Supplementary Material

Oshrit Shtossel[1], Akiva Goldberg[2], Sondra Turjeman[3], Erel A. Shtossel[4], Shani Finkelstein[1], Nadav Shnerb[2], Omry Koren[3], and Yoram Louzoun[1,*]

[1]Department of Mathematics, Bar-Ilan University, Ramat Gan 52900, Israel
[2]Department of Physics, Bar-Ilan University, Ramat Gan 52900, Israel
[3]The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel
[4]Department of Computer Science, Bar-Ilan University, Ramat Gan 52900, Israel
[*]Corresponding author: Yoram Louzoun, louzouy@math.biu.ac.il

February 6, 2025

1 Simulations details

Transitions can be explained using a simple multi-equilibrium ecological model, where each equilibrium consists of a small number of microbe strains. The Generalized Lotka-Volterra Model (GLVM)[1, 2, 3, 4, 5] offers a relatively straightforward way to describe such dynamics, and has recently been shown[4] to be a generic framework that captures the essential features of many more complex models. To account for transitions between equilibrium states, we introduced strain-specific stochastic variations in the growth rates, driven by random environmental fluctuations. A similar approach to microbiome dynamics was used in [6, 7, 8].

Specifically, we consider a community of S microbes, the abundance of each is given by n_i, where the index i runs from 1 to S. The dynamics of the i-th microbe is govern by the equation,

$$\frac{dn_i}{dt} = n_i \left(1 - n_i - \sum_{j \neq i} \alpha_{i,j} n_j\right) + \lambda_i + \sigma_e \eta_i(t) n_i. \tag{1}$$

Here, the interaction matrix term $\alpha_{i,j}$ corresponds to the pressure put by microbe j on microbe i. For a given abundance of microbe j, The larger $\alpha_{i,j}$ is, the larger is the suffering of i from competition with j. λ_i is the rate by which new immigrants reinforce the i-th population, and the σ_e term represents the stochasticity associated with environmental variations: $\eta_i(t)$ is a white noise process, so the growth rate of each microbe fluctuates erratically in time.

Additional elements can be incorporated into the model to enhance its realism, such as varying carrying capacities, species-specific growth rates, or Holling-type response functions. However, it was recently demonstrated that the core dynamics and their primary phases are fully captured by the simple model (1) [4]. Furthermore, as long as $\lambda > 0$, the results remain unchanged for different values of λ. Accordingly, we follow recent literature [2] and set $\lambda = 10^{-10}$ (uniform across all i). The values of $\alpha_{i,j}$ were randomly drawn from a normal distribution with mean α and variance σ^2.

In the absence of stochasticity ($\sigma_e = 0$), The community splits into two types of microbes: those whose abundance is much greater than the square root of λ, and those whose abundance is smaller, approximately equal to λ. The microbes of the first type are "residents" forming a stable clique. The microbes of the second type are transients, unable to invade the resident clique. Competition with the residents would lead to their extinction, if not for the weak inward migration at a rate of λ. This behavior is demonstrated in Figure 1(A).

This division between a clique of species with high abundance and a collection of transients is not necessarily unique [2]. When interactions between microbes are relatively strong, as can be expected in cases of high niche overlap, alternative stable states emerge. Stochasticity allows the system to transition between these alternative states [1], as demonstrated in Figure 1(B).

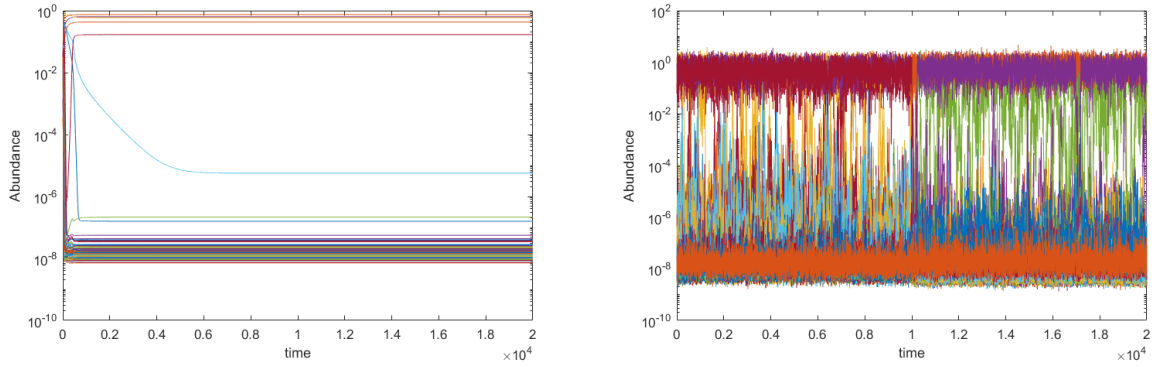

Figure 1: Community dynamics with and without stochasticity.**A.** shows the dynamics of $S = 100$ competing microbe strains as described by Eq. (1), with no stochasticity ($\sigma_e = 0$). Each line represents the abundance of a single strain, starting from random initial conditions. The community rapidly settles into a state where a few resident microbes, with large abundances, outcompete all other strains, which persist only due to immigration. **B.** presents the time evolution of the same community with identical parameters, but now stochasticity has been introduced. The dynamics become more erratic, and a regime shift is clearly observable. The model parameters are $\alpha = 0.65$, $\sigma = 0.25$, $\lambda = 10^{-10}$, and (for panel B) $\sigma_e = 0.7$. The interaction matrix is symmetric, i.e., $\alpha_{i,j} = \alpha_{j,i}$. Eq. (1) was integrated numerically using the Euler method with $dt = 0.01$. For the stochastic case, the Stratonovich integration procedure was implemented.

Table 1: Acronym table

Acronym	**Meaning**
FMT	Fecal Microbiota Transplantation
RSM	Regime Shifting Microbes
WGS	Whole-Genome Sequencing
QSS	Quasi-Steady States
BIC	Bayesian Information Criterion
LV	Lotka-Volterra
RPT	Reported Probiotic Taxa
IFMT	Influential FMT
SCC	Spearman Correlation Coefficient
LR	Logistic Regression
RF	Random Forest
AUC	Area Under the Receiver Operating Characteristic Curve
S.D.	Standard Deviation
ANOVA	Analysis of Variance
NEC	Necrotizing Enterocolitis
IBD	Inflammatory Bowel Disease
ARD	Automatic Relevance Determination
GDM	Gestational Diabetes
ML	Machine Learning
SVR	Support Vector Machine Regression
RBF	Radial Basis Function
LSTM	Long Short-Term Memory
iMic	iMage Microbiome

Table 2: All dataset details

Dataset	Phenotype	Number of samples	Max number of time points	Avg. number of time points	16S vs. WGS	Reference
GDM	GDM	655	3	3	16S	[9]
PRJNA730851	Infant allergy	954	19	6	16S	[10]
PRJEB14529	Early dynamics 2	807	43	18	16S	[11]
PRJEB6456	Early dynamics 1	400	4	4	WGS	[12]
PRJNA1130109	Obesity	203	5	4	WGS	SRA accession PRJNA1130109
PRJEB39500	T2D	202	3	2	WGS	[13]
PRJNA345144	Eczema	646	5	3	WGS	[14]
PRJNA290729	Fatty liver	92	6	6	WGS	[15]
PRJNA273761	NEC	60	9	6	WGS	SRA accession PRJNA273761
PRJNA301903	Preterm infants	510	20	6	WGS	SRA accession PRJNA301903
PRJNA395569	IBDMDB	612	18	3	WGS	[16]
PRJNA510445	CF	166	16	2	WGS	[17]
PRJNA806984	Healthy	207	6	2	WGS	[18]

Table 3: Statistical tests on distance distributions between each two consecutive samples. The table includes results for: the BIC and F-test comparing bimodal to unimodal and three-modal distributions (Bimodal or multimodal > 3). Host sample distribution between Gaussians is measured by the fraction of host samples in more than one Gaussian (Host ratio between Gaussians). Kolmogorov-Smirnov test comparing time distributions across different Gaussians (Time distributions across Gaussians). Phenotype Chi-square test results (Phenotype Chi-square).

Dataset	Phenotype	Bimodal or multimodal (> 3)	Host ratio between Gaussians	Time distributions across Gaussians	Phenotype Chi-square
GDM	GDM	Multimodal	0.07	n.s	n.s
PRJNA730851	Infant allergy	Multimodal	0.66	n.s	Not available
PRJEB14529	Early dynamics 2	Bimodal	1	n.s	Only controls
PRJEB6456	Early dynamics 1	Bimodal	0.69	n.s	n.s
PRJNA1130109	Obesity	Bimodal	0.7	n.s	n.s
PRJEB39500	T2D	Bimodal	0.06	n.s	**significant**
PRJNA345144	Eczema	Bimodal	0.55	n.s	n.s
PRJNA290729	Fatty liver	Bimodal	0.75	n.s	**significant**
PRJNA273761	NEC	Multimodal	0.67	n.s	Not available
PRJNA301903	Preterm infants	Multimodal	0.58	n.s	Not available
PRJNA395569	IBDMDB	Bimodal	0.58	n.s	**significant**
PRJNA510445	CF	Bimodal	0.09	n.s	Not available
PRJNA806984	Healthy	Bimodal	0.13	n.s	Only controls

Table 4: Summary of Reported Probiotic Taxa (RPT)

Genus	Species/ strain	Function
	Lactobacillus acidophilus	Treatment of travellers' diarrhea [19, 20]; Reduction of hospital stay of children with acute diarrhea [21]; Antifungal activity (L. acidophilus ATCC-4495) [22]; Prevention or treatment of bacterial vaginosis [23]; Treatment of C. difficile-associated diarrhea [22]; Reduction of incidence of febrile urinary tract infections in children [120]; Reduction of irritable bowel syndrome symptoms [24, 20]; Alleviate cancer [25].
	Lacticaseibacillus casei	Treatment of functional constipation in adults (L. casei Lcr35 and L. casei Shirota) [26]; Treatment of C. difficile-associated diarrhoea [27]; Restoration of vaginal flora of patient with bacterial vaginosis (L. casei Lcr35) [28]; Reduction of irritable bowel syndrome symptoms and gingivitis [24, 29]; Reduction of diarrhea duration of antibiotic-associated diarrhea in geriatric patients (L. casei Shirota) [30]; Immunomodulatory mechanisms (L. casei Shirota) [31]; Improvement of rheumatoid arthritis status (L. casei 01) [32]; Protection against Salmonella infection (L. casei CRL-431) [33]; Prevention of Salmonella-induced synovitis [34]; Treatment of intravaginal staphylococcosis (L. casei IMV B-7280) [35].
	Lactobacillus rhamnosus	Reduction of viral-associated pulmonary damage (L. rhamnosus CRL1505)[36, 37] Prevention and reduction of severity of atopic dermatitis in children (L. rhamnosus GG) [38]; Reduction of risk for developing allergic disease (L. rhamnosus GG) [38, 26], (L. rhamnosus HN001 [39]; Anti-diabetic potential (various strains from human infant faecal samples) [40]; Prevention of necrotizing enterocolitis in newborns (L. rhamnosus GG) [41, 42]; Prevention or treatment of bacterial vaginosis (L. rhamnosus GR-1) [23]; Aid in weight loss of obese women (L. rhamnosus CGMCC1.3724) [43, 44]; Treatment of acute gastroenteritis in children (L. rhamnosus GG) [45]; Reduction of risk for rhinovirus infections in preterm infants (L. rhamnosus GG and L. rhamnosus ATCC 53103) [46]; Protection of human colonic muscle from lipopolysaccharide-induced damage (L. rhamnosus GG) [47]; Has an effect on symptoms of maternal depression and anxiety during the postpartum period [48].
	Lactiplantibacillus plantarum	Prevention of endotoxin production [49]; Antifungal activity (L. plantarum NRRL B-4496) [22]; Cholesterol lowering activity [50]; Reduction of irritable bowel syndrome symptoms [48].
	Lactobacillus reuteri	Reduction of low-density lipoprotein cholesterol (L. reuteri NCIMB 30242) [51]; Treatment of acute gastroenteritis in children [45]; Reduction of diarrhea duration in children (L. reuteri ATCC 55730) [52]; Management of infant colic (L. reuteri ATCC 55730 and L. reuteri DSM 17938) [53]; Reduction of onset of gastrointestinal disorders in infants (L. reuteri DSM 17938) [54]; Reduction of frequency of proven sepsis, feeding intolerance and duration of hospital stay in preterm infants (L. reuteri DSM 17938) [54]; Treatment of gingivitis in pregnant women and chronic periodontitis [55, 56, 57].

Table 4 continued from previous page

Genus	Species/ strain	Function
Lactobacillus	Lactobacillus fermentum	Prevention or treatment of bacterial vaginosis (L. fermentum RC-14) [23]; Blockage of adherence of pathogenic microorganisms on vaginal epithelium [58]; Antistaphylococcal action (L. fermentum ATCC 11739) [59]; Potential for reduction of insulin resistance and hypercholesterolemia (L. fermentum NCIMB 5221) [60].
	Lactobacillius delbrueckii subsp. bulgaricus	Antibiotic resistance of yogurt starter culture [61] Enhancement of systemic immunity in elderly (L. delbrueckii subsp. bulgaricus 8481) [62]; Antibacterial action against E. coli [63]; Modulation of brain activity [64].
	Lactobacillius brevis	Protective role in bile salt tolerance (L. brevis KB290) [65]; Reduction in plague acidogenicity (L. brevis CD2) [66].
	Lactobacillus johnsonii	Impact on adaptive immunity for protection against respiratory insults [67]; Reduction of occurrence of gastritis and risk of H. pylori infection (L. johnsonii MH-68) [68]; Inhibition of S. sonnei activity (L. johnsonii F0421) [69]; Treatment of perennial allergic rhinitis in children together with levocetirizine (L. johnsonii EM1) [70].
Bifidobacterium	Bifidobacterium infantis	Reduction of irritable bowel syndrome symptoms [27, 71]; Reduction of necrotizing enterocolitis in preterm infants [72, 73, 74]; Inhibition the secretion of allergen induced IgE [57].
	Bifidobacterium animalis subsp. lactis	Treatment of functional constipation in adults (B. animalis subsp. lactis DN-173 010) [75]; Reduction of incidence of febrile urinary tract infections in children [24]; Modulation of brain activity [64]; Reduction of necrotizing enterocolitis in preterm infants [72]; Reduction of total microbial counts in dental plaque (B. animalis subsp. lactis DN-173 010) [76]; Reduction of total cholesterol (B. animalis subsp. lactis MB 202/DSMZ 23733) [77]; Reduction of risk of upper respiratory illness (B. animalis subsp. lactis BI-04) [78].
	Bifidobacterium bifidum	Reduction of hospital stay of children with acute diarrhea [21]; Reduction of necrotizing enterocolitis in preterm infants [73, 74]; Reduction of total cholesterol (B. bifidum MB 109/DSMZ 23731) [77].
	Bifidobacterium longum	Prevention and treatment of necrotizing enterocolitis in newborns [79]; Reduction of radiation induced diarrhea [80, 81]; Reduction of necrotizing enterocolitis with Bifidobacteria cocktail (B. breve, B. infantis, B. bifidum, B. longum) [74]; Reduction of irritable bowel syndrome symptoms [27]; Treatment of gastrointestinal diseases (B. longum CMCC P0001) [82]; Modulation of the immune system through IL-10 production [83]; Perinatal intervention against onset of allergic sensitization (B. longum CCM 7952) [84].
	Bifidobacterium adolescentis	Reducing inflammation of the spleen and brain and changes the microbiota of cecum and colon [85]
	Bifidobacterium breve	Prevention and treatment of necrotizing enterocolitis in newborns [79]; Reduction of necrotizing enterocolitis with Bifidobacteria cocktail (B. breve, B. infantis, B. bifidum, B. longum) [74]; Reduction of cholesterol (B. breve MB 113/DSMZ 23732) [77].
Saccharomyces	Saccharomyces boulardi	Treatment of travellers' diarrhea [19]; Treatment and reduction of diarrhea duration regardless of cause [86, 87, 88, 89, 90]; Treatment of irritable bowel syndrome [91]; Treatment of moderate ulcerative colitis [92, 93]; Treatment and reduction of recurrent pseudomembrane colitis infection caused by C. difficile [94]; Treatment of acute gastroenteritis in children [45].

Table 4 continued from previous page

Genus	Species/ strain	Function
Lactococcus	Lactococcus lactis subsp. lactis	Treatment of antibiotic-associated diarrhea [87]; Adhesion to vaginal epithelial cells (L. lactis subsp. lactis KLDS4.0325) [95]; Nisin production (L. lactis subsp. lactis CV56) [96]; Modulation of brain activity [64]; Antimicrobial activity against C. difficile [97]; Antimicrobial and probiotic properties (L. lactis subsp. lactis ATCC 11454) [98].
Enterococcus	Enterococcus durans	Antibiotic and antioxidant activity (E. durans LAB18s) [99], Adherence to colonic tissue and anti-inflammatory activity [100].
	Enterococcus faecium	Treatment of antibiotic-associated diarrhea [101]; Modulation of the Th2-mediated [102, 103] Efficient animal probiotic [104].
Streptococcus	Streptococcus thermophilus	Reduction of irritable bowel syndrome symptoms [27]; Antibiotic resistance of yogurt starter culture [61]; Producing some antioxidant compounds and mitigating the risk of some types of cancer [105] Reduction of necrotizing enterocolitis in preterm infants [72, 73].
Pediococcus	Pediococcus acidilactici	Pediocin production with antimicrobial and probiotic properties (P. acidilactici UL5) [98]; Bacteriocin production [106]; Elimination of H. pylori infections (P. acidilactici BA28) [107].
Leuconostoc	Leuconostoc mesenteroides	Leucoin production, probiotic profile (survival at low pH, in presence of bile salts, in presence of pepsin) (L. mesenteroides B7) [108].
Bacillus	**Bacillus** coagulans	Treatment of antibiotic-associated diarrhea [101, 109], Treatment of bacterial vaginosis (B. coagulans ATCC PTA-11748) [110]; Immunological support (B. coagulans GandenBC30) [111]; Prevention of caries in children [112**?**].
	Bacillus subtilis	Efficient animal probiotic [113, 114]; Treatment of diarrhea and aiding in H. pylori eradication (B. subtilis R0179) [115]; Production of vitamin K [48]; Production of nitric oxide [116].
	Bacillus cereus	Efficient animal probiotic (B. cereus NVH75/95) [117].
Escherichia	Escherichia coli Nissle 1917	Treatment of functional constipation in adults [24]; Treatment of inflammatory bowel disease [118]; Treatment of gastrointestinal disorders [119]; Pro-inflammatory potential [120]; Prevention of surface ocular diseases [121]; Reduction of Salmonella enterica Typhimurium intestinal colonization by iron competition [122].

Table 5: Characteristics of all published human to human datasets used for defining the influential taxa within FMT (IFMT).

Accession number	Disease	Abx	Sample size	FMT	16S region	Reference
ERP021216	CDI	T	86	20	V4	[123]
PRJDB4959	IBD	F	28	10	V1V2	[124]
PRJNA221789	CDI	T	20	10	V1-V3	[125]
PRJNA238042	CDI	T	22	11	V3-V5	[126]
PRJNA238486	CDI	T	23	3	V6	[127]
PRJNA380944	IBD	T	83	21	V4	[128]
PRJNA412501	IBD	T	52	19	V3V4	[129]
PRJNA428898	IBD	F	35	9	V4V5	[130]

Table 6: Gut colonization data of ingested *Lactobacillus* and *Bifidobacterium* strains in the gut of infants or mother–infant pairs. Taxa that appear in the top 5th percentile of S.D. people are highlighted in blue.

