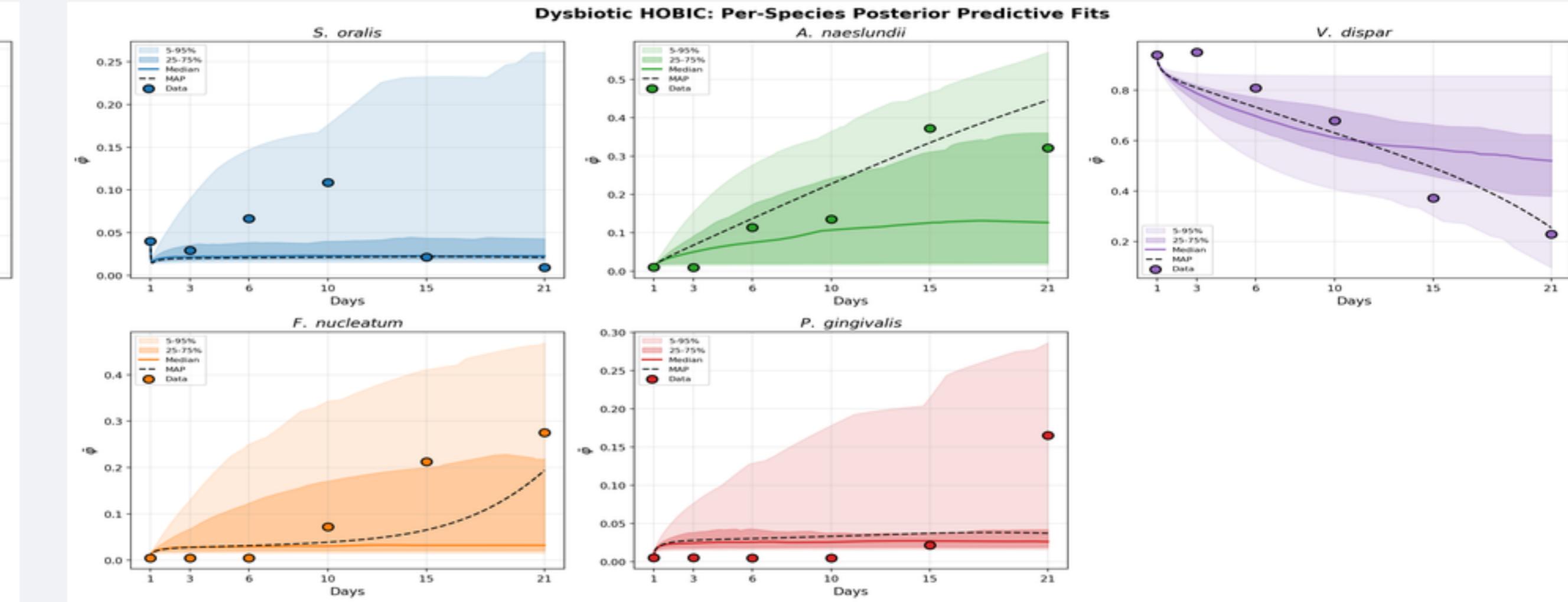
Dysbiotic Static



Commensal HOBIC



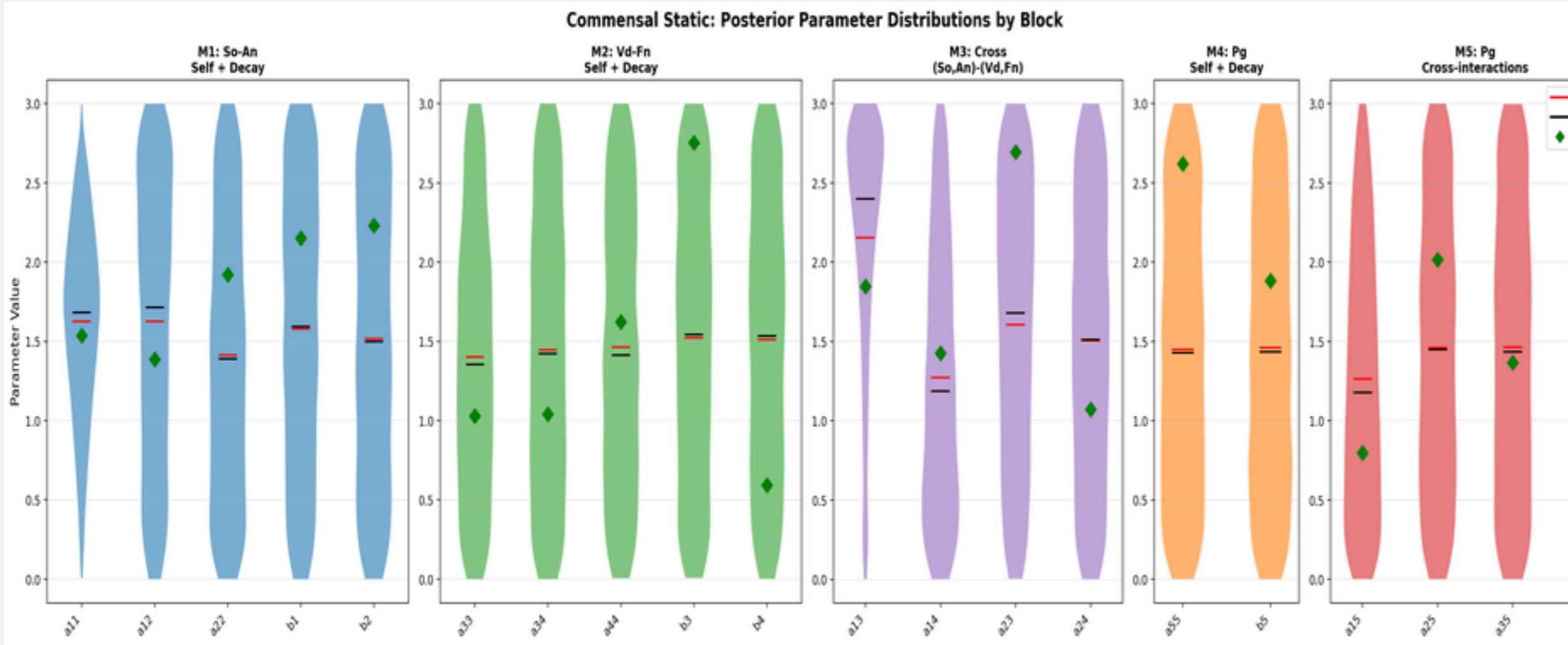
