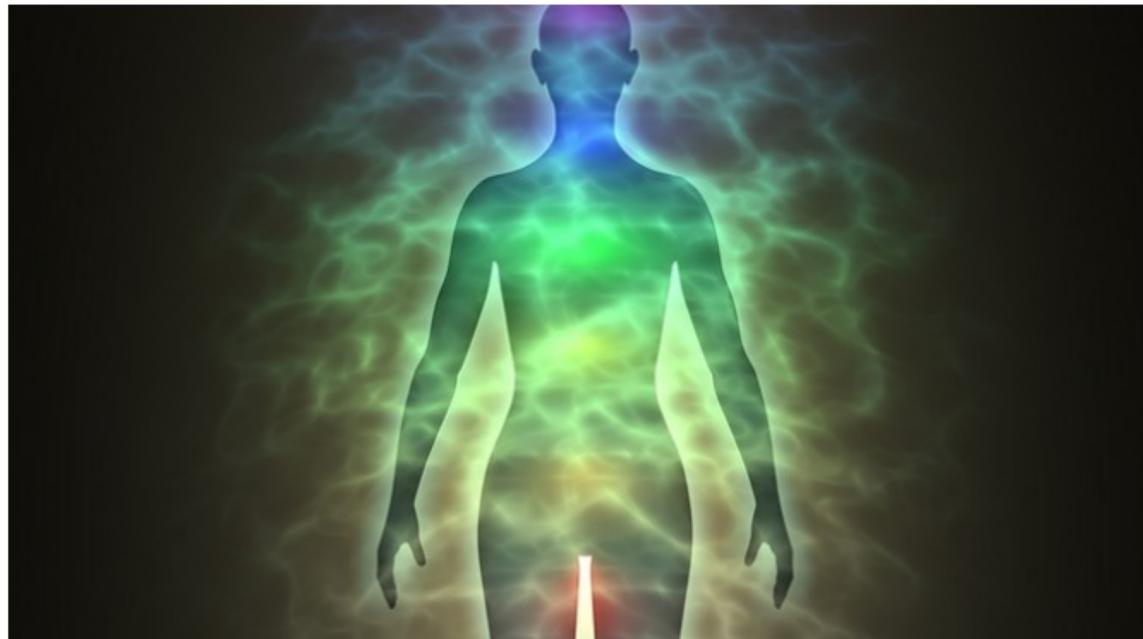


The human microbiome: from individuals to populations

Leo Lahti | leo.lahti@iki.fi | <http://www.iki.fi/Leo.Lahti>

University of Turku, Finland & VIB/KU Leuven, Belgium



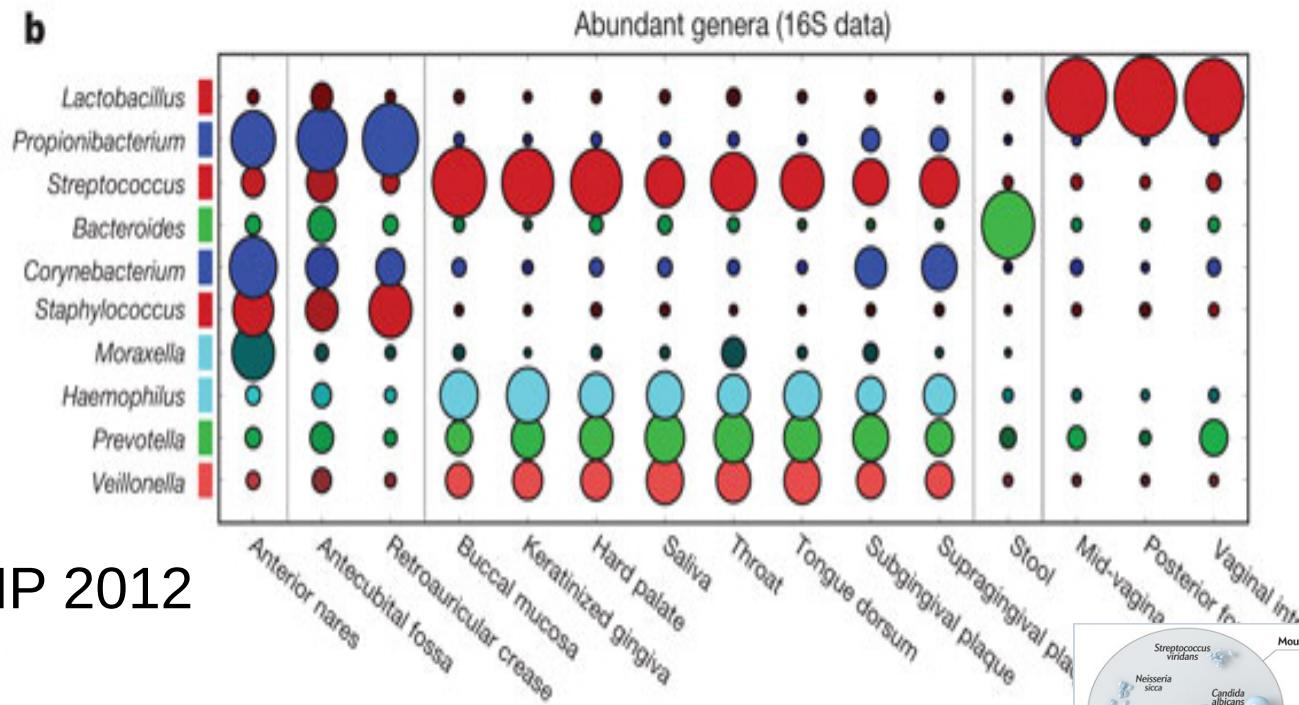
Emitting over 10 million biological particles per hour – personal cloud from cradle to grave. Meadows et al. PeerJ 2015 – Metcalf et al. Science 2015

Wednesday outline

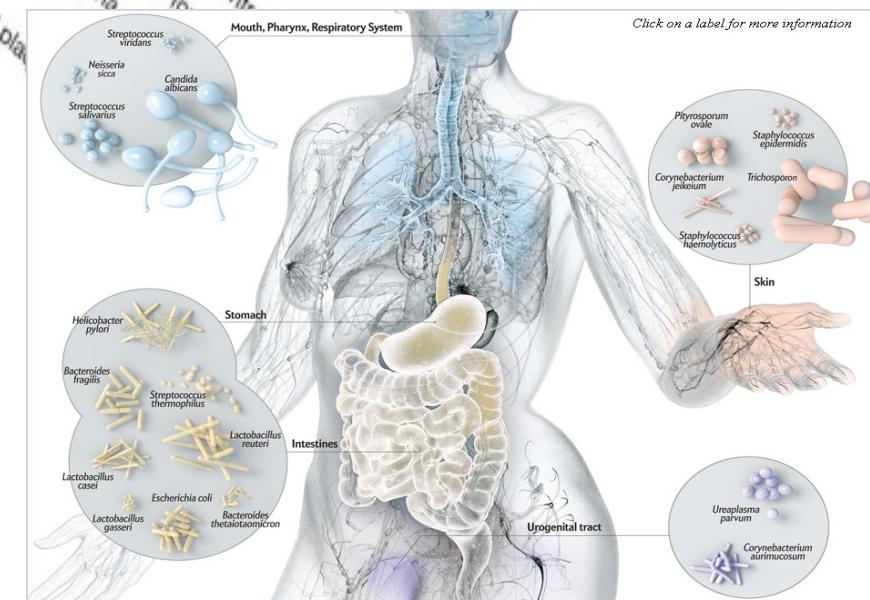
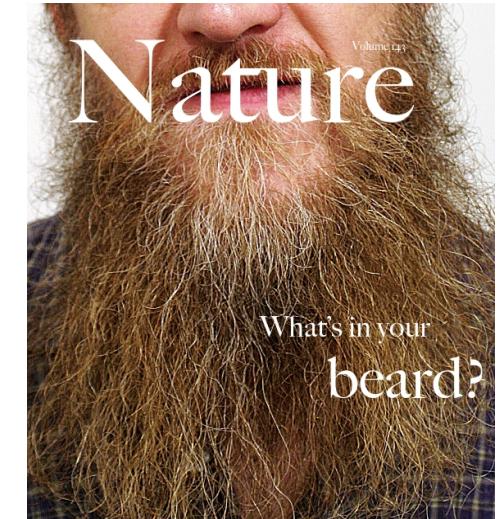
- Network pharmacology modelling to predict personalized drug combinations (Jing Tang)
- Tipping points in ecological networks (Vasilis Dakos)
- Evolving web of antagonistic interactions among digital organisms (Miguel A Fortuna)
- Tutorial: human gut microbiome population-level analysis (Leo Lahti & Karoline Faust)

Microbial composition differs among body sites

b



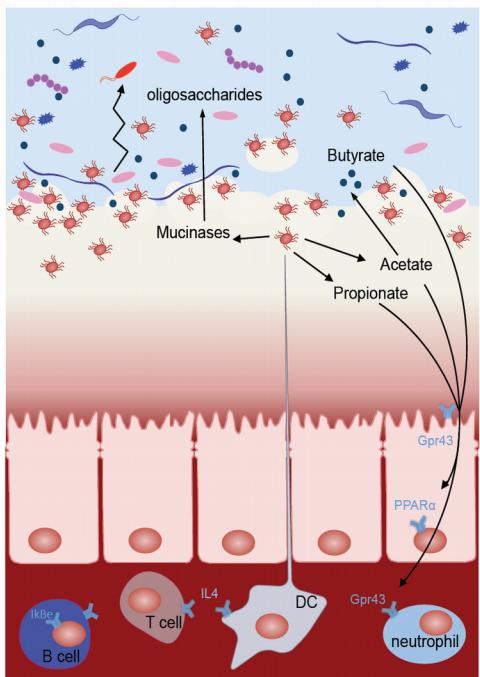
HMP 2012



Microbes live on all surfaces that interact with outside world

Gut microbiome inhabits 300-400 m² intestinal surface

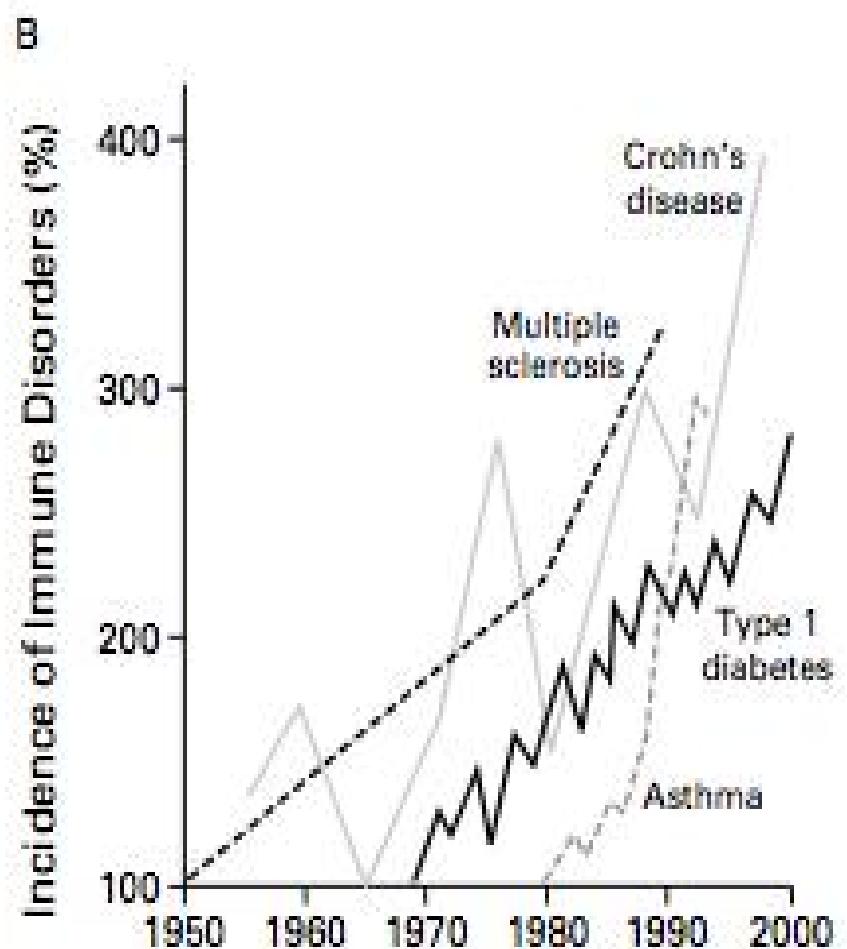
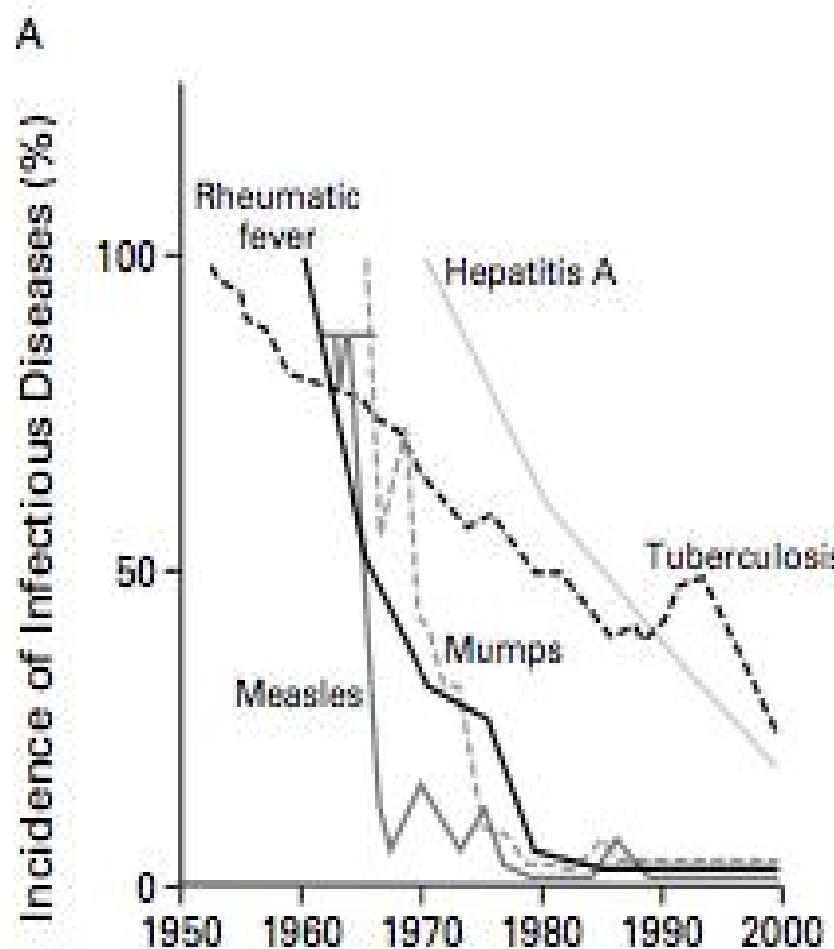
- ~ bacterial cells outnumber our own
- ~ 100 billion bacteria / gram in the gut
- ~ 10,000 gut bacterial species
- ~ 10M uniq genes (500x human genome)
- ~ Plastic, varies in time



Brussel central square flower carpet



Diseases linked to gut microbiome have become more prevalent !



Reality check: We don't even know what a healthy flora means!

Microbiome state-of-the-art:

MetaHIT, HMP + specific lab studies combined 2-3000 individuals,
still biased cut of the population



Genetics: 10.000-100.000s
individuals profiled

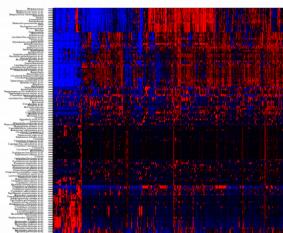
Variation in clinically relevant population = unknown
Temporal variation = largely unknown
Factors influencing gut flora composition = largely unknown
Effect environment = unknown

Clinical end points for functional foods, pre-/pro/synbiotics, pharma-/nutriceutical interventions etc are *unknown*

Data availability: large & standardized population cohorts

HITChip Atlas (microarrays):

- > 10,000 samples
- > 5,000 subjects
- > 1,000 phylotypes (~0.1%)
- versatile geography
- highly reproducible (>98%)
- long follow-ups (10+ y)
- open data: Lahti et al. 2014



Challenges for data availability:

- Protocol & metadata standardization
- Custom tools & reproducible workflows
- Ethical considerations

Analysis & visualization tools:
<http://microbiome.github.io>

Other collections: MetaHIT, Human Microbiome Project, American Gut...

HITChip Atlas: Gut microbiota high-throughput profiling
10,000 samples ~ 5000 individuals ~ 1000 phylotypes
-> Microbial composition is individual and variable !

Highly standardized & reproducible platform

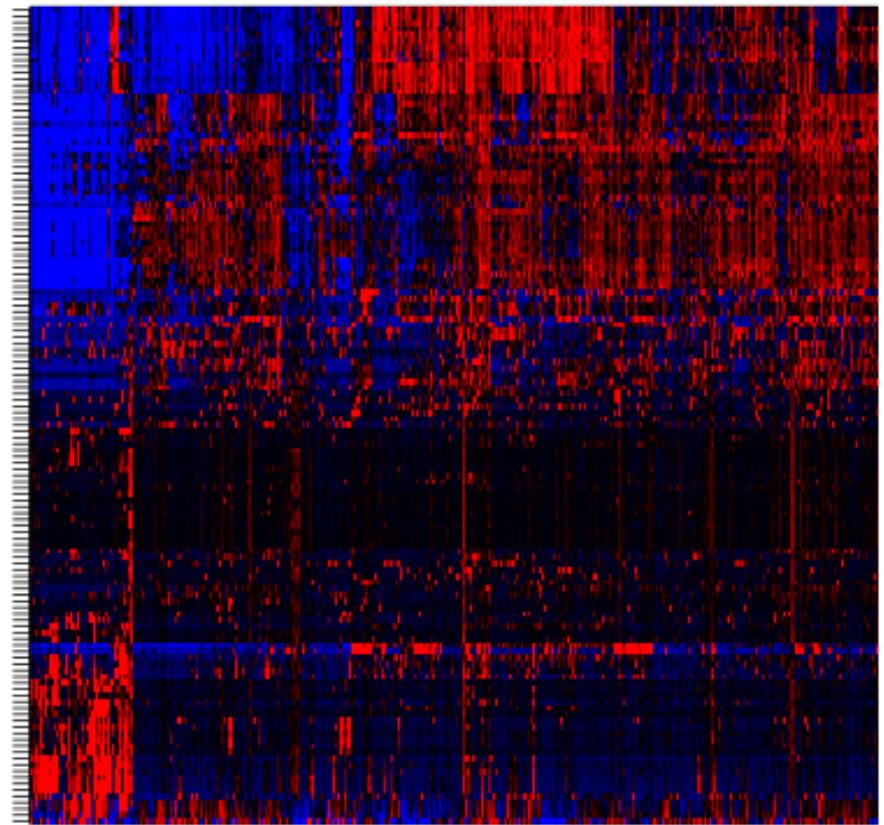
Deep phylotype level profiling

Open data & source code: Lahti et al. Nature Comm. 2014



1000 bacterial phyotypes

$N \sim 10,000$

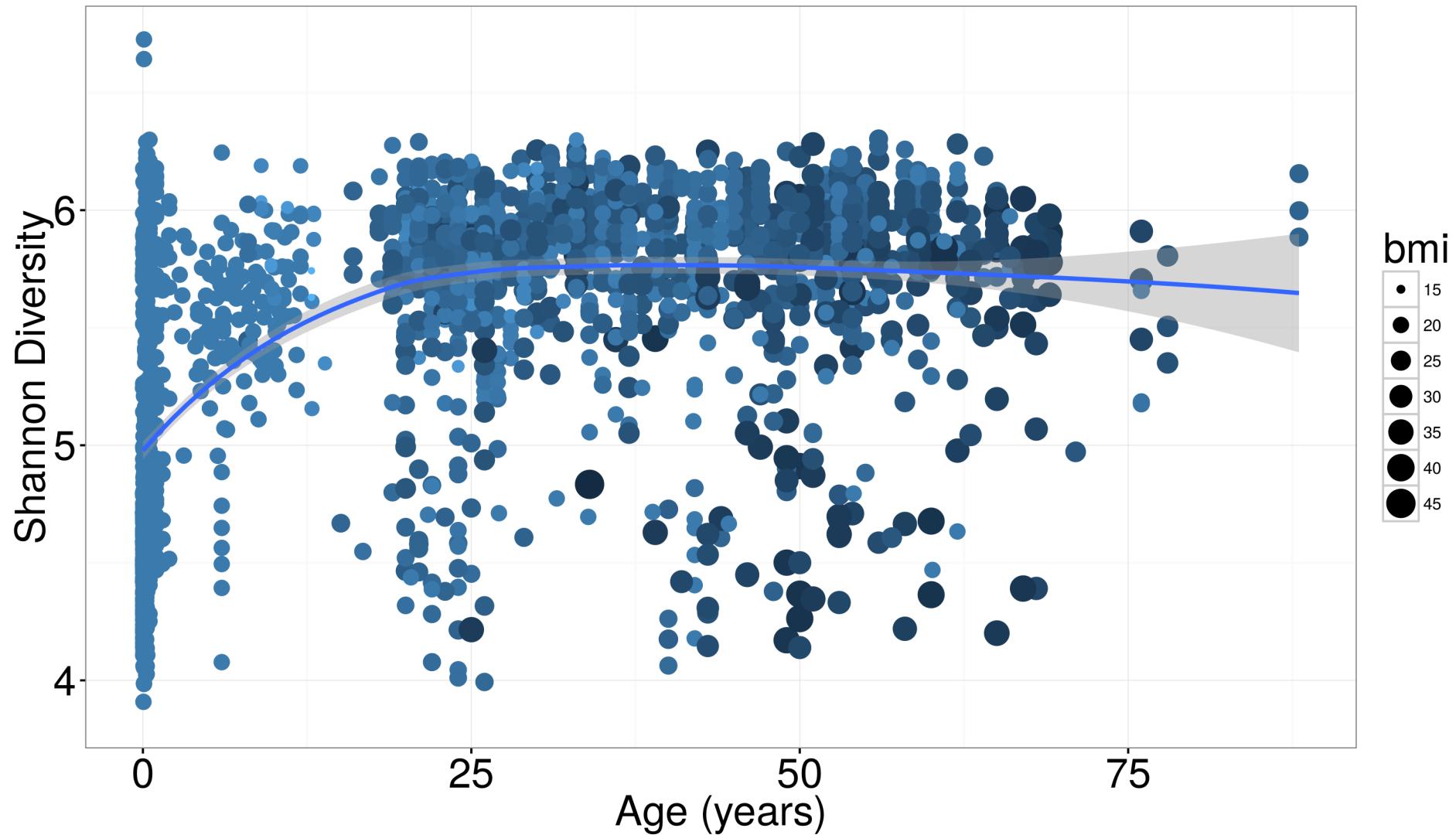


<http://microbiome.github.io>

Standardized – cost efficient – accurate at 0.1% relative abundance
Rajilic-Stojanovic et al. Env. Microbiol. 2009

