Quantifying gut microbiota metabolism in theory and practice

11. Nachhaltigkeitstagung, Agroscope

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Markus Arnoldini, 25.12.2024

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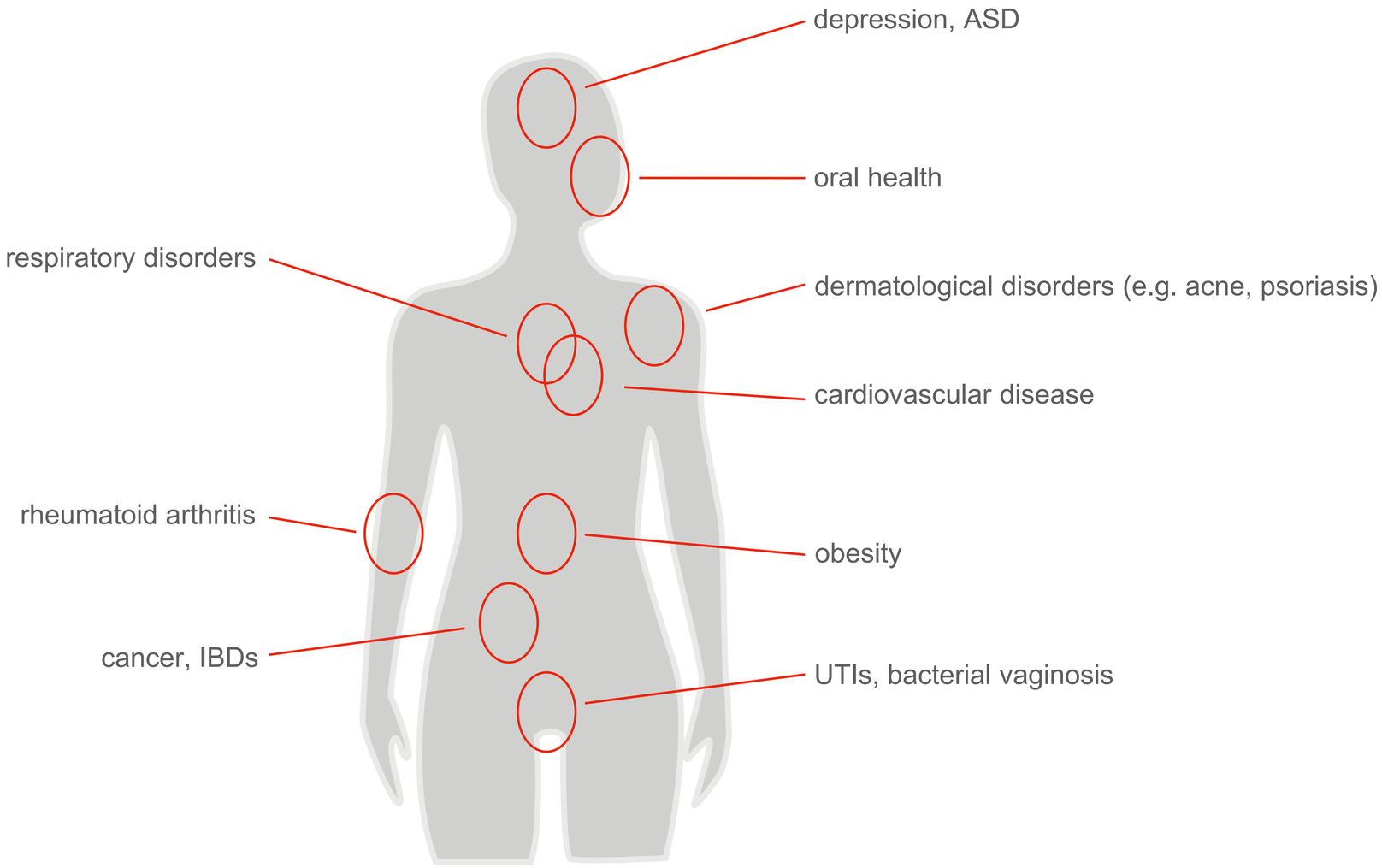
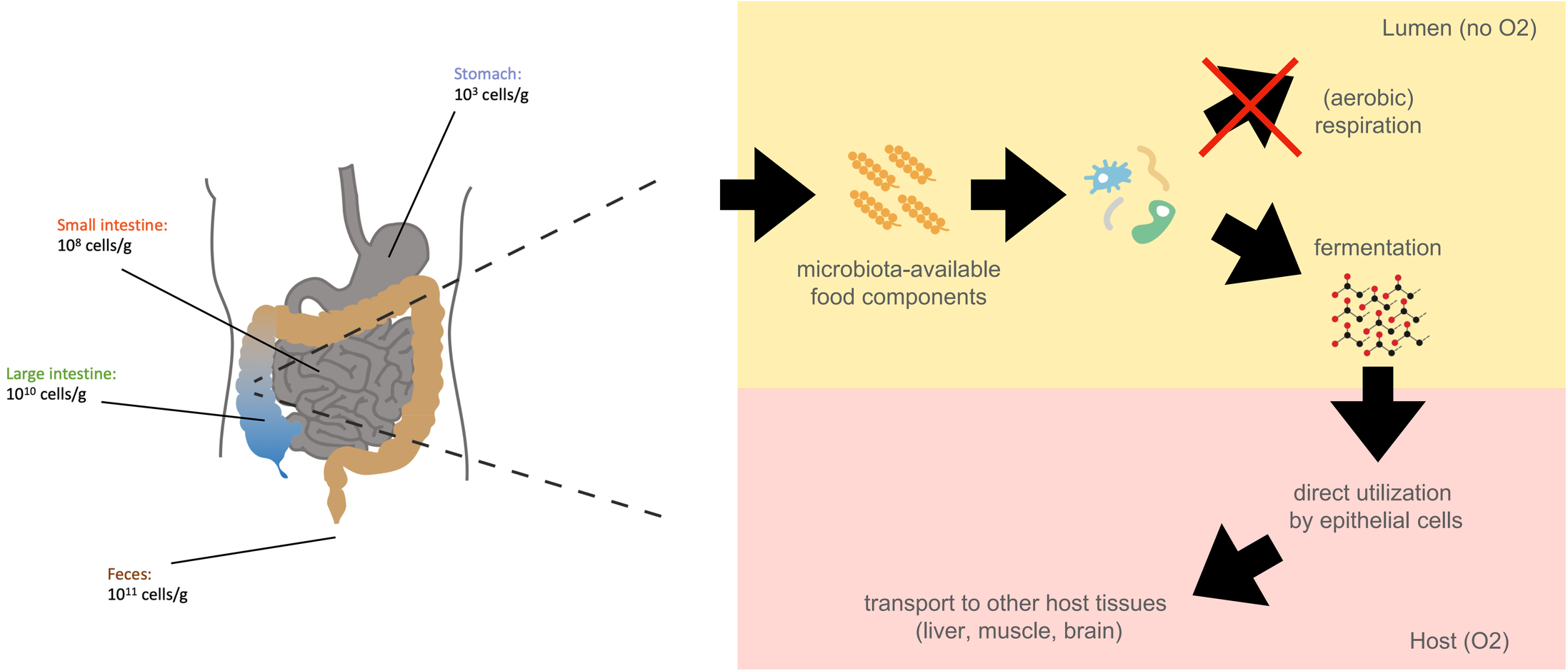
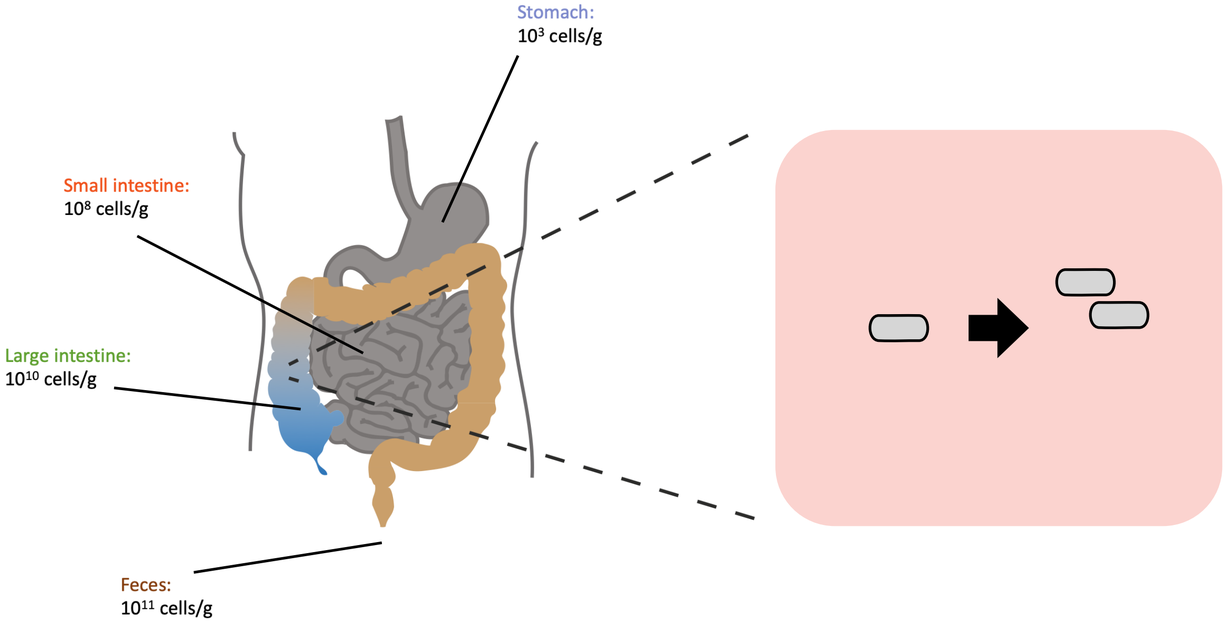
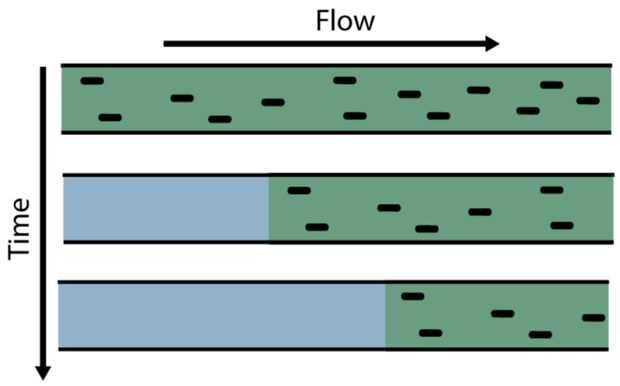

