

1 Title:

2 Supplemental material of "Health and disease  
3 imprinted in the time variability of the human  
4 microbiome"

5 Running title:

6 Supplemental material of "Microbiota, are you sick?"

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**Supplementary Table S1.** Taylor parameters. Individuals with either animal-based (A) or plant-based (P) diets (1). Previous to diet, the population sampled is described by  $\bar{V} = 0.09 \pm 0.05$ ,  $\bar{\beta} = 0.77 \pm 0.04$ .

Metadata	V	$\beta$	$\bar{R}^2$	$V_{st}$	$\beta_{st}$
A	$0.26 \pm 0.05$	$0.826 \pm 0.025$	0.918	$3.1 \pm 0.9$	$1.2 \pm 0.6$
A	$0.32 \pm 0.06$	$0.857 \pm 0.025$	0.924	$4.4 \pm 1.1$	$2.0 \pm 0.6$
A	$0.194 \pm 0.033$	$0.813 \pm 0.024$	0.918	$1.9 \pm 0.6$	$0.9 \pm 0.6$
A	$0.24 \pm 0.04$	$0.824 \pm 0.020$	0.924	$2.7 \pm 0.7$	$1.2 \pm 0.5$
A	$0.34 \pm 0.06$	$0.855 \pm 0.024$	0.931	$4.7 \pm 1.1$	$1.9 \pm 0.6$
A	$0.30 \pm 0.05$	$0.847 \pm 0.022$	0.921	$3.9 \pm 1.0$	$1.7 \pm 0.5$
A	$0.133 \pm 0.021$	$0.784 \pm 0.023$	0.916	$0.7 \pm 0.4$	$0.2 \pm 0.6$
A	$0.25 \pm 0.04$	$0.831 \pm 0.024$	0.929	$3.0 \pm 0.8$	$1.4 \pm 0.6$
P	$0.23 \pm 0.05$	$0.804 \pm 0.035$	0.885	$2.6 \pm 0.9$	$0.7 \pm 0.8$
P	$0.097 \pm 0.018$	$0.705 \pm 0.031$	0.891	$0.03 \pm 0.34$	$-1.6 \pm 0.7$
P	$0.037 \pm 0.006$	$0.642 \pm 0.025$	0.881	$-1.12 \pm 0.11$	$-3.1 \pm 0.6$
P	$0.118 \pm 0.019$	$0.723 \pm 0.025$	0.895	$0.4 \pm 0.4$	$-1.2 \pm 0.6$
P	$0.17 \pm 0.04$	$0.78 \pm 0.04$	0.842	$1.5 \pm 0.7$	$0.1 \pm 0.9$
P	$0.123 \pm 0.020$	$0.757 \pm 0.026$	0.914	$0.5 \pm 0.4$	$-0.4 \pm 0.6$
P	$0.19 \pm 0.05$	$0.77 \pm 0.04$	0.871	$1.8 \pm 0.9$	$-0.0 \pm 0.9$
P	$0.121 \pm 0.020$	$0.736 \pm 0.027$	0.921	$0.5 \pm 0.4$	$-0.9 \pm 0.6$
P	$0.187 \pm 0.034$	$0.771 \pm 0.030$	0.908	$1.8 \pm 0.7$	$-0.1 \pm 0.7$
P	$0.097 \pm 0.015$	$0.735 \pm 0.025$	0.922	$0.05 \pm 0.28$	$-0.9 \pm 0.6$

**Supplementary Table S2.** Taylor parameters for individuals taking antibiotics (2). Prior to antibiotics intake, the population sampled is described by  $\bar{V} = 0.12 \pm 0.05$ ,  $\bar{\beta} = 0.75 \pm 0.04$ .

Metadata	V	$\beta$	$\bar{R}^2$	$V_{st}$	$\beta_{st}$
Ab	$0.35 \pm 0.07$	$0.81 \pm 0.04$	0.925	$4.3 \pm 1.4$	$1.3 \pm 0.9$
Ab	$0.41 \pm 0.09$	$0.82 \pm 0.04$	0.908	$5.6 \pm 1.8$	$1.6 \pm 0.9$
Ab	$0.23 \pm 0.04$	$0.770 \pm 0.031$	0.920	$2.1 \pm 0.8$	$0.5 \pm 0.7$
Ab	$0.165 \pm 0.029$	$0.738 \pm 0.031$	0.928	$0.9 \pm 0.6$	$-0.3 \pm 0.7$
Ab	$0.34 \pm 0.06$	$0.812 \pm 0.032$	0.936	$4.1 \pm 1.2$	$1.5 \pm 0.7$
Ab	$0.26 \pm 0.05$	$0.798 \pm 0.033$	0.931	$2.8 \pm 0.9$	$1.1 \pm 0.8$

**Supplementary Table S3.** Taylor parameters for persons diagnosed with irritable bowel syndrome (IBS) (3). Healthy individuals sampled in this study are characterized by  $\bar{V} = 0.134 \pm 0.009$ ,  $\bar{\beta} = 0.691 \pm 0.025$ .