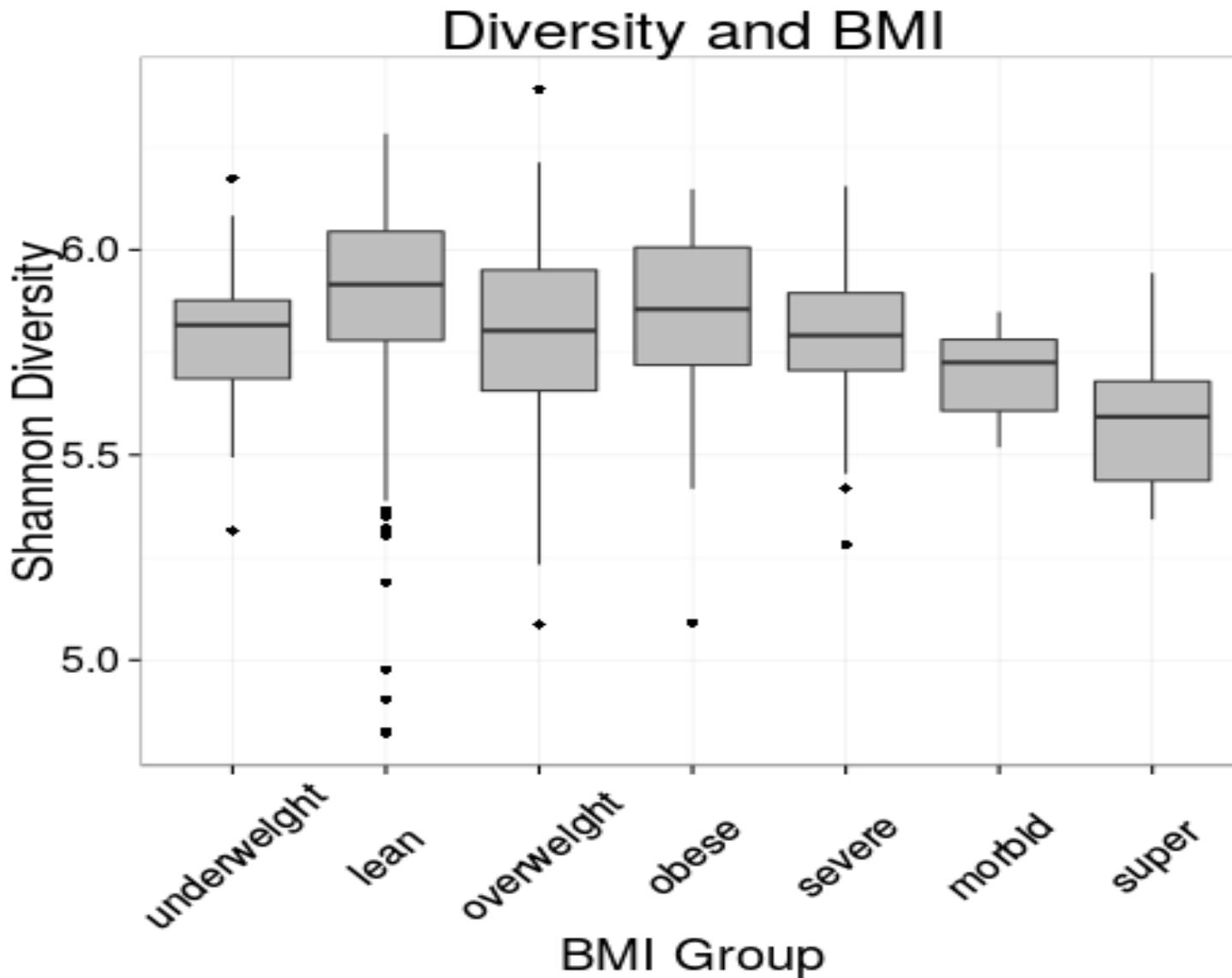
Microbiome diversity and age: healthy & normal obese subjects

N = 2363



Data: HITChip Atlas;
healthy fecal RBB samples

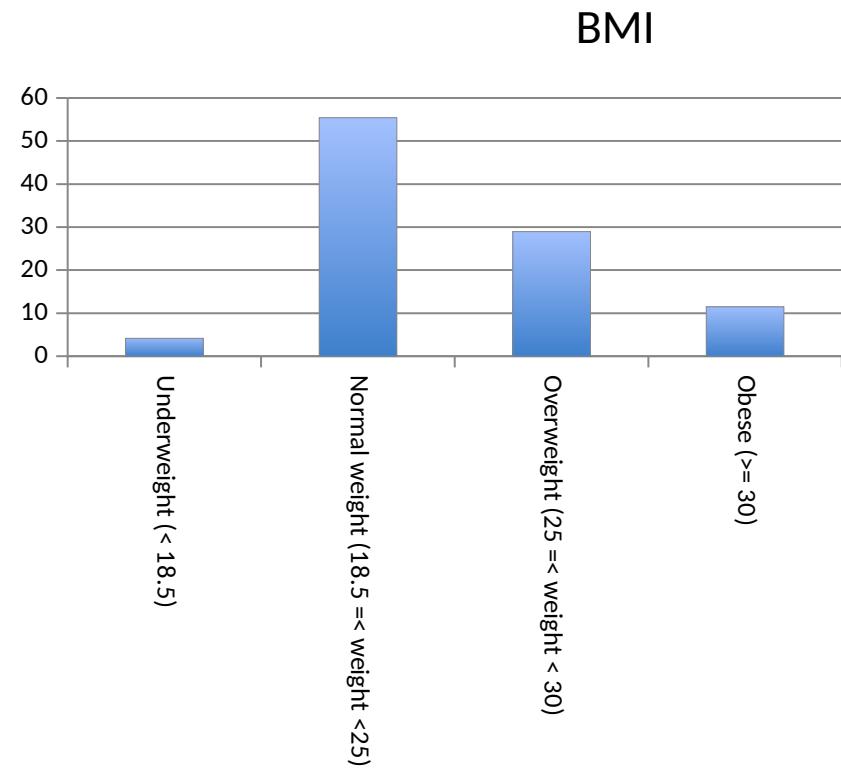
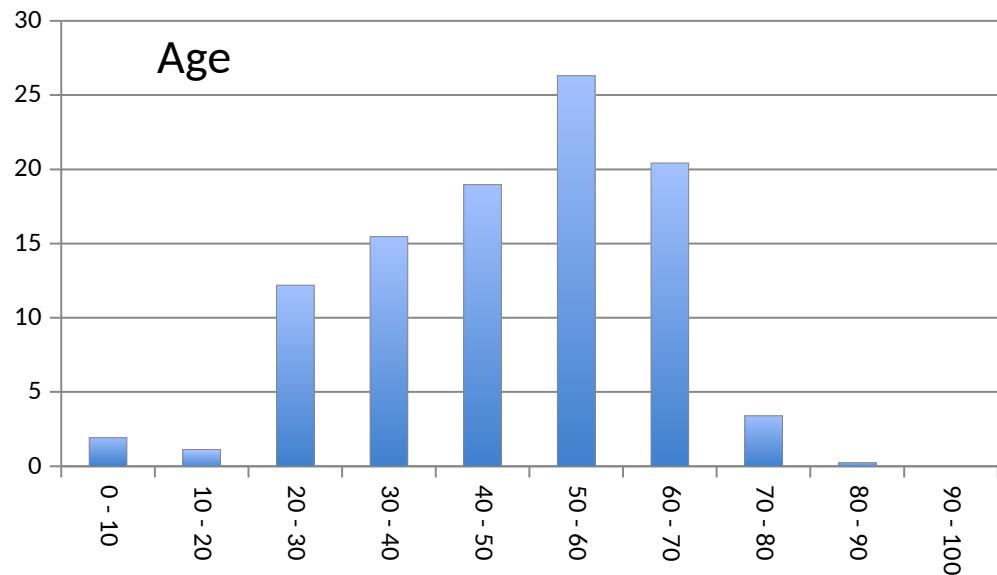
Microbial diversity decreases with obesity



Flemish gut flora project: longitudinal study of +-5000 volunteers spread over a confined geographic region



Population statistics in Flemish Gut Flora Project

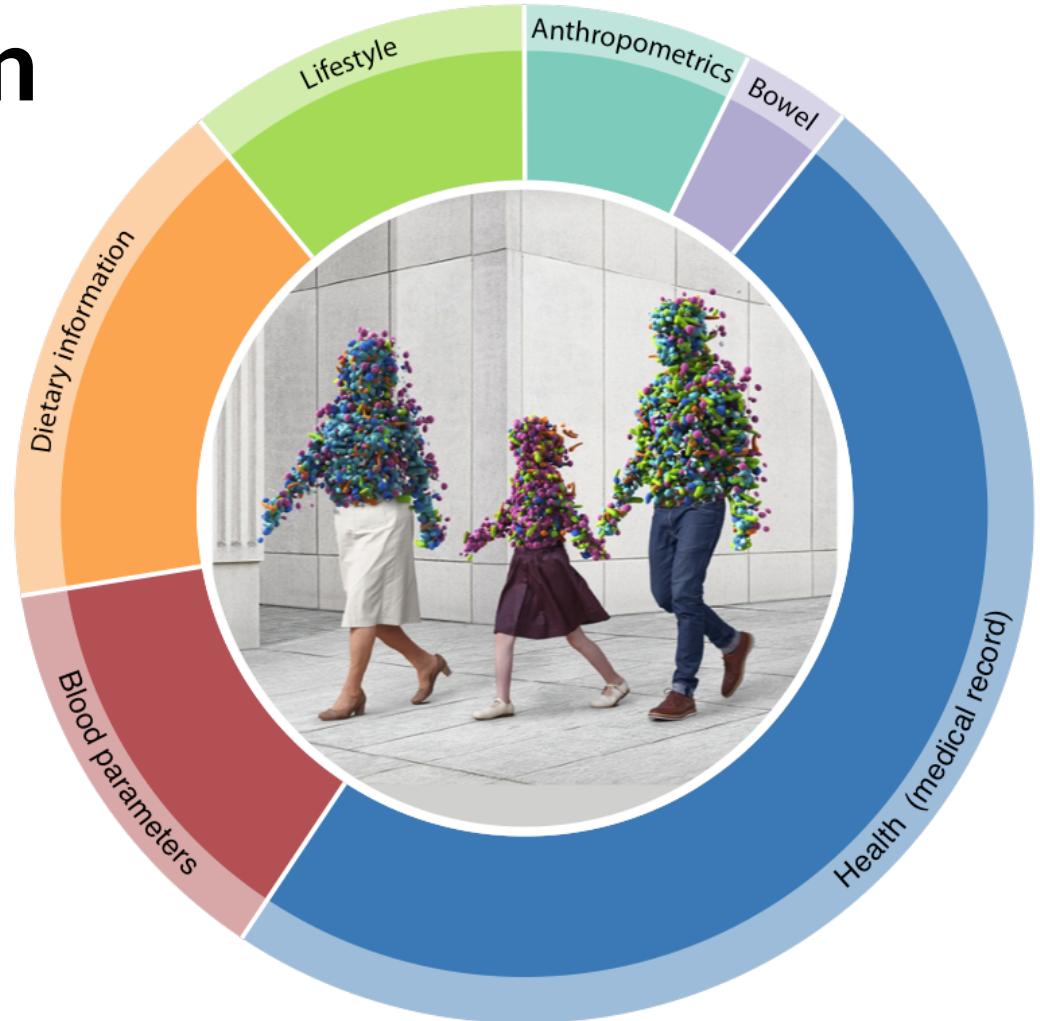


40/60 M/F ratio

98.5% of Western or Eastern European ethnicity; 96.8% born in Belgium

FGFP sample collection

- Collection of faecal, blood (GP) and saliva samples
 - Questionnaires:
 - Self-reported health
 - Detailed health (GP)
 - Diet (incl probiotics, drugs)
 - Wellbeing/QoL
 - Hygiene
 - Bowel habit/Bristol scale
 - Travel, Stress etc
 - Blood analysis: metabolic (e.g. glucose, HDL triglycerides, insulin,...) and immunological/inflammatory readouts (cell interleukins, CRP,...)
 - Secured database, patient encoding



Het Vlaams Darmflora-project	
Stoelgangscore	
www.vdb.be/darmflora	
	 Universiteit Gent
	
Via onderstaande kleuren en beschrijvingen kan je je stoeling een score tussen 1 en 7 geven. Schrijf deze code op het stickerlabel en breng dit bij de hand-wasser die je vandaag vingerspoelt!	
	Score 1 Hartie, losse krentels. Meestal moeizig.
	Score 2 Saengerklaafdekkende krentels
	Score 3 Wermoechte moeizig. Brokkelig van structuur.
	Score 4 Wermoechte moeizig. Zacht en glad van structuur.
	Score 5 Zacht, makkelijk te openen. Dekkende, slappe consistency.
	Score 6 Zacht en niet-indeelbaar. Ook makkelijk te openen.
	Score 7 Tikkende moeizig, geen structuur aanwezig. Gedekt vloeiwater.

Het Vlaams Darmflora-project

Staalkaartje
www.bbv.be/darmflora

 Universiteit Gent

 Vlaams
Regering

Dit kaartje moet je niet te bewaren voor je steekproef. Houd het volledig bij de hand & vulten je de online vragenlijst (zie de link in de vorderen ontvangers) nu wél a! (het "Steekproefblad").

Naam: _____

Voornaam: _____

Datum staalkaartje: _____

Tijdsduur staalkaartje: _____

Vorige oefening: Minder dan 4 sur geleden
 Tussen 4 en 12 sur geleden
 Tussen 12 en 18 sur geleden
 Tussen 18 en 24 sur geleden
 Tussen 24 en 36 sur geleden
 Tussen 36 en 48 sur geleden
 Langer dan 48 sur geleden

Onderstaand je steekproefnummer: 1 2 3 4 5 6 7

13 / 59

Current status: 3400 sample sets collected

Core microbiota, healthy western adults (n=456)

Top-10 genus-level groups

Faecalibacterium prausnitzii et rel.
Ruminococcus obeum et rel.
Subdoligranulum variable at rel.
Dorea formicigenerans et rel.
Oscillospira guillermondii et rel.
Lachnospira pectinoschiza et rel.
Bifidobacterium
Clostridium symbiosum et rel.
Clostridium orbiscindens et rel.
Clostridium sphenoides et rel.

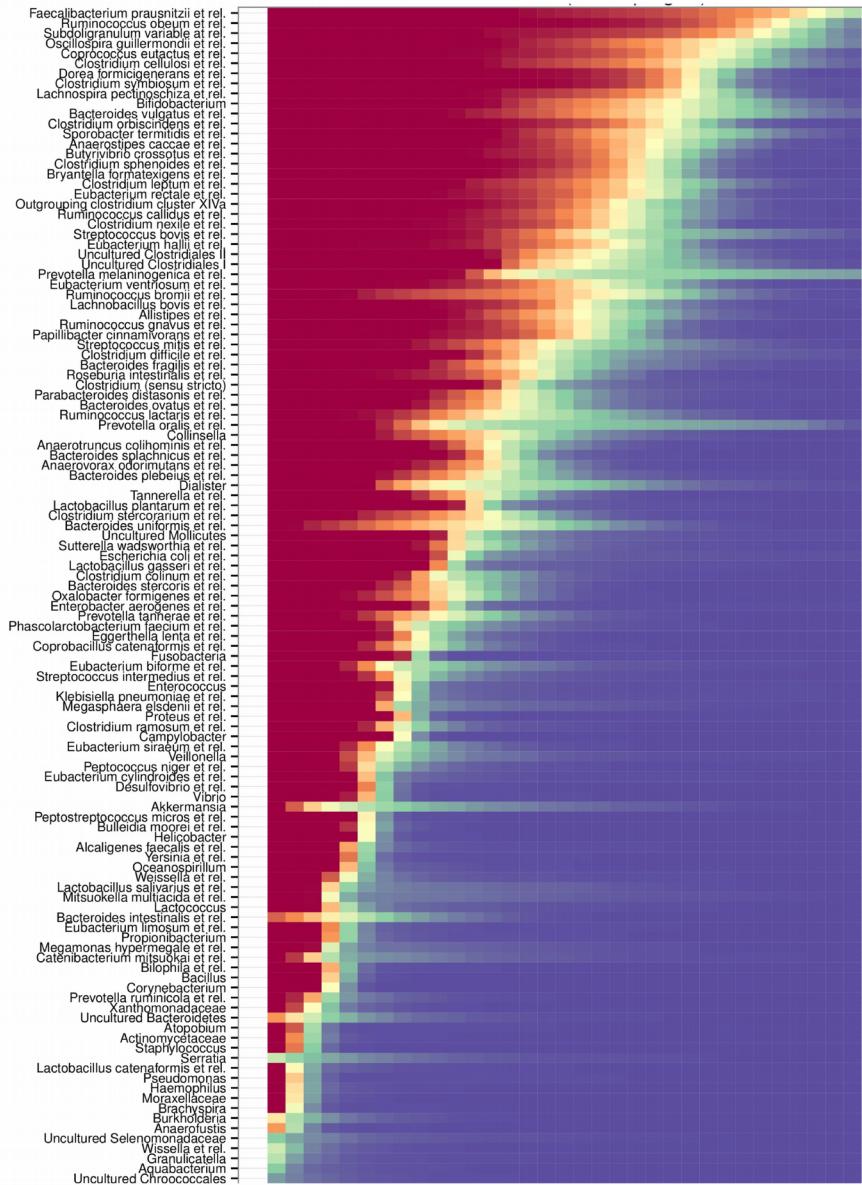
Jalanka-Tuovinen et al. (2011) PLoS One

6:e23035

Salonen et al. (2012) Clinical microbiology and
infection 18:16–20.



Code: [microbiome.github.com](https://github.com/microbiome/gut microbiome)



Detection threshold (abundance)

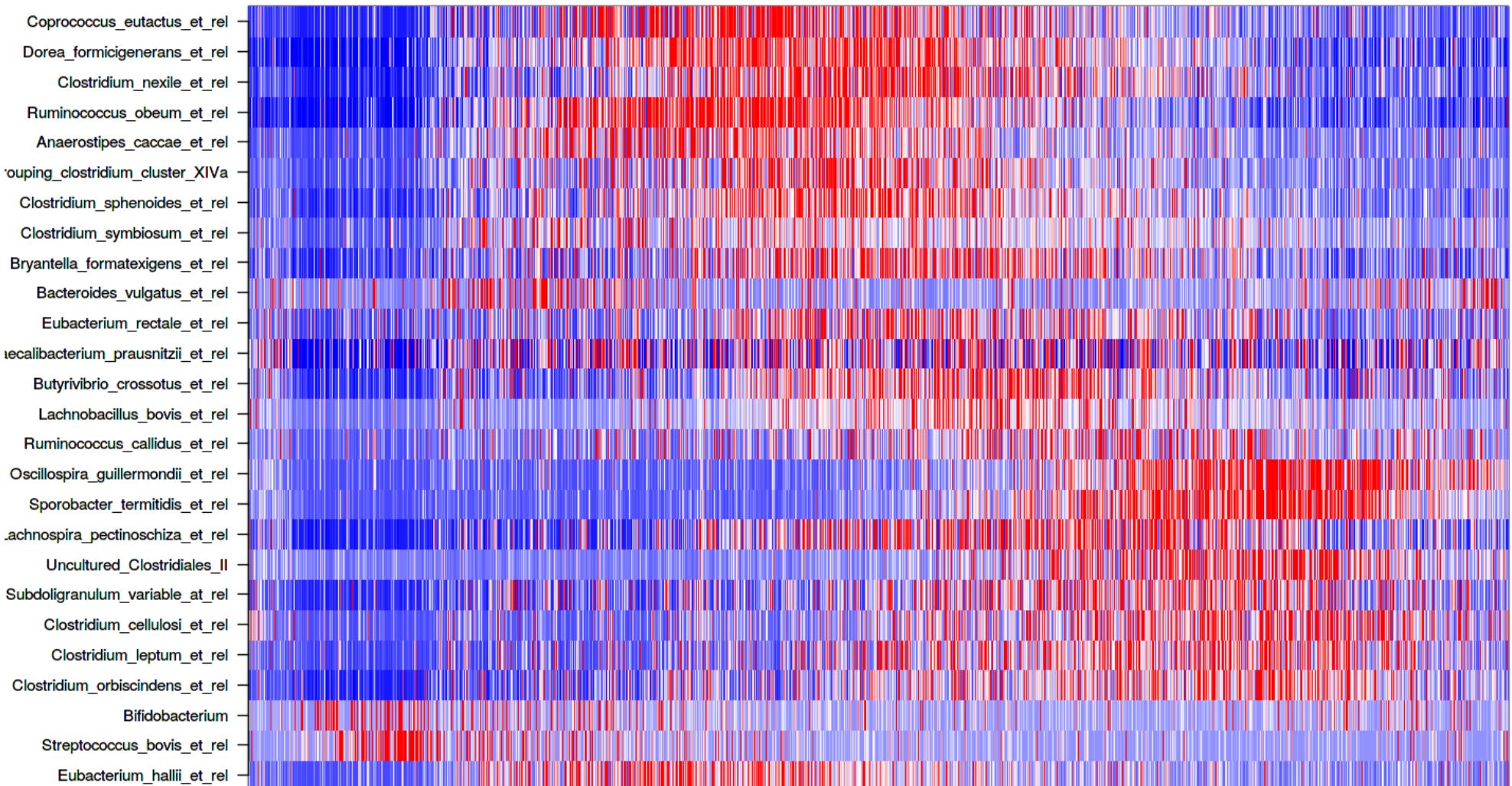
HITChip Atlas. Shetty et al. FEMS Microbiol. Reviews 2017, fuw045.
Data from Lahti et al. Nat Comm, 2014.