depression, ASD
oral health
respiratory disorders
dermatological disorders (e.g. acne, psoriasis)
cardiovascular disease
rheumatoid arthritis
obesity
cancer, IBDs
UTIs, bacterial vaginosis


Stomach:
10^3 cells/g
Small intestine:
10^8 cells/g
Large intestine:
10^{10} cells/g
Feces:
10^{11} cells/g
Lumen (no O2)
(aerobic)
respiration
microbiota-available
food components
fermentation
direct utilization
by epithelial cells
transport to other host tissues
(liver, muscle, brain)
Host (O2)

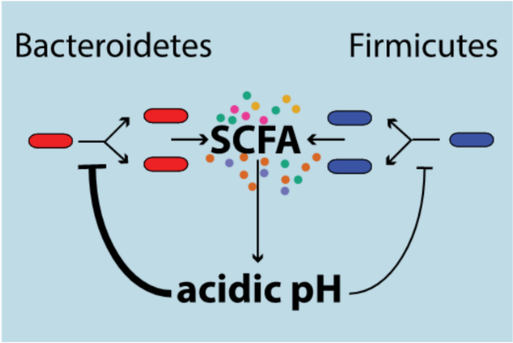
The microbiota has to grow and therefore produces FPs

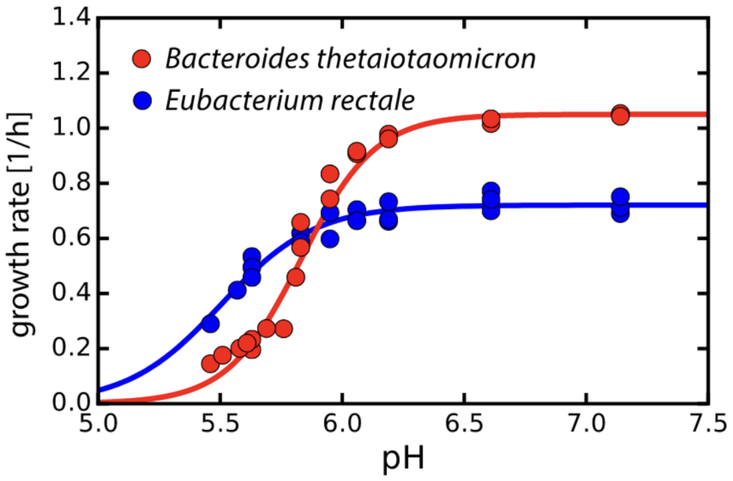
FPs have roles in
- immune regulation
- epithelial integrity
- satiety signaling
- behavior etc





Cremer et al, PNAS 2016





Cremer, Arnoldini, Hwa, PNAS 2017

Effect of FPs are dose dependent

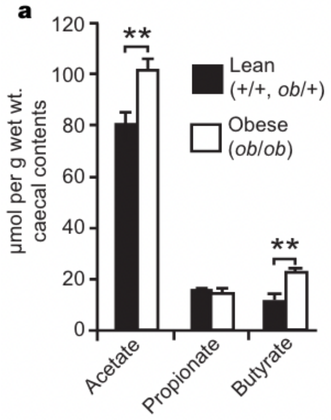
measurements…

Table 2 *pH, Short chain fatty acid and other organic anions* in the human intestine*

	Small intestine			*Large Intestine*			
	Jejunum	*Ileum*	*Caecum*	*Ascending*	*Transverse*	*Descending*	*Sigmoid/rectum*
pH	5·9 (0·1)	6·3 (0·1)	5·6 (0·2)	5·7 (0·2)	6·2 (0·1)	6·6 (0·1)	6·3 (0·2)
Acetate	0·6 (0·6)	7·9 (4·1)	69·1 (5·0)	63·4 (6·8)	57·9 (5·4)	43·5 (11·1)	50·1 (16·2)
Propionate	—	1·5 (1·0)	25·3 (3·7)	26·7 (4·0)	23·1 (2·8)	14·2 (3·1)	19·5 (6·7)
Iso-butyrate	—	0·3 (0·2)	2·1 (0·4)	1·8 (0·2)	2·6 (0·5)	2·3 (0·4)	1·9 (0·8)
Butyrate	—	2·3 (1·3)	26·1 (3·8)	24·5 (4·2)	24·4 (2·2)	14·7 (2·9)	17·9 (5·6)
Iso-valerate	—	0·1 (0·1)	2·7 (0·5)	2·7 (0·5)	3·4 (0·4)	3·5 (0·1)	3·7 (0·9)
Valerate	—	0·2 (0·1)	4·5 (0·5)	3·6 (0·8)	4·2 (0·2)	2·8 (0·1)	4·3 (0·9)
Iso-caproate	—	0·1 (0·1)	0·6 (0·3)	0·2 (0·2)	‡	—	0·9 (0·3)
Caproate	—	0·3 (0·2)	1·4 (0·5)	1·7 (0·8)	1·7 (0·6)	0·3 (0·2)	1·5 (0·3)
Lactate	2·0 (1·2)	13·5 (5·5)	4·5 (1·4)	3·1 (1·7)	3·5 (2·2)	3·1 (2·1)	1·5 (1·5)
Succinate	3·7 (1·3)	8·3 (3·2)	0·9 (0·2)	3·1 (0·9)	1·7 (0·4)	1·9 (0·6)	2·1 (1·0)
N†	6	6	6	6	5	4	5

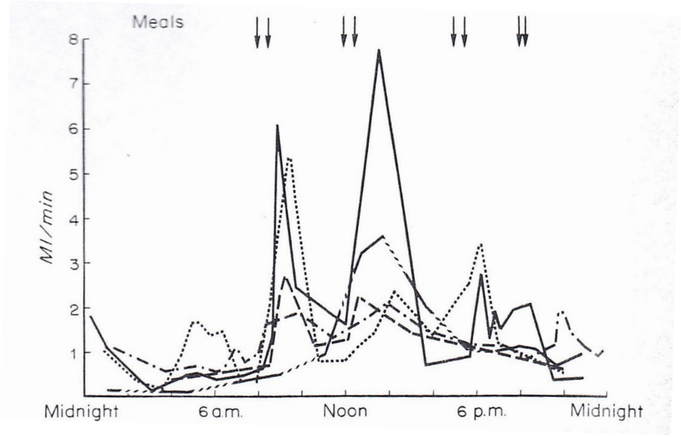
*mmol/kg contents (±1 SEM); †number of samples. In some cases areas of the large intestine did not contain enough material for analysis; ‡none detected (less than 0·1 mmol/kg).