Metadata	V	$\beta$	$\bar{R}^2$	$V_{st}$	$\beta_{st}$
IBS	$0.204 \pm 0.034$	$0.739 \pm 0.029$	0.916	$7.6 \pm 3.7$	$1.9 \pm 1.2$
IBS	$0.35 \pm 0.05$	$0.793 \pm 0.023$	0.935	$23.1 \pm 5.9$	$4.0 \pm 0.9$

**Supplementary Table S4.** Taylor parameters for the healthy subject of the discordant twins (4). This table continues in Supplementary Table 5. The population of healthy twins is characterized by  $\bar{V} = 0.25 \pm 0.10$ ,  $\bar{\beta} = 0.863 \pm 0.028$ .

Metadata	V	$\beta$	$\bar{R}^2$	$V_{st}$	$\beta_{st}$
DH	$0.27 \pm 0.04$	$0.835 \pm 0.016$	0.925	$0.2 \pm 0.4$	$-1.0 \pm 0.6$
DH	$0.36 \pm 0.06$	$0.858 \pm 0.015$	0.929	$1.1 \pm 0.6$	$-0.2 \pm 0.5$
DH	$0.35 \pm 0.06$	$0.859 \pm 0.014$	0.926	$1.0 \pm 0.5$	$-0.1 \pm 0.5$
DH	$0.25 \pm 0.04$	$0.829 \pm 0.014$	0.911	$0.0 \pm 0.4$	$-1.2 \pm 0.5$
DH	$0.30 \pm 0.05$	$0.844 \pm 0.014$	0.920	$0.5 \pm 0.4$	$-0.7 \pm 0.5$
DH	$0.29 \pm 0.05$	$0.850 \pm 0.016$	0.915	$0.4 \pm 0.5$	$-0.5 \pm 0.5$
DH	$0.28 \pm 0.05$	$0.848 \pm 0.016$	0.921	$0.3 \pm 0.5$	$-0.5 \pm 0.6$
DH	$0.35 \pm 0.07$	$0.861 \pm 0.017$	0.918	$0.9 \pm 0.6$	$-0.0 \pm 0.6$
DH	$0.31 \pm 0.04$	$0.833 \pm 0.012$	0.916	$0.6 \pm 0.4$	$-1.1 \pm 0.4$
DH	$0.33 \pm 0.05$	$0.843 \pm 0.013$	0.925	$0.8 \pm 0.5$	$-0.7 \pm 0.5$
DH	$0.31 \pm 0.05$	$0.852 \pm 0.014$	0.925	$0.6 \pm 0.5$	$-0.4 \pm 0.5$
DH	$0.31 \pm 0.05$	$0.853 \pm 0.015$	0.930	$0.6 \pm 0.5$	$-0.4 \pm 0.5$
DH	$0.203 \pm 0.033$	$0.815 \pm 0.015$	0.907	$-0.44 \pm 0.32$	$-1.7 \pm 0.5$

**Supplementary Table S5.** Taylor parameters for the kwashiorkor part of the discordant twins (4). This is a continuation of Supplementary Table 4. The population of healthy twins is characterized by  $\bar{V} = 0.25 \pm 0.10$ ,  $\bar{\beta} = 0.863 \pm 0.028$ .

Metadata	V	$\beta$	$\bar{R}^2$	$V_{st}$	$\beta_{st}$
DK	$0.40 \pm 0.07$	$0.859 \pm 0.017$	0.926	$1.5 \pm 0.7$	$-0.1 \pm 0.6$
DK	$0.44 \pm 0.08$	$0.868 \pm 0.016$	0.919	$1.8 \pm 0.8$	$0.2 \pm 0.6$
DK	$0.196 \pm 0.031$	$0.819 \pm 0.014$	0.916	$-0.50 \pm 0.30$	$-1.5 \pm 0.5$
DK	$0.160 \pm 0.026$	$0.798 \pm 0.015$	0.904	$-0.85 \pm 0.25$	$-2.3 \pm 0.5$
DK	$0.30 \pm 0.05$	$0.845 \pm 0.014$	0.924	$0.5 \pm 0.4$	$-0.6 \pm 0.5$
DK	$0.23 \pm 0.04$	$0.834 \pm 0.014$	0.908	$-0.1 \pm 0.4$	$-1.0 \pm 0.5$
DK	$0.27 \pm 0.05$	$0.848 \pm 0.015$	0.930	$0.2 \pm 0.4$	$-0.5 \pm 0.5$
DK	$0.35 \pm 0.07$	$0.860 \pm 0.019$	0.916	$1.0 \pm 0.7$	$-0.1 \pm 0.7$
DK	$0.34 \pm 0.05$	$0.835 \pm 0.012$	0.917	$0.9 \pm 0.5$	$-1.0 \pm 0.4$
DK	$0.25 \pm 0.04$	$0.831 \pm 0.012$	0.912	$0.0 \pm 0.4$	$-1.1 \pm 0.4$
DK	$0.36 \pm 0.06$	$0.858 \pm 0.013$	0.918	$1.1 \pm 0.5$	$-0.2 \pm 0.5$
DK	$0.31 \pm 0.06$	$0.851 \pm 0.016$	0.924	$0.6 \pm 0.6$	$-0.4 \pm 0.6$
DK	$0.149 \pm 0.022$	$0.799 \pm 0.013$	0.905	$-0.96 \pm 0.22$	$-2.2 \pm 0.5$

**Supplementary Table S6.** Taylor parameters for individuals with different degrees of overweight and obesity (5). Healthy people in this study, whom were not obese, are characterized by  $\bar{V} = 0.19 \pm 0.06$ ,  $\bar{\beta} = 0.806 \pm 0.034$ .