Species	**Strain**	**Persistence time during washout period**	**Strain-specific**
L. rhamnosus	19070-2, GG, DR20, LC705	[< 5–11 days, > 21 days]	Yes
L. rhamnosus	GG	[> 6 months, 0–18 months]	NA
L. reuteri	DSM 12246, 108, 47 (R2LC), ATCC PTA 6475, DSM 17938, ATCC 55730	[< 1 days, > 28 days]	Yes
L. casei	CHCC 3137, LC10, Shirota, 136, 98, 271 , Lcr35	[< 1 days, > 3 weeks]	Yes
L. casei	GG	> 2 weeks	NA
L. plantarum	LPT, 283, 299, 299v	[< 1 days, > 11 days]	Yes
L. plantarum	ATCC 20195	> 6 months	NA
L. crispatus	M247, MU5	[< 8 days, > 8 days]	Yes
L. delbrueckii	CHCC 2329	< 5 days	NA
L. paracasei	IMPC 2.1	< 7 days	NA
B. longum	AH1206, SBT2928	[> 6–30 days, > 6 months]	NA
B. infantis	NA	< 3 weeks	NA
B. lactis	NA	> 3 weeks	NA
L. salivarius	132, 280, UCC118	[< 1 days, 3 weeks]	NA
L. acidophilus	DDS-1	< 8 days	NA

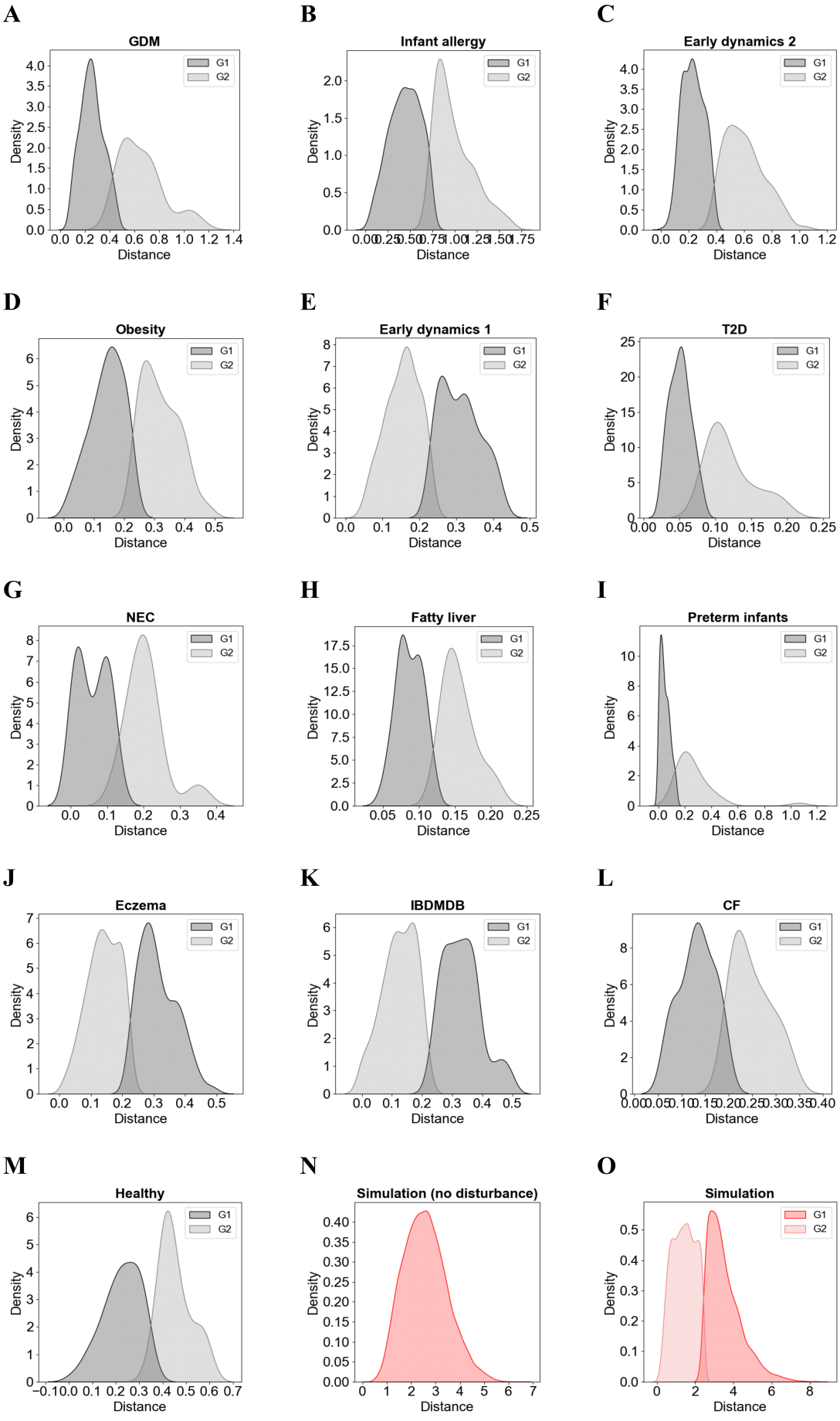

Figure 2: Histograms of microbiota distance between consecutive time points across different cohorts **(A-M)**. These histograms represent the distribution of microbiota distances measured between two successive time points for each cohort, providing insights into how microbiota compositions change over time within each group. **N, O.** Histograms of simulated microbiota distance between consecutive time points across a simulation with no disturbance **(N)** and a simulation with disturbance **(O)**.

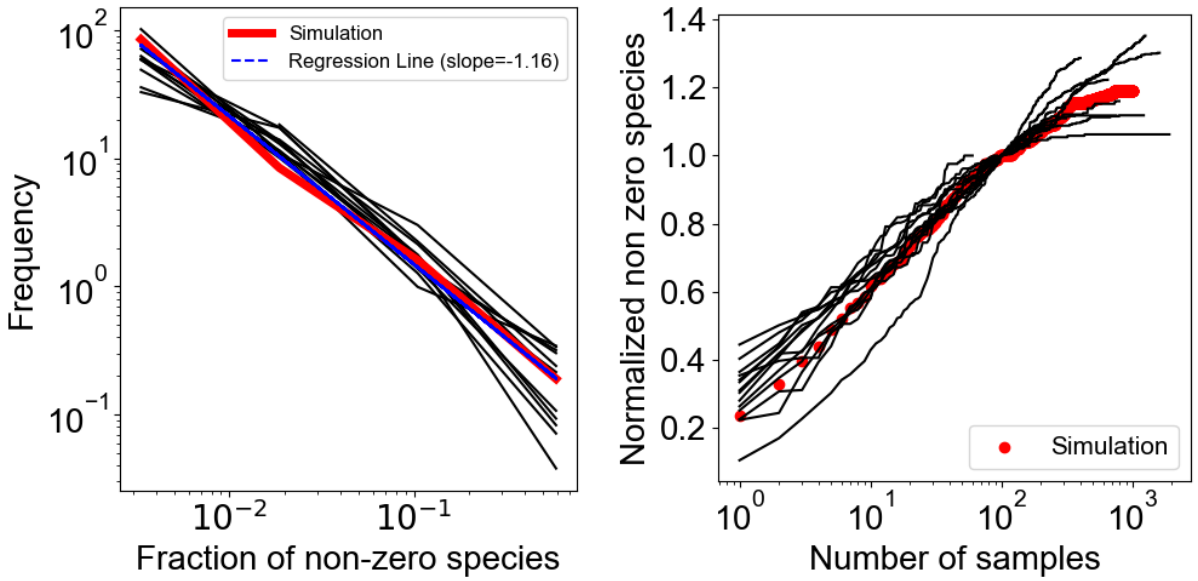

Figure 3: The species microbiome system exhibits generic features, such as TOP **(left)** and DTN **(right)**. Each black line represents a separate study. The red lines represent the simulation, while the blue line in the left plot depicts the regression line based on all points from all studies.

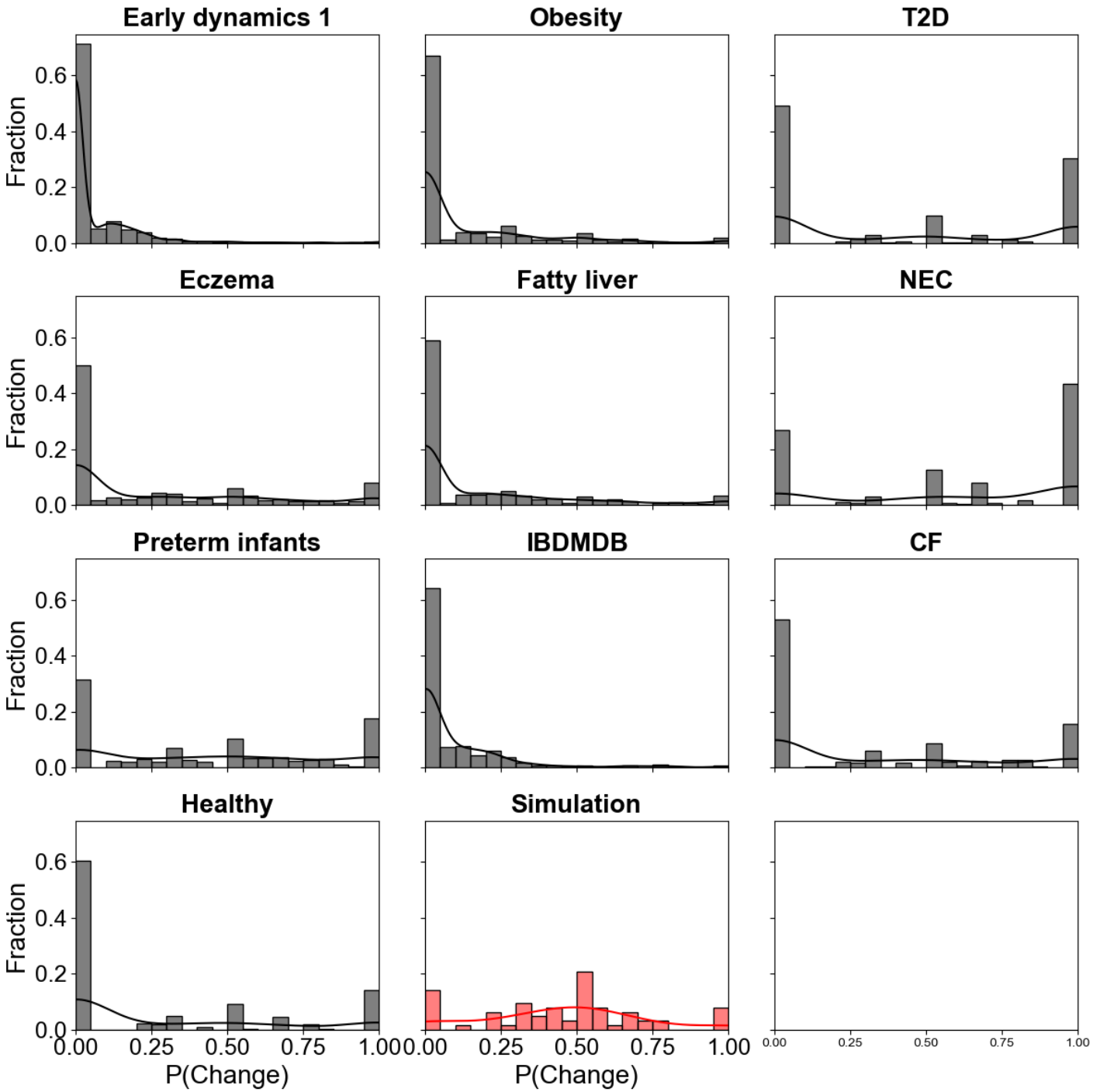

Figure 4: Probability to change distribution over the different cohorts (black) and the simulation (red) analyzed at the **strain-level**. P(change) was measured by the $P(011)$ probability, which represents the likelihood of a taxon that is absent at a certain time step to appear in the next step and remain in the subsequent one. This is divided by the $P(01X)$ probability, representing the likelihood of a taxon appearing at a time step when it was not previously present in the sample.

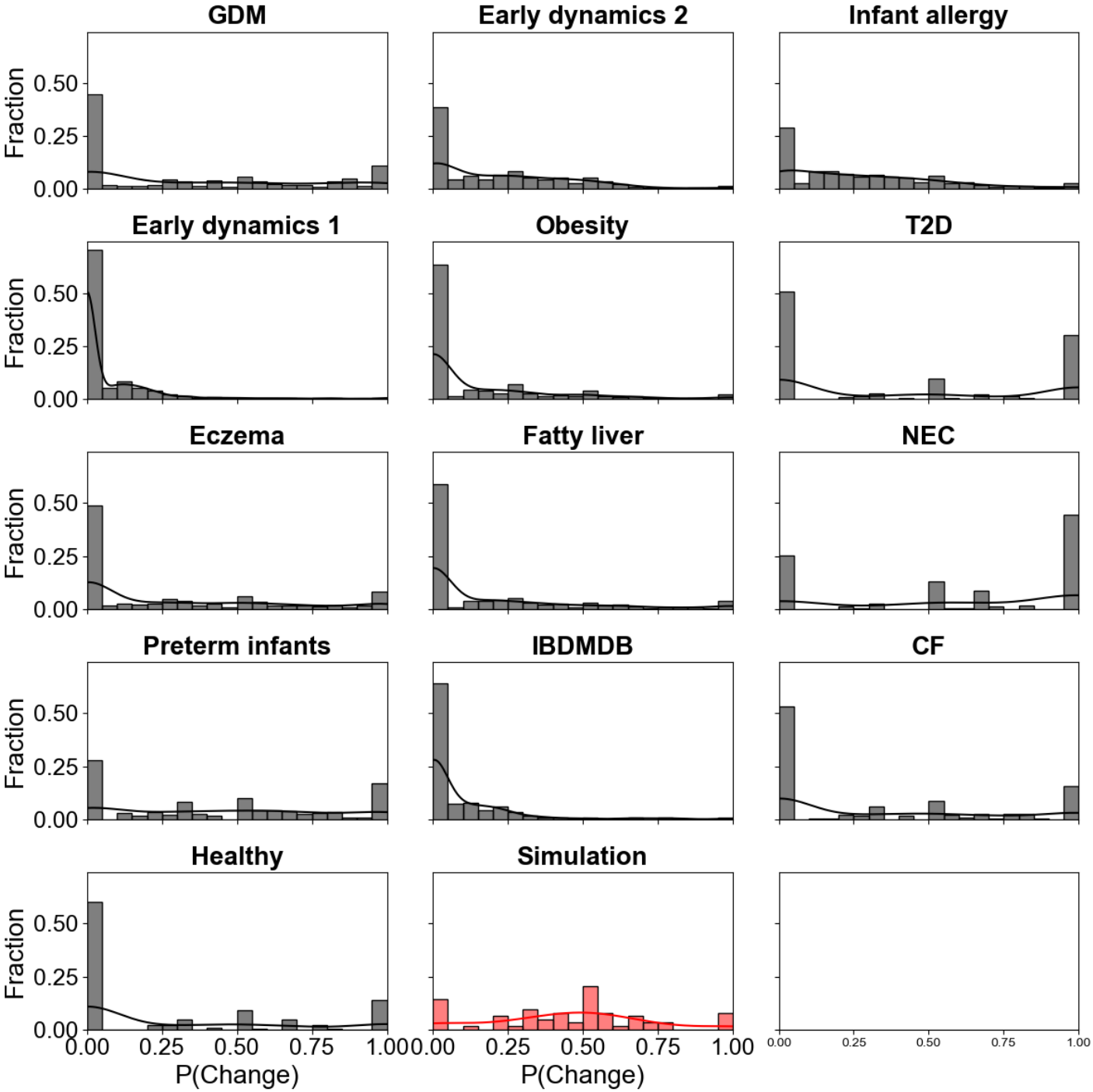

Figure 5: Probability to change distribution over the different cohorts (black) and the simulation (red) analyzed at the **species-level**. P(Change) was measured by the $P(011)$ probability, which represents the likelihood of a taxon that is absent at a certain time step to appear in the next step and remain in the subsequent one. This is divided by the $P(01X)$ probability, representing the likelihood of a taxon appearing at a time step when it was not previously present in the sample.

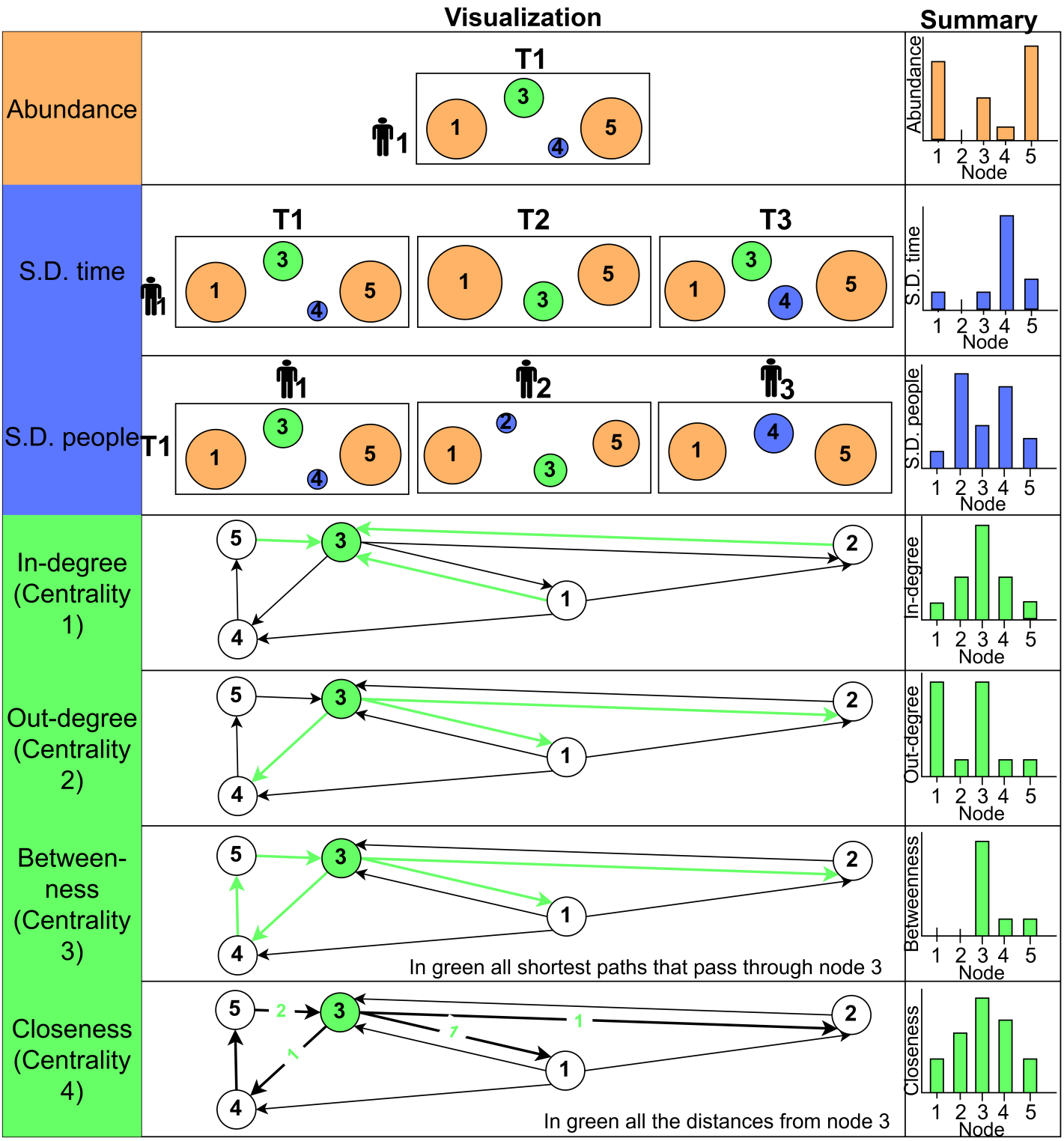

Figure 6: Visuaization of the different microbial features divided to the 3 groups of abundance, fluctuation and centrality.

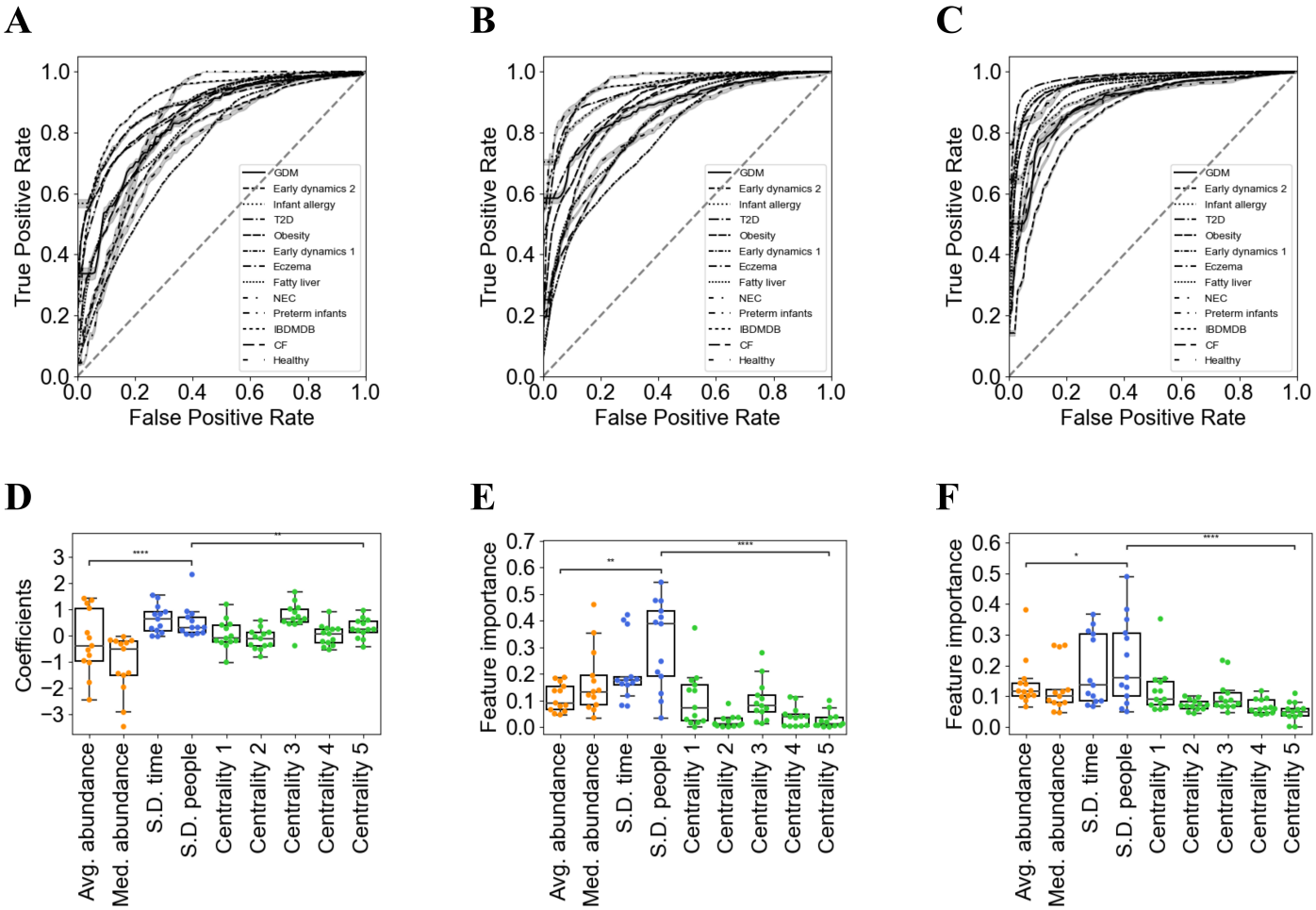

Figure 7: Prediction of RSM using non-log normalized microbiome data, demonstrating consistent performance across different models and cohorts. **A-C.** ROC curves show the predictive accuracy of RSM across various cohorts using three models: **A** depicts results from the LR model, **B** from the RF model, and **C** from XGBOOST. **D-F.** Patchy features emerge as the most informative predictors. This is evident in the LR coefficients (**D**), as well as the feature importance (FI) scores for RF (**E**) and XGBOOST (**F**). The results highlight the robustness of patchy microbial features in predicting regime shifts across multiple models. The stars represent the p-values of t-tests between the fluctuating features (S.D. time and S.D. people) vs. the highly abundant features (average and median) and the central features (in-degree, out-degree, betweenness and closeness), such that * for $p - value < 0.05$, ** for $p - value < 0.01$, *** for $p - value < 0.001$ and **** for $p - value < 0.0001$.