Dysbiotic HOBIC (Surge)



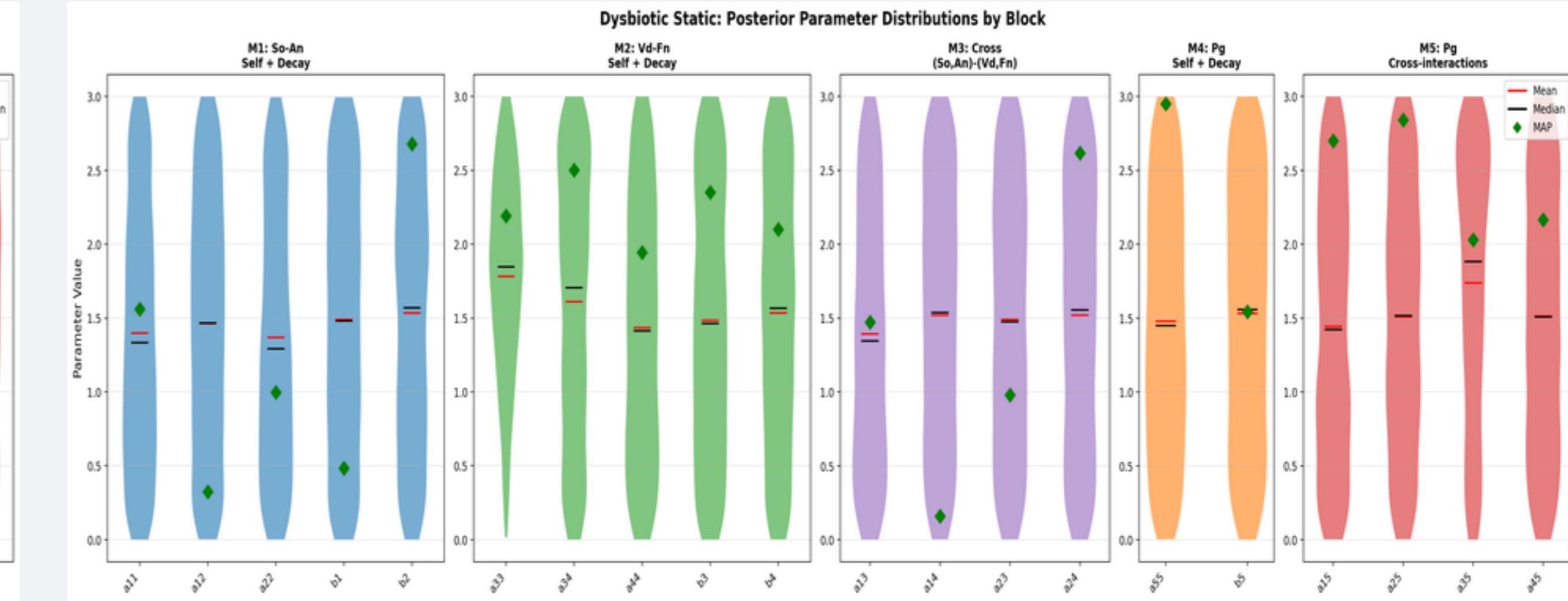
Parameter Uncertainty Comparison (All 4 Conditions)