Cummings et al , 1987

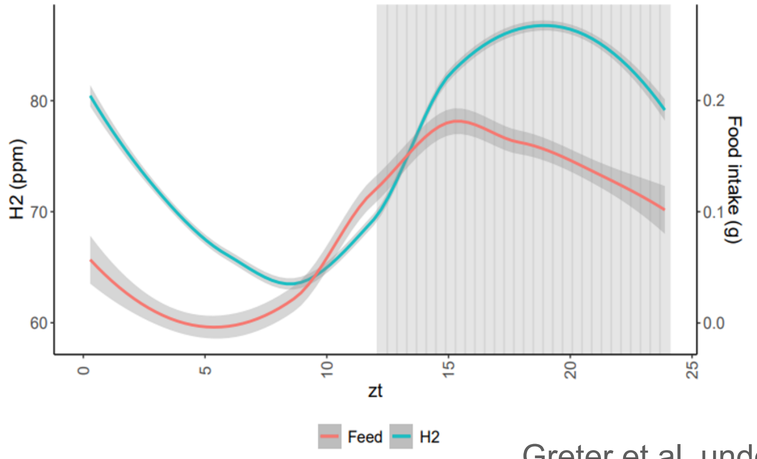


Turnbaugh et al , 1987

…are snapshots



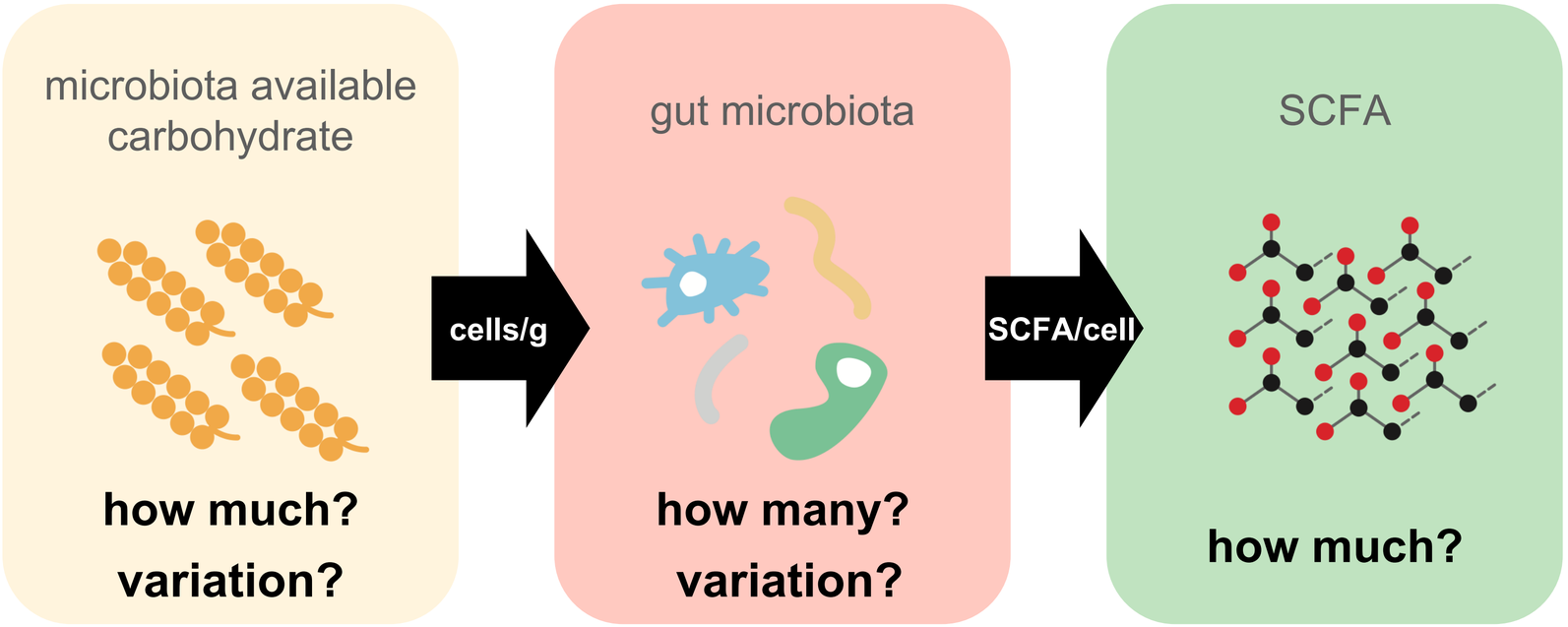