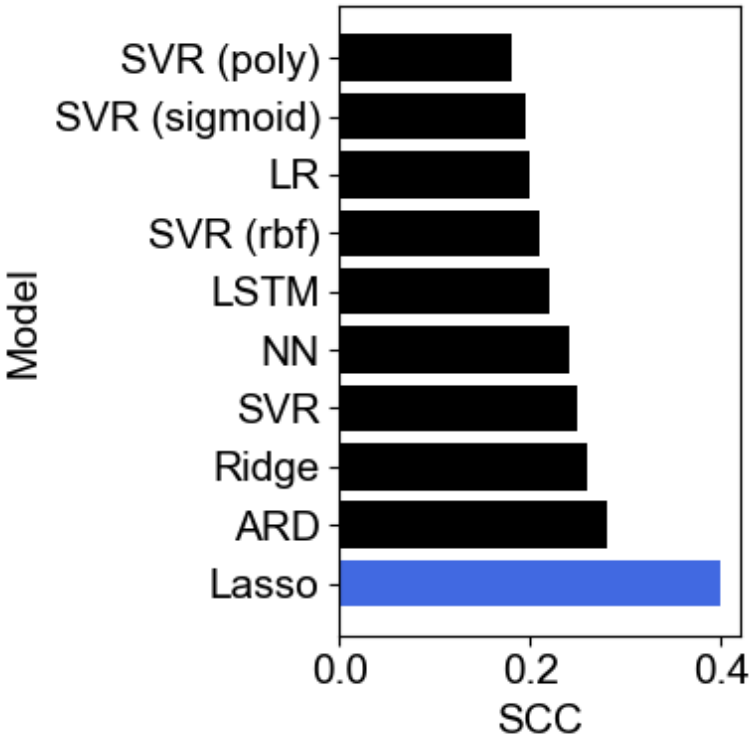

Figure 8: Overall average SCC between predicted and actual taxon differences over time across models. This plot shows the overall average Spearman correlation coefficient (SCC) between the differences predicted for each taxon and the real observed differences over time, as a function of the model used for prediction. The best correlations were achieved using the Lasso model (blue).

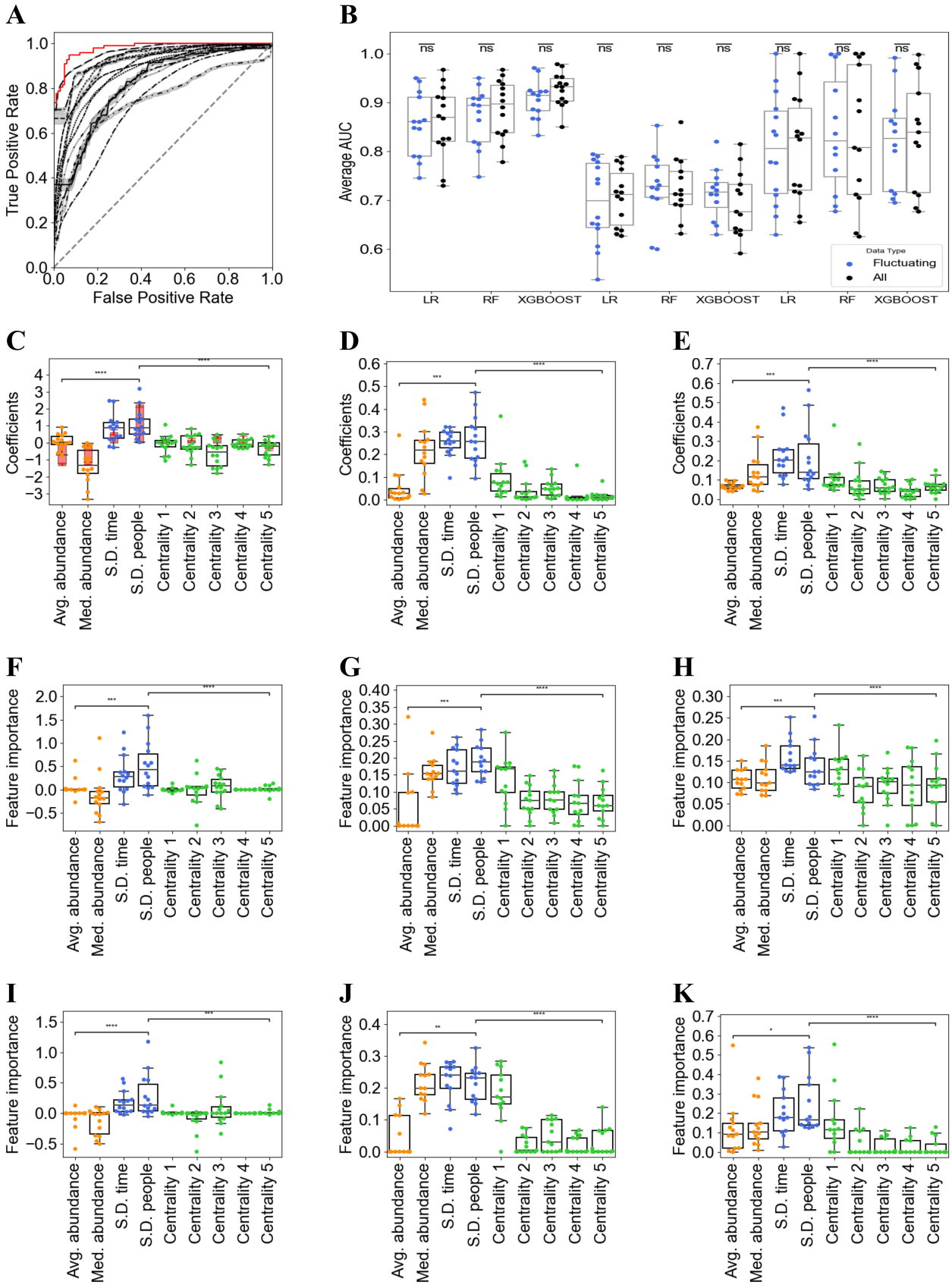

Figure 9: Microbial features accurately predict RSM (species), primarily through fluctuating microbes. **A.** ROC AUCs for predicting RSM taxa (colonization success measured by high $P(Change)$) using the LR model across 10 WGS cohorts (black) and in a simulation (red). **B.** Comparison of prediction performance using only fluctuating features (blue) versus all features (black). Each point represents the average AUC from the test set of a different study. No significant difference is observed between models using all features and those using fluctuating measures alone. **C-I.** The most informative features for predicting RSM capture variability and define fluctuating taxa, consistently performing well across various RSM definitions and models. These features include predictions of taxa with high likelihood to colonize (light grey C-E), RPT (pink F-H), or influential FMT (yellow I-K) across different models, including LR models (C,F,I), RF models (D,G,J), and XGBOOST models (E,H,K). Feature contributions are measured by coefficients in LR models and feature importance (FI) in RF and XGBOOST models. Blue features consistently show significantly higher positive contributions across all tasks. Stars indicate p-values from paired t-tests comparing blue features with orange and green features such that *-$p < 0.05$, **-$p < 0.01$, ***-$p < 0.001$.

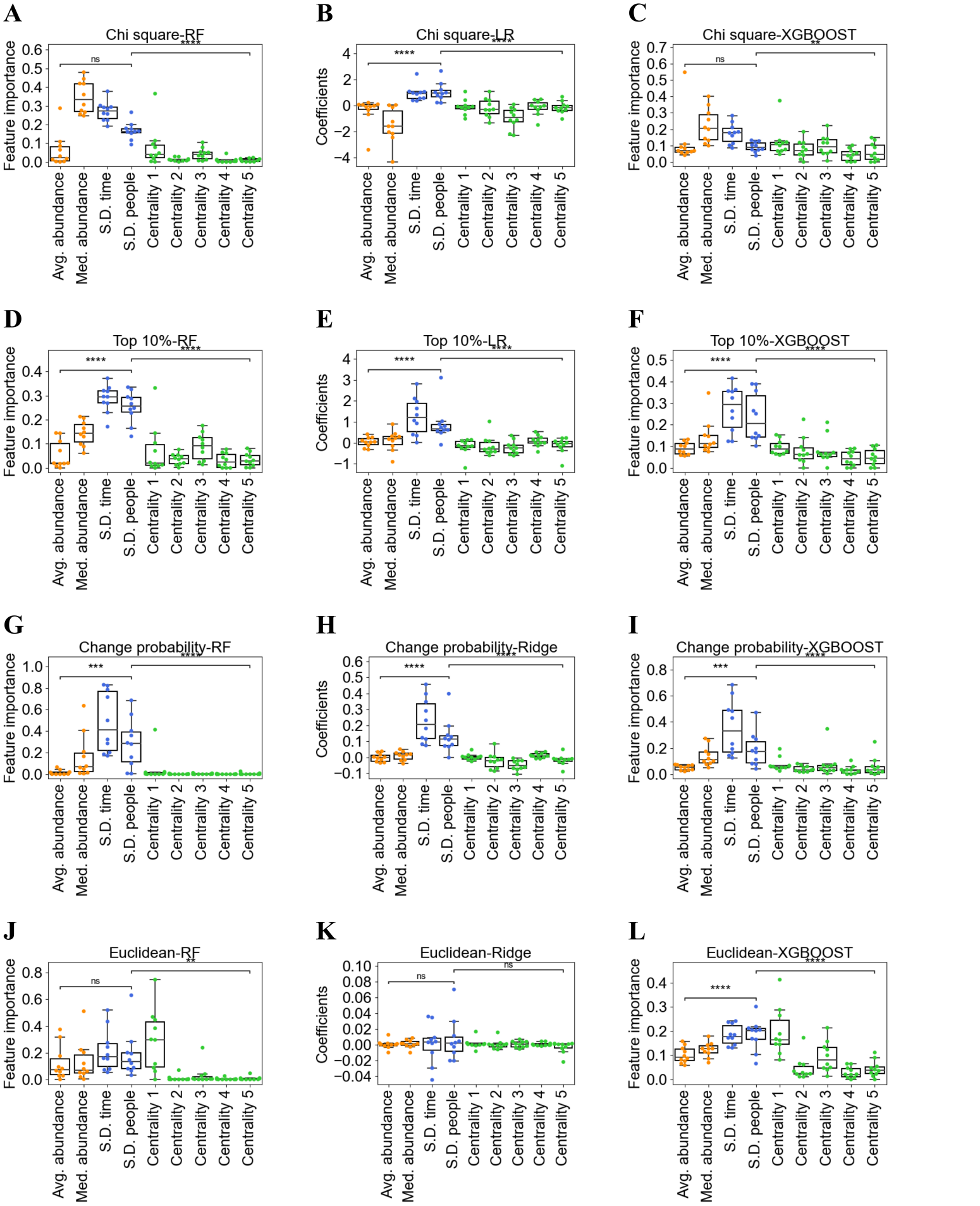

Figure 10: Taxa fluctuation (blue) emerged as the most influential factor contributing to the predictive accuracy of identifying RSM taxa across multiple definitions and models. These include using a fixed cutoff of 0.8, where taxa with a probability to change above this threshold are classified as changing ME taxa **(A-C)**, or selecting the top percentile of taxa **(D-F)**. Additionally, continuous prediction tasks were explored, such as predicting the probability of change itself **(G-H)**, or the Euclidean distance between RSM taxa and other taxa. This analysis was applied at the **strain-level** only to the WGS cohorts.

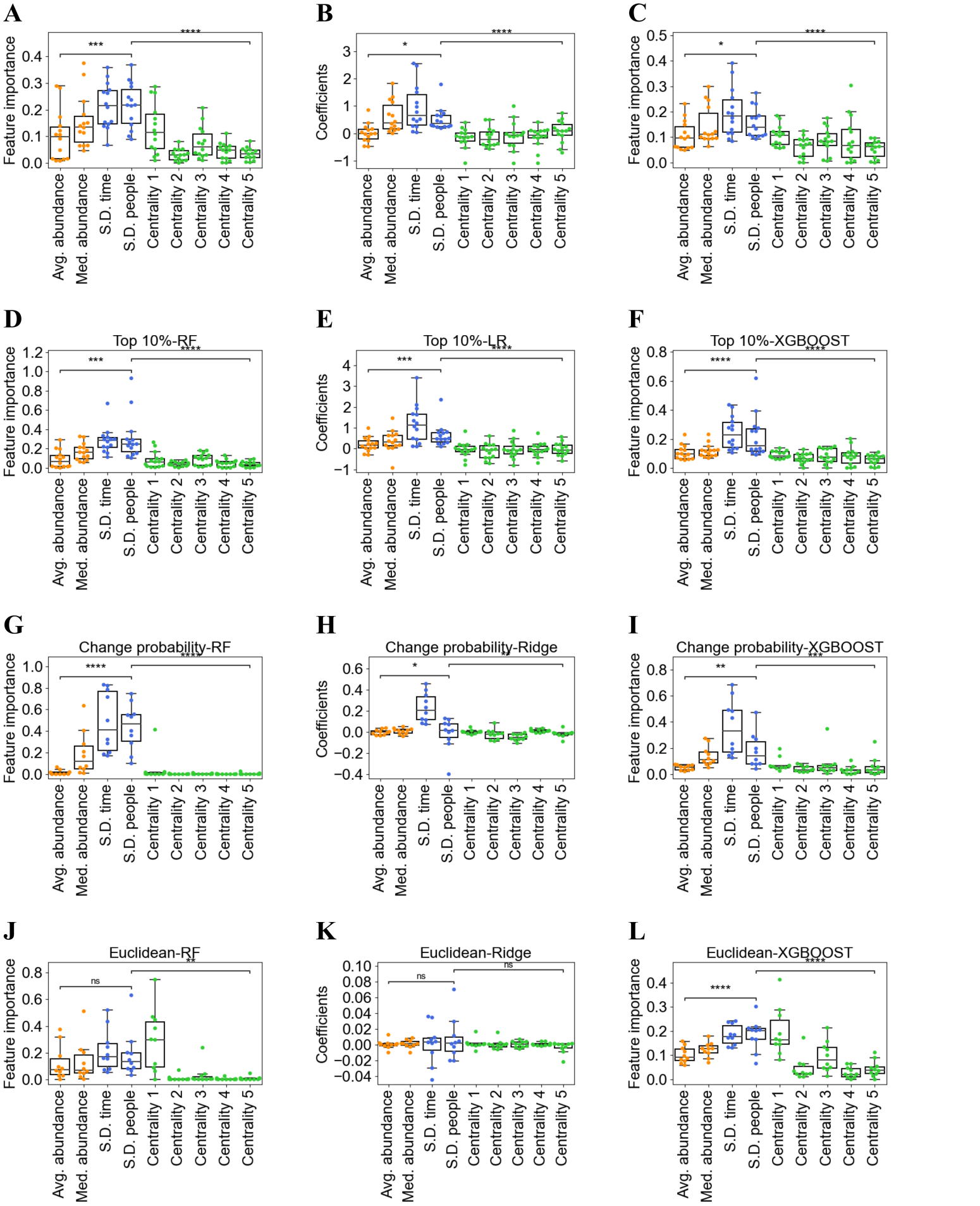

Figure 11: Taxa dynamics (blue) emerged as the most influential factors contributing to the predictive accuracy of identifying RSM taxa across multiple definitions and models. These include using a fixed cutoff of 0.8, where taxa with a probability to change above this threshold are classified as changing ME taxa **(A-C)**, or selecting the top percentile of taxa **(D-F)**. Additionally, continuous prediction tasks were explored, such as predicting the probability of change itself **(G-H)**, or the Euclidean distance between changing ME taxa and other taxa. This analysis was applied at the **species-level** both to WGS and 16S cohorts.

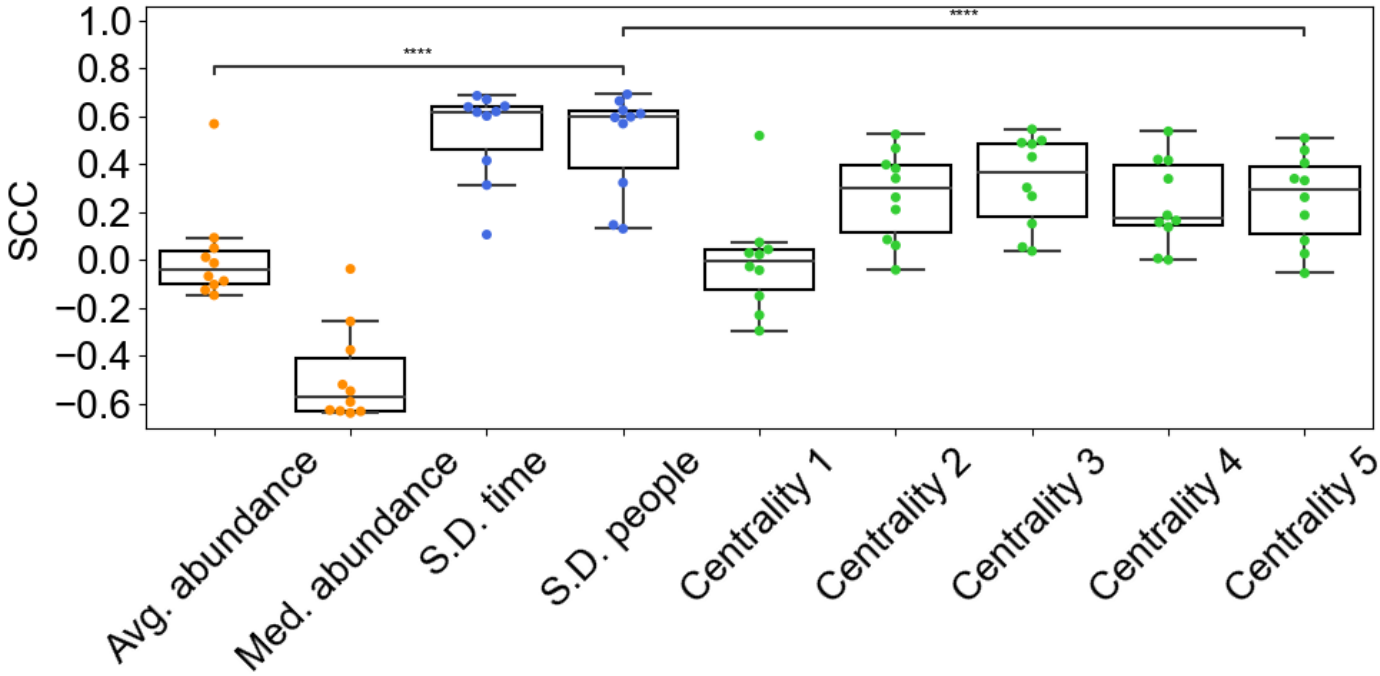

Figure 12: Spearman Correlation Coefficients (SCCs) between the probability to change and various taxa characteristics: average abundance (orange), dynamics (standard deviation of time and population in blue), and interaction network metrics (such as Fiedler vector, in-degree, out-degree, betweenness centrality, and closeness centrality in green) across different dynamic cohorts. Notably, the highest correlations were observed with taxa dynamics. This analysis was applied at the **strain-level** only to the WGS cohorts.