パラメータ不確実性の比較 – 全4条件

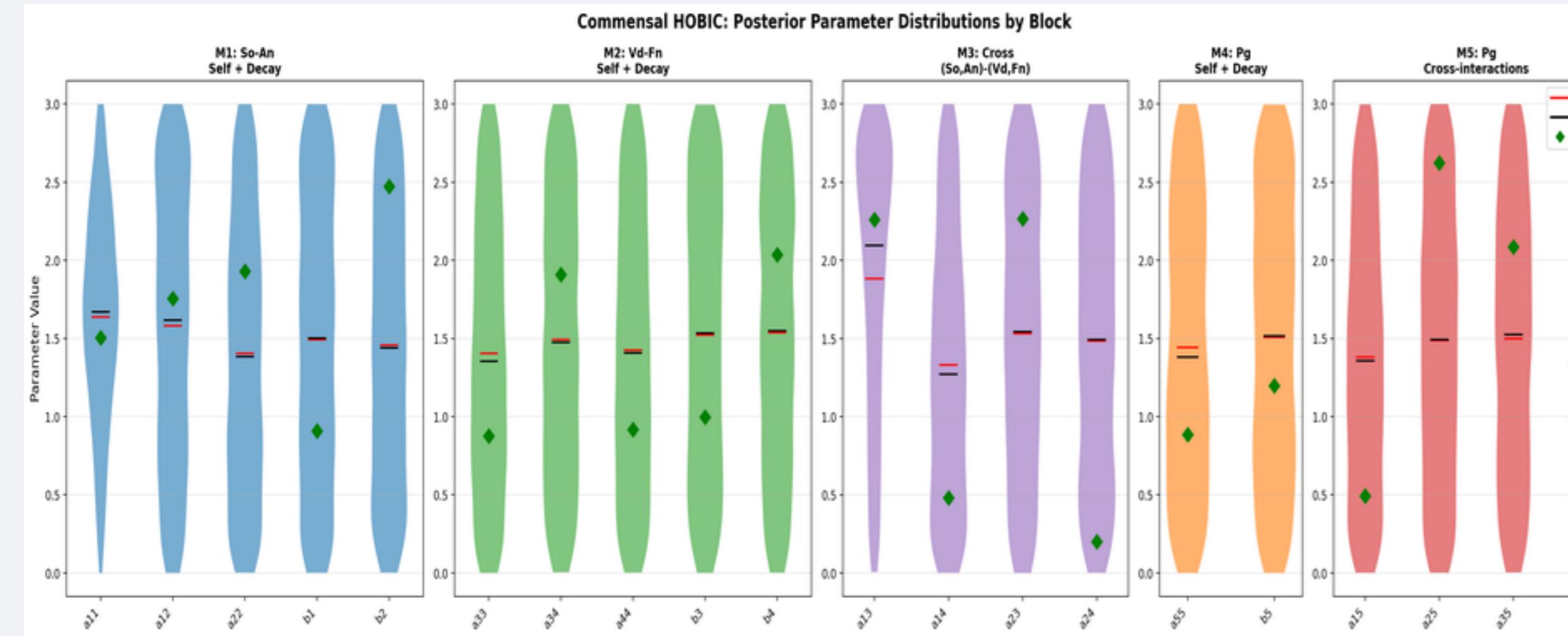
Commensal Static



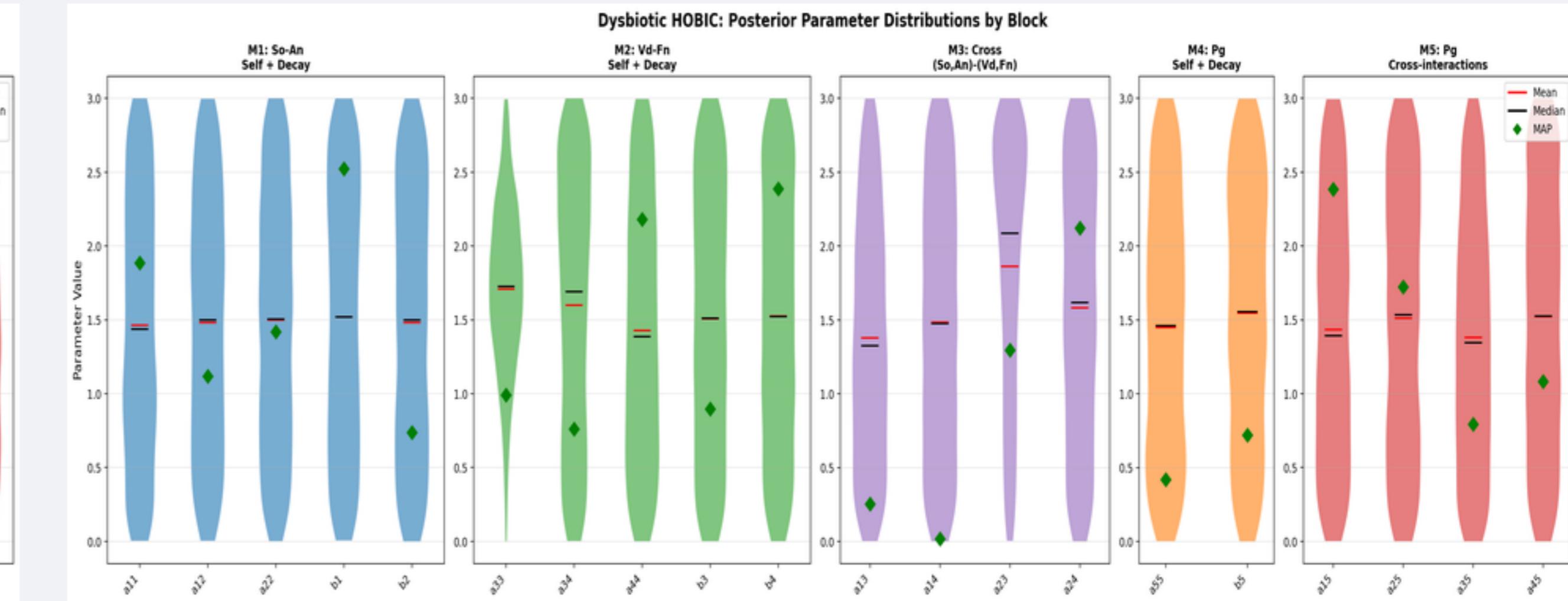
Dysbiotic Static



Commensal HOBIC



Dysbiotic HOBIC (Surge)



Commensal vs. Dysbiotic — Key Differences

健康 vs 疾患 – 主な違い

Commensal (Healthy)

健康状態

- Early colonizers (S.o, A.n) dominate
初期定着菌 (S.o, A.n) が優位
- Pathogen (P.g) interactions suppressed
病原菌 (P.g) の相互作用が抑制
- Interaction matrix: competitive (blue)
相互作用行列: 競合的 (青) ブロックが支配
- Narrow posteriors = high identifiability
狭い事後分布 = 高い識別性
- Strict locks reinforce biological knowledge
厳格なロックが生物学的知識を強化

Dysbiotic (Disease)

疾患状態

- P. gingivalis interactions become positive
P.g の相互作用が正 (協力的) に転換
- Veillonella–P.g cross-feeding emerges
Vei–P.g クロスフィーディングが出現
- Full dysbiosis requires flow (HOBIC)
完全な疾患にはHOBIC (流れ) が必要
- 'Surge' in HOBIC: explosive P.g growth
HOBIC での 'Surge': P.g の爆発的増殖
- Discovery Mode essential to capture dynamics
Discovery Mode が動態の捕捉に不可欠