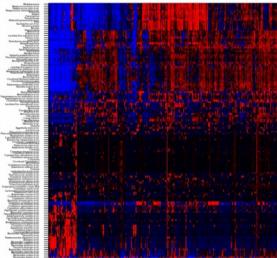
Abundances of the shared core taxa are highly individual

Z-score across subjects: **red – high abundance & blue – low abundance**

Core microbiota shows remarkable variation across population.

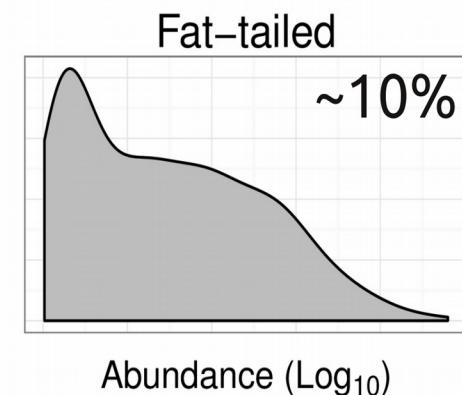
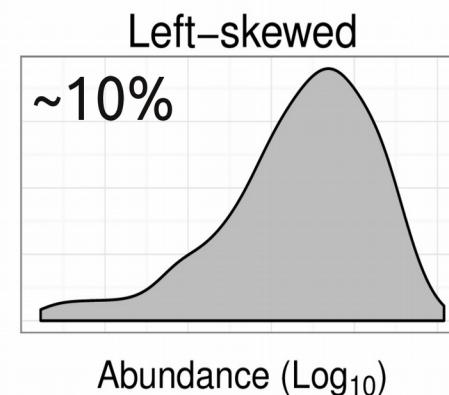
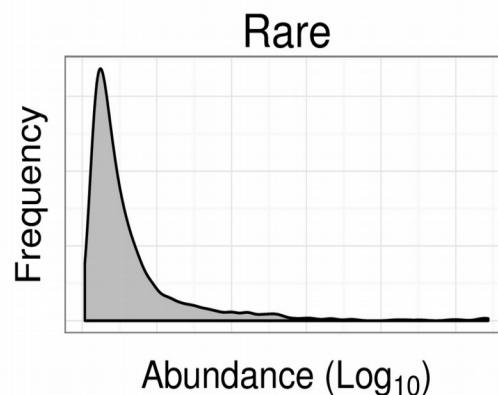
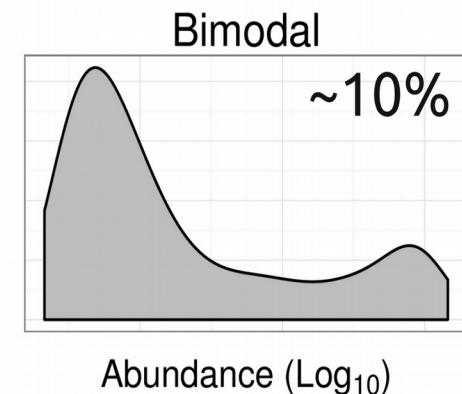
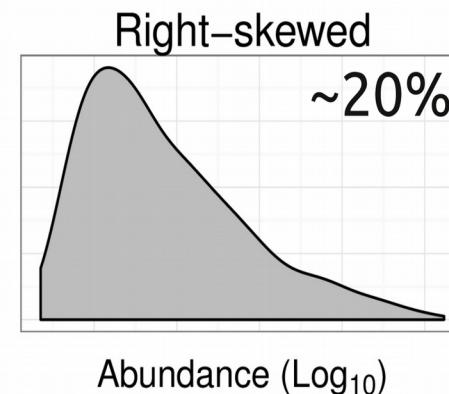
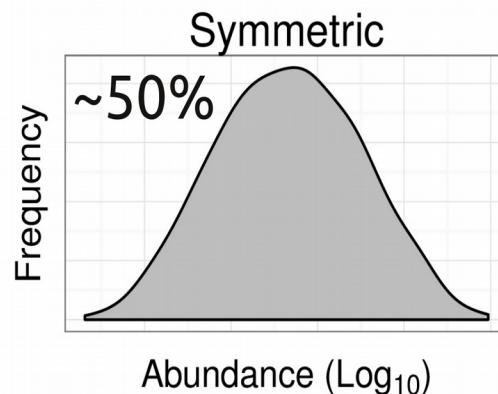
(HITChip Atlas; N = 5005)





Bacterial 'abundance types' in 1000 western adults:

~% indicates proportion among prevalent taxa

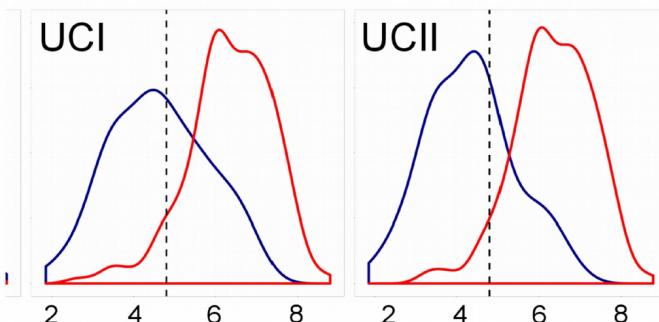


Effect on the overall ecosystem

Prevotella states seen at ecosystem level

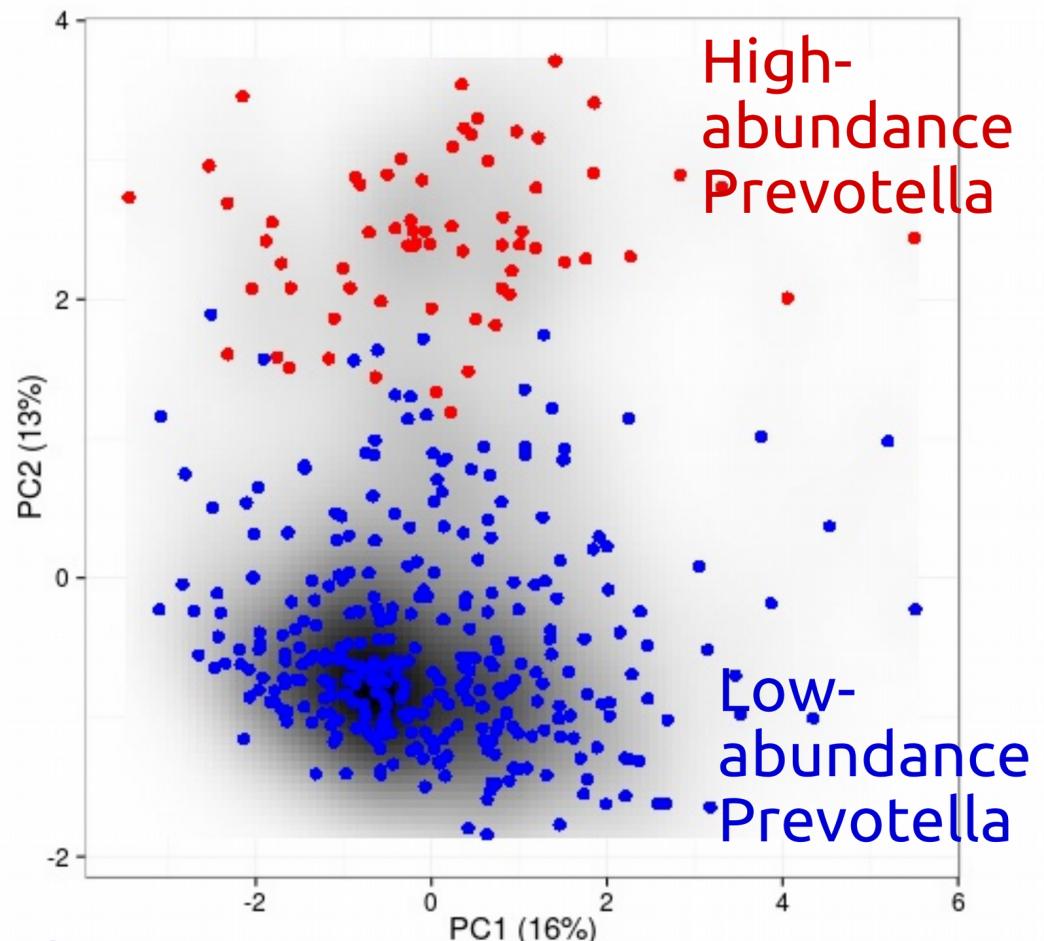
High ~10% relative abundance !

Other bi-stable taxa:
<2% relative abundance,
no ecosystem-level switches are visible



Uncultured Clostridiales associated with overall metagenomic richness

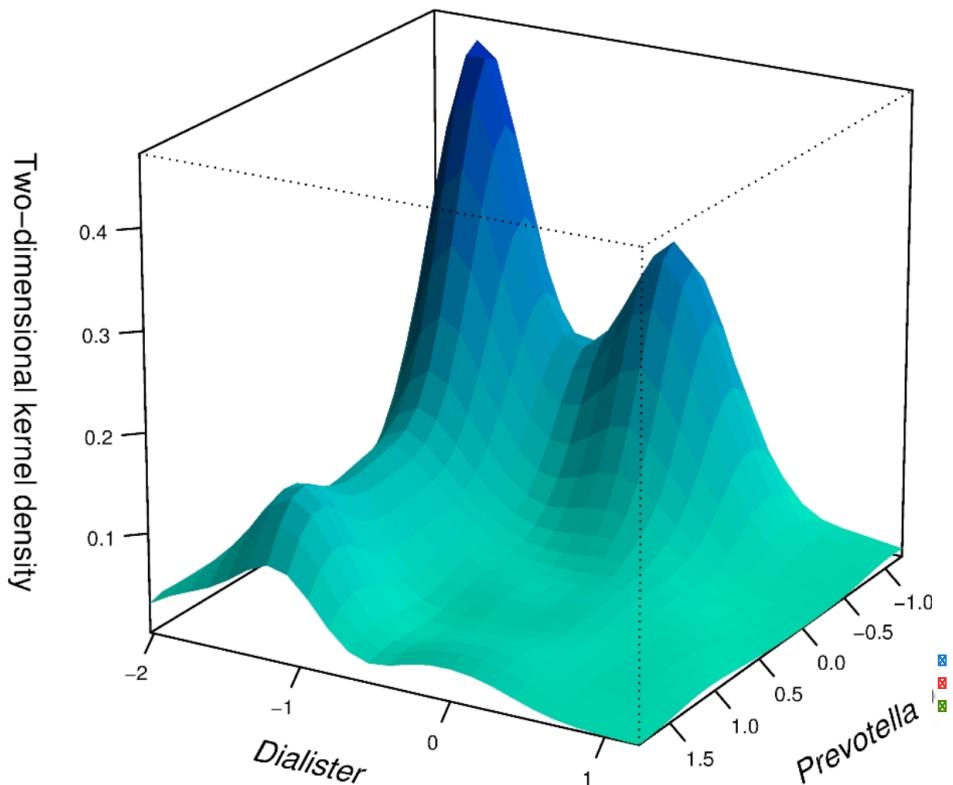
PCA +
Correlation (Spearman)



N = 401 western adults

Enterotype landscape of the Flemish Population shows density peaks of 'preferred' ecosystem constellations

(B)



B

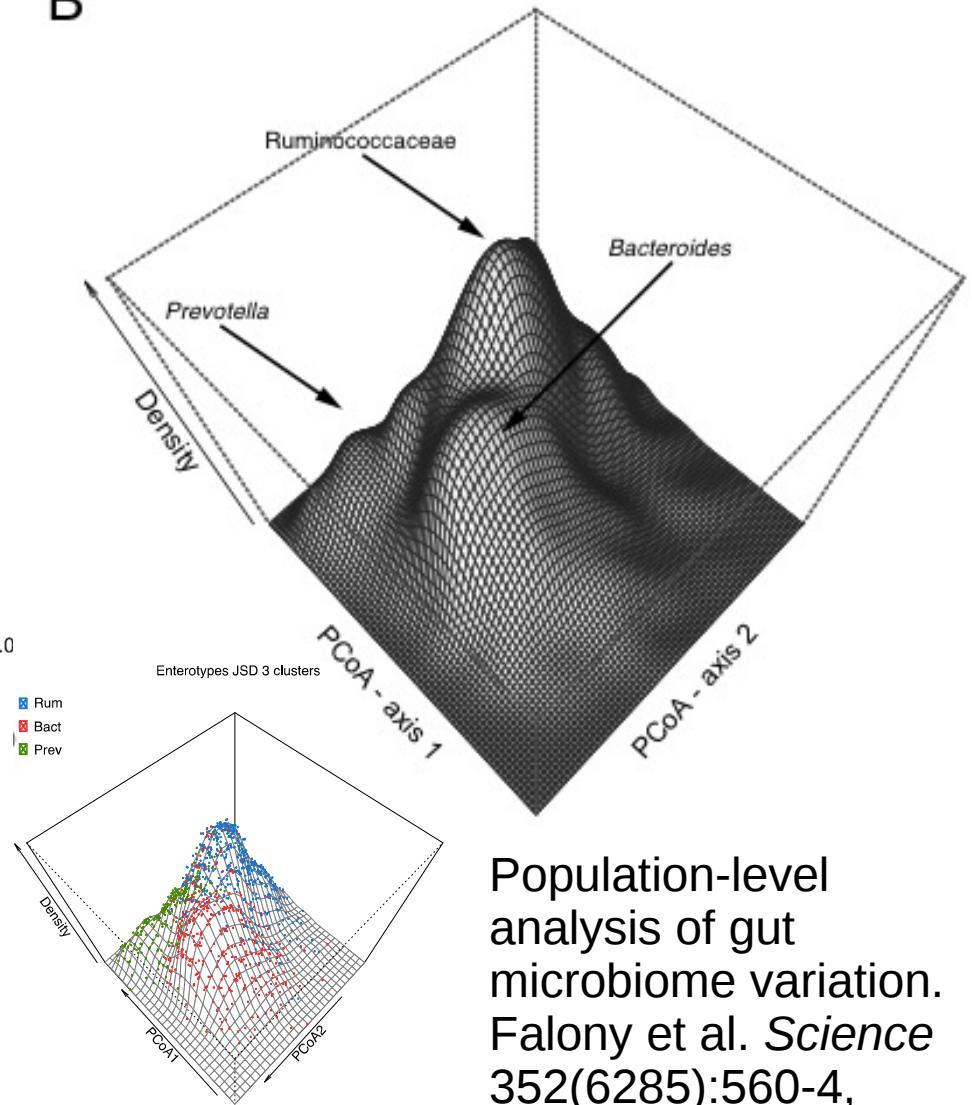
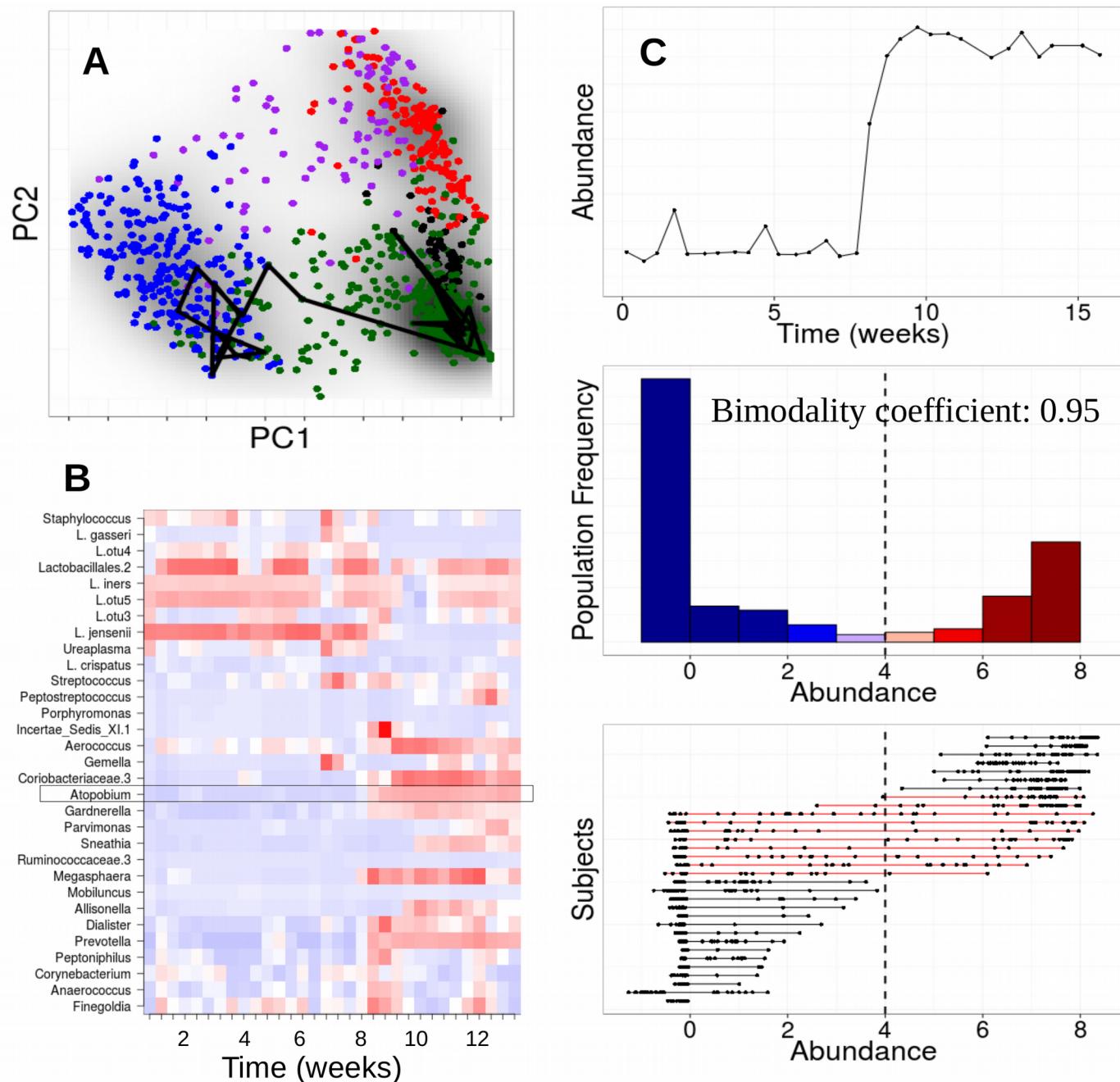


Figure: Intestinal microbiome landscaping: insight in community assemblage and implications for microbial modulation strategies.
Shetty et al. 2017 FEMS Microbiol Rev.
2017 – Data: Lahti et al. Nat Comm 5:4344, 2014

Population-level analysis of gut microbiome variation.
Falony et al. Science 352(6285):560-4, 2016

Community states and dynamics in normal vaginal microbiome of reproductive-age women