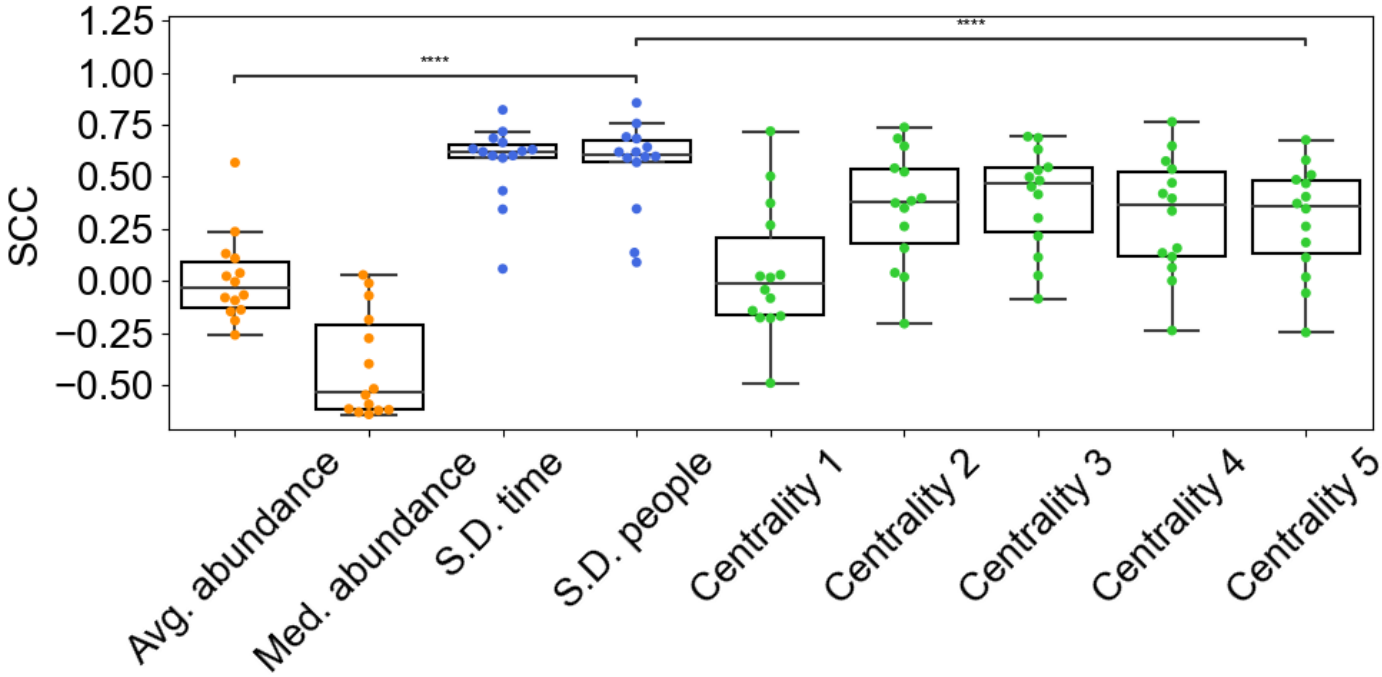

Figure 13: Spearman Correlation Coefficients (SCCs) between the probability to change and various taxa characteristics: average abundance (orange), dynamics (standard deviation of time and population in blue), and interaction network metrics (such as Fiedler vector, in-degree, out-degree, betweenness centrality, and closeness centrality in green) across different dynamic cohorts. Notably, the highest correlations were observed with taxa dynamics. This analysis was applied at the **species-level** both to WGS and 16S cohorts.

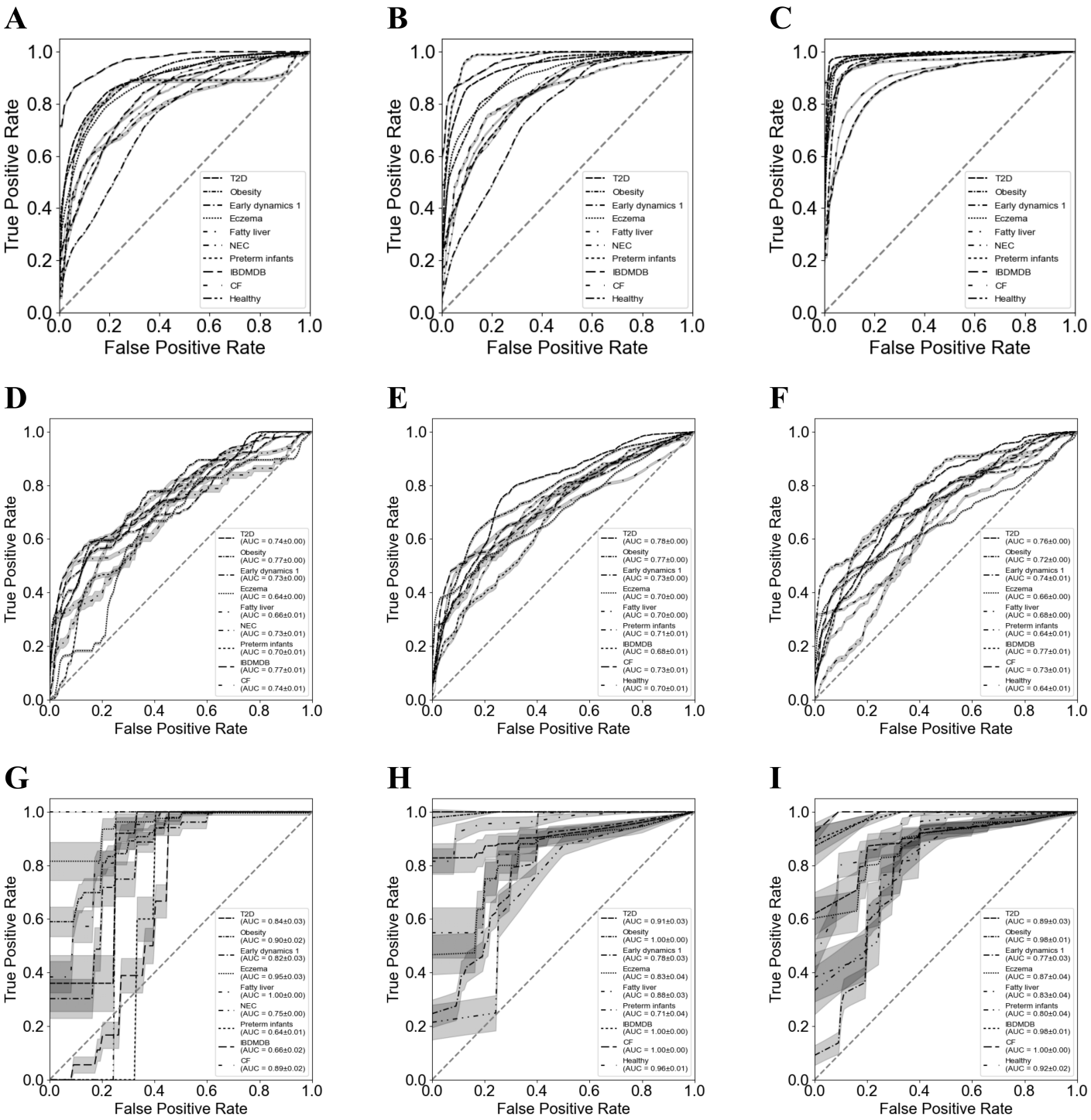

Figure 14: All ROC curves over different tasks and different models. **A-C.** ROC curves of predicting changing ME taxa by LR **(A)**, RF **(B)**, and XGBOOST **(C)**. **D-F.** ROC curves of predicting RPT taxa by LR **(D)**, RF **(E)**, and XGBOOST **(F)**. **G-I.** ROC curves of predicting dominant within FMT taxa by LR **(G)**, RF **(H)**, and XGBOOST **(I)**.The dotted line represents random performance with an AUC of 0.5. Different line styles indicate the average ROC curves for different cohorts, and the standard deviation across runs is shown as a shaded region. This analysis was applied at the **strain-level** only to the WGS cohorts.

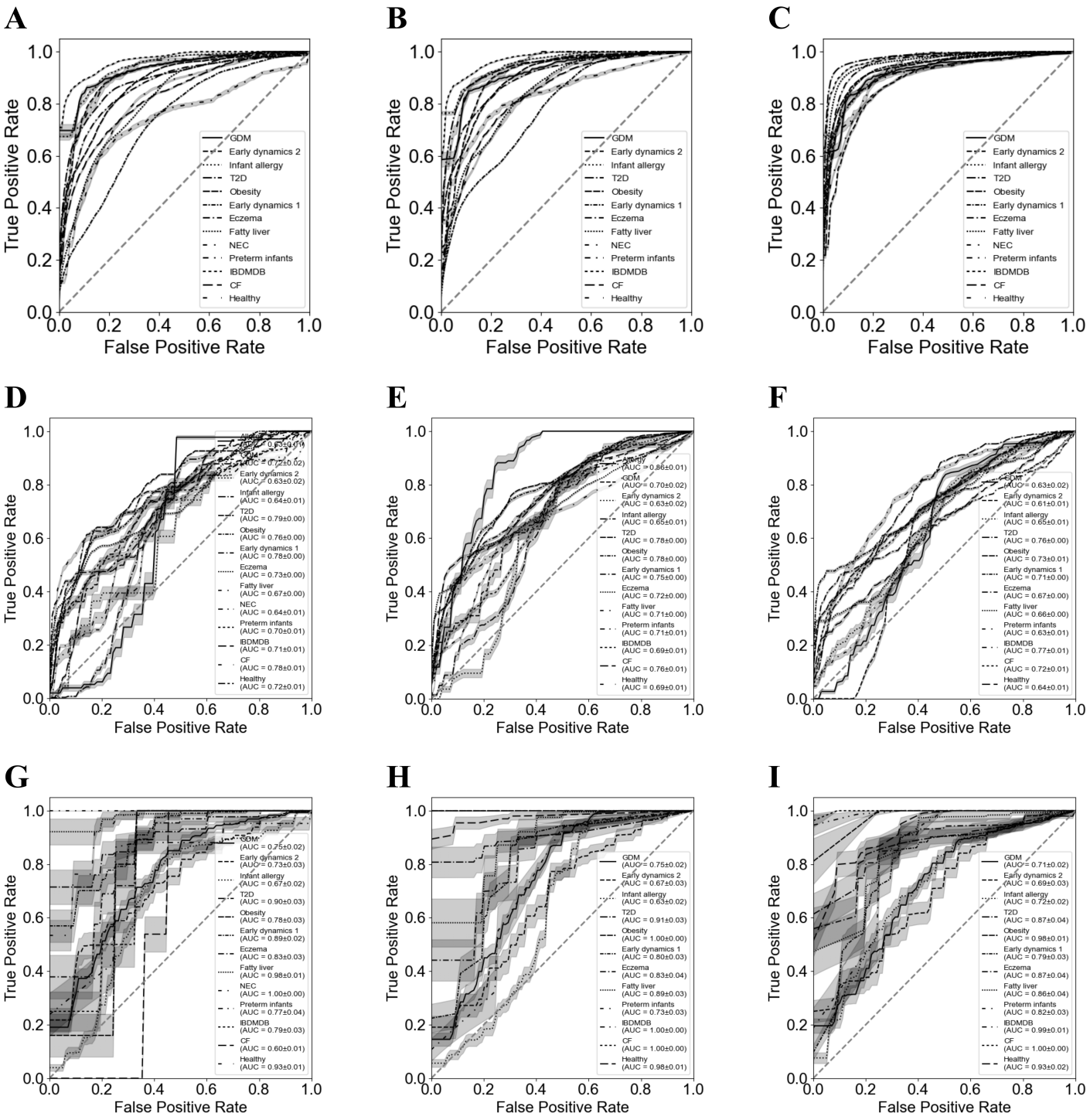

Figure 15: All ROC curves over different tasks and different models. **A-C.** ROC curves of predicting changing ME taxa by LR **(A)**, RF **(B)**, and XGBOOST **(C)**. **D-F.** ROC curves of predicting RPT taxa by LR **(D)**, RF **(E)**, and XGBOOST **(F)**. **G-I.** ROC curves of predicting dominant within FMT taxa by LR **(G)**, RF **(H)**, and XGBOOST **(I)**.The dotted line represents random performance with an AUC of 0.5. Different line styles indicate the average ROC curves for different cohorts, and the standard deviation across runs is shown as a shaded region. This analysis was applied at the **strain-level** only to the WGS cohorts.

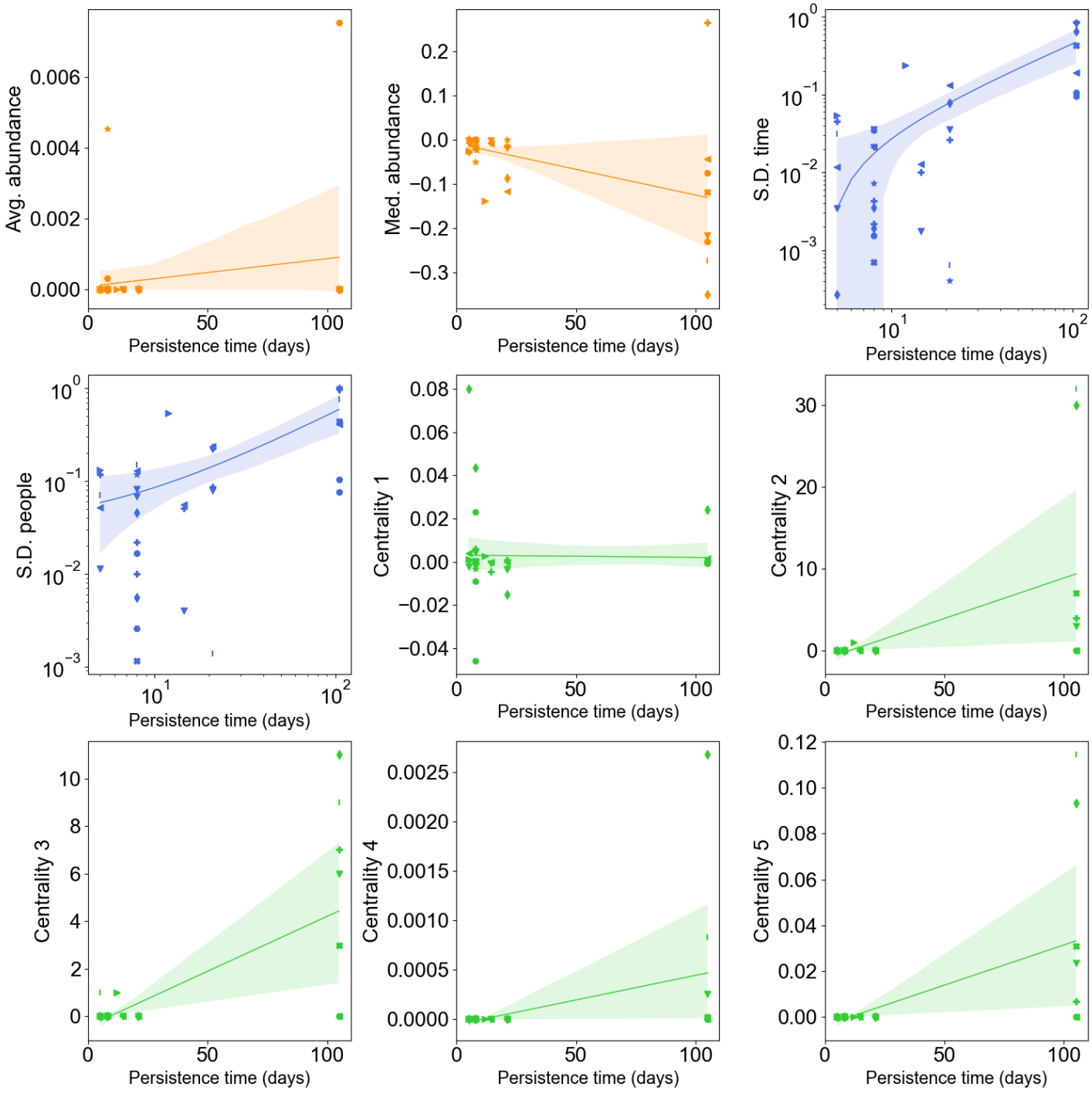

Figure 16: Variability shows a positive correlation with probiotics persistence times. The scatter plots with the black trend lines depict the relationships between probiotics' persistence times and various microbiome attributes such as frequency (orange), patchy (blue), and centrality (green). Each shape represents another dataset. This analysis was applied only to the WGS cohorts at the **strain-level**.

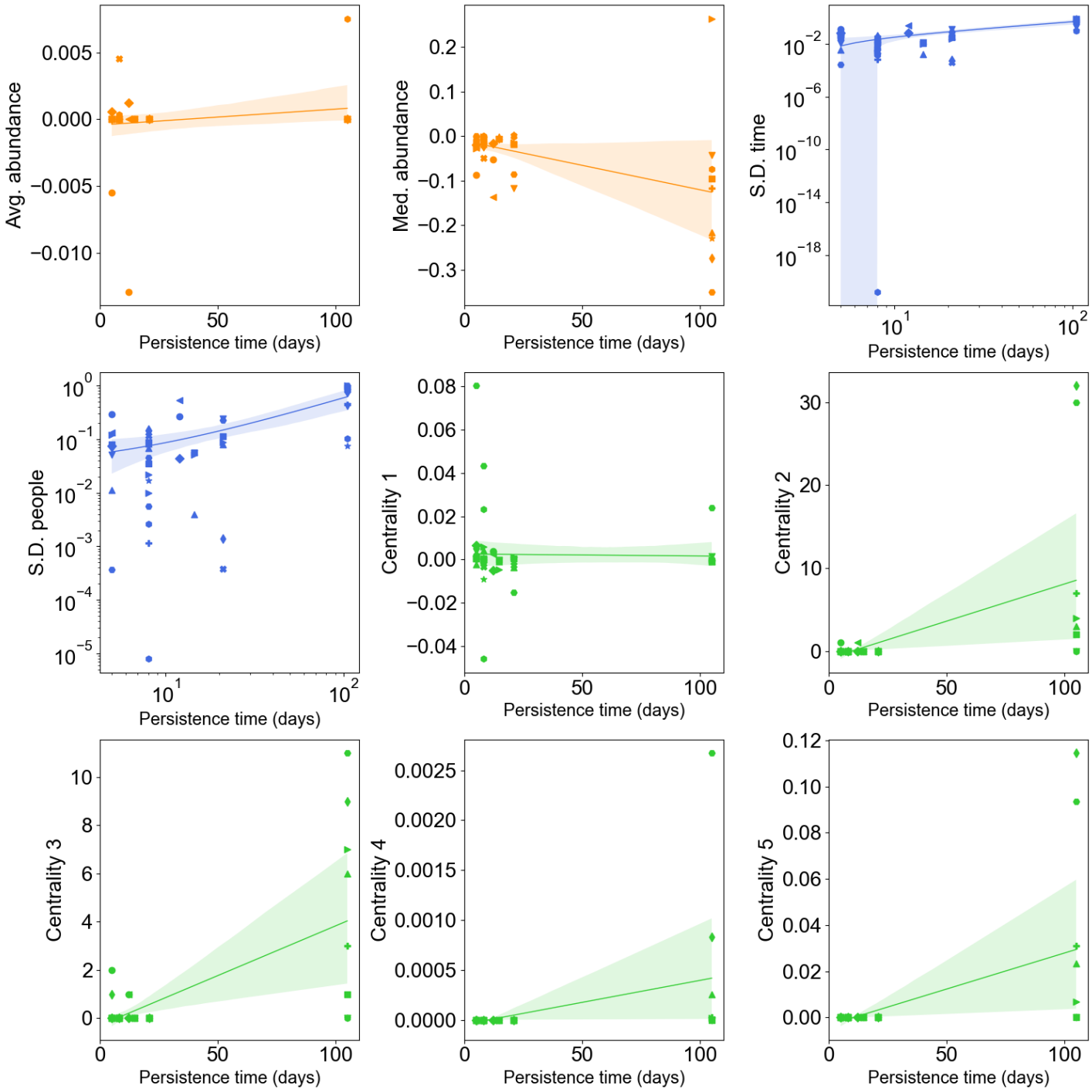

Figure 17: Variability shows a positive correlation with probiotics persistence times. The scatter plots with the black trend lines depict the relationships between probiotics' persistence times and various microbiome attributes such as frequency (orange), patchy (blue), and centrality (green). Each shape represents another dataset. This analysis was applied both to the WGS and 16S cohorts at the **species-level**.