Static vs. HOBIC – Effect of Saliva Flow

静的 vs 流動 – 唾液流の影響

Static Culture

静的培養

- Nutrient-limited environment
栄養制限環境
- Stable but low biomass steady states
安定だが低バイオマスの定常状態
- Metabolite accumulation limits pathogens
代謝産物蓄積が病原菌を制限
- Narrower posterior distributions
より狭い事後分布
- Less complex dynamics → easier estimation
より単純な動態 → 容易な推定

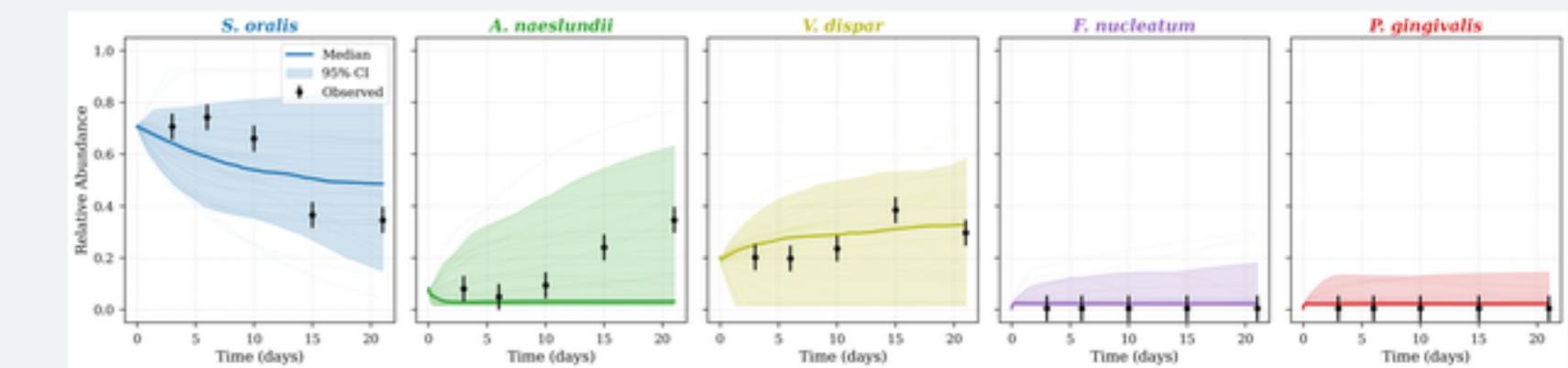
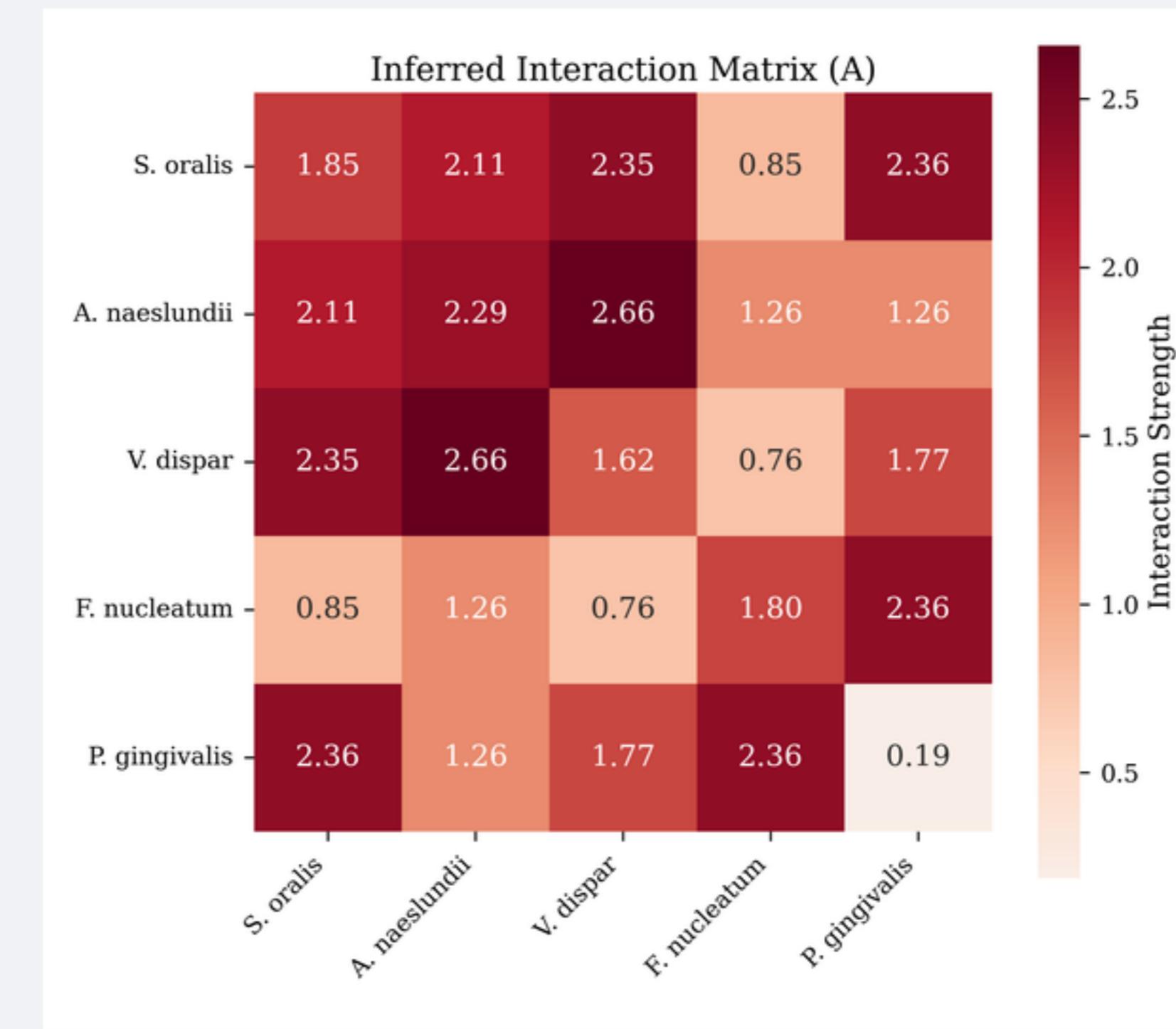
HOBIC (Flow)