Phillips & Giller, 1973



Greter et al, under review

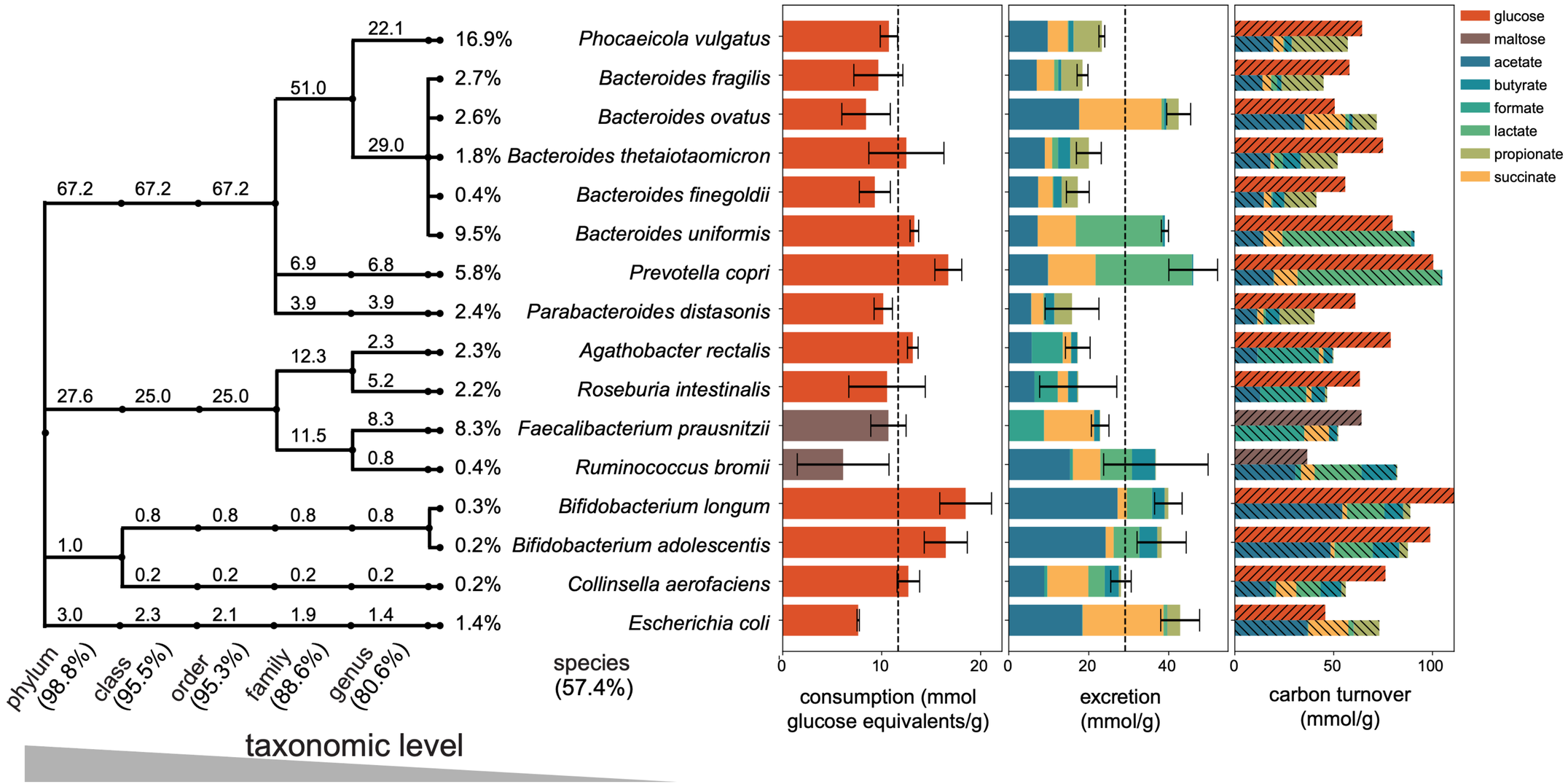
Quantifying the total FP harvest from a human gut microbiota