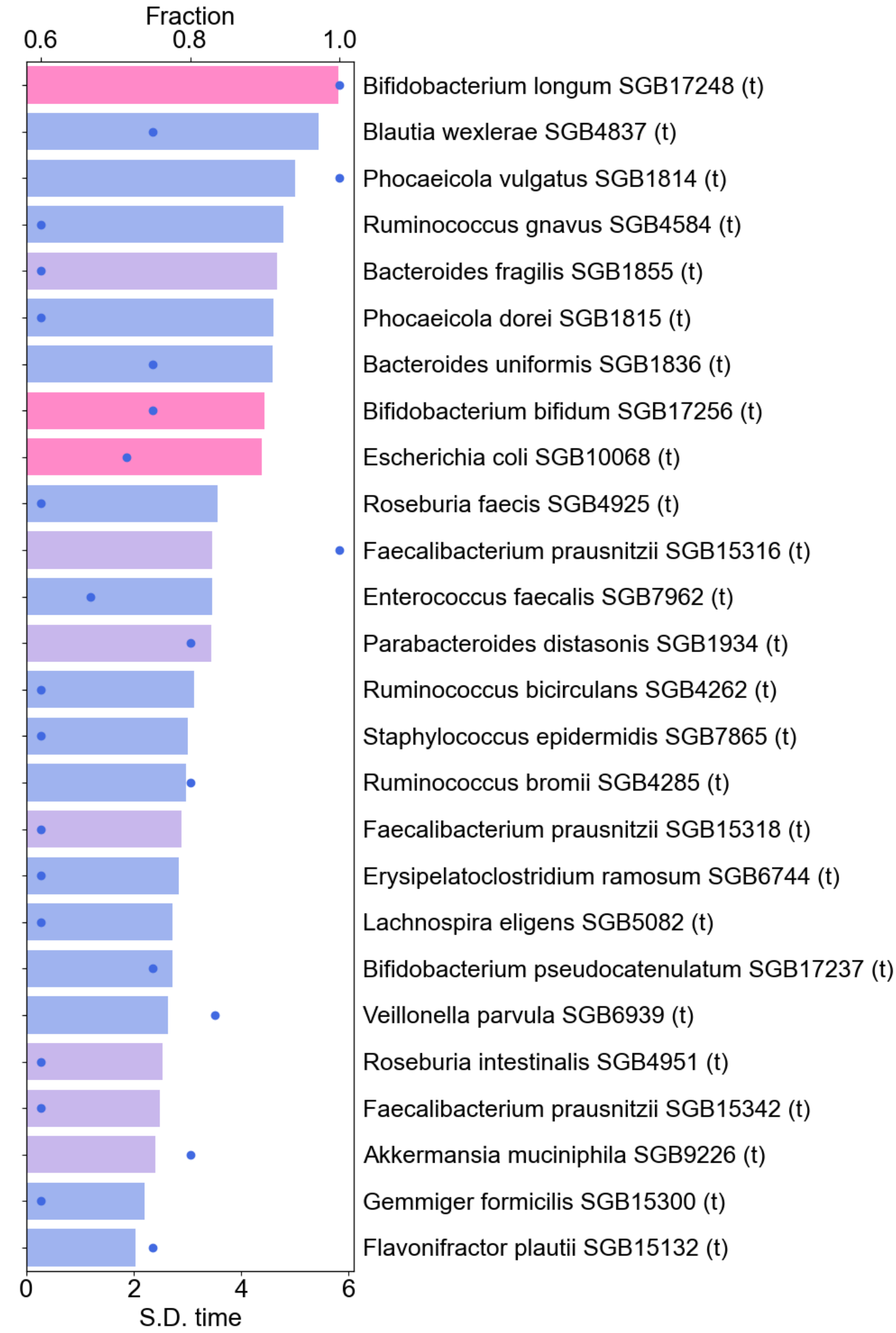
Fraction
0.6
0.8
1.0
Bifidobacterium longum SGB17248 (t)
Blautia wexlerae SGB4837 (t)
Phocaeicola vulgatus SGB1814 (t)
Ruminococcus gnavus SGB4584 (t)
Bacteroides fragilis SGB1855 (t)
Phocaeicola dorei SGB1815 (t)
Bacteroides uniformis SGB1836 (t)
Bifidobacterium bifidum SGB17256 (t)
Escherichia coli SGB10068 (t)
Roseburia faecis SGB4925 (t)
Faecalibacterium prausnitzii SGB15316 (t)
Enterococcus faecalis SGB7962 (t)
Parabacteroides distasonis SGB1934 (t)
Ruminococcus bicirculans SGB4262 (t)
Staphylococcus epidermidis SGB7865 (t)
Ruminococcus bromii SGB4285 (t)
Faecalibacterium prausnitzii SGB15318 (t)
Erysipelatoclostridium ramosum SGB6744 (t)
Lachnospira eligens SGB5082 (t)
Bifidobacterium pseudocatenulatum SGB17237 (t)
Veillonella parvula SGB6939 (t)
Roseburia intestinalis SGB4951 (t)
Faecalibacterium prausnitzii SGB15342 (t)
Akkermansia muciniphila SGB9226 (t)
Gemmiger formicilis SGB15300 (t)
Flavonifractor plautii SGB15132 (t)
0
2
4
6
S.D. time

Figure 18: List of fluctuating based on std time, consistent in at least three studies and within the top 5th percentile. The bar plots represent the average S.D. people score of the taxa (bottom x-axis), while the dots represent the consistency of fluctuation as a fraction of the studies in which it ranks in the top percentile of all studies it appears in (top x-axis). Dark pink bars correspond to taxa already known as probiotics (RPT), light pink bars represent taxa identified as next-generation probiotics, and blue bars indicate newly identified taxa.

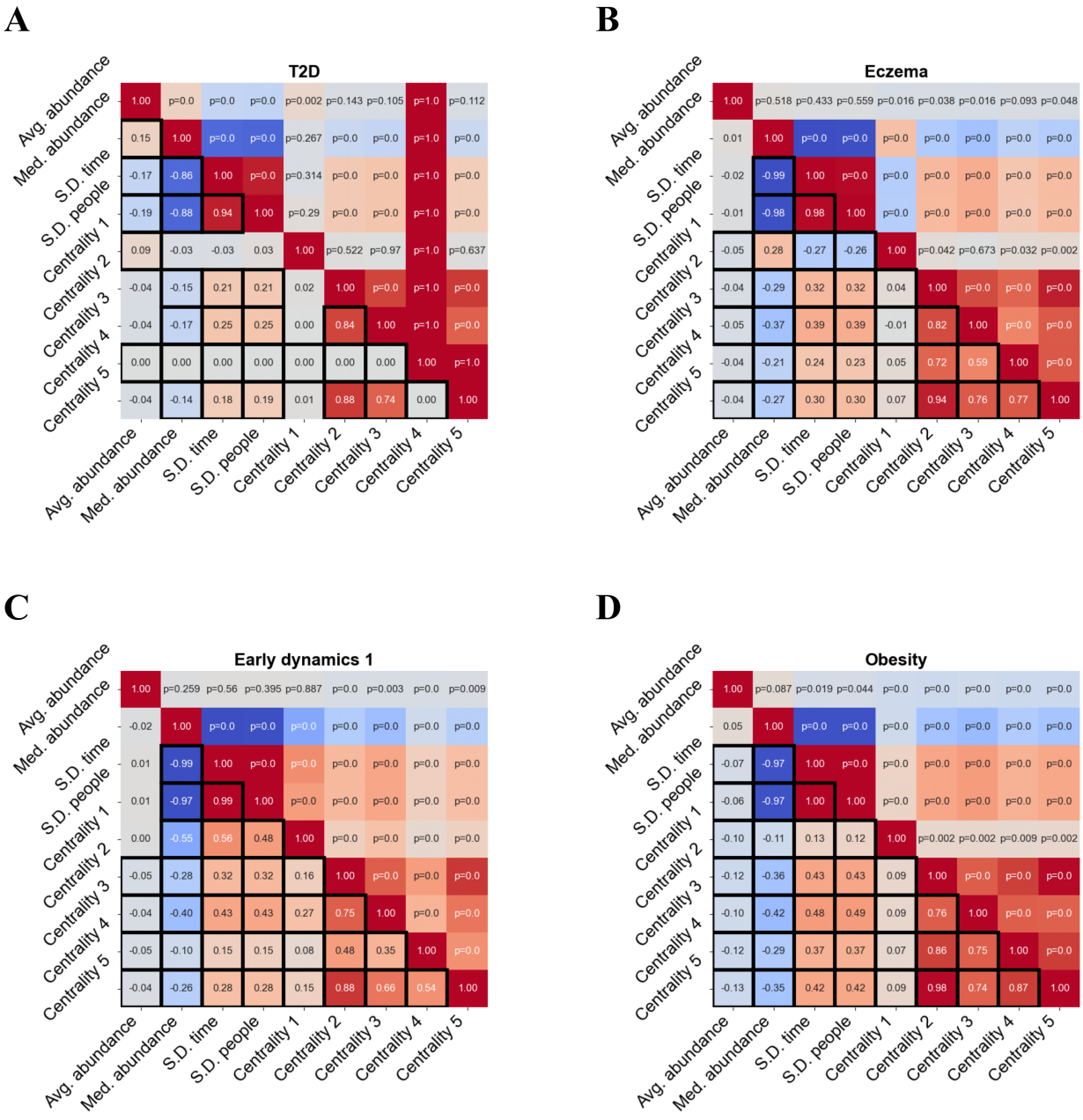

Figure 19: Spearman correlation heatmaps of microbial features at the **strain level** across **T2D**, **Eczema**, **early dynamic 1** and **obesity** cohorts. Below the diagonal, statistical correlation values are shown, with significant correlations highlighted by a black border. Above the diagonal, the corresponding p-values are displayed to indicate the strength of the correlations.

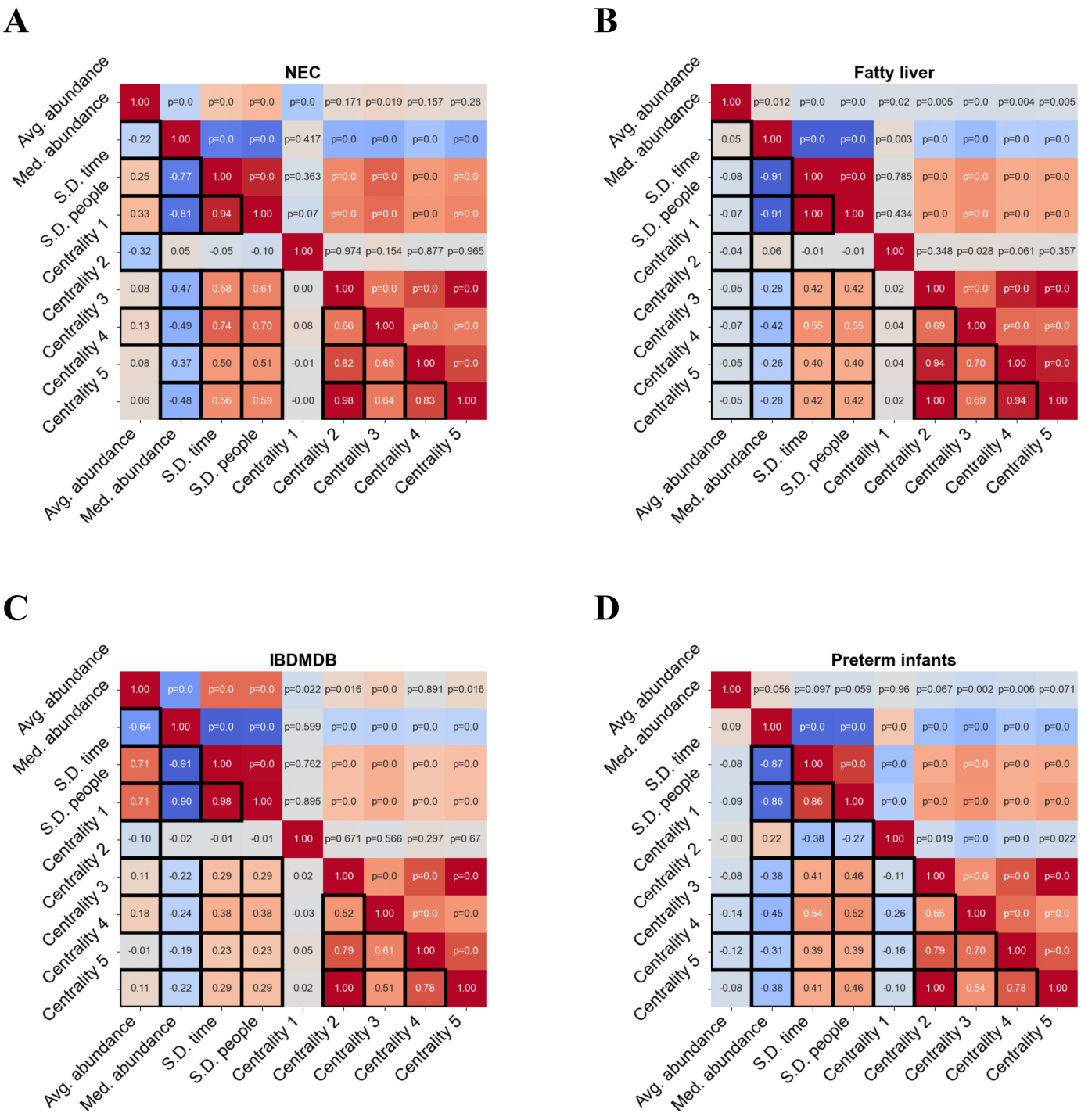

Figure 20: Spearman correlation heatmaps of microbial features at the **strain level** across **NEC**, **Fatty liver**, **IBDMDB** and **Preterm infants** cohorts. Below the diagonal, statistical correlation values are shown, with significant correlations highlighted by a black border. Above the diagonal, the corresponding p-values are displayed to indicate the strength of the correlations.

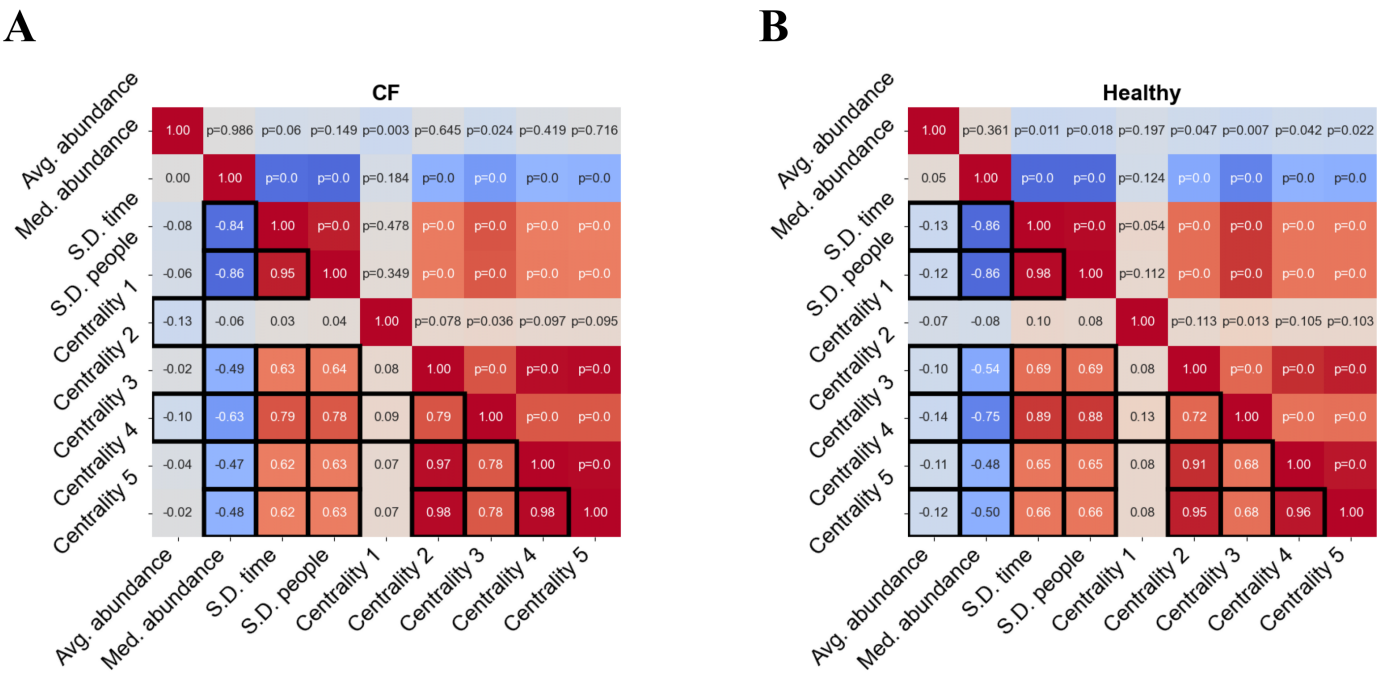

Figure 21: Spearman correlation heatmaps of microbial features at the **strain level** across **CF**, **Healthy** cohorts. Below the diagonal, statistical correlation values are shown, with significant correlations highlighted by a black border. Above the diagonal, the corresponding p-values are displayed to indicate the strength of the correlations.

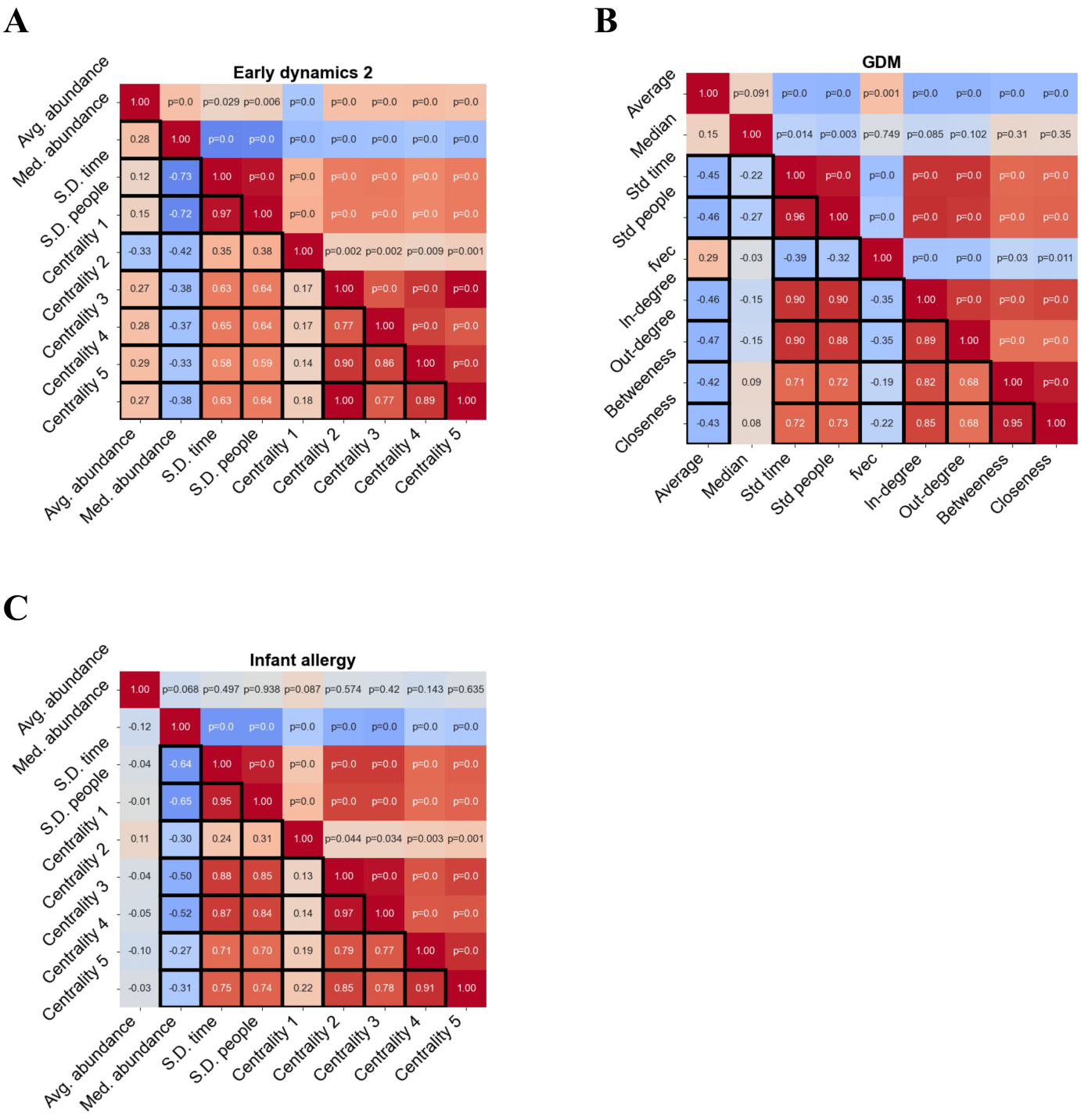

Figure 22: Spearman correlation heatmaps of microbial features at the **species level** across **GDM**, **Infant allergy** and **Early dynamics 2** cohorts. Below the diagonal, statistical correlation values are shown, with significant correlations highlighted by a black border. Above the diagonal, the corresponding p-values are displayed to indicate the strength of the correlations.