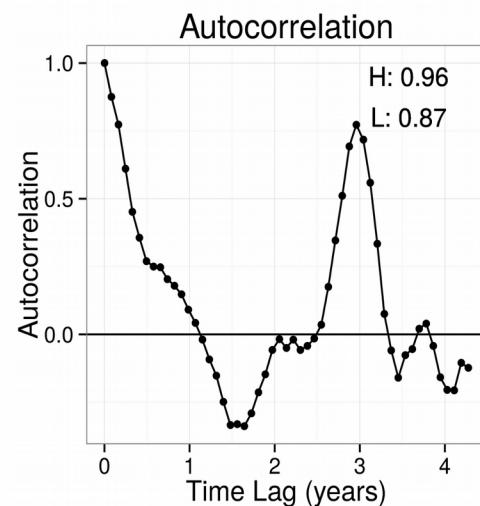
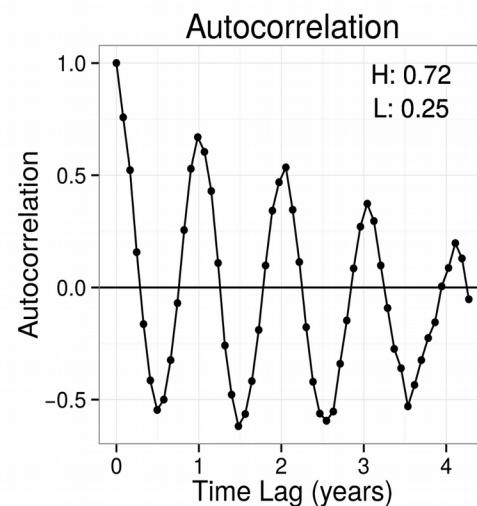
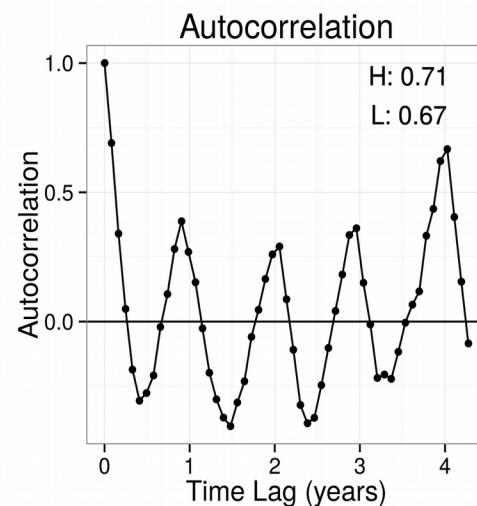
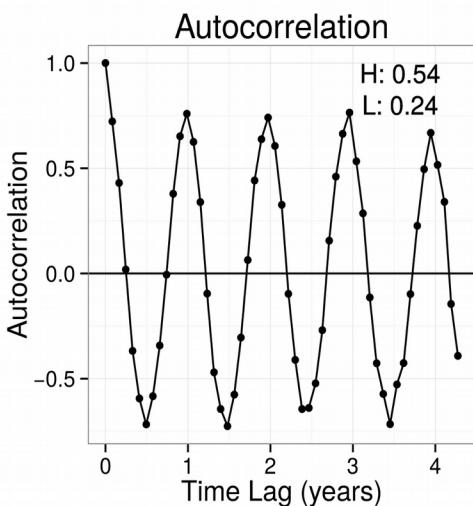
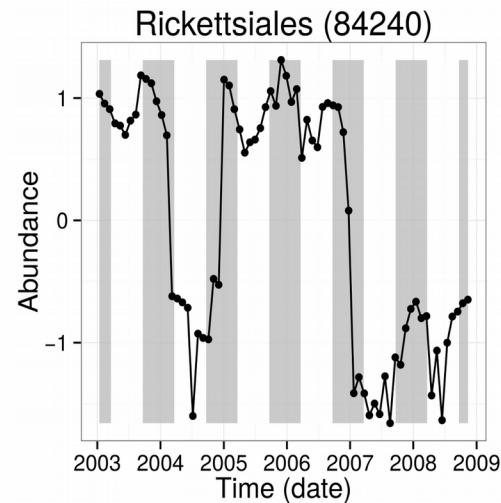
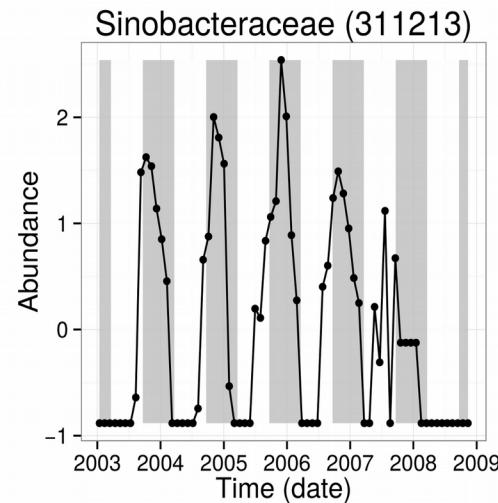
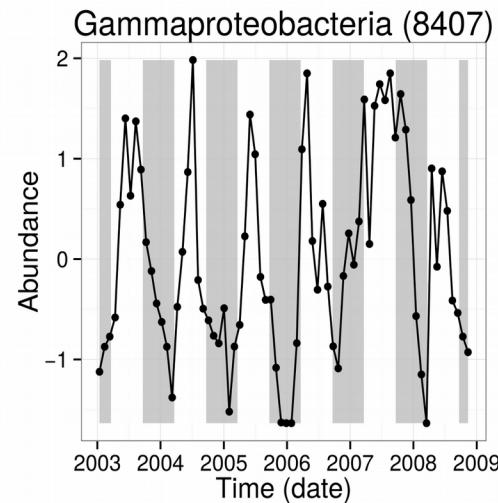
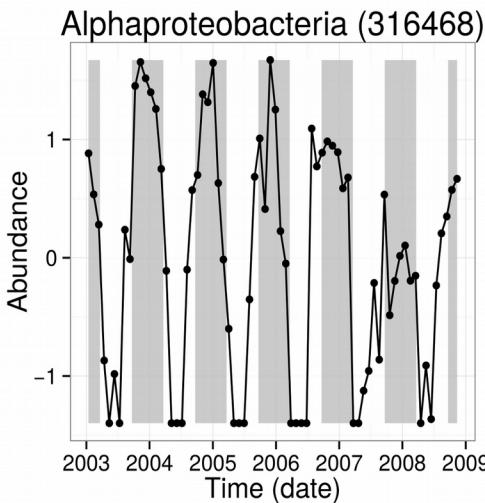
Figure: Faust et al. Curr.
Op. Microbiol. 2015
Data: Gajer et al. 2012



Periodicity, Chaos, and Environmental factors

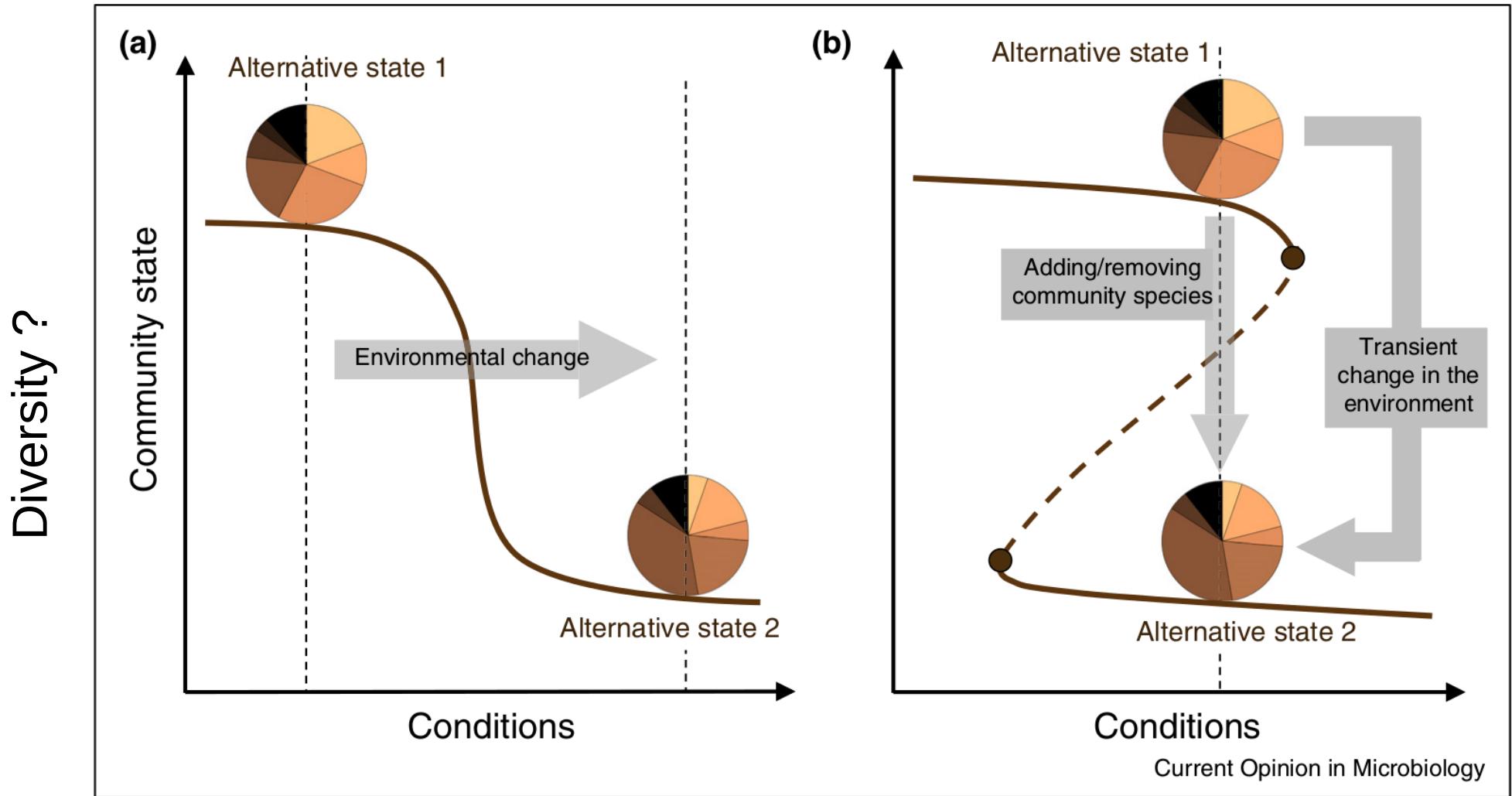
Hurst exponent – quantifies periodicity or persisting trends

Lyapunov exponent – quantifies chaos



Alternative (transient?) states are induced by external factors

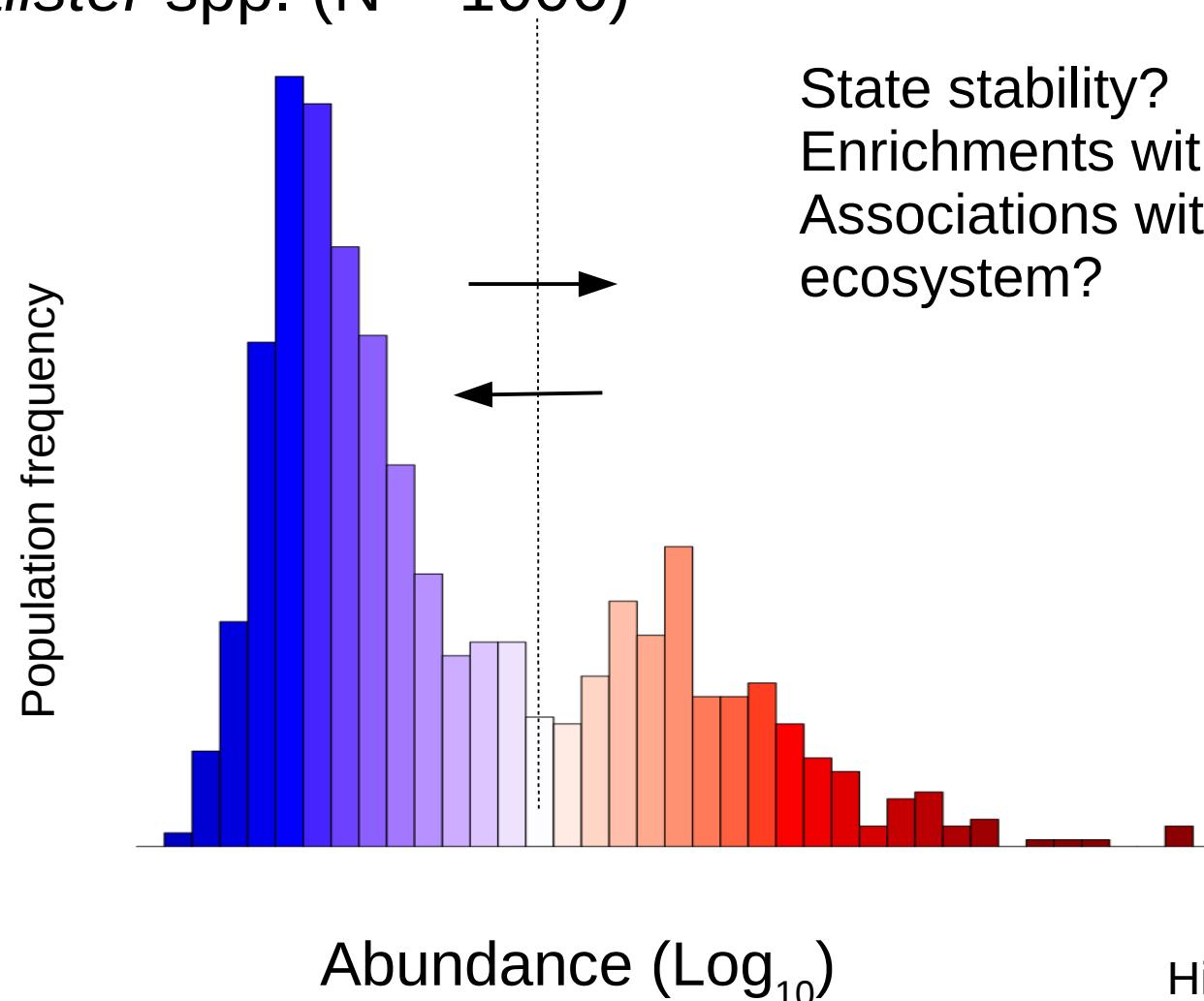
Alternative stable states are resilient to external factors



Environmental or host factor (e.g. body-mass index)

Alternative states in specific bacterial groups ?
→ Bimodal population distribution is one indicator

Dialister spp. (N = 1006)



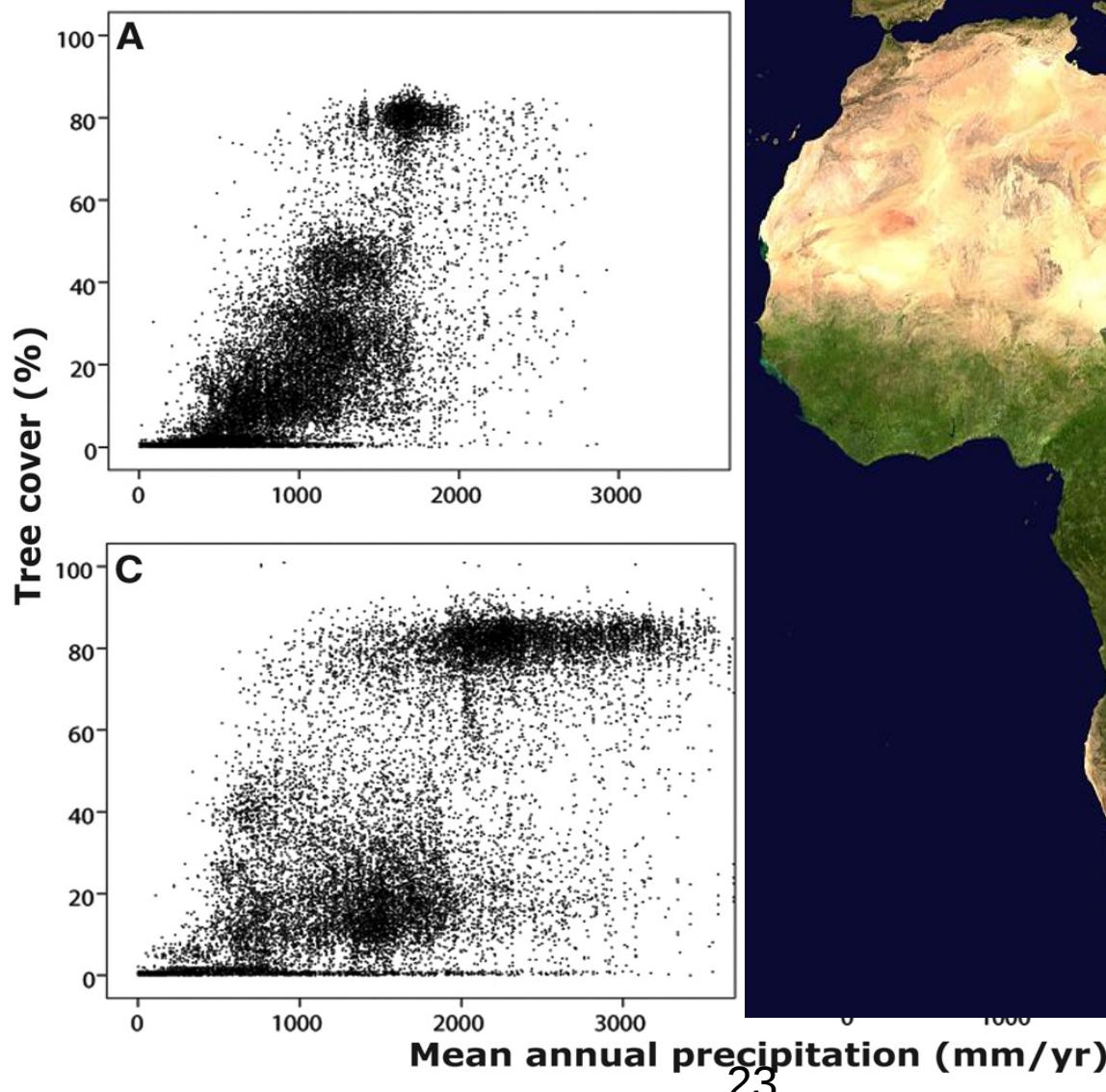
State stability?
Enrichments with diet / health / etc.?
Associations with the overall ecosystem?

Hirota et al. Science 2011
Livina et al. Clim Past. 2010
Lahti et al. Nat. Comm 2014

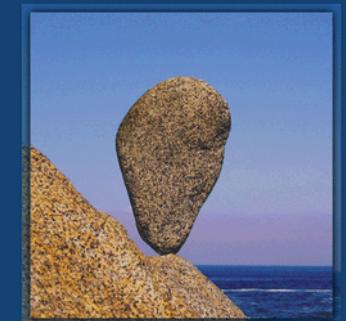
REPORT

Global Resilience of Tropical Forest and Savanna to Critical Transitions

Marina Hirota¹, Milena Holmgren^{2,*}, Egbert H. Van Nes¹, Marten Scheffer¹



Critical Transitions
in Nature and Society



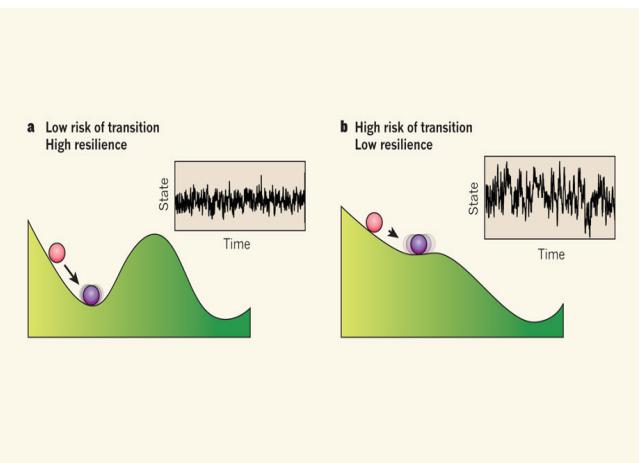
Marten Scheffer

PRINCETON STUDIES IN COMPLEXITY

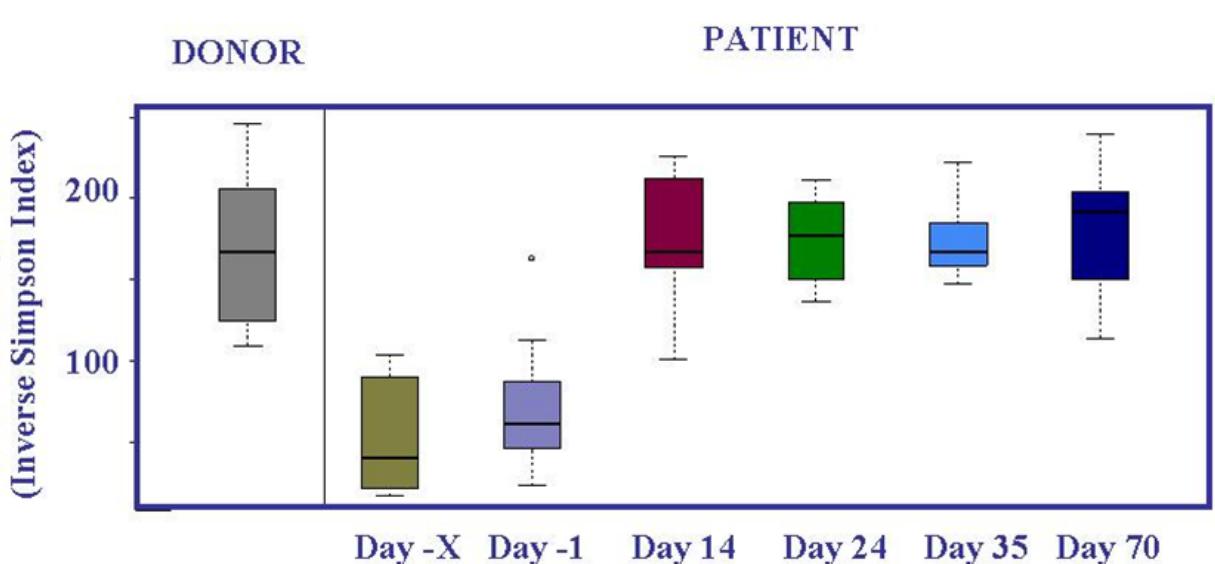
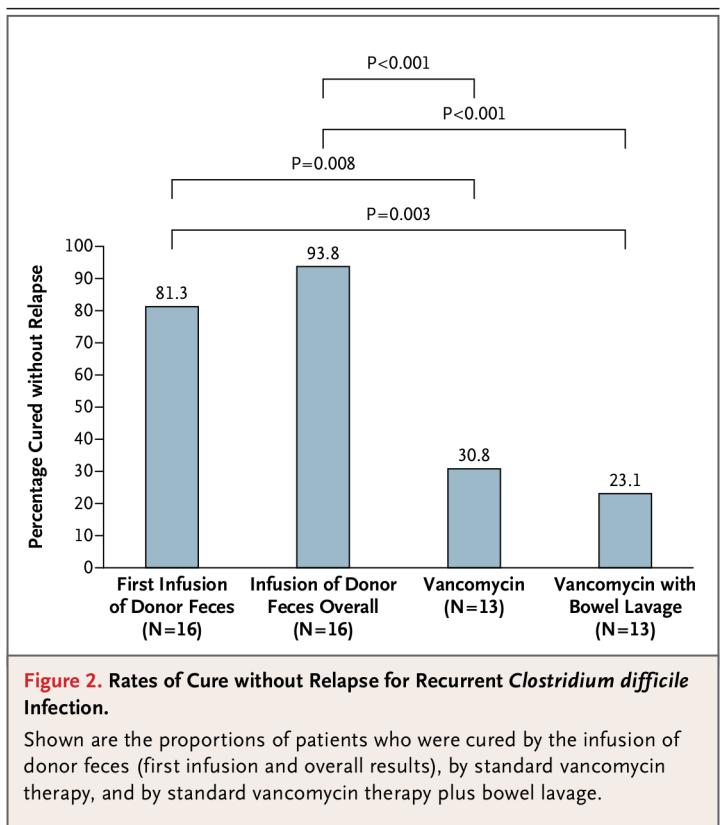
Fecal transplant induced ecosystem level state shift

Efficient treatment in *C. difficile* infected patients.
Shift from Bacilli- and Proteobacteria-dominated state to a healthy state dominated by *Bacteroides* and many butyrate producing taxa

Better than antibiotics !