Jonas Cremer, Stanford

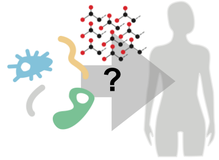


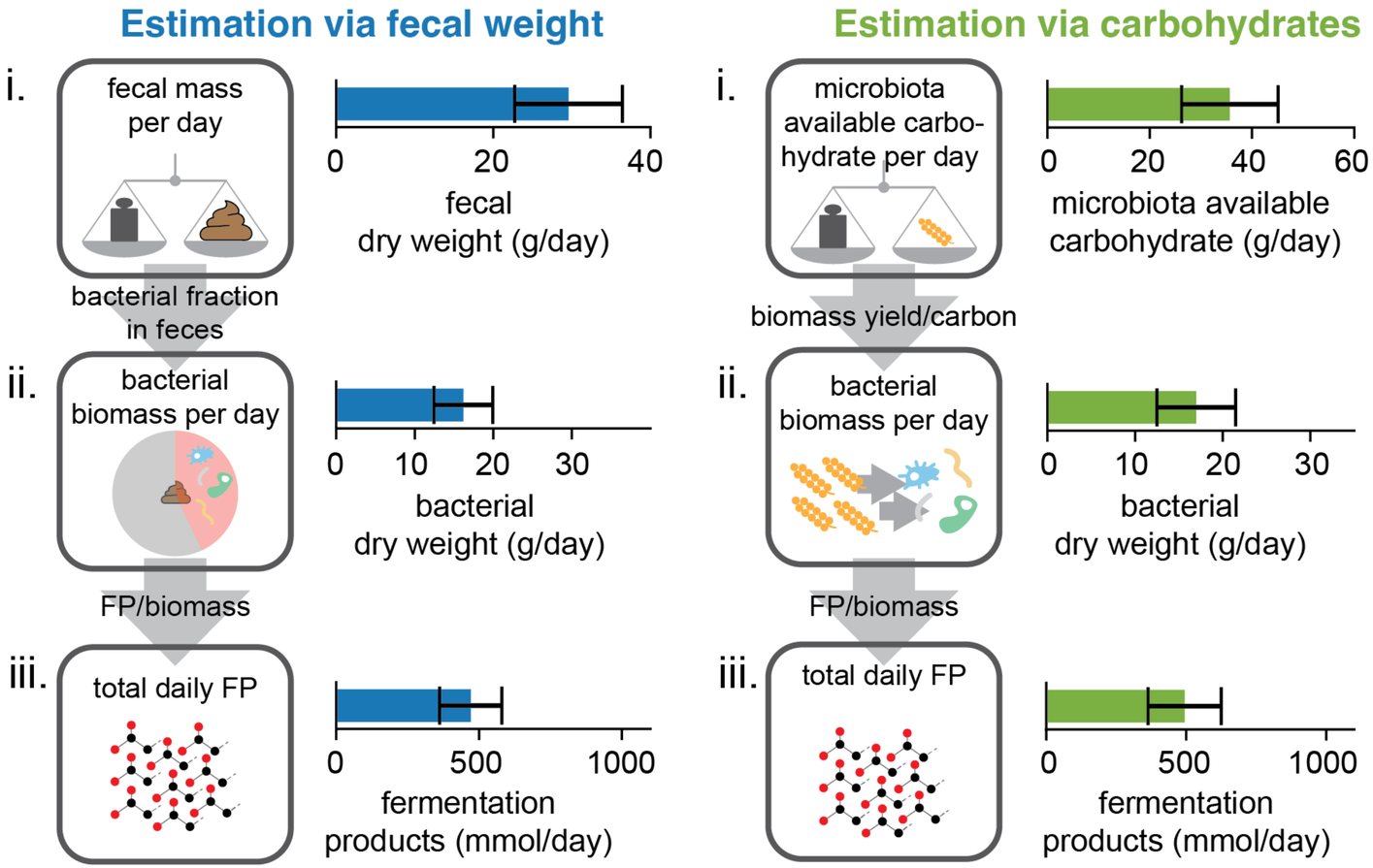
Estimating diversity in FP secretion

Claudia Moresi, ETHZ
Richa Sharma, Stanford

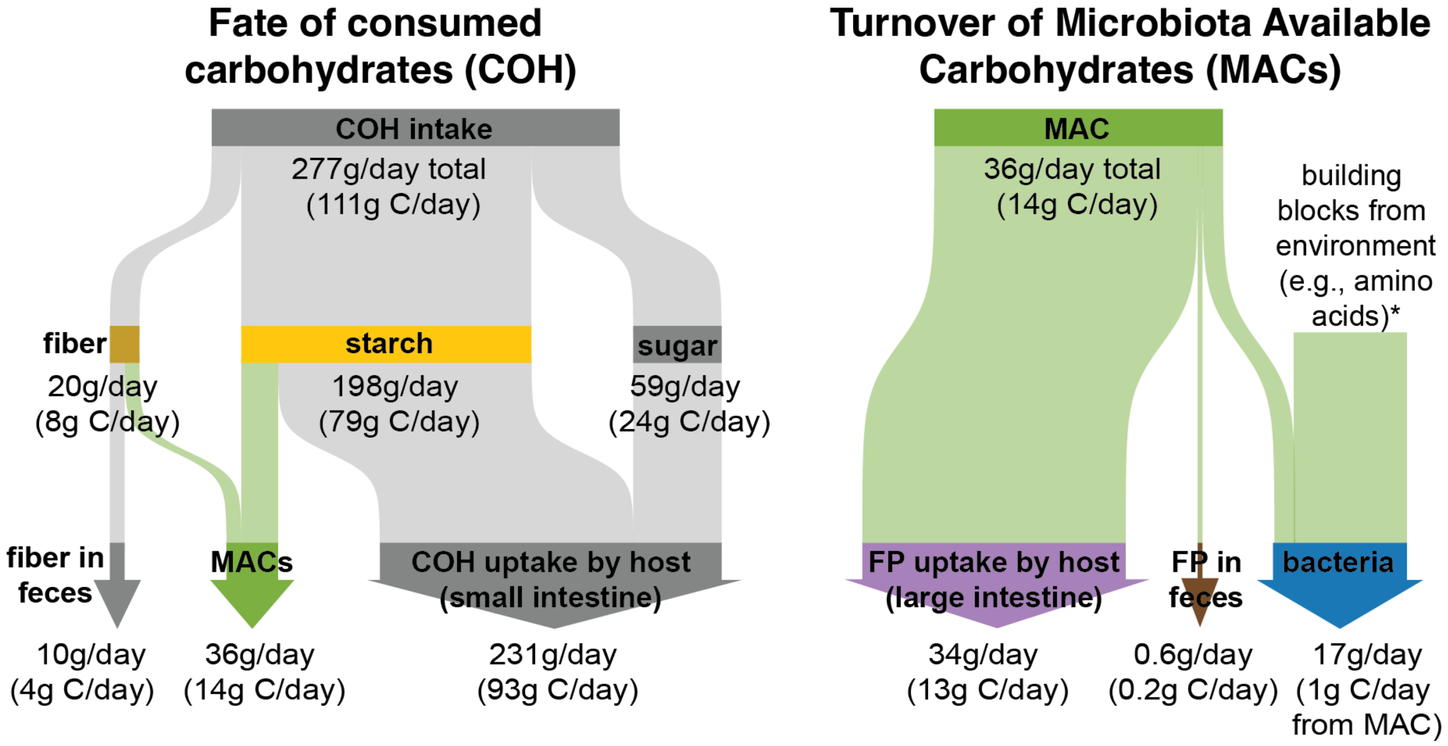


A point estimate for FP production

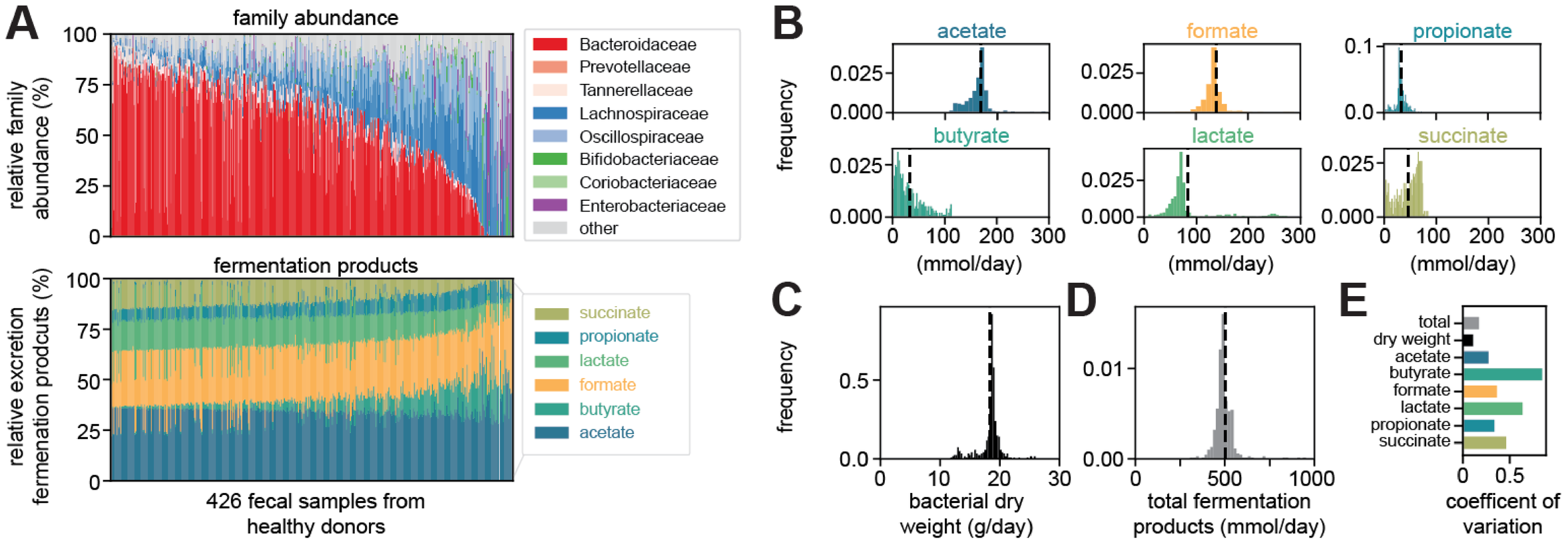




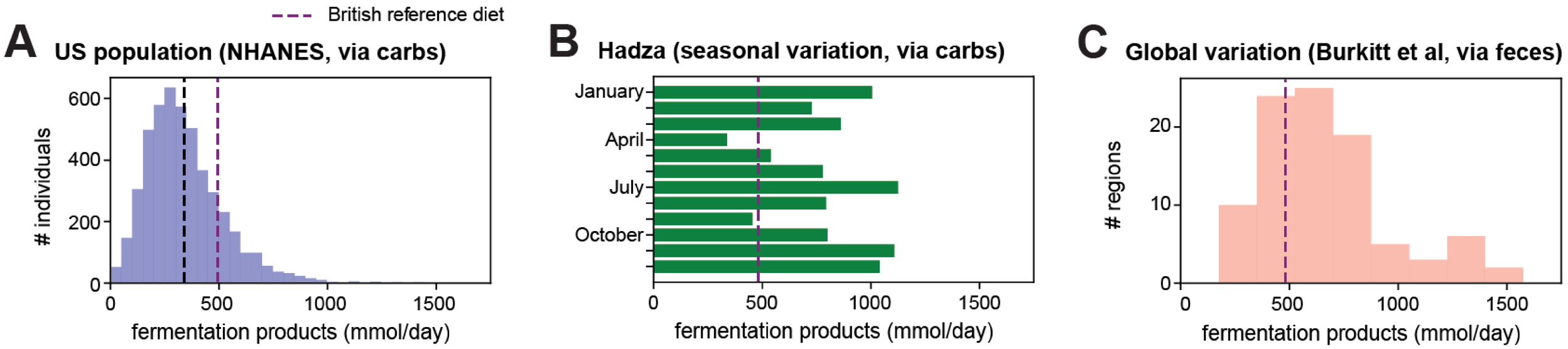
Fate of carbohydrates in a human host



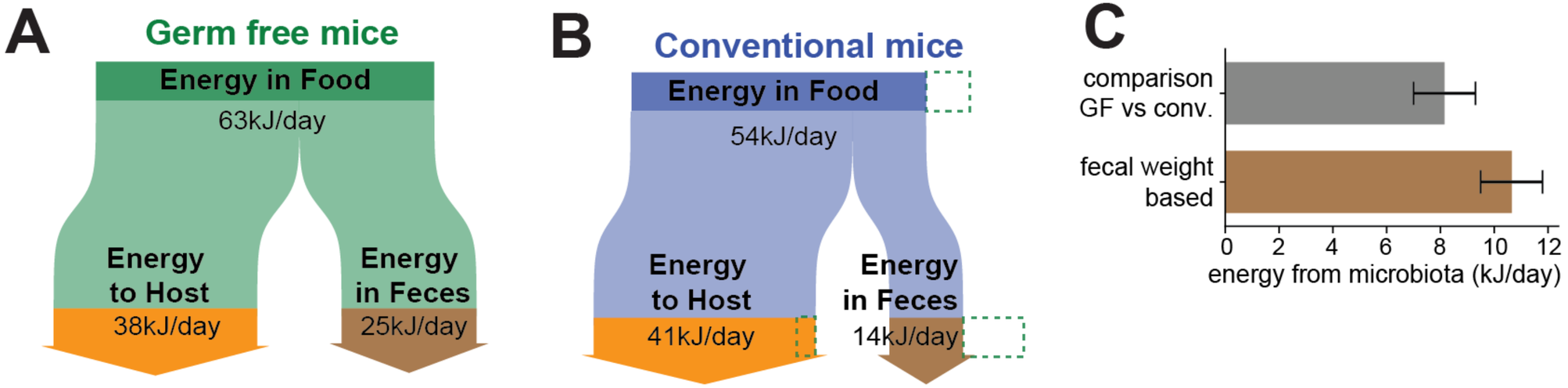
Variation with microbiota composition



Variation with diet and lifestyle

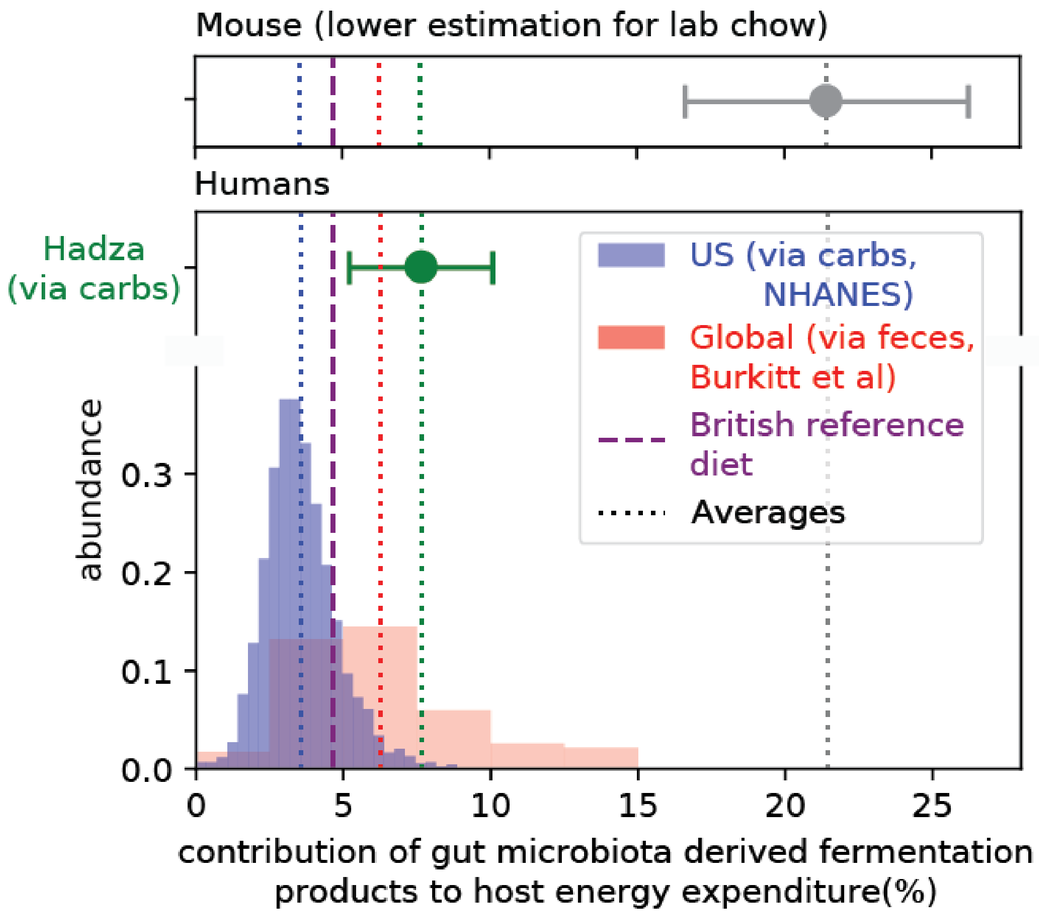


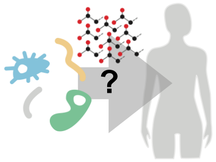
And in mice?



Data based on Hoces et al, PLOS BIOL 2022

Energy harvest from the gut microbiota across diets, life styles, and even species





We can provide a reference value for one of the main interaction routes between microbiota and host.

Microbiota composition does not play a major role in determining quantity of FPs.

Diet seems to be major determining factor.

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MUCOSAL IMMUNOLOGY

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NCCR MICROBIOMES

Global and local difference in FP load between humans and mice

global

70kg

30g

4.8mmol/kg/day

230mmol/kg/day

mice, relative to humans…

- **have higher systemic SCFA levels**
- **generate more energy form SCFA**
- **effects on satiety signaling, gut-brain axis…?**

local

SCFA have local effects
(immune regulation/activation, epithelial integrity)

70kg

30g

0.03m^2/kg

2.3m^2/kg

160mmol FP/m^2/day

100mmol FP/m^2/day

Casteleyn et al, 2010 (mouse)
Helander & Fändriks, 2014 (human)

Dependence of experimental FP and biomass yields on growth medium