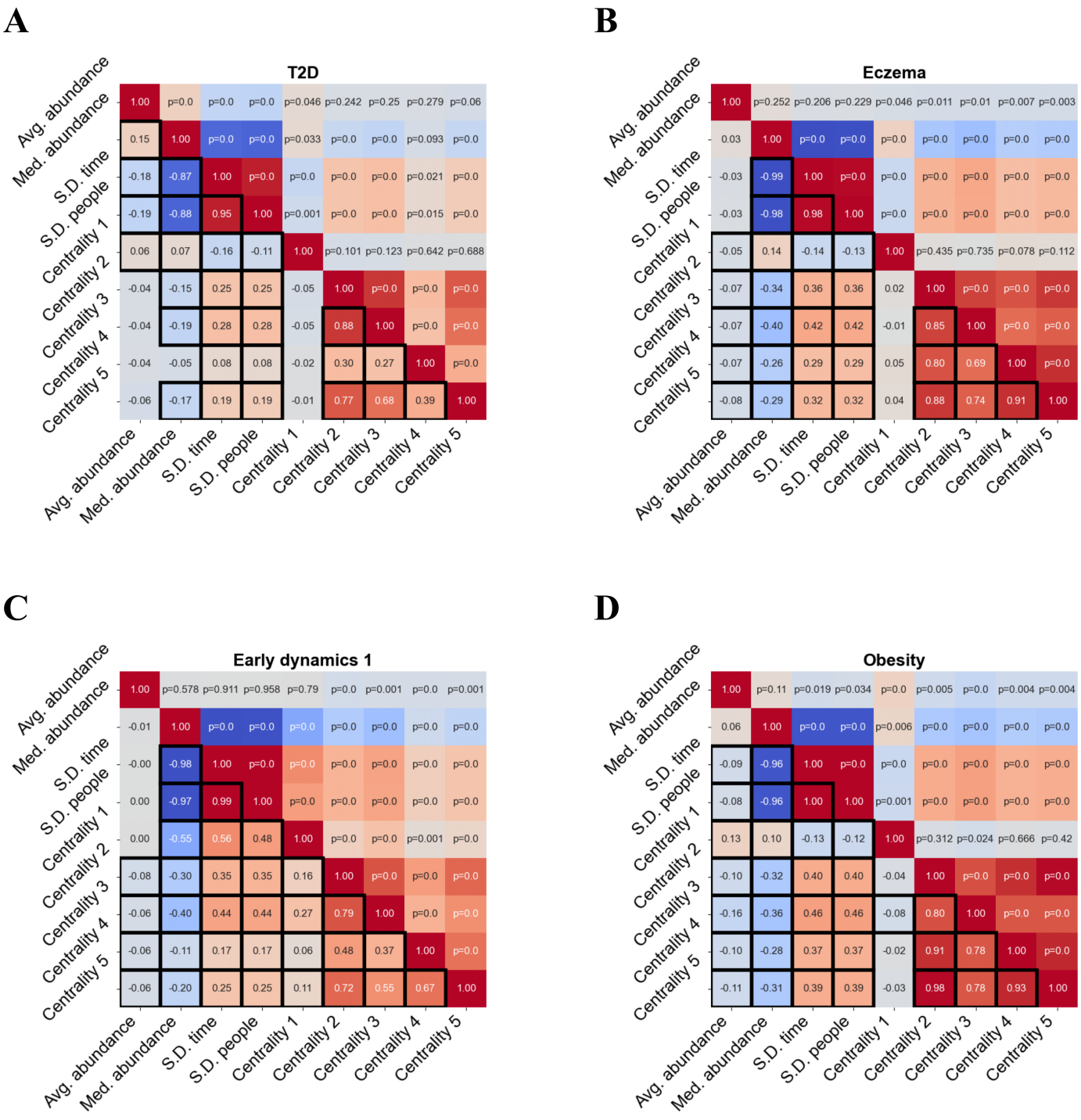

Figure 23: Spearman correlation heatmaps of microbial features **species level** across **T2D**, **Eczema**, **early dynamic 1** and **obesity** cohorts. Below the diagonal, statistical correlation values are shown, with significant correlations highlighted by a black border. Above the diagonal, the corresponding p-values are displayed to indicate the strength of the correlations.

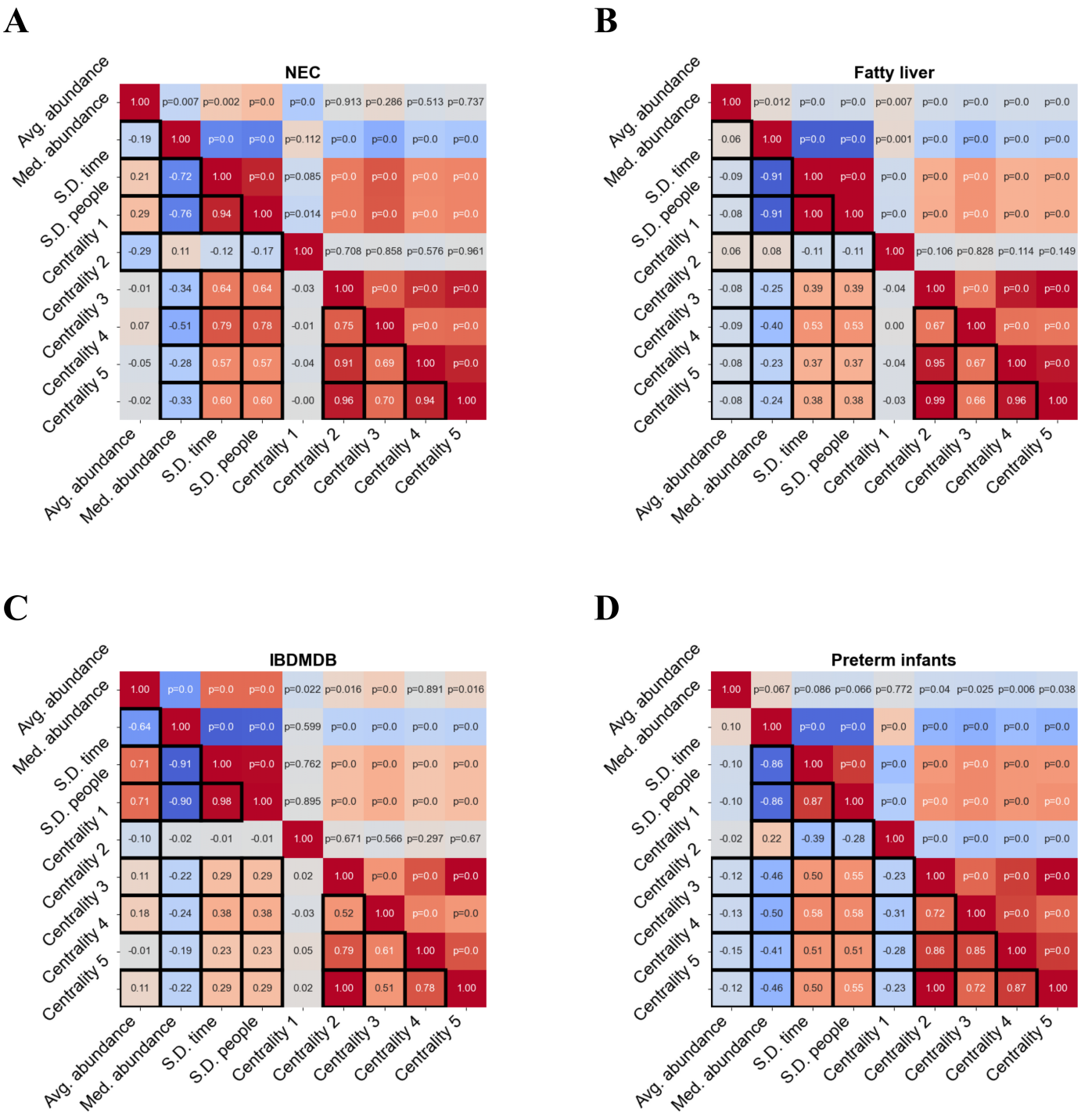

Figure 24: Spearman correlation heatmaps of microbial features **species level** across **NEC**, **Fatty liver**, **IBDMDB** and **Preterm infants** cohorts. Below the diagonal, statistical correlation values are shown, with significant correlations highlighted by a black border. Above the diagonal, the corresponding p-values are displayed to indicate the strength of the correlations.

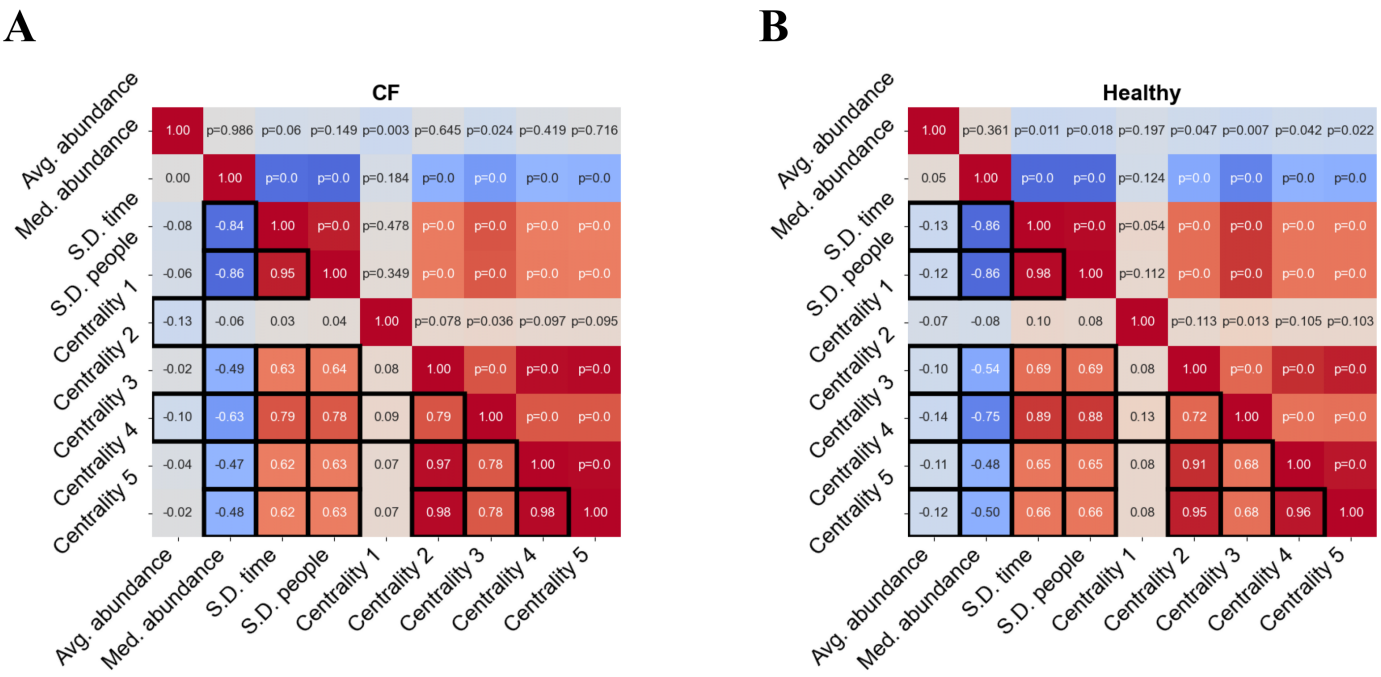

Figure 25: Spearman correlation heatmaps of microbial features **species level** across **CF** and **Healthy** cohorts. Below the diagonal, statistical correlation values are shown, with significant correlations highlighted by a black border. Above the diagonal, the corresponding p-values are displayed to indicate the strength of the correlations.

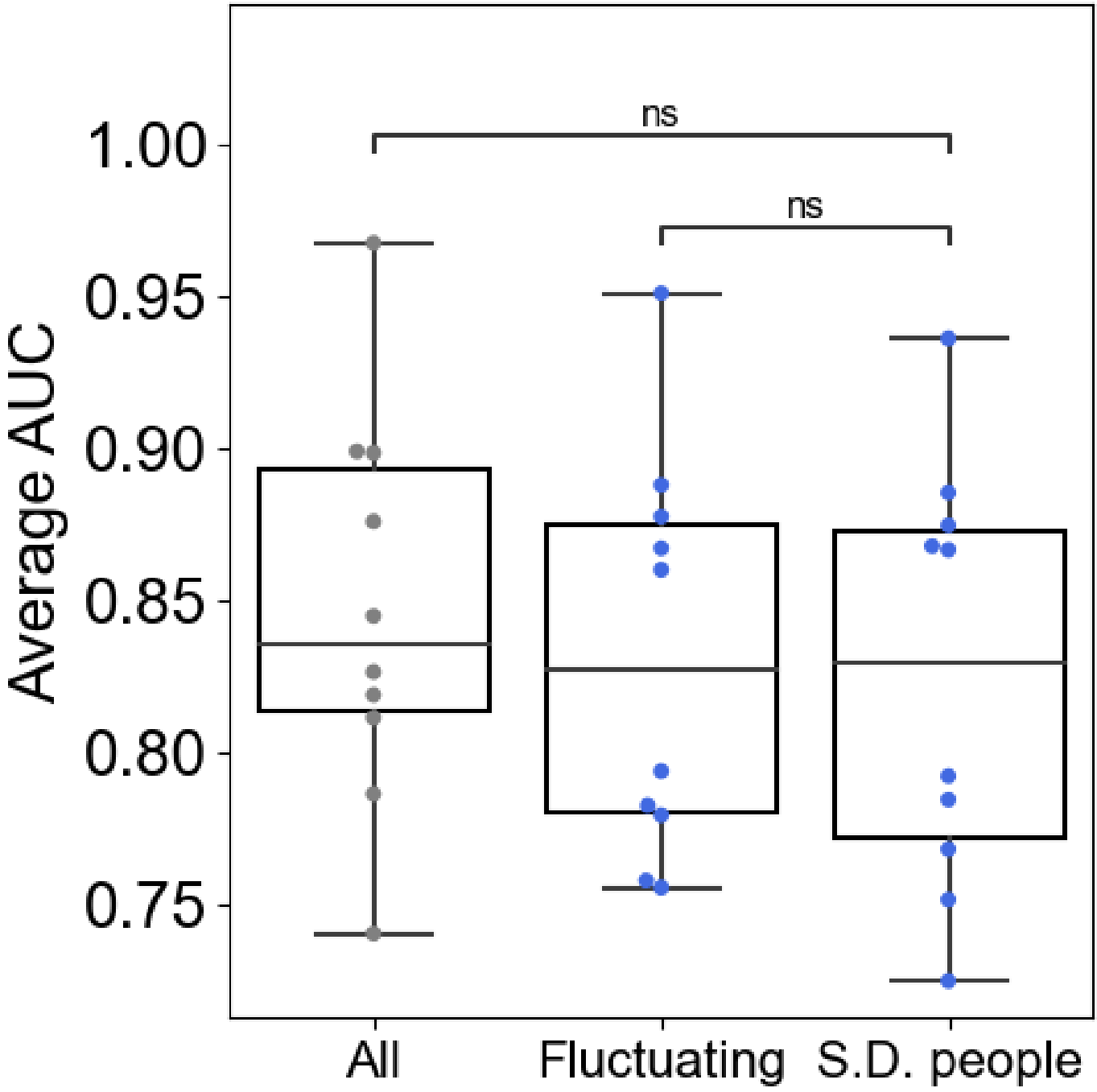

Figure 26: The S.D. over the host alone suffices as an RSM predictor. Swarm plot of average AUCs across 10 WGS studies, where each point represents the average AUC of a single study. Grey dots indicate results from logistic regression (LR) using all nine features, central blue dots show results from LR using only fluctuating features (S.D. time and S.D. people), and right blue dots show AUCs based solely on the S.D. people feature. No significant differences were observed between the groups

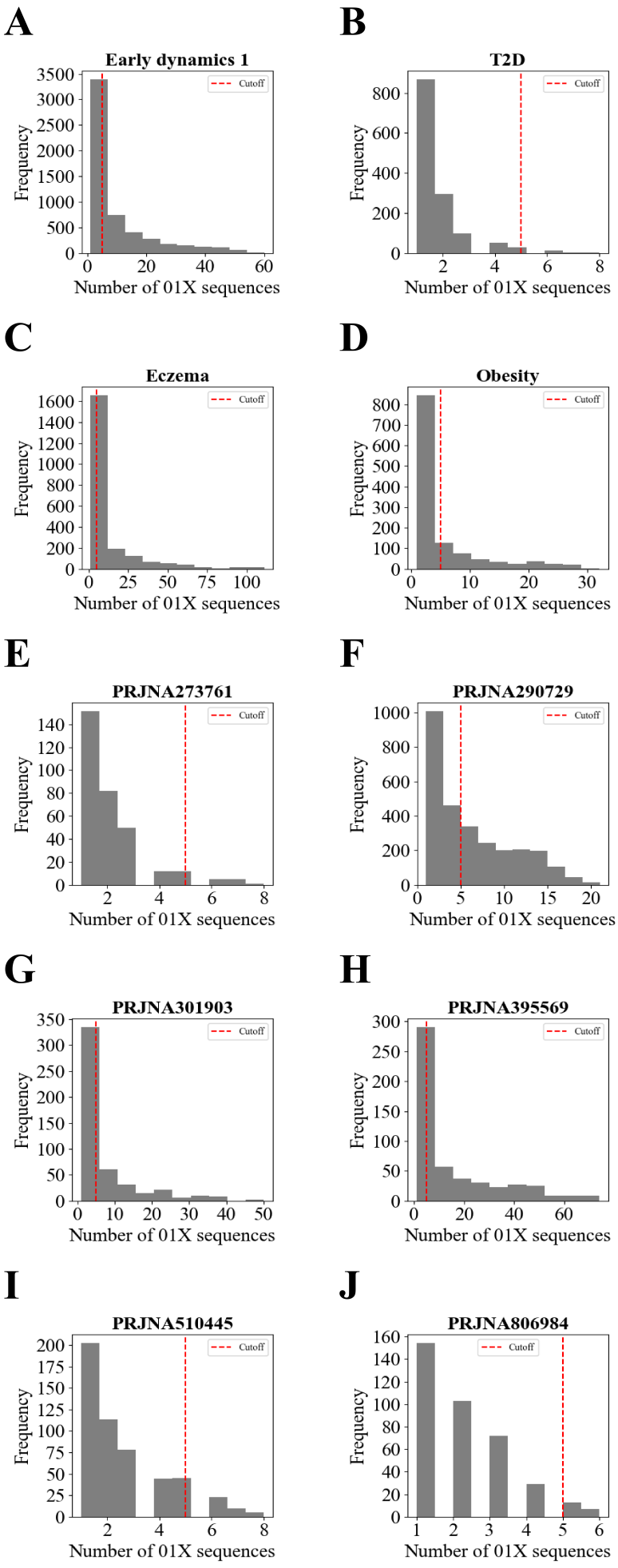

Figure 27: All 0, 1, X distributions over the different cohorts. The red line represents the cutoff of 5 samples, such that taxa with less than 5 appearances in the whole cohort were removed from the analysis. This analysis was applied at the **species-level** both to WGS and 16S cohorts

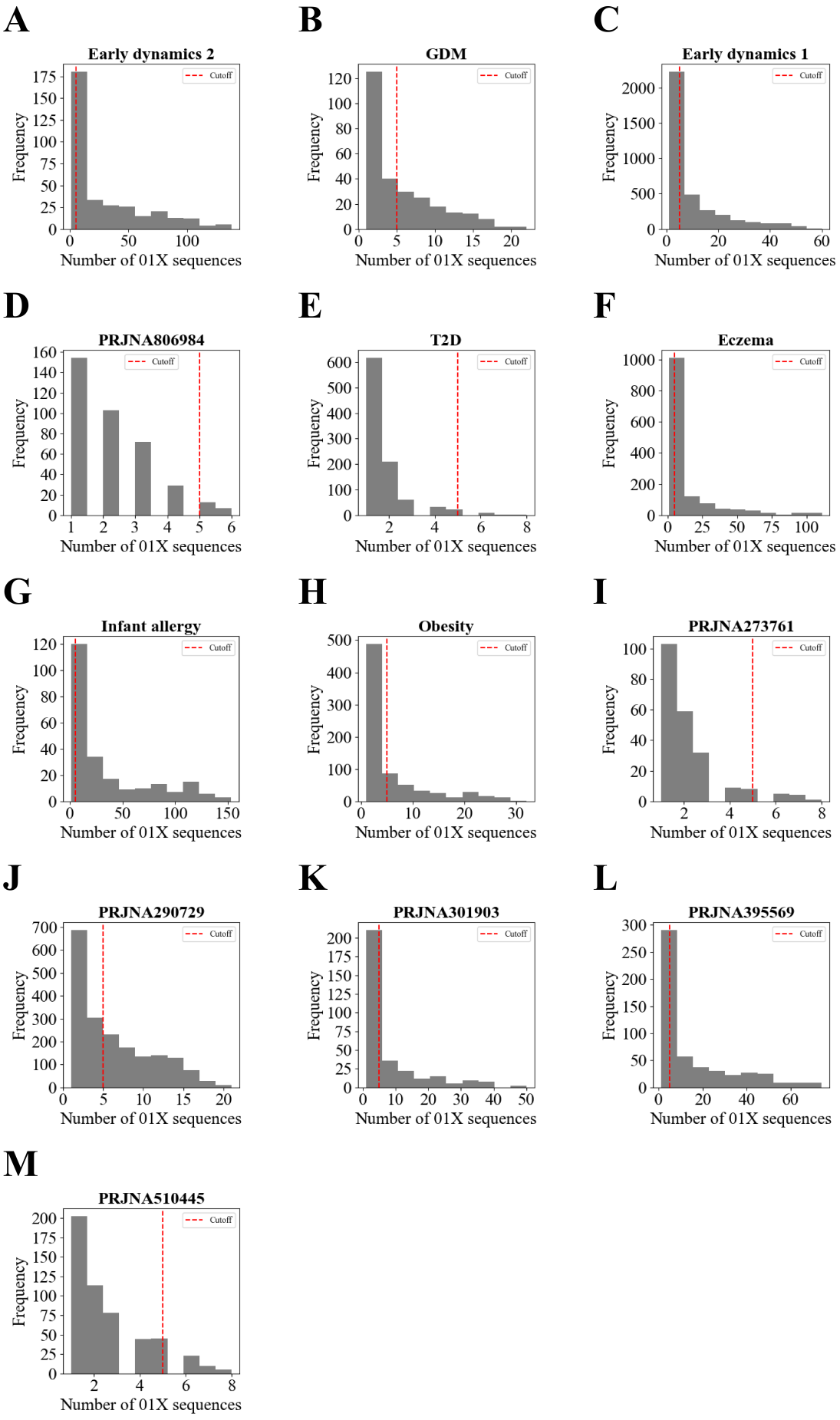

Figure 28: All 0, 1, X distributions over the different cohorts. The red line represents the cutoff of 5 samples, such that taxa with less than 5 appearances in the whole cohort were removed from the analysis. This analysis was applied at the **species-level** both to WGS and 16S cohorts

References

[1] David A Kessler and Nadav M Shnerb. Generalized model of island biodiversity. *Physical Review E*, 91(4):042705, 2015.