Metadata	V	$\beta$	$\bar{R}^2$	$V_{st}$	$\beta_{st}$
OW	$0.59 \pm 0.12$	$0.894 \pm 0.034$	0.920	$6.6 \pm 2.0$	$2.6 \pm 1.0$
OW	$0.22 \pm 0.04$	$0.830 \pm 0.030$	0.904	$0.5 \pm 0.6$	$0.7 \pm 0.9$
OBI	$0.28 \pm 0.04$	$0.855 \pm 0.022$	0.958	$1.5 \pm 0.6$	$1.4 \pm 0.6$
OBI	$0.33 \pm 0.07$	$0.870 \pm 0.031$	0.916	$2.4 \pm 1.1$	$1.9 \pm 0.9$
OBII	$0.223 \pm 0.032$	$0.823 \pm 0.023$	0.938	$0.6 \pm 0.5$	$0.5 \pm 0.7$
OBII	$0.208 \pm 0.029$	$0.844 \pm 0.022$	0.935	$0.4 \pm 0.5$	$1.1 \pm 0.7$
OBIII	$0.34 \pm 0.05$	$0.855 \pm 0.025$	0.943	$2.5 \pm 0.9$	$1.4 \pm 0.7$
OBIII	$0.26 \pm 0.04$	$0.845 \pm 0.026$	0.954	$1.1 \pm 0.7$	$1.2 \pm 0.8$
OBIII	$0.33 \pm 0.06$	$0.870 \pm 0.027$	0.908	$2.4 \pm 1.0$	$1.9 \pm 0.8$
OBIII	$0.200 \pm 0.026$	$0.843 \pm 0.020$	0.949	$0.2 \pm 0.4$	$1.1 \pm 0.6$
OBIII	$0.30 \pm 0.05$	$0.846 \pm 0.026$	0.929	$1.9 \pm 0.8$	$1.2 \pm 0.7$
OBIII	$0.176 \pm 0.029$	$0.826 \pm 0.026$	0.894	$-0.2 \pm 0.5$	$0.6 \pm 0.8$
OBIII	$0.30 \pm 0.06$	$0.841 \pm 0.031$	0.896	$1.8 \pm 0.9$	$1.0 \pm 0.9$
OBIII	$0.28 \pm 0.04$	$0.857 \pm 0.025$	0.941	$1.5 \pm 0.7$	$1.5 \pm 0.7$
OBIII	$0.122 \pm 0.018$	$0.822 \pm 0.024$	0.930	$-1.05 \pm 0.30$	$0.5 \pm 0.7$
OBIIIId	$0.47 \pm 0.08$	$0.872 \pm 0.023$	0.945	$4.7 \pm 1.3$	$1.9 \pm 0.7$
OBIIIId	$0.38 \pm 0.06$	$0.846 \pm 0.023$	0.951	$3.2 \pm 1.0$	$1.2 \pm 0.7$
OBIIIId	$0.36 \pm 0.06$	$0.842 \pm 0.022$	0.954	$2.9 \pm 0.9$	$1.1 \pm 0.6$

## References

1. David LA, Maurice CE, Carmody RN, Gootenberg DB, Button JE, Wolfe BE, Ling A V, Devlin AS, Varma Y, Fischbach MA, Biddinger SB, Dutton RJ, Turnbaugh PJ. 2014. Diet rapidly and reproducibly alters the human gut microbiome. *Nature* **505**:559–63.
2. Dethlefsen L, Relman DA. 2011. Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation. *Proc Natl Acad Sci* **108**:4554–61.
3. Durbán A, Abellán JJ, Jiménez-Hernández N, Artacho A, Garrigues V, Ortiz V, Ponce J, Latorre A, Moya A. 2013. Instability of the faecal microbiota in diarrhoea-predominant irritable bowel syndrome. *FEMS Microbiol Ecol* **86**:581–589.
4. Smith MI, Yatsunenko T, Manary MJ, Trehan I, Mkakosya R, Cheng J, Kau AL, Rich SS, Concannon P, Mychaleckyj JC, Liu J, Hought E, Li J V, Holmes E, Nicholson J, Knights D, Ursell LK, Knight R, Gordon JI. 2013. Gut microbiomes of Malawian twin pairs discordant for kwashiorkor. *Science* **339**:548–54.
5. Faith JJ, Guruge JL, Charbonneau M, Subramanian S, Seedorf H, Goodman AL, Clemente JC, Knight R, Heath AC, Leibel RL, Rosenbaum M, Gordon JI. 2013. The long-term stability of the human gut microbiota. *Science* **341**:1237439.