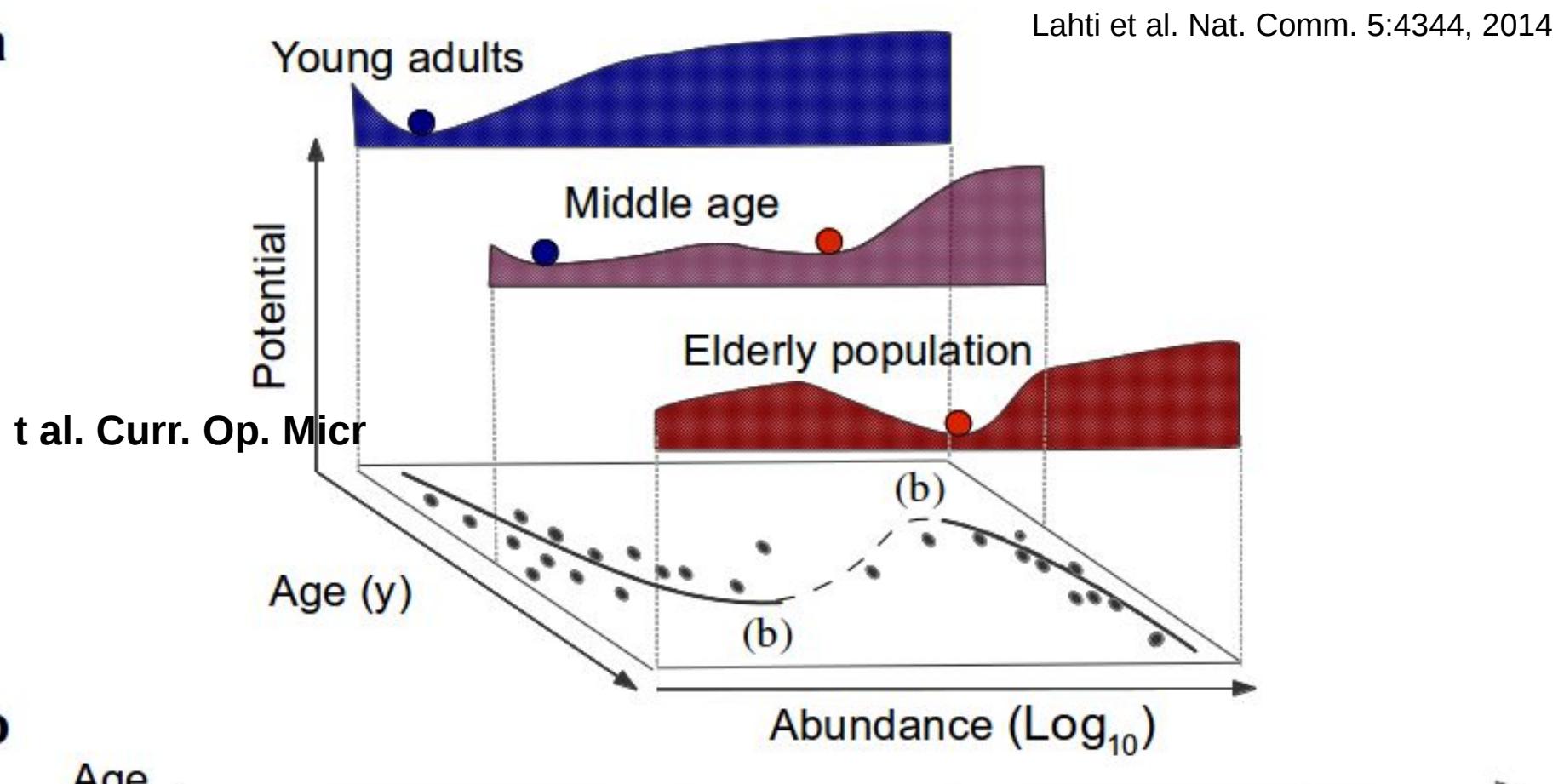
Patient gets donor microbiota -> Donor farms!?



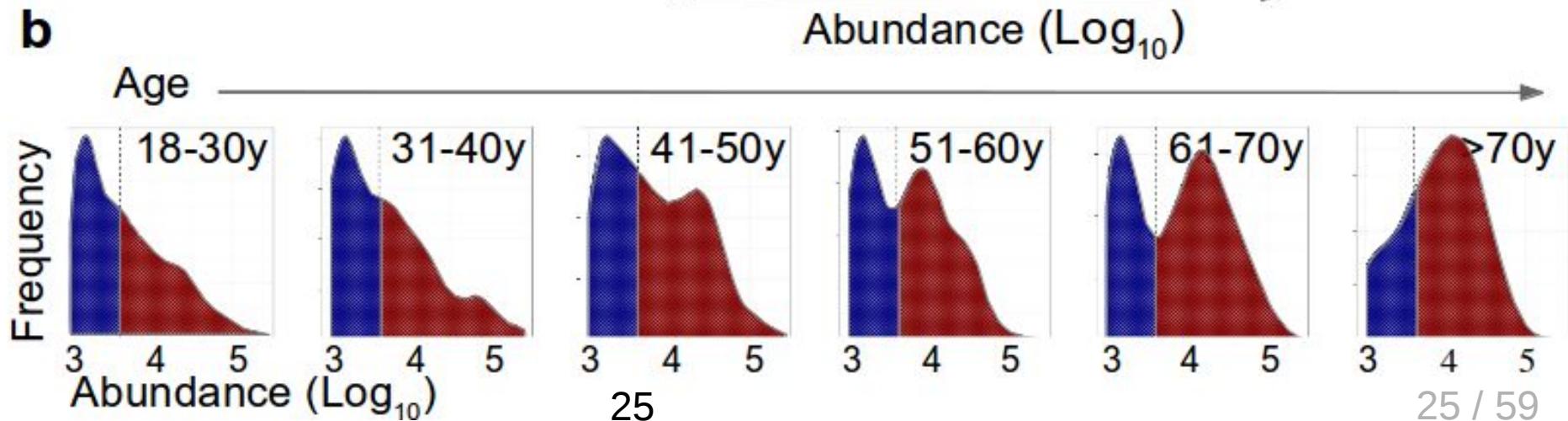
Els van Nood et al., NEJM 368(5) 2013
Fuentes et al. ISME J, 8:1621-33, 2014

Tipping elements of the human gut microbiota: Uncultured Clostridiales I

a

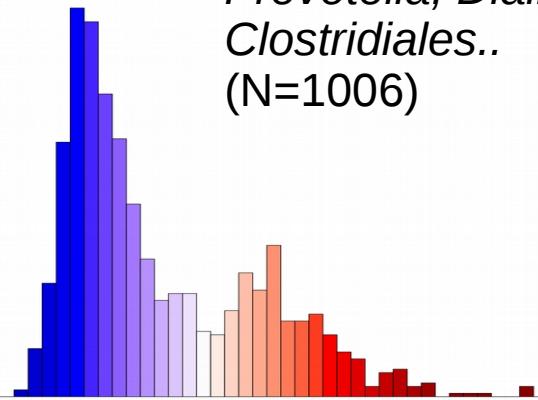


b

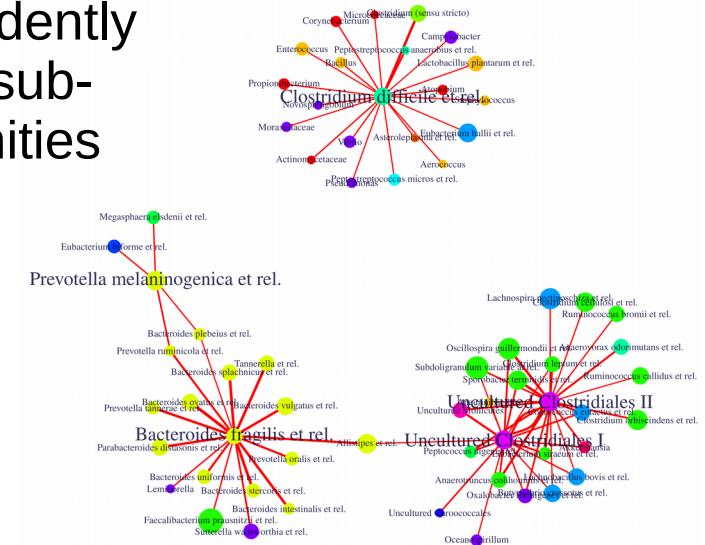


Subject stratification into community types based on simple tipping elements could reduce complexity

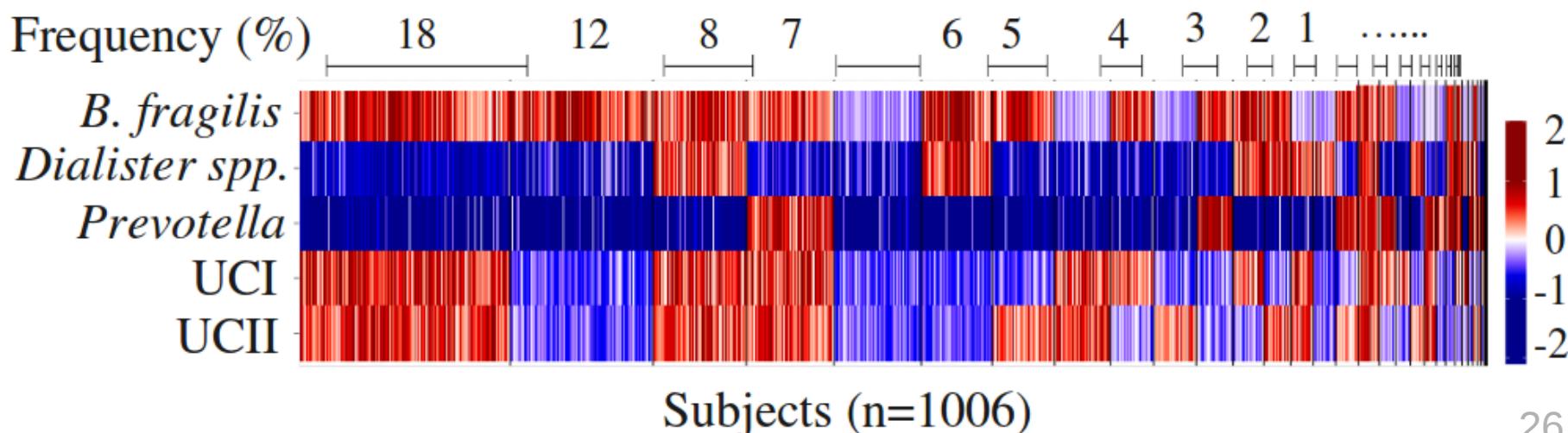
Bistable taxa:
Prevotella, *Dialister*,
Clostridiales..
(N=1006)



Independently varying sub-communities



Ecosystem states are rich combinations of independent tipping elements ? Lahti et al. Nat. Comm. 2014



Bi-stable taxa:

Prevotella groups
(oralis & melaninogenica)

Dialister spp.

Uncultured Clostridiales I-II

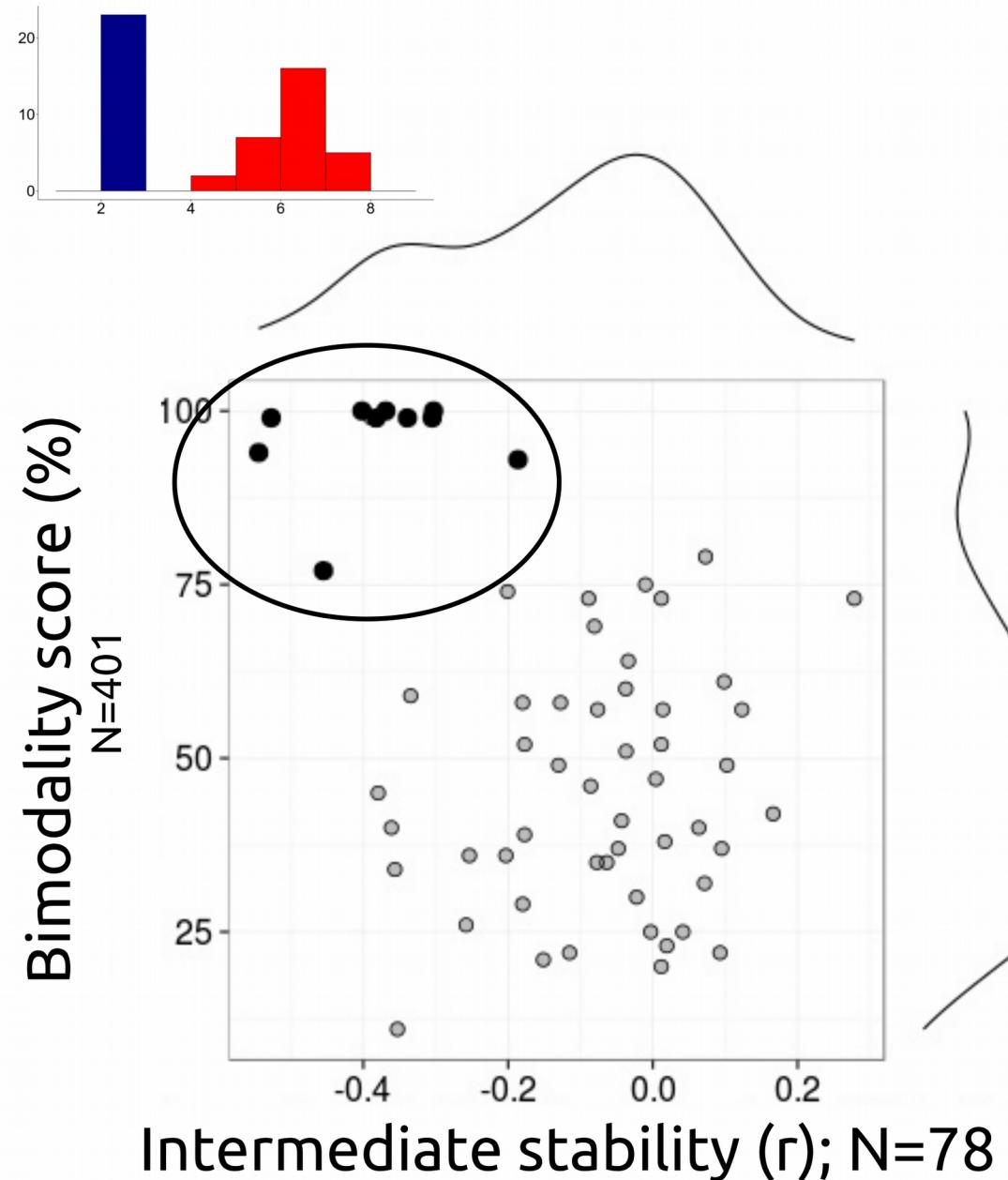
B. fragilis group

Uncultured Mollicutes

Clostridium groups
(difficile, colinum,
sensu stricto)

Lactobacillus plantarum

+ methanogenic archaea

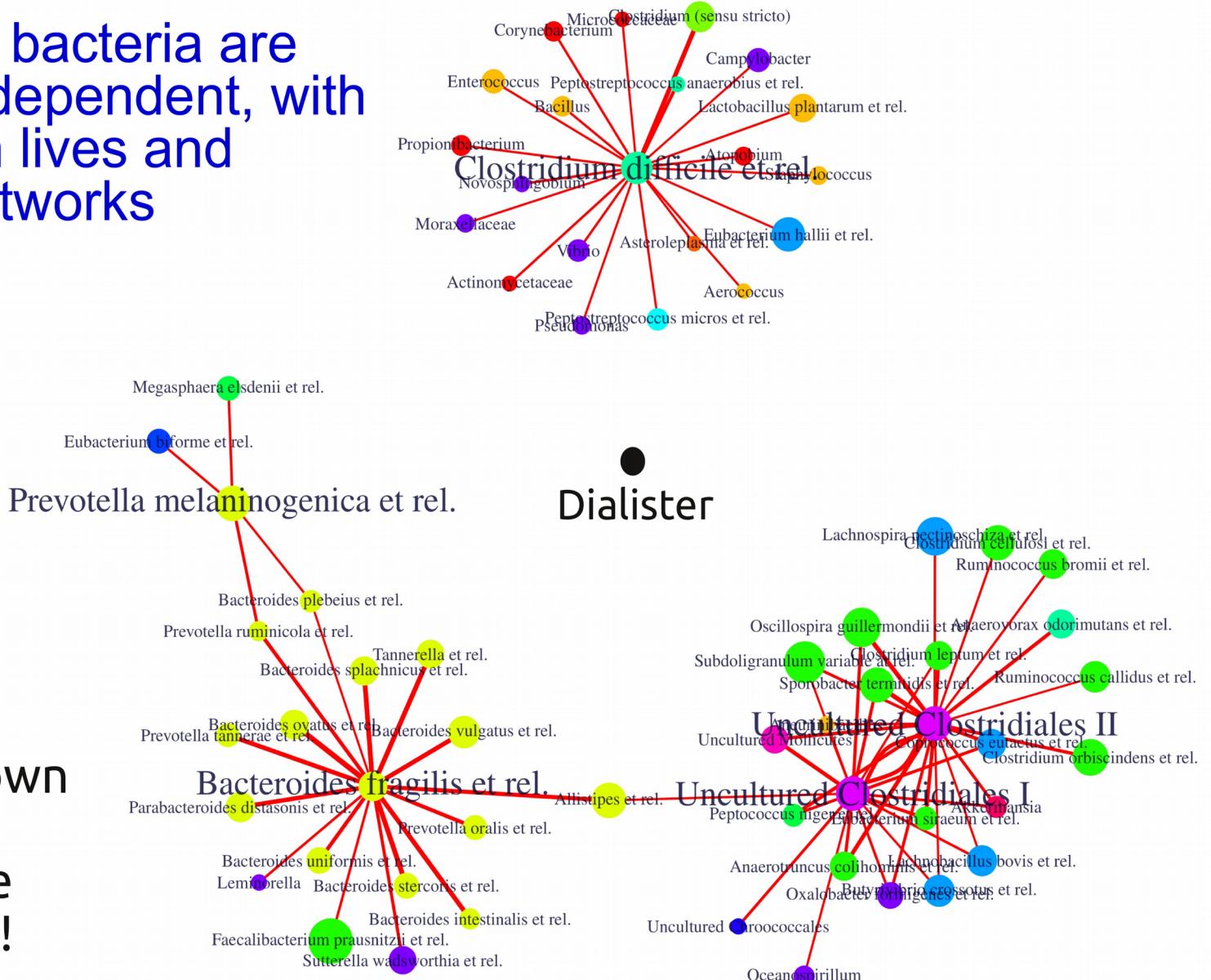


Lahti et al. Nat. Comm. 5:4344, 2014

Bi-stable bacteria are rather independent, with their own lives and social networks

$|r| > 0.33$ shown

Only positive correlations !