流動培養 (HOBIC)

- Simulates oral saliva flow
口腔の唾液流を模倣
- More dynamic steady states
より動的な定常状態
- Higher variance in decay rate posteriors
減衰率事後分布の分散が増大
- Enables 'Blue Bloom' (Commensal)
'Blue Bloom' を可能にする (健康)
- Enables 'Surge' (Dysbiotic)
'Surge' を可能にする (疾患)

Publication-Quality Comparison Figures

論文品質の比較図



MAP fit comparison

Interaction heatmap comparison

Fit comparison

Key Contributions / 主な貢献

- ① Biologically-constrained parameter reduction: $30 \rightarrow 20 \rightarrow 15$ free parameters
生物学的制約に基づくパラメータ削減: $30 \rightarrow 20 \rightarrow 15$ 自由パラメータ
- ② TMCMC successfully applied to all 4 experimental conditions with 1000 particles
TMCMCを1000粒子で4つの全実験条件に適用成功
- ③ Unlock All (Discovery Mode) essential for Dysbiotic HOBIC 'Surge' detection
全ロック解除 (Discovery Mode) がDysbiotic HOBIC 'Surge' の検出に不可欠
- ④ Inferred interaction matrices provide quantitative health → disease transition map
推定相互作用行列が健康 → 疾患遷移の定量的マップを提供
- ⑤ 4-stage sequential estimation enables condition-specific Bayesian inference
4段階逐次推定が条件特異的ベイズ推論を実現

Future Work / 今後の課題

- Increase particle count ($N > 5000$)
粒子数の増加 ($N > 5000$)
- Time-varying interaction parameters
時間変化する相互作用パラメータ
- In silico therapeutic testing
治療介入のin silicoテスト

Clinical Impact / 臨床的インパクト

- Quantitative dysbiosis biomarkers
定量的ディスバイオシスバイオマー
- Personalized peri-implantitis risk
個別化インプラント周囲炎リスク
- Framework for multi-species analysis
多菌種解析の枠組み

Thank You

ご清聴ありがとうございます

Keisuke Nishioka ─ Institut für Kontinuumsmechanik (IKM) ─ Leibniz Universität Hannover

February 2026