[2] Guy Bunin. Ecological communities with lotka-volterra dynamics. *Physical Review E*, 95(4):042414, 2017.

[3] Giulio Biroli, Guy Bunin, and Chiara Cammarota. Marginally stable equilibria in critical ecosystems. *New Journal of Physics*, 20(8):083051, 2018.

[4] Matthieu Barbier, Jean-François Arnoldi, Guy Bunin, and Michel Loreau. Generic assembly patterns in complex ecological communities. *Proceedings of the National Academy of Sciences*, 115(9):2156–2161, 2018.

[5] Matthieu Barbier, Claire De Mazancourt, Michel Loreau, and Guy Bunin. Fingerprints of high-dimensional coexistence in complex ecosystems. *Physical Review X*, 11(1):011009, 2021.

[6] Travis E Gibson, Amir Bashan, Hong-Tai Cao, Scott T Weiss, and Yang-Yu Liu. On the origins and control of community types in the human microbiome. *PLoS computational biology*, 12(2):e1004688, 2016.

[7] Tyler A Joseph, Liat Shenhav, Joao B Xavier, Eran Halperin, and Itsik Pe'er. Compositional lotka-volterra describes microbial dynamics in the simplex. *PLoS computational biology*, 16(5):e1007917, 2020.

[8] Libai Xu, Ximing Xu, Dehan Kong, Hong Gu, and Toby Kenney. Stochastic generalized lotka-volterra model with an application to learning microbial community structures. *arXiv preprint arXiv:2009.10922*, 2020.

[9] Yishay Pinto, Sigal Frishman, Sondra Turjeman, Adi Eshel, Meital Nuriel-Ohayon, Oshrit Shrossel, Oren Ziv, William Walters, Julie Parsonnet, Catherine Ley, et al. Gestational diabetes is driven by microbiota-induced inflammation months before diagnosis. *Gut*, 72(5):918–928, 2023.

[10] Victoria Martin, Yamini Virkud, Ehud Dahan, Hannah Seay, Hera Vlamakis, Ramnik Xavier, Wayne Shreffler, Qian Yuan, and Moran Yassour. Longitudinal disease-associated gut microbiome differences in infants with early food allergic manifestations. 2021.

[11] Nicholas A Bokulich, Jennifer Chung, Thomas Battaglia, Nora Henderson, Melanie Jay, Huilin Li, Arnon D. Lieber, Fen Wu, Guillermo I Perez-Perez, Yu Chen, et al. Antibiotics, birth mode, and diet shape microbiome maturation during early life. *Science translational medicine*, 8(343):343ra82–343ra82, 2016.

[12] Fredrik Bäckhed, Josefine Roswall, Yangqing Peng, Qiang Feng, Huijue Jia, Petia Kovatcheva-Datchary, Yin Li, Yan Xia, Hailiang Xie, Huanzi Zhong, et al. Dynamics and stabilization of the human gut microbiome during the first year of life. *Cell host & microbe*, 17(5):690–703, 2015.

[13] Ilze Elbere, Ivars Silamikelis, Ilze Izabella Dindune, Ineta Kalnina, Monta Ustinova, Linda Zaharenko, Laila Silamikele, Vita Rovite, Dita Gudra, Ilze Konrade, et al. Baseline gut microbiome composition predicts metformin therapy short-term efficacy in newly diagnosed type 2 diabetes patients. *PLoS One*, 15(10):e0241338, 2020.

[14] Christine Barthow, Kristin Wickens, Thorsten Stanley, Edwin A Mitchell, Robyn Maude, Peter Abels, Gordon Purdie, Rinki Murphy, Peter Stone, Janice Kang, et al. The probiotics in pregnancy study (pip study): rationale and design of a double-blind randomised controlled trial to improve maternal health during pregnancy and prevent infant eczema and allergy. *BMC Pregnancy and Childbirth*, 16:1–14, 2016.

[15] Sandrine Louis, Rewati-Mukund Tappu, Antje Damms-Machado, Daniel H Huson, and Stephan C Bischoff. Characterization of the gut microbial community of obese patients following a weight-loss intervention using whole metagenome shotgun sequencing. *PLoS One*, 11(2):e0149564, 2016.

[16] Jason Lloyd-Price, Cesar Arze, Ashwin N Ananthakrishnan, Melanie Schirmer, Julian Avila-Pacheco, Tiffany W Poon, Elizabeth Andrews, Nadim J Ajami, Kevin S Bonham, Colin J Brislawn, et al. Multi-omics of the gut microbial ecosystem in inflammatory bowel diseases. *Nature*, 569(7758):655–662, 2019.

[17] Magdalena Durda-Masny, Joanna Goździk-Spychalska, Katarzyna Morańska, Natalia Pawłowska, Michał Mazurkiewicz, Iwona Skrzypczak, Szczepan Cofta, and Anita Szwed. Gut microbiota in adults with cystic fibrosis: Implications for the severity of the cftr gene mutation and nutritional status. *Journal of Cystic Fibrosis*, 23(5):977–983, 2024.

[18] Shirajum Monira, Shota Nakamura, Kazuyoshi Gotoh, Kaori Izutsu, Haruo Watanabe, Nur Haque Alam, Hubert Ph Endtz, Alejandro Cravioto, Sk Imran Ali, Takaaki Nakaya, et al. Gut microbiota of healthy and malnourished children in bangladesh. *Frontiers in microbiology*, 2:228, 2011.

[19] Lynne V McFarland. Meta-analysis of probiotics for the prevention of traveler's diarrhea. *Travel medicine and infectious disease*, 5(2):97–105, 2007.

[20] Siyong You, Yuchen Ma, Bowen Yan, Wenhui Pei, Qiming Wu, Chao Ding, and Caoxing Huang. The promotion mechanism of prebiotics for probiotics: A review. *Frontiers in Nutrition*, 9:1000517, 2022.

[21] Nopaorn Phavichitr, Praewpun Puwdee, and Ruangvith Tantibhaedhyangkul. Cost-benefit analysis of the probiotic treatment of children hospitalized for acute diarrhea in bangkok, thailand. *Southeast Asian J Trop Med Public Health*, 44(6):1065–71, 2013.

[22] O Cortés-Zavaleta, A López-Malo, A Hernández-Mendoza, and HS García. Antifungal activity of lactobacilli and its relationship with 3-phenyllactic acid production. *International journal of food microbiology*, 173:30–35, 2014.

[23] Aziz Homayouni, Parvin Bastani, Somayeh Ziyadi, Sakineh Mohammad-Alizadeh-Charandabi, Morad Ghalibaf, Amir Mohammad Mortazavian, and Elnaz Vaghef Mehrabany. Effects of probiotics on the recurrence of bacterial vaginosis: a review. *Journal of lower genital tract disease*, 18(1):79–86, 2014.

[24] L Ortiz, F Ruiz, L Pascual, and L Barberis. Effect of two probiotic strains of lactobacillus on in vitro adherence of listeria monocytogenes, streptococcus agalactiae, and staphylococcus aureus to vaginal epithelial cells. *Current microbiology*, 68:679–684, 2014.

[25] Emma Mani-López, Daniela Arrioja-Bretón, and Aurelio López-Malo. The impacts of antimicrobial and antifungal activity of cell-free supernatants from lactic acid bacteria in vitro and foods. *Comprehensive Reviews in Food Science and Food Safety*, 21(1):604–641, 2022.

[26] Nieke Westerik, Remco Kort, Wilbert Sybesma, and Gregor Reid. Lactobacillus rhamnosus probiotic food as a tool for empowerment across the value chain in africa. *Frontiers in microbiology*, 9:1501, 2018.

[27] Zhi-Juan Wu, DU Xi, and Jian Zheng. Role oflactobacillusin the prevention ofclostridium difficile-associated diarrhea: a meta-analysis of randomized controlled trials, 2013.

[28] S Kovachev and R Dobrevski-Vacheva. Effect of lactobacillus casei var rhamnosus (gynophilus) in restoring the vaginal flora by female patients with bacterial vaginosis–randomized, open clinical trial. *Akusherstvo i ginekologiia*, 52:48–53, 2013.

[29] S Slawik, I Staufenbiel, Reinhard Schilke, Sonja Nicksch, Knut Weinspach, Meike Stiesch, and Jörg Eberhard. Probiotics affect the clinical inflammatory parameters of experimental gingivitis in humans. *European journal of clinical nutrition*, 65(7):857–863, 2011.

[30] Kelly Wright, Heathcote Wright, and Michael Murray. Probiotic treatment for the prevention of antibiotic-associated diarrhoea in geriatric patients: A multicentre randomised controlled pilot study. *Australasian Journal on Ageing*, 34(1):38–42, 2015.

[31] Kan Shida and Koji Nomoto. Probiotics as efficient immunopotentiators: translational role in cancer prevention. *Indian Journal of Medical Research*, 138(5):808–814, 2013.

[32] Elnaz Vaghef-Mehrabany, Beitullah Alipour, Aziz Homayouni-Rad, Sakineh-Khatoon Sharif, Mohammad Asghari-Jafarabadi, and Sema Zavvari. Probiotic supplementation improves inflammatory status in patients with rheumatoid arthritis. *Nutrition*, 30(4):430–435, 2014.

[33] Natalia Alejandra Castillo, A De Moreno De Leblanc, C M. Galdeano, and G Perdigón. Comparative study of the protective capacity against salmonella infection between probiotic and nonprobiotic lactobacilli. *Journal of Applied Microbiology*, 114(3):861–876, 2013.

[34] Mariangeles Noto Llana, Sebastián Hernán Sarnacki, María del Rosario Aya Castañeda, María Isabel Bernal, Mónica Nancy Giacomodonato, and María Cristina Cerquetti. Consumption of lactobacillus casei fermented milk prevents salmonella reactive arthritis by modulating il-23/il-17 expression. *PLoS One*, 8(12):e82588, 2013.

[35] LP Babenko, LM Lazarenko, LM Shynkarenko, VV Mokrozub, VS Pidgorskyi, and M Ja Spivak. The effect of lacto-and bifidobacteria in monoculture on the vaginal microflora in norm and in cases of intravaginal staphylococcosis. , (75,№ 3):46–55, 2013.

[36] Hortensia Zelaya, Kohichiro Tsukida, Eriko Chiba, Gabriela Marranzino, Susana Alvarez, Haruki Kitazawa, Graciela Agüero, and Julio Villena. Immunobiotic lactobacilli reduce viral-associated pulmonary damage through the modulation of inflammation–coagulation interactions. *International immunopharmacology*, 19(1):161–173, 2014.

[37] Busra Aktas, Travis J De Wolfe, Kanokwan Tandee, Nasia Safdar, Benjamin J Darien, and James L Steele. The effect of lactobacillus casei 32g on the mouse cecum microbiota and innate immune response is dose and time dependent. *PloS one*, 10(12):e0145784, 2015.

[38] N Foolad and AW Armstrong. Prebiotics and probiotics: the prevention and reduction in severity of atopic dermatitis in children. *Beneficial microbes*, 5(2):151–160, 2014.

[39] K Wickens, TV Stanley, EA Mitchell, C Barthow, P Fitzharris, G Purdie, R Siebers, PN Black, and J Crane. Early supplementation with lactobacillus rhamnosus hn 001 reduces eczema prevalence to 6 years: does it also reduce atopic sensitization? *Clinical & Experimental Allergy*, 43(9):1048–1057, 2013.

[40] Harsh Panwar, Danielle Calderwood, Irene R Grant, Sunita Grover, and Brian D Green. Lactobacillus strains isolated from infant faeces possess potent inhibitory activity against intestinal alpha-and beta-glucosidases suggesting anti-diabetic potential. *European Journal of Nutrition*, 53:1465–1474, 2014.

[41] Brett M Jakaitis and Patricia W Denning. Commensal and probiotic bacteria may prevent nec by maturing intestinal host defenses. *Pathophysiology*, 21(1):47–54, 2014.

[42] P Manzoni, M Mostert, ML Leonessa, C Priolo, D Farina, C Monetti, MA Latino, and G Gomirato. Oral supplementation with lactobacillus casei subspecies rhamnosus prevents enteric colonization by candida species in preterm neonates: a randomized study. *Clinical infectious diseases*, 42(12):1735–1742, 2006.

[43] Marina Sanchez, Christian Darimont, Vicky Drapeau, Shahram Emady-Azar, Melissa Lepage, Enea Rezzonico, Catherine Ngom-Bru, Bernard Berger, Lionel Philippe, Corinne Ammon-Zuffrey, et al. Effect of lactobacillus rhamnosus cgmcc1. 3724 supplementation on weight loss and maintenance in obese men and women. *British Journal of Nutrition*, 111(8):1507–1519, 2014.

[44] Michał Wiciński, Jakub Gebalski, Jakub Gołebiewski, and Bartosz Malinowski. Probiotics for the treatment of overweight and obesity in humans—a review of clinical trials. *Microorganisms*, 8(8):1148, 2020.

[45] Simona Ciccarelli, Ilaria Stolfi, and Giuseppe Caramia. Management strategies in the treatment of neonatal and pediatric gastroenteritis. *Infection and drug resistance*, pages 133–161, 2013.

[46] Raakel Luoto, Olli Ruuskanen, Matti Waris, Marko Kalliomäki, Seppo Salminen, and Erika Isolauri. Prebiotic and probiotic supplementation prevents rhinovirus infections in preterm infants: a randomized, placebo-controlled trial. *Journal of Allergy and Clinical Immunology*, 133(2):405–413, 2014.

[47] F Ammoscato, Annunziata Scirocco, A Altomare, P Matarrese, C Petitta, B Ascione, Roberto Caronna, M Guarino, M Marignani, M Cicala, et al. L actobacillus rhamnosus protects human colonic muscle from pathogen lipopolysaccharide-induced damage. *Neurogastroenterology & Motility*, 25(12):984–e777, 2013.

[48] Nicoleta-Maricica Maftei, Cosmin Raducu Raileanu, Alexia Anastasia Balta, Lenuta Ambrose, Monica Boev, Denisa Batîr Marin, and Elena Lacramioara Lisa. The potential impact of probiotics on human health: An update on their health-promoting properties. *Microorganisms*, 12(2):234, 2024.

[49] Sin Ji Lee, Shambhunath Bose, Jae-Gu Seo, Won-Seok Chung, Chi-Yeon Lim, and Hojun Kim. The effects of co-administration of probiotics with herbal medicine on obesity, metabolic endotoxemia and dysbiosis: a randomized double-blind controlled clinical trial. *Clinical nutrition*, 33(6):973–981, 2014.

[50] Adele Costabile, Ivan Buttarazzi, Sofia Kolida, Sara Quercia, Jessica Baldini, Jonathan R Swann, Patrizia Brigidi, and Glenn R Gibson. An in vivo assessment of the cholesterol-lowering efficacy of lactobacillus plantarum ecgc 13110402 in normal to mildly hypercholesterolaemic adults. *PloS one*, 12(12):e0187964, 2017.

[51] Douglas B DiRienzo. Effect of probiotics on biomarkers of cardiovascular disease: implications for heart-healthy diets. *Nutrition reviews*, 72(1):18–29, 2014.

[52] H Szajewska, M Urbańska, A Chmielewska, Z Weizman, and R Shamir. Meta-analysis: Lactobacillus reuteri strain dsm 17938 (and the original strain atcc 55730) for treating acute gastroenteritis in children. *Beneficial microbes*, 5(3):285–293, 2014.

[53] Jasim Anabrees, Flavia Indrio, Bosco Paes, and Khalid AlFaleh. Probiotics for infantile colic: a systematic review. *BMC pediatrics*, 13:1–9, 2013.

[54] Flavia Indrio, Antonio Di Mauro, Giuseppe Riezzo, Elisa Civardi, Cristina Intini, Luigi Corvaglia, Elisa Ballardini, Massimo Bisceglia, Mauro Cinquetti, Emanuela Brazzoduro, et al. Prophylactic use of a probiotic in the prevention of colic, regurgitation, and functional constipation: a randomized clinical trial. *JAMA pediatrics*, 168(3):228–233, 2014.

[55] Ulrich Schlagenhauf, Lena Jakob, Martin Eigenthaler, Sabine Segerer, Yvonne Jockel-Schneider, and Monika Rehn. Regular consumption of lactobacillus reuteri-containing lozenges reduces pregnancy gingivitis: an rct. *Journal of clinical periodontology*, 43(11):948–954, 2016.

[56] Merve Tekce, Gizem Ince, Hare Gursoy, Sebnem Dirikan Ipci, Gokser Cakar, Tanju Kadir, and Selçuk Yılmaz. Clinical and microbiological effects of probiotic lozenges in the treatment of chronic periodontitis: a 1-year follow-up study. *Journal of clinical periodontology*, 42(4):363–372, 2015.

[57] Wim Teughels, Andaç Durukan, Onur Ozcelik, Martine Pauwels, Marc Quirynen, and Mehmet Cenk Haytac. Clinical and microbiological effects of lactobacillus reuteri probiotics in the treatment of chronic periodontitis: a randomized placebo-controlled study. *Journal of clinical periodontology*, 40(11):1025–1035, 2013.

[58] María Ortiz-Lucas, Aurelio Tobias, JJ Sebastián, and P Saz. Effect of probiotic species on irritable bowel syndrome symptoms: A bring up to date meta-analysis. Technical report, 2013.

[59] Po-Wen Chen, Trista Tingyun Jheng, Ching-Ling Shyu, and Frank Chiahung Mao. Synergistic antibacterial efficacies of the combination of bovine lactoferrin or its hydrolysate with probiotic secretion in curbing the growth of meticillin-resistant staphylococcus aureus. *Journal of medical microbiology*, 62(12):1845–1851, 2013.

[60] Catherine Tomaro-Duchesneau, Shyamali Saha, Meenakshi Malhotra, Mitchell L Jones, Alain Labbé, Laetitia Rodes, Imen Kahouli, and Satya Prakash. Effect of orally administered l. fermentum ncimb 5221 on markers of metabolic syndrome: an in vivo analysis using zdf rats. *Applied microbiology and biotechnology*, 98:115–126, 2014.

[61] Yuxuan Qin, Jing Li, Qiuya Wang, Kexin Gao, Baoli Zhu, and Na Lv. Identification of lactic acid bacteria in commercial yogurt and their antibiotic resistance. *Wei sheng wu xue bao= Acta microbiologica Sinica*, 53(8):889–897, 2013.

[62] Marco Antonio Moro-García, Rebeca Alonso-Arias, Maria Baltadjieva, Carlos Fernández Benítez, Manuel Amadeo Fernández Barrial, Enrique Díaz Ruisánchez, Ricardo Alonso Santos, Magdalena Álvarez Sánchez, Juan Saavedra Miján, and Carlos López-Larrea. Oral supplementation with lactobacillus delbrueckii subsp. bulgaricus 8481 enhances systemic immunity in elderly subjects. *Age*, 35:1311–1326, 2013.

[63] D Abedi, S Feizizadeh, V Akbari, and A Jafarian-Dehkordi. In vitro anti-bacterial and anti-adherence effects of lactobacillus delbrueckii subsp bulgaricus on escherichia coli. *Research in pharmaceutical sciences*, 8(4):260, 2013.