Health associations of bi-stable tipping elements

Health status	Bimodal group	Enriched state	Compromised (%)	Controls (%)	FDR (%)
Severe obesity (n=136)	UCI	Low abundance	29	55	<0.1
Severe obesity	UCII	Low abundance	38	61	<0.1
IBS (n=106)	UCII	Low abundance	50	61	1
MetS (n=66)	<i>B.fragilis</i> group	High abundance	89	78	<0.1
MetS	<i>Prevotella</i> group	Low abundance	11	22	11
MetS	<i>Dialister</i>	High abundance	36	28	13

- Causality: drivers or passengers?
- Diagnostic & prognostic indicators ?
- Targets for manipulation?
- Early warnings signals of state shift ?

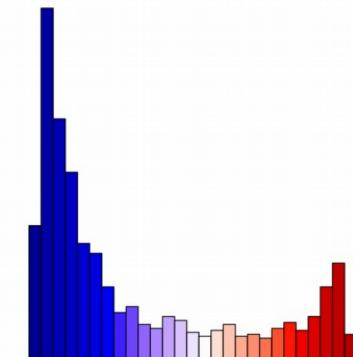
Received 23 Jan 2014 | Accepted 9 Jun 2014 | Published 8 Jul 2014

DOI: 10.1038/ncomms5344

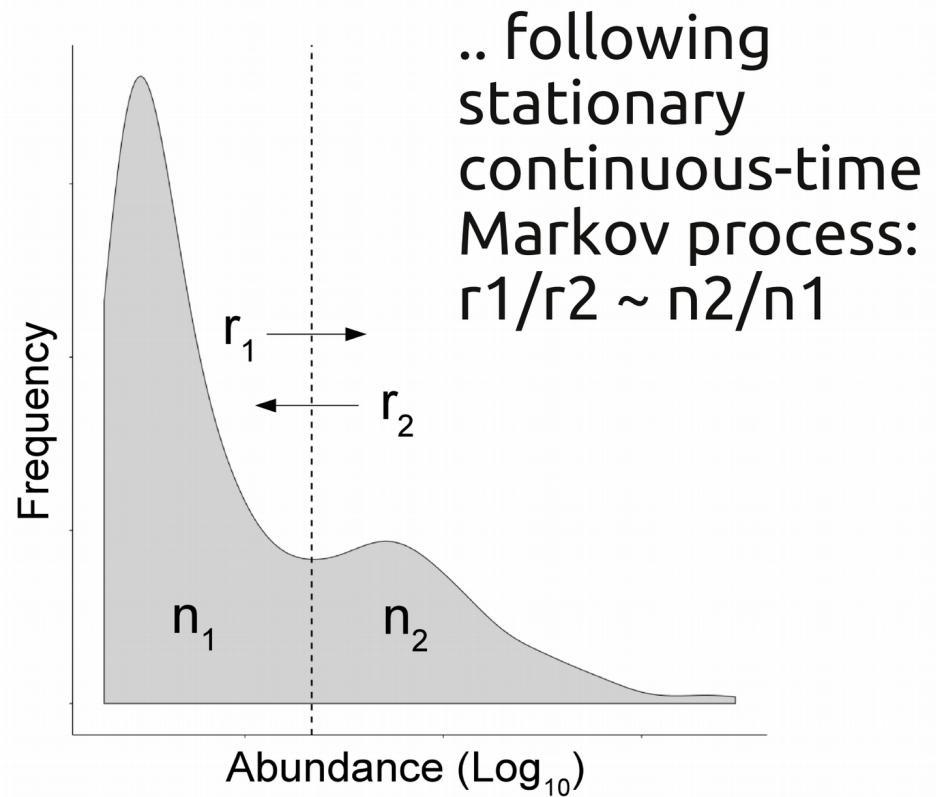
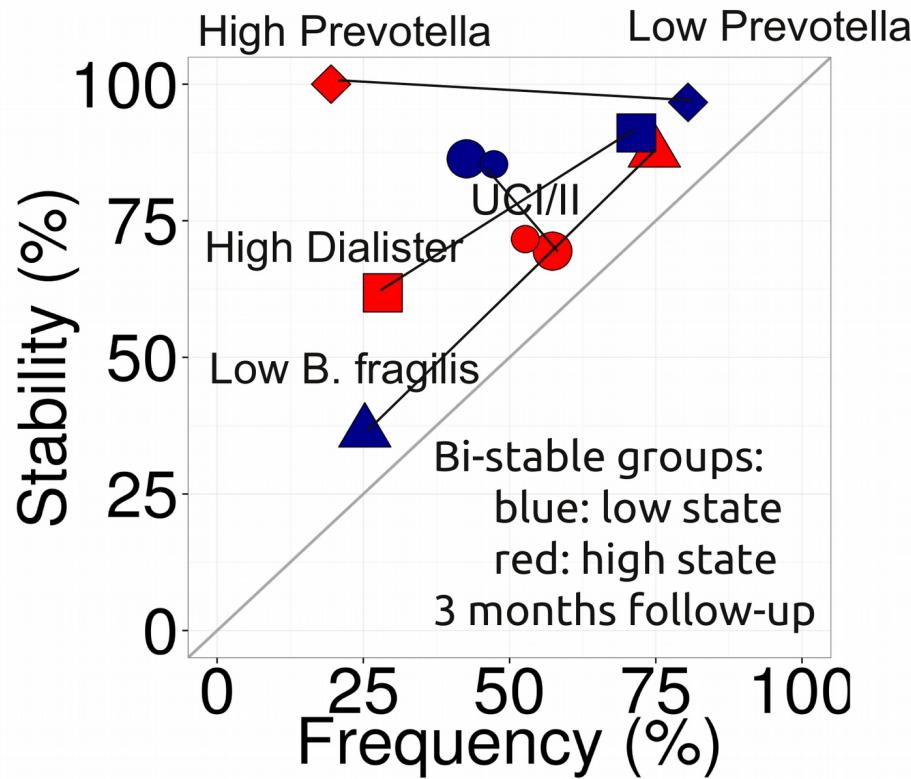
OPEN

Tipping elements in the human intestinal ecosystem

Leo Lahti^{1,2}, Jarkko Salojärvi^{1,*}, Anne Salonen^{3,*}, Marten Scheffer⁴ & Willem M. de Vos^{1,2,3}



How stable ? more frequent states are more stable



- > Notable stability differences between taxa
- > Exception: high-abundance Prevotella is the most stable state!
- > bi-stable states are robust to dietary changes in short term
- > individual responses

Salonen et al. ISME J. 2014

Early warning signals to predict state shifts ?

Early warning signals for a critical transition in a time series generated by a model of a harvested population⁷⁷ driven slowly across a bifurcation.

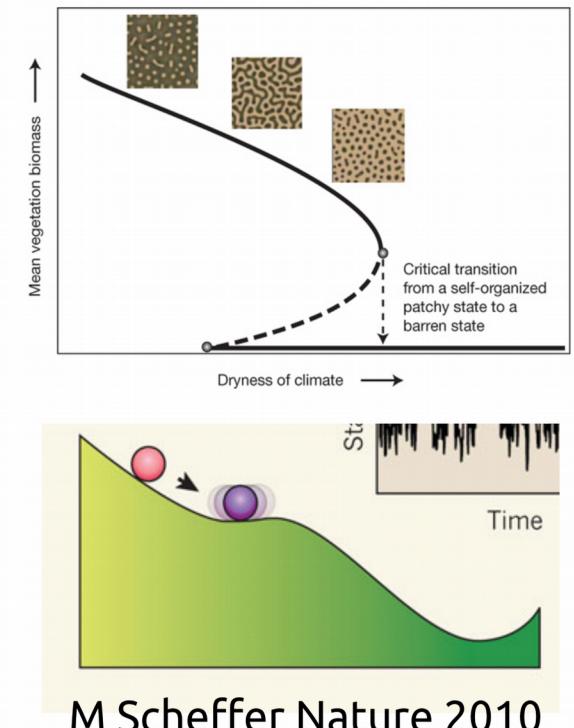
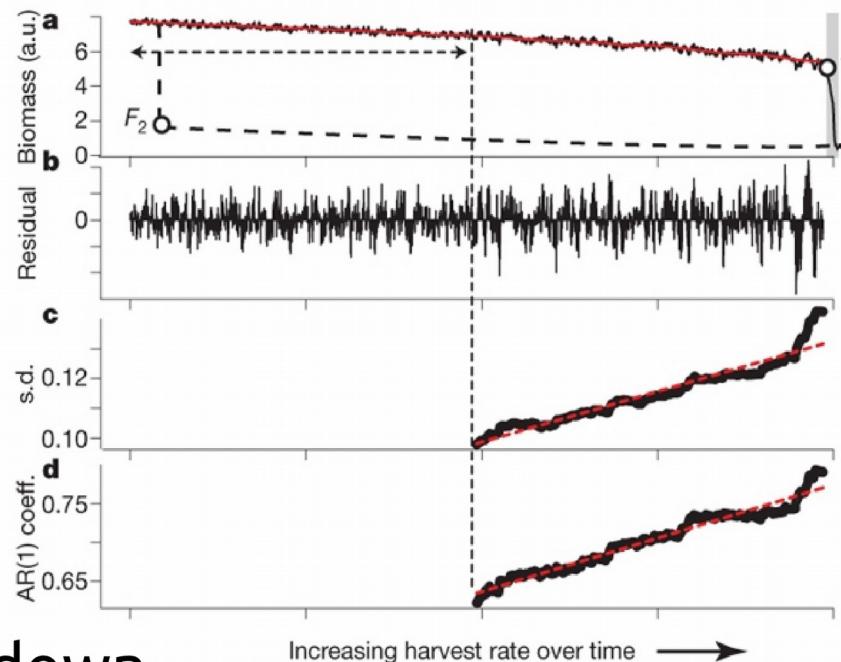
Autocorrelation

Variance

Skewness

Flickering

Critical slowing down



M Scheffer Nature 2010

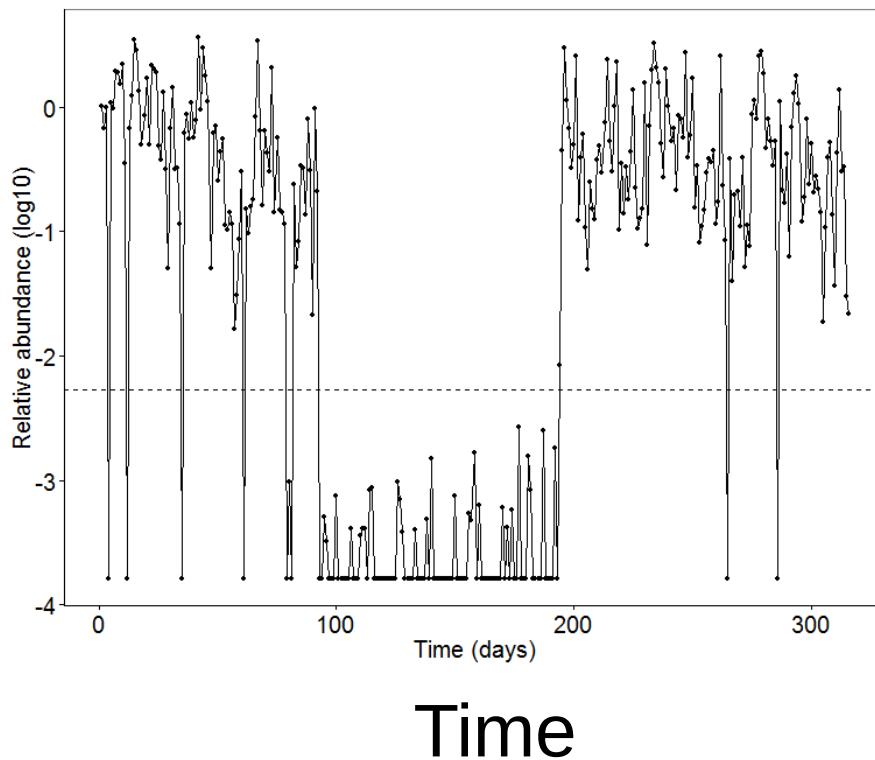
M Scheffer et al. *Nature* **461**, 53-59 (2009) doi:10.1038/nature08227

CRAN: earlywarnings R package
V. Dakos & L. Lahti

nature

Detecting a tipping point: temporal instability at intermediate abundances as an indicator of bistability

One long time series:
Lachnospiraceae

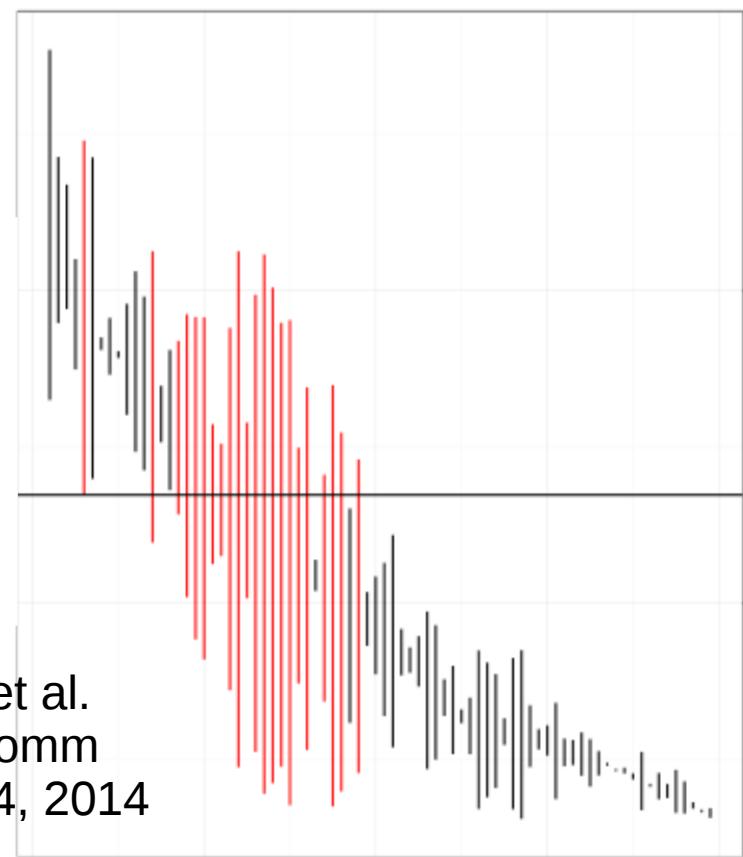


Data: David et al. 2014; Figure: T Blake 2015

Many short time series:
Dialister spp.

Abundance

Lahti et al.
Nat Comm
5:4344, 2014



Can random chance explain the observed diversity of the human gut microbiomes ?

Linking statistical and ecological theory: Hubbell's unified neutral theory of biodiversity as a hierarchical Dirichlet process ¹

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- Unified Neutral Theory of Biodiversity
- Connection to Hierarchical Dirichlet Process
- Validation & Experiments

How to explain the observed variation -classical niche model:

"When we look at the plants and bushes clothing an entangled bank, we are tempted to attribute their proportional numbers and kinds to what we call chance. But how false a view is this!"

- Charles Darwin, The Origin of Species.



Neutral vs. niche models in ecology ?

After >25 years on the Barro Colorado Island tropical forests, Hubbell controversially proposed that.. random chance may in fact be the best explanation of the observed biodiversity (Hubbell 2001).



Mainland – Island model

Metacommunity ('mainland') diversity is affected by **size, speciation and extinction rates**

Local community ('island') is also governed by the **immigration rate**

Caswell (1976):

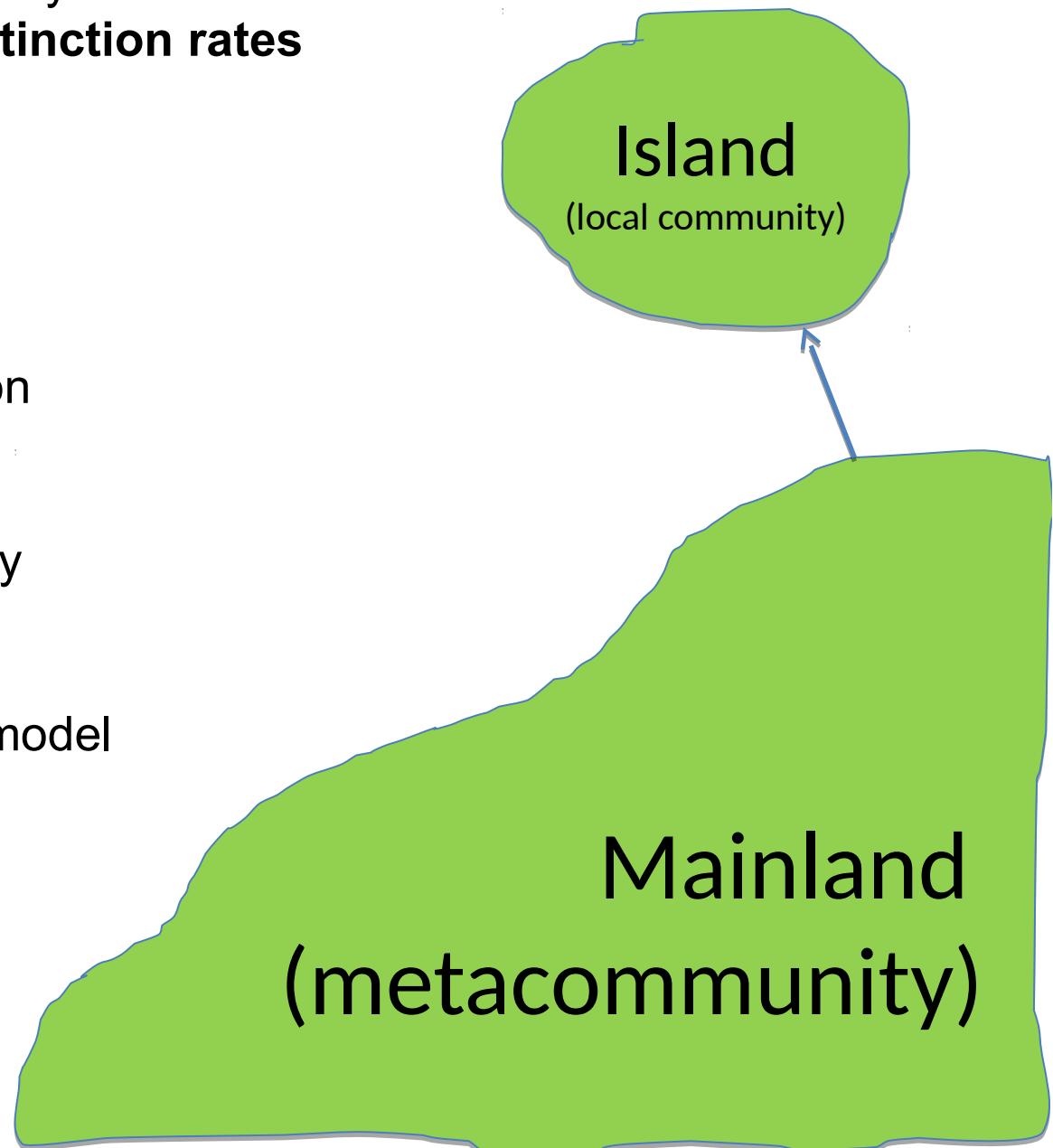
- single local community + migration

Hubbell (2001)

- many local communities + neutrality

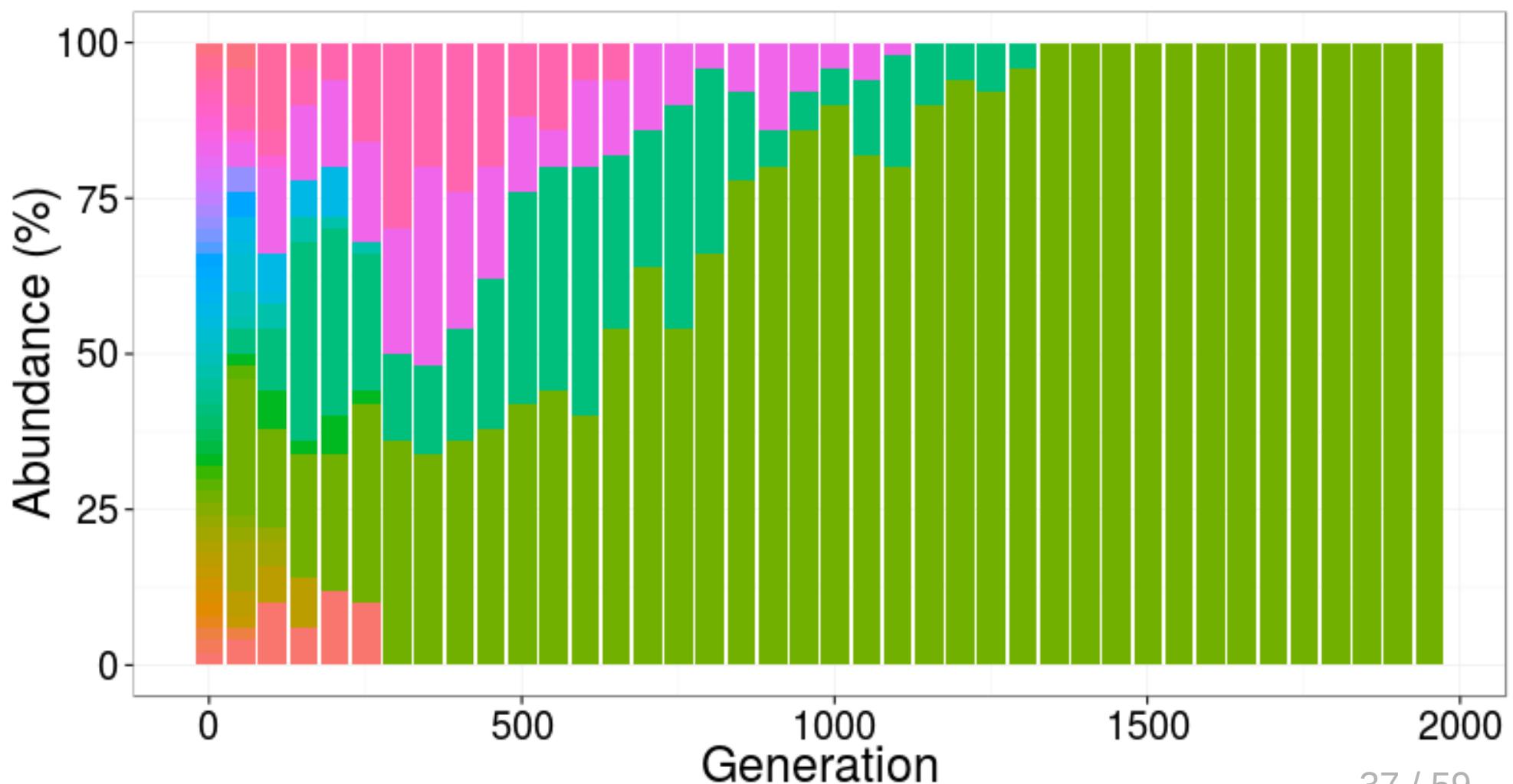
Etienne (2004):

- exact likelihood for the single-site model



Single-species dominance also from random walk !

Random drift + No migration + Fixed community size



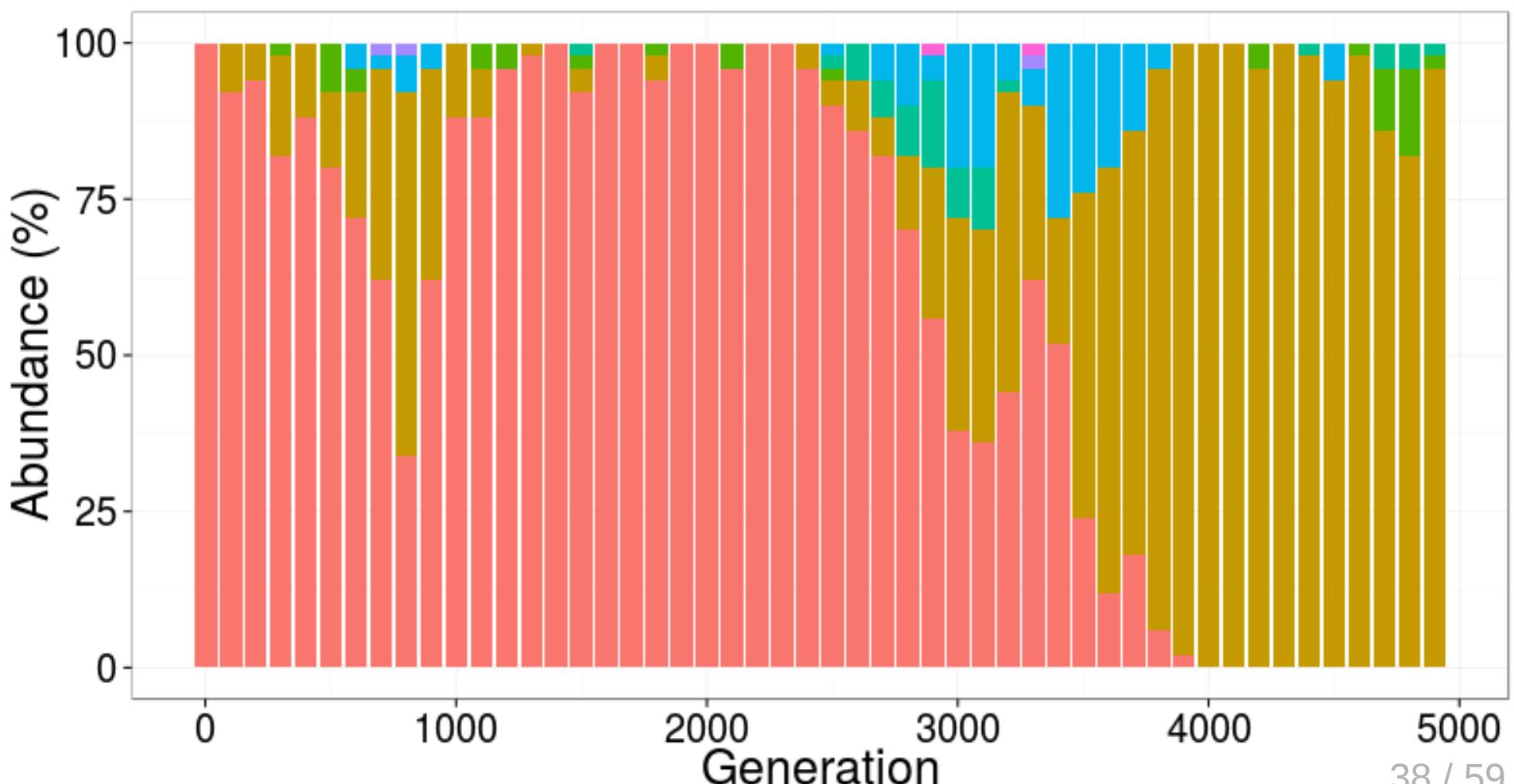
Random migration as ecological driver ?

Random drift + Small migration / speciation + Fixed community size

Drastic shifts in community dominance by different species !

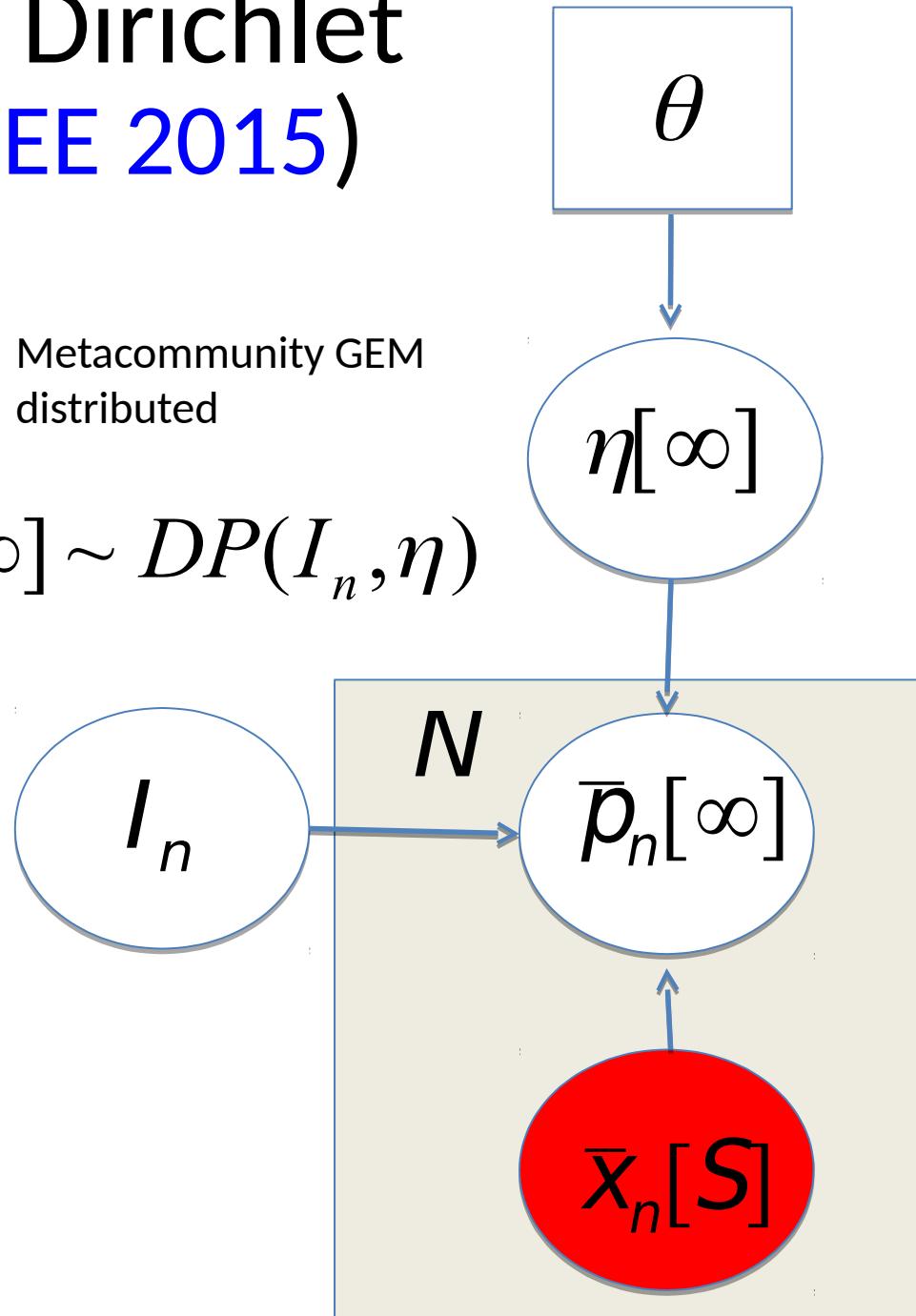
UNTB (migration probability 0.01)

Species 1 2 3 4 5 6 7



UNTB as a Hierarchical Dirichlet Process (Harris et al. PIEEE 2015)

- Mainland-island neutral dynamics converges to Hierarchical Dirichlet Process (Teh et al. 2006)
- Maintains neutrality, fixed community size, and variable immigration
- Robust to differences in local community dynamics
- Metacommunity can be estimated
- Efficient, scalable approximation for full multi-site UNTB from existing HDP fitting strategy
- Bayesian approach: full posterior distribution for model parameters obtained instead of maximum-likelihood point estimates



Gut microbiome neutrality ?

- Neutrality depends on taxonomic level
- Bacteroidetes have lower immigration than the spore-forming Firmicutes.

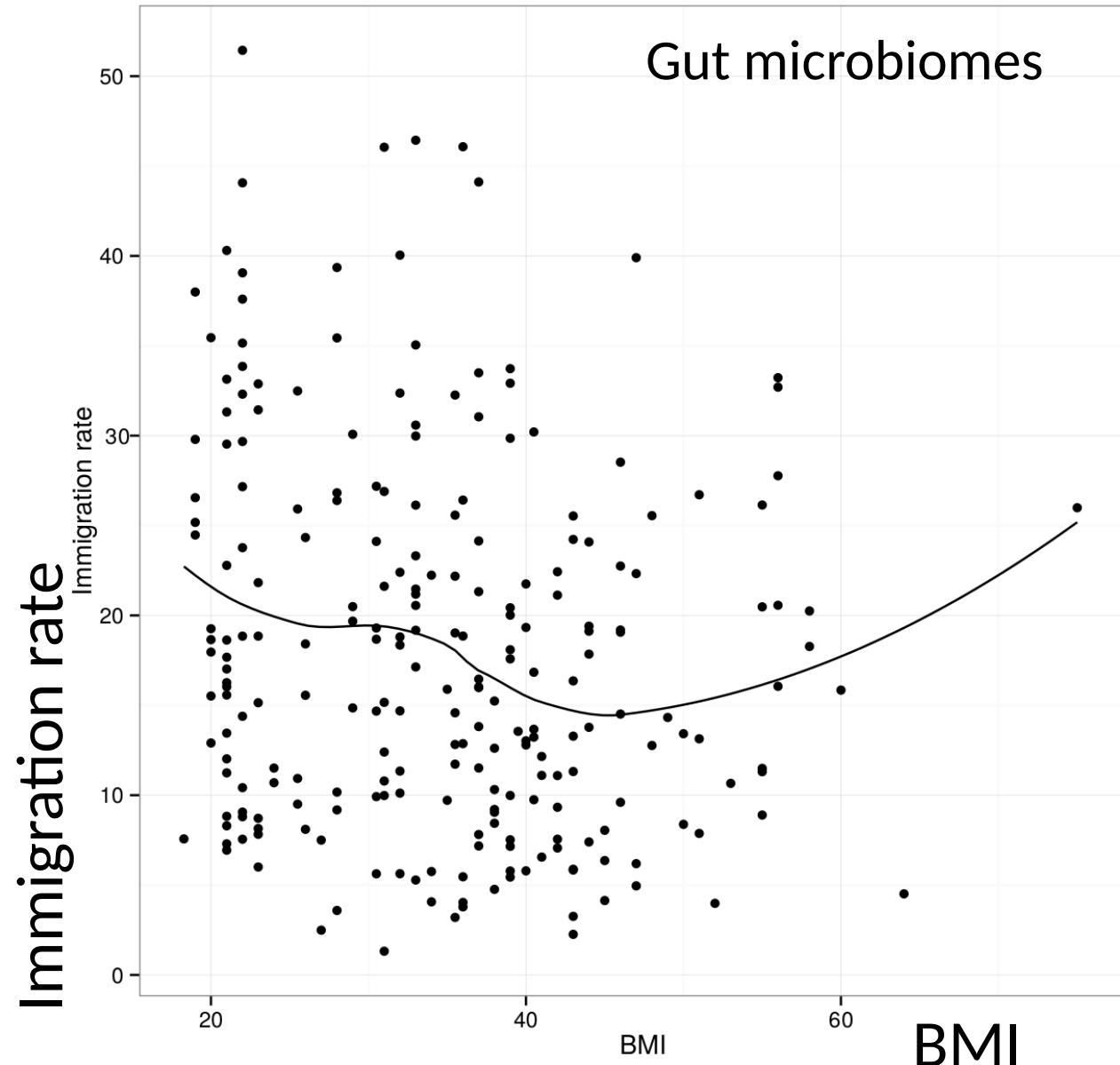
Table 2. Fitting the UNTB-HDP model to human gut microbiota.

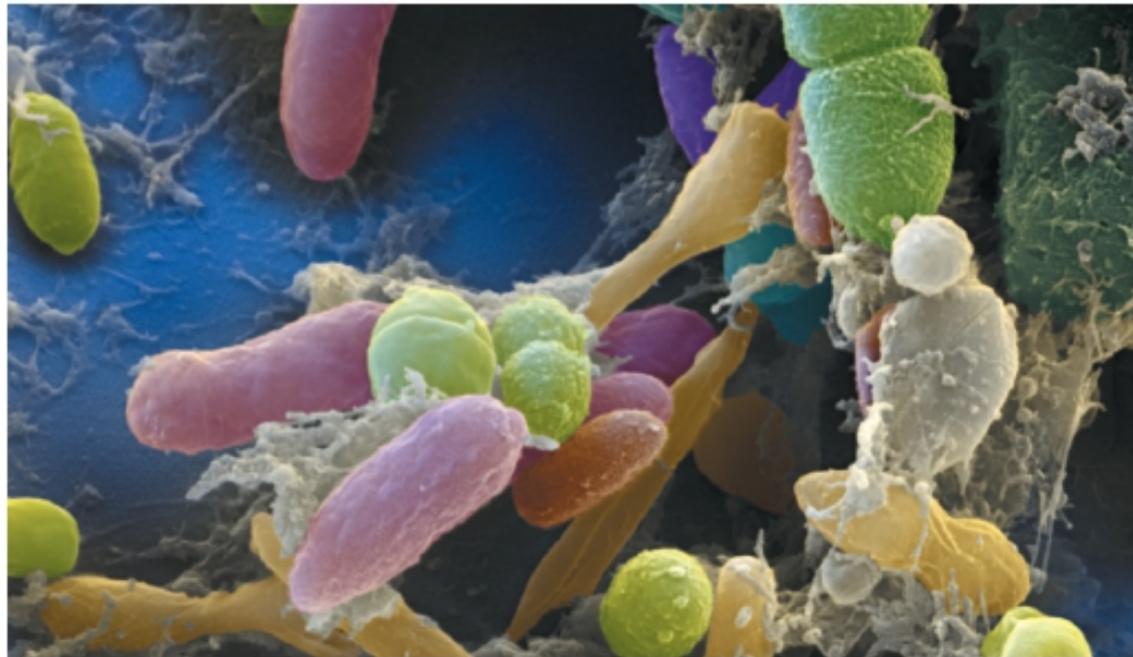
Taxa	N	S	\tilde{J}	θ	I_i			p_N	p_L
					l	m	u		
Bacteroidetes	231	569	596	148.6	1.5	5.5	13.7	0.0 (0.0)	0.0 (0.0)
Bacteroidaceae	208	224	506	51.4	0.7	3.3	7.6	0.0 (0.0)	0.03 (0.0)
Bacteroides	208	224	506	51.4	0.7	3.3	7.6	0.0 (0.0)	0.03 (0.0)
Firmicutes	277	4770	1009	1382.3	21.4	44.8	81.0	0.0 (0.0)	0.0 (0.0)
Incertae Sedis XIV	87	176	264	39.2	1.7	9.8	27.5	0.0 (0.0)	0.05 (0.004)
Blautia	87	175	264	38.9	1.6	10.1	27.1	0.0 (0.0)	0.06 (0.003)
Lachnospiraceae	164	873	248	262.9	6.5	13.0	21.2	0.0 (0.0)	0.0 (0.0)
Ruminococcaceae	239	1471	409	411.0	4.5	16.1	38.1	0.0 (0.0)	0.0 (0.0)
Faecalibacterium	141	301	297	71.7	1.0	7.5	21.4	0.0 (0.0)	0.004 (0.0)

Results are given for 3% OTUs at different levels, quantities given in the table are: N - the no. of samples with > 150 reads; S - the number of 3% OTUs; \tilde{J} - the median sample size; θ - the fitted biodiversity parameter; I_i - the fitted immigration rates where l, m and u are the lower 2.5%, median and upper 97.5% quantiles respectively; p_N - the proportion of simulated neutral samples exceeding the observed data likelihood; and p_L - the proportion of simulated locally neutral samples exceeding the observed data likelihood. The figures in parentheses give pseudo p-values for the equivalent complete gut microbiome data set randomly sampled down to the same size as the individual taxa.

Immigration and clinical parameters ?

Negative correlation
between body mass
index (BMI) and
Ruminococcaceae
immigration rates





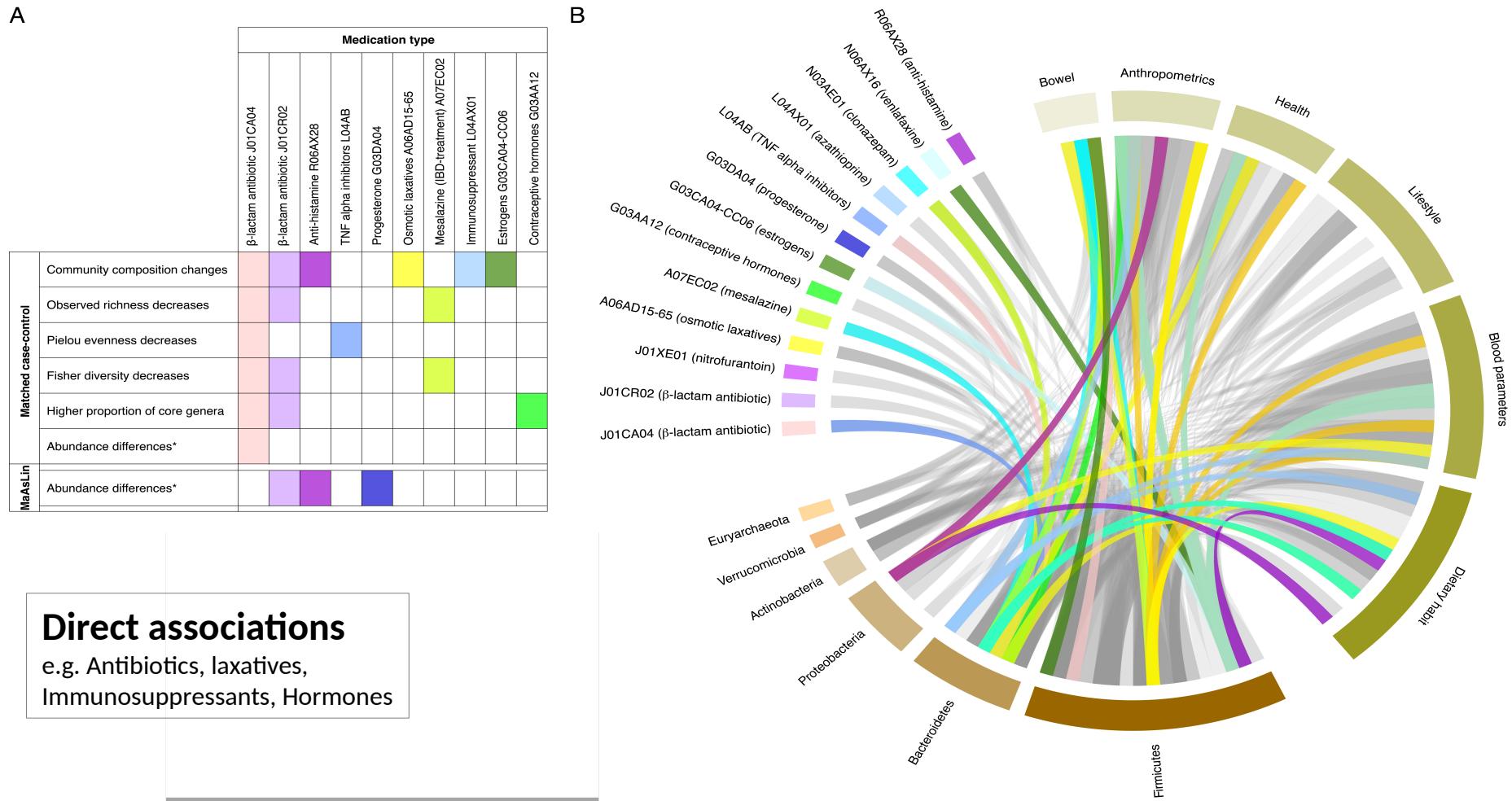
A scanning electron micrograph of bacteria in human faeces, in which 50% of species originate from the gut.

Microbiome science needs a healthy dose of scepticism

To guard against hype, those interpreting research on the body's microscopic communities should ask five questions, says William P. Hanage.

Comment August 2014 Nature

Identification of microbiota-drug associations: Majority of genera thus far associated to disease are also confounded by other covariates, incl drugs



Confounding variables: stool consistency showed the largest effect size on microbiota variation

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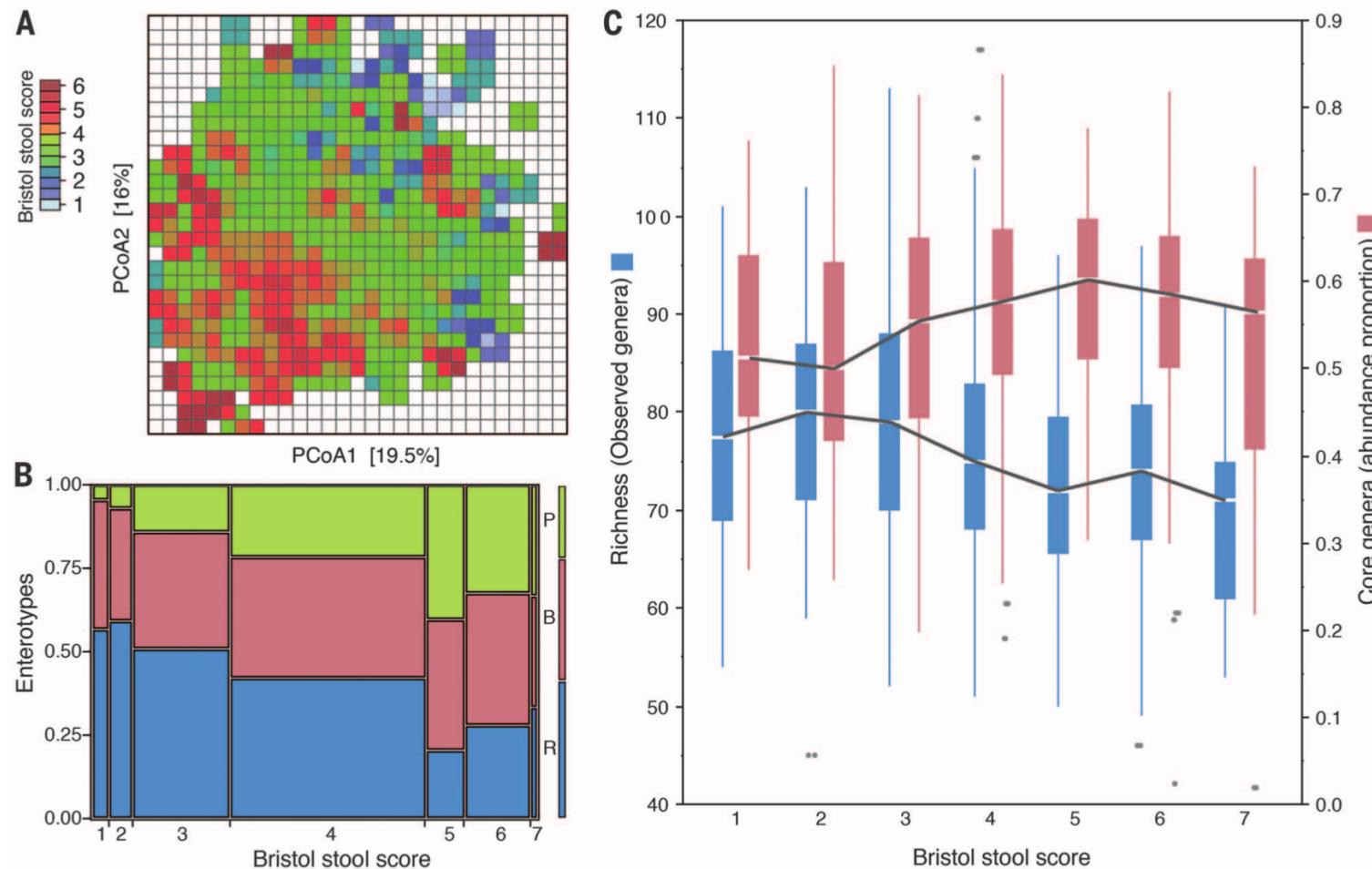
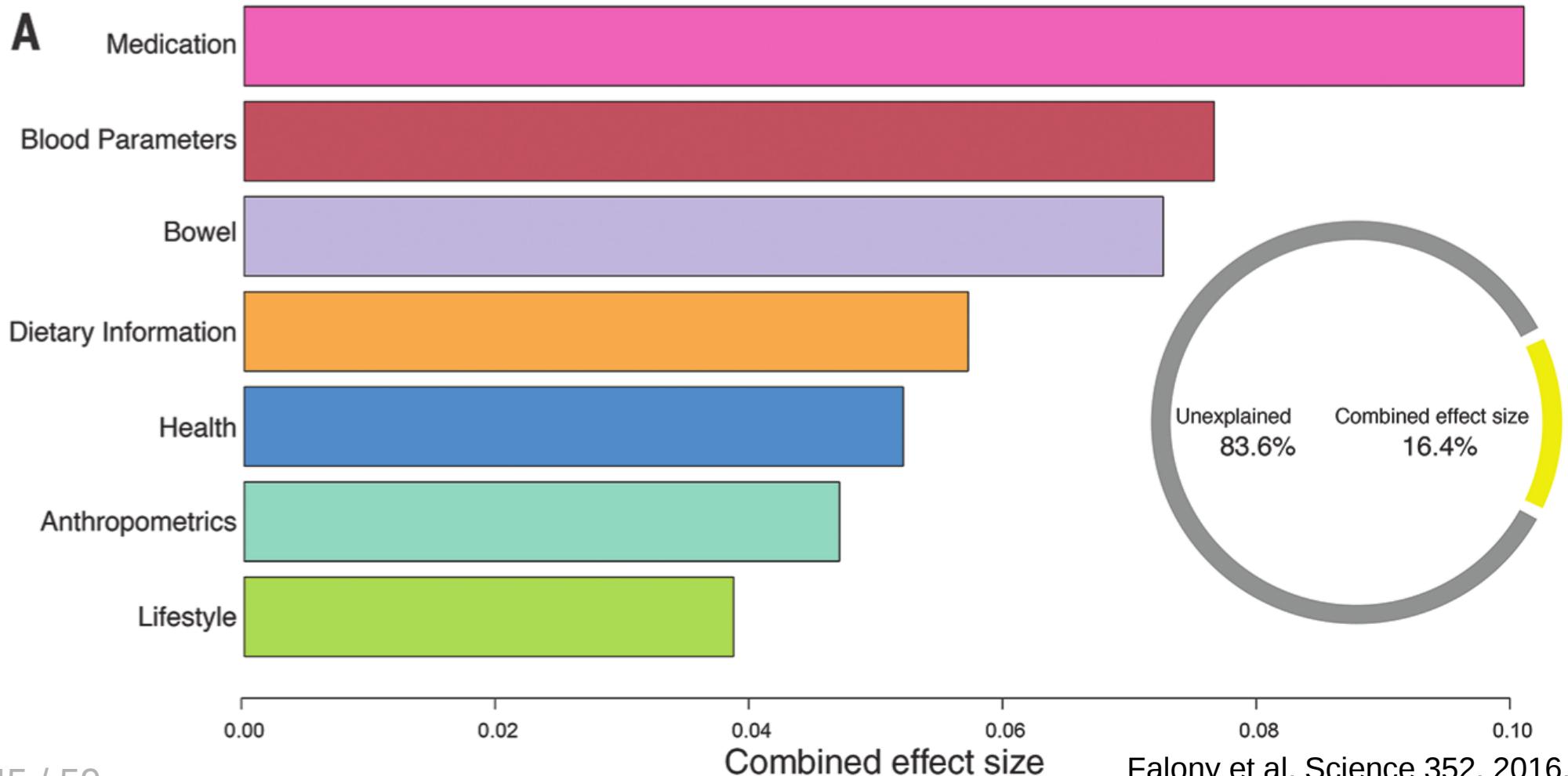


Fig. 4. BSS score association to microbiota variation. (A) BSS score variation across the FGFP cohort, as represented on the genus-level PCoA ordination (Bray-Curtis dissimilarity). Each cell is colored according to median BSS score of individual samples allocated to the cell coordinates. (B) Enterotype distribution over BSS scores [JSD enterotyping (18)] showing an increase in *Prevotella* individuals with looser stool consistency. (C) Median differences in abundance of the core microbiota (FGFP genus-level core at 99%) and in observed genus richness across BSS score.

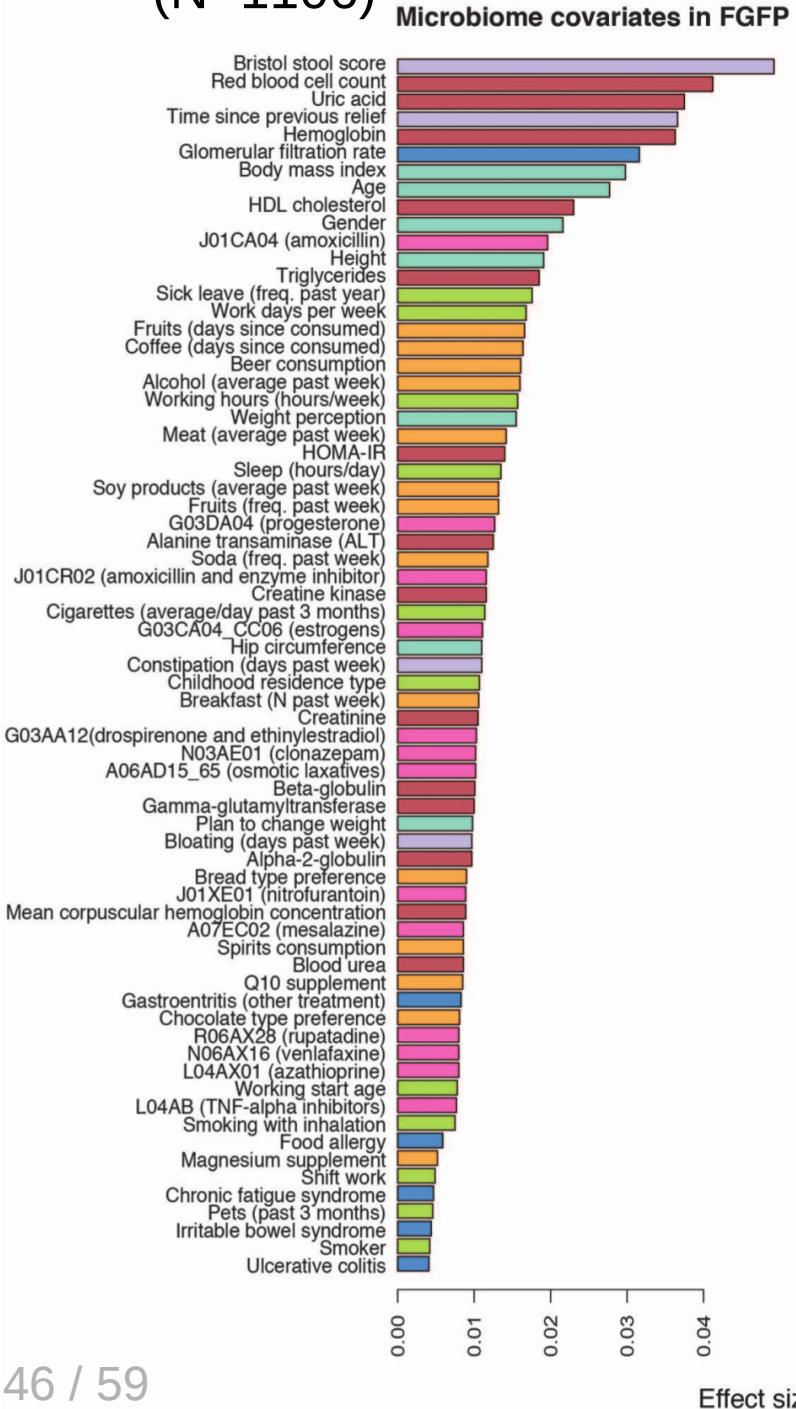
Total explained variation: 16.4%

(Flemish Gut Flora Project)

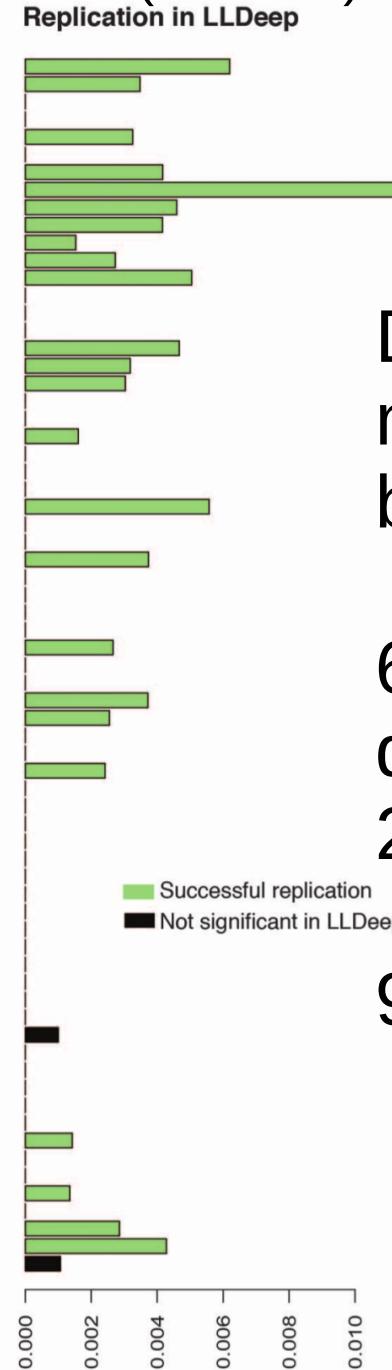
Proposed disease marker genera associated to host covariates and medication - inclusion in study design is essential !



Flemish Gut Flora (N=1106)



Dutch LifeLines- DEEP (N=1135)



Determinants of
microbiota
composition ?

Diet, health, lifestyle,
medication, host variables,
blood, bowel habits..

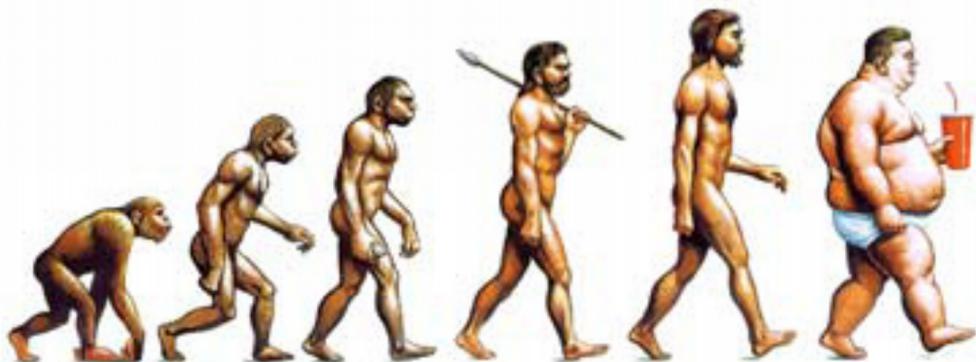
69 covariates (clinical &
questionnaire) in FGFP;
26 shared with DEEP

92% replication rate !

Falony et al. Science 352, 2016.

Bowel cancer risk may be reduced by rural African diet, study finds

Tests on subjects who swapped a fatty, meat-heavy diet for foods rich in beans and vegetables found a drop in biological markers for cancer in just two weeks



Diet swap – Two weeks ?

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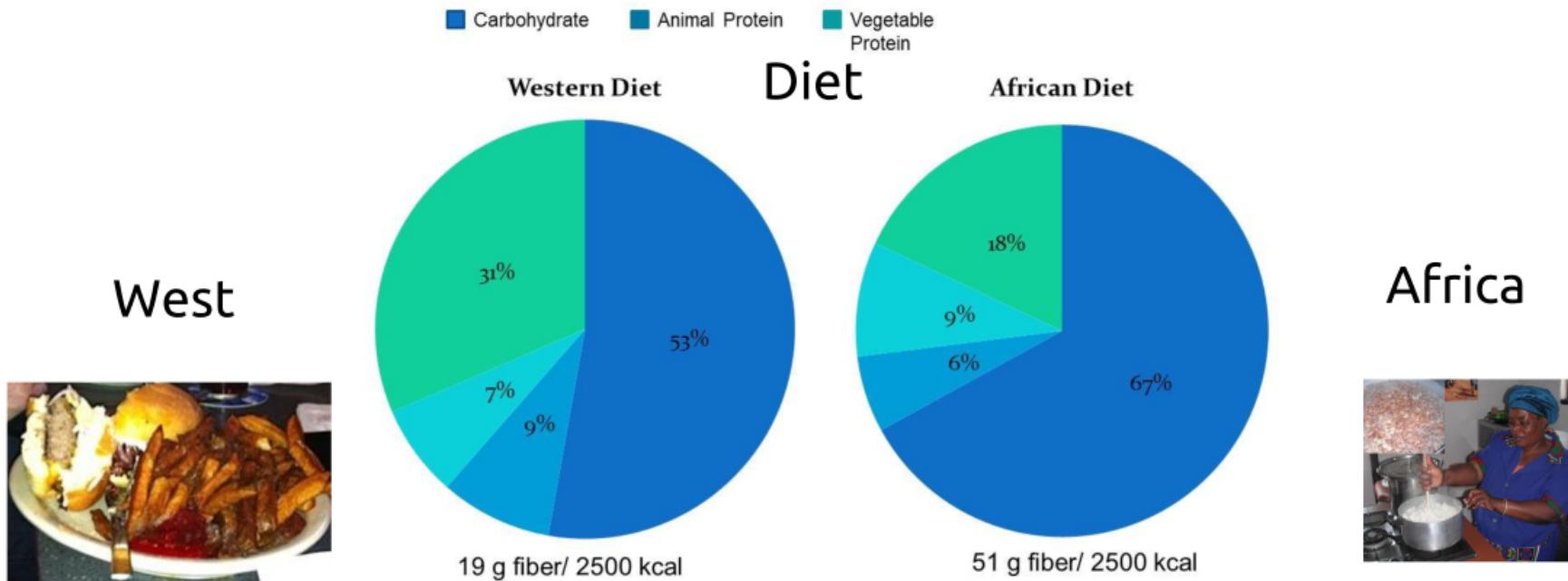
Fat, fibre and cancer risk in African Americans and rural Africans

Stephen J. D. O'Keefe, Jia V. Li, Leo Lahti, Junhai Ou, Franck Carbonero, Khaled Mohammed, Joram M. Posma, James Kinross, Elaine Wahl, Elizabeth Ruder, Kishore Vipperla, Vasudevan Naidoo, Lungile Mtshali, Sebastian Tims, Philippe G. B. Puylaert, James DeLany, Alyssa Krasinskas, Ann C. Benefiel, Hatem O. Kaseb, Keith Newton * et al.

Affiliations | Contributions | Corresponding author

Nature Communications 6, Article number: 6342 | doi:10.1038/ncomms7342
Received 23 May 2014 | Accepted 20 January 2015 | Published 28 April 2015

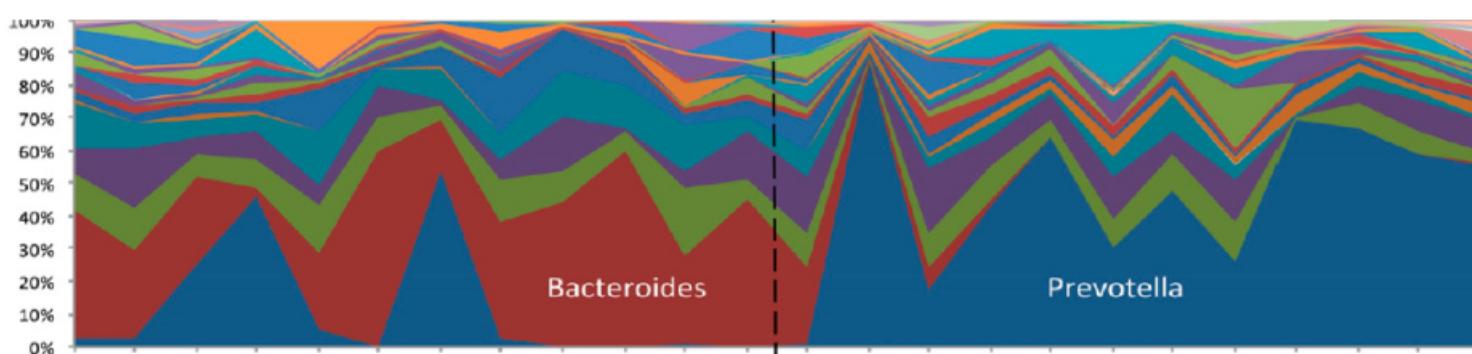
Diet is a major driver of gut microbiome composition