[64] Kirsten Tillisch, Jennifer Labus, Lisa Kilpatrick, Zhiguo Jiang, Jean Stains, Bahar Ebrat, Denis Guyonnet, Sophie Legrain-Raspaud, Beatrice Trotin, Bruce Naliboff, et al. Consumption of fermented milk product with probiotic modulates brain activity. *Gastroenterology*, 144(7):1394–1401, 2013.

[65] Shigenori Suzuki, Takafumi Yakabe, Hiroyuki Suganuma, Masanori Fukao, Tadao Saito, and Nobuhiro Yajima. Cell-bound exopolysaccharides of lactobacillus brevis kb290: protective role and monosaccharide composition. *Canadian journal of microbiology*, 59(8):549–555, 2013.

[66] Guglielmo Campus, Fabio Cocco, Giovanna Carta, Maria Grazia Cagetti, Charlotte Simark-Mattson, Laura Strohmenger, and Peter Lingström. Effect of a daily dose of lactobacillus brevis cd2 lozenges in high caries risk schoolchildren. *Clinical oral investigations*, 18:555–561, 2014.

[67] Kei E Fujimura, Tine Demoor, Marcus Rauch, Ali A Faruqi, Sihyug Jang, Christine C Johnson, Homer A Boushey, Edward Zoratti, Dennis Ownby, Nicholas W Lukacs, et al. House dust exposure mediates gut microbiome lactobacillus enrichment and airway immune defense against allergens and virus infection. *Proceedings of the National Academy of Sciences*, 111(2):805–810, 2014.

[68] Pei-Shan Hsieh, Yi-Chun Tsai, Yi-Chun Chen, Su-Fen Teh, Chung-Mou Ou, and V An-Erl King. Eradication of h elicobacter pylori infection by the probiotic strains l actobacillus johnsonii mh-68 and l. salivarius ssp. salicinius ap-32. *Helicobacter*, 17(6):466–477, 2012.

[69] Ying-Chun Zhang, Lan-Wei Zhang, Wei Ma, Hua-Xi Yi, Xin Yang, Ming Du, Yu-Juan Shan, Xue Han, and Li-Li Zhang. Screening of probiotic lactobacilli for inhibition of shigella sonnei and the macromolecules involved in inhibition. *Anaerobe*, 18(5):498–503, 2012.

[70] Ko-Haung Lue, Hai-Lun Sun, Ko-Hsiu Lu, Min-Sho Ku, Ji-Nan Sheu, Ching-Hui Chan, and Yun-Hu Wang. A trial of adding lactobacillus johnsonii em1 to levocetirizine for treatment of perennial allergic rhinitis in children aged 7–12 years. *International journal of pediatric otorhinolaryngology*, 76(7):994–1001, 2012.

[71] Fuqiang Yuan, Huijuan Ni, Carl V Asche, Minchul Kim, Saqib Walayat, and Jinma Ren. Efficacy of bifidobacterium infantis 35624 in patients with irritable bowel syndrome: a meta-analysis. *Current medical research and opinion*, 33(7):1191–1197, 2017.

[72] Susan E Jacobs, Jacinta M Tobin, Gillian F Opie, Susan Donath, Sepehr N Tabrizi, Marie Pirotta, Colin J Morley, and Suzanne M Garland. Probiotic effects on late-onset sepsis in very preterm infants: a randomized controlled trial. *Pediatrics*, 132(6):1055–1062, 2013.

[73] D Li, G Rosito, and T Slagle. Probiotics for the prevention of necrotizing enterocolitis in neonates: an 8-year retrospective cohort study. *Journal of clinical pharmacy and therapeutics*, 38(6):445–449, 2013.

[74] Annie Janvier, Josianne Malo, and Keith J Barrington. Cohort study of probiotics in a north american neonatal intensive care unit. *The Journal of pediatrics*, 164(5):980–985, 2014.

[75] Anna Chmielewska and Hania Szajewska. Systematic review of randomised controlled trials: probiotics for functional constipation. *World journal of gastroenterology: WJG*, 16(1):69, 2010.

[76] GS Pinto, MS Cenci, MS Azevedo, M Epifanio, and MH Jones. Effect of yogurt containing bifidobacteriumanimalis subsp. lactis dn-173010 probiotic on dental plaque and saliva in orthodontic patients. *Caries research*, 48(1):63–68, 2014.

[77] Alessandra Bordoni, Alberto Amaretti, Alan Leonardi, Elisa Boschetti, Francesca Danesi, Diego Matteuzzi, Lucia Roncaglia, Stefano Raimondi, and Maddalena Rossi. Cholesterol-lowering probiotics: in vitro selection and in vivo testing of bifidobacteria. *Applied Microbiology and Biotechnology*, 97:8273–8281, 2013.

[78] Nicholas P West, Peggy L Horn, David B Pyne, Val J Gebski, Sampo J Lahtinen, Peter A Fricker, and Allan W Cripps. Probiotic supplementation for respiratory and gastrointestinal illness symptoms in healthy physically active individuals. *Clinical Nutrition*, 33(4):581–587, 2014.

[79] Diana Di Gioia, Irene Aloisio, Giuseppe Mazzola, and Bruno Biavati. Bifidobacteria: their impact on gut microbiota composition and their applications as probiotics in infants. *Applied microbiology and biotechnology*, 98:563–577, 2014.

[80] Mimi Demers, Anne Dagnault, and Josée Desjardins. A randomized double-blind controlled trial: impact of probiotics on diarrhea in patients treated with pelvic radiation. *Clinical nutrition*, 33(5):761–767, 2014.

[81] Jean Guy LeBlanc, Florian Chain, Rebeca Martín, Luis G Bermúdez-Humarán, Stéphanie Courau, and Philippe Langella. Beneficial effects on host energy metabolism of short-chain fatty acids and vitamins produced by commensal and probiotic bacteria. *Microbial cell factories*, 16:1–10, 2017.

[82] Hongjing Yu, Lu Liu, Zhen Chang, Shasha Wang, Bin Wen, Peijun Yin, Datao Liu, Bei Chen, and Jundong Zhang. Genome sequence of the bacterium bifidobacterium longum strain cmcc p0001, a probiotic strain used for treating gastrointestinal disease. *Genome announcements*, 1(5):10–1128, 2013.

[83] Ella-Noora Rahkola, Samuli Rautava, Henni Hiltunen, Chandler Ross, Leo Lahti, and Erika Isolauri. The preterm gut microbiota and administration routes of different probiotics: a randomized controlled trial. *Pediatric Research*, 94(4):1480–1487, 2023.

[84] Martin Schwarzer, Dagmar Srutkova, Irma Schabussova, Tomas Hudcovic, Johnnie Akgün, Ursula Wiedermann, and Hana Kozakova. Neonatal colonization of germ-free mice with bifidobacterium longum prevents allergic sensitization to major birch pollen allergen bet v 1. *Vaccine*, 31(46):5405–5412, 2013.

[85] Nadia Osman, Diya Adawi, Göran Molin, Siv Ahrne, Anna Berggren, and Bengt Jeppsson. Bifidobacterium infantis strains with and without a combination of oligofructose and inulin (ofi) attenuate inflammation in dss-induced colitis in rats. *BMC gastroenterology*, 6:1–10, 2006.

[86] Angélica T Vieira, Mauro M Teixeira, and Flaviano S Martins. The role of probiotics and prebiotics in inducing gut immunity. *Frontiers in immunology*, 4:445, 2013.

[87] Bradley C Johnston, Joshua Z Goldenberg, Per O Vandvik, Xin Sun, and Gordon H Guyatt. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. *Cochrane Database of Systematic Reviews*, (11), 2011.

[88] Ener Cagri Dinleyici, Makbule Eren, Metehan Ozen, Zeynel Abidin Yargic, and Yvan Vandenplas. Effectiveness and safety of saccharomyces boulardii for acute infectious diarrhea. *Expert opinion on biological therapy*, 12(4):395–410, 2012.

[89] L Shan, P Hou, Z Wang, F Liu, N Chen, L Shu, and Y Shang. Prevention and treatment of diarrhoea with saccharomyces boulardii in children with acute lower respiratory tract infections. 4 (december), 329–334, 2013.

[90] H Szajewska and J Mrukowicz. Meta-analysis: non-pathogenic yeast saccharomyces boulardii in the prevention of antibiotic-associated diarrhoea. *Alimentary pharmacology & therapeutics*, 22(5):365–372, 2005.

[91] Chang Hwan Choi, Sun Young Jo, Hyo Jin Park, Sae Kyung Chang, Jeong-Sik Byeon, and Seung-Jae Myung. A randomized, double-blind, placebo-controlled multicenter trial of saccharomyces boulardii in irritable bowel syndrome: effect on quality of life. *Journal of Clinical Gastroenterology*, 45(8):679–683, 2011.

[92] Mario Guslandi, Gianni Mezzi, Massimo Sorghi, and Pier Alberto Testoni. Saccharomyces boulardii in maintenance treatment of crohn's disease. *Digestive diseases and sciences*, 45:1462–1464, 2000.

[93] Mario Guslandi, Patrizia Giollo, and Pier Alberto Testoni. A pilot trial of saccharomyces boulardii in ulcerative colitis. *European journal of gastroenterology & hepatology*, 15(6):697–698, 2003.

[94] Leo R Fitzpatrick. Probiotics for the treatment of clostridium difficile associated disease. *World Journal of Gastrointestinal Pathophysiology*, 4(3):47, 2013.

[95] Xiaochun Yang, Yutang Wang, and Guicheng Huo. Complete genome sequence of lactococcus lactis subsp. lactis klds4. 0325. *Genome announcements*, 1(6):10–1128, 2013.

[96] Yong Gao, Ying Lu, Kun-Ling Teng, Mei-Ling Chen, Hua-Jun Zheng, Yong-Qiang Zhu, and Jin Zhong. Complete genome sequence of lactococcus lactis subsp. lactis cv56, a probiotic strain isolated from the vaginas of healthy women, 2011.

[97] Joong-Su Lee, Myung-Jun Chung, and Jae-Gu Seo. In vitro evaluation of antimicrobial activity of lactic acid bacteria against clostridium difficile. *Toxicological research*, 29(2):99–106, 2013.

[98] B Fernandez, R Hammami, P Savard, J Jean, and I Fliss. Pediococcus acidilactici ul5 and lactococcus lactis atcc 11454 are able to survive and express their bacteriocin genes under simulated gastrointestinal conditions. *Journal of applied microbiology*, 116(3):677–688, 2014.

[99] Simone Pieniz, Robson Andreazza, Jamile Queiroz Pereira, Flávio Anastácio de Oliveira Camargo, and Adriano Brandelli. Production of selenium-enriched biomass by enterococcus durans. *Biological trace element research*, 155:447–454, 2013.

[100] Irit Raz, Natan Gollop, Sylvie Polak-Charcon, and Betty Schwartz. Isolation and characterisation of new putative probiotic bacteria from human colonic flora. *British Journal of Nutrition*, 97(4):725–734, 2007.

[101] Susanne Hempel, Sydne J Newberry, Alicia R Maher, Zhen Wang, Jeremy NV Miles, Roberta Shanman, Breanne Johnsen, and Paul G Shekelle. Probiotics for the prevention and treatment of antibiotic-associated diarrhea: a systematic review and meta-analysis. *Jama*, 307(18):1959–1969, 2012.

[102] Tasuku Ogita, Megumi Nakashima, Hidetoshi Morita, Yasuo Saito, Takuya Suzuki, and Soichi Tanabe. Streptococcus thermophilus st28 ameliorates colitis in mice partially by suppression of inflammatory th17 cells. *BioMed Research International*, 2011(1):378417, 2011.

[103] Man-Kwang Rho, Young-Eun Kim, Hyun-In Rho, Tae-Rahk Kim, Yoon-Bum Kim, Won-Kyung Sung, Tae-Woo Kim, Dae-Ok Kim, and Hee Kang. Enterococcus faecium fc-k derived from kimchi is a probiotic strain that shows anti-allergic activity. *Journal of Microbiology and Biotechnology*, 27(6):1071–1077, 2017.

[104] GT Cao, XF Zeng, AG Chen, L Zhou, L Zhang, YP Xiao, and CM Yang. Effects of a probiotic, enterococcus faecium, on growth performance, intestinal morphology, immune response, and cecal microflora in broiler chickens challenged with escherichia coli k88. *Poultry science*, 92(11):2949–2955, 2013.

[105] Hiroya Mizuno, Kae Tomotsune, Md Aminul Islam, Ryutaro Funabashi, Leonardo Albarracin, Wakako Ikeda-Ohtsubo, Hisashi Aso, Hideki Takahashi, Katsunori Kimura, Julio Villena, et al. Exopolysaccharides from streptococcus thermophilus st538 modulate the antiviral innate immune response in porcine intestinal epitheliocytes. *Frontiers in Microbiology*, 11:894, 2020.

[106] Ridhi Mehta, Ridhima Arya, Karan Goyal, Mahipal Singh, and Anil K Sharma. Bio-preservative and therapeutic potential of pediocin: recent trends and future perspectives. *Recent patents on biotechnology*, 7(3):172–178, 2013.

[107] Baljinder Kaur, Neena Garg, Atul Sachdev, and Balvir Kumar. Effect of the oral intake of probiotic pediococcus acidilactici ba28 on helicobacter pylori causing peptic ulcer in c57bl/6 mice models. *Applied biochemistry and biotechnology*, 172:973–983, 2014.

[108] Zineb Benmechernene, Hanane Fatma Chentouf, Bellil Yahia, Ghazi Fatima, Marcos Quintela-Baluja, Pilar Calo-Mata, and Jorge Barros-Velázquez. Technological aptitude and applications of leuconostoc mesenteroides bioactive strains isolated from algerian raw camel milk. *BioMed research international*, 2013(1):418132, 2013.

[109] Shira Idit Doron, Patricia L Hibberd, and Sherwood L Gorbach. Probiotics for prevention of antibiotic-associated diarrhea. *Journal of Clinical Gastroenterology*, 42:S58–S63, 2008.

[110] M Ratna Sudha, Kanan A Yelikar, and Sonali Deshpande. Clinical study of bacillus coagulans unique is-2 (atcc pta-11748) in the treatment of patients with bacterial vaginosis. *Indian journal of microbiology*, 52:396–399, 2012.

[111] Kathleen F Benson, Kimberlee A Redman, Steve G Carter, David Keller, Sean Farmer, John R Endres, and Gitte S Jensen. Probiotic metabolites from bacillus coagulans ganedenbc30tm support maturation of antigen-presenting cells in vitro. *World Journal of Gastroenterology: WJG*, 18(16):1875, 2012.

[112] G Jindal, RK Pandey, J Agarwal, and M Singh. A comparative evaluation of probiotics on salivary mutans streptococci counts in indian children. *European Archives of Paediatric Dentistry*, 12:211–215, 2011.

[113] Nadja Larsen, Line Thorsen, Elmer Nayra Kpikpi, Birgitte Stuer-Lauridsen, Mette Dines Cantor, Bea Nielsen, Elke Brockmann, Patrick MF Derkx, and Lene Jespersen. Characterization of bacillus spp. strains for use as probiotic additives in pig feed. *Applied microbiology and biotechnology*, 98:1105–1118, 2014.

[114] Hadi Zokaeifar, Nahid Babaei, Che Roos Saad, Mohd Salleh Kamarudin, Kamaruzaman Sijam, and Jose Luis Balcazar. Administration of bacillus subtilis strains in the rearing water enhances the water quality, growth performance, immune response, and resistance against vibrio harveyi infection in juvenile white shrimp, litopenaeus vannamei. *Fish & shellfish immunology*, 36(1):68–74, 2014.

[115] T Tompkins, X Xu, and J Ahmarani. A comprehensive review of post-market clinical studies performed in adults with an asian probiotic formulation. *Beneficial microbes*, 1(1):93–106, 2010.

[116] Laura C Clark and Jonathan Hodgkin. Commensals, probiotics and pathogens in the c aenorhabditis elegans model. *Cellular microbiology*, 16(1):27–38, 2014.

[117] Martin Trapecar, Thomas Leouffre, Morgane Faure, Henrik E Jensen, Per E Granum, Avrelija Cencic, and Simon P Hardy. The use of a porcine intestinal cell model system for evaluating the food safety risk of bacillus cereus probiotics and the implications for assessing enterotoxigenicity. *Apmis*, 119(12):877–884, 2011.

[118] Judith Behnsen, Elisa Deriu, Martina Sassone-Corsi, and Manuela Raffatellu. Probiotics: properties, examples, and specific applications. *Cold Spring Harbor perspectives in medicine*, 3(3):a010074, 2013.

[119] Pengpeng Xia, Jun Zhu, and Guoqiang Zhu. Escherichia coli nissle 1917 as safe vehicles for intestinal immune targeted therapy–a review. *Wei Sheng wu xue bao= Acta Microbiologica Sinica*, 53(6):538–544, 2013.

[120] S Bereswill, A Fischer, IR Dunay, AA Kühl, UB Göbel, O Liesenfeld, and MM Heimesaat. Pro-inflammatory potential of escherichia coli strains k12 and nissle 1917 in a murine model of acute ileitis. *European Journal of Microbiology and Immunology*, 3(2):126–134, 2013.

[121] Elisabeth Stein, Aleksandra Inic-Kanada, Sandra Belij, Jacqueline Montanaro, Nora Bintner, Simone Schlacher, Ulrike Beate Mayr, Werner Lubitz, Marijana Stojanovic, Hristo Najdenski, et al. In vitro and in vivo uptake study of escherichia coli nissle 1917 bacterial ghosts: cell-based delivery system to target ocular surface diseases. *Investigative ophthalmology & visual science*, 54(9):6326–6333, 2013.

[122] Elisa Deriu, Janet Z Liu, Milad Pezeshki, Robert A Edwards, Roxanna J Ochoa, Heidi Contreras, Stephen J Libby, Ferric C Fang, and Manuela Raffatellu. Probiotic bacteria reduce salmonella typhimurium intestinal colonization by competing for iron. *Cell host & microbe*, 14(1):26–37, 2013.

[123] Sahil Khanna, Yoshiki Vazquez-Baeza, Antonio González, Sophie Weiss, Bradley Schmidt, David A Muñiz-Pedrogo, John F Rainey, Patricia Kammer, Heidi Nelson, Michael Sadowsky, et al. Changes in microbial ecology after fecal microbiota transplantation for recurrent c. difficile infection affected by underlying inflammatory bowel disease. *Microbiome*, 5(1):1–8, 2017.

[124] Shinta Mizuno, Kosaku Nanki, Katsuyoshi Matsuoka, Keiichiro Saigusa, Keiko Ono, Mari Arai, Shinya Sugimoto, Hiroki Kiyohara, Moeko Nakashima, Kozue Takeshita, et al. Single fecal microbiota transplantation failed to change intestinal microbiota and had limited effectiveness against ulcerative colitis in Japanese patients. *Intestinal Research*, 15(1):68, 2017.

[125] Yang Song, Shashank Garg, Mohit Girotra, Cynthia Maddox, Erik C Von Rosenvinge, Anand Dutta, Sudhir Dutta, and W Florian Fricke. Microbiota dynamics in patients treated with fecal microbiota transplantation for recurrent clostridium difficile infection. *PloS One*, 8(11):e81330, 2013.

[126] Anna M Seekatz, Johannes Aas, Charles E Gessert, Timothy A Rubin, Daniel M Saman, Johan S Bakken, and Vincent B Young. Recovery of the gut microbiome following fecal microbiota transplantation. *MBio*, 5(3):e00893–14, 2014.

[127] Vijay Shankar, Matthew J Hamilton, Alexander Khoruts, Amanda Kilburn, Tatsuya Unno, Oleg Paliy, and Michael J Sadowsky. Species and genus level resolution analysis of gut microbiota in clostridium difficile patients following fecal microbiota transplantation. *Microbiome*, 2(1):1–10, 2014.

[128] Alka Goyal, Andrew Yeh, Brian R Bush, Brian A Firek, Leah M Siebold, Matthew Brian Rogers, Adam D Kufen, and Michael J Morowitz. Safety, clinical response, and microbiome findings following fecal microbiota transplant in children with inflammatory bowel disease. *Inflammatory Bowel Diseases*, 24(2):410–421, 2018.

[129] Michael Mintz, Shanawaj Khair, Suman Grewal, Joseph F LaComb, Jiyhe Park, Breana Channer, Ramona Rajapakse, Juan Carlos Bucobo, Jonathan M Buscaglia, Farah Monzur, et al. Longitudinal microbiome analysis of single donor fecal microbiota transplantation in patients with recurrent clostridium difficile infection and/or ulcerative colitis. *PloS one*, 13(1):e0190997, 2018.

[130] Pan Li, Ting Zhang, Yandong Xiao, Liang Tian, Bota Cui, Guozhong Ji, Yang-Yu Liu, and Faming Zhang. Timing for the second fecal microbiota transplantation to maintain the long-term benefit from the first treatment for crohn's disease. *Applied Microbiology and Biotechnology*, 103(1):349–360, 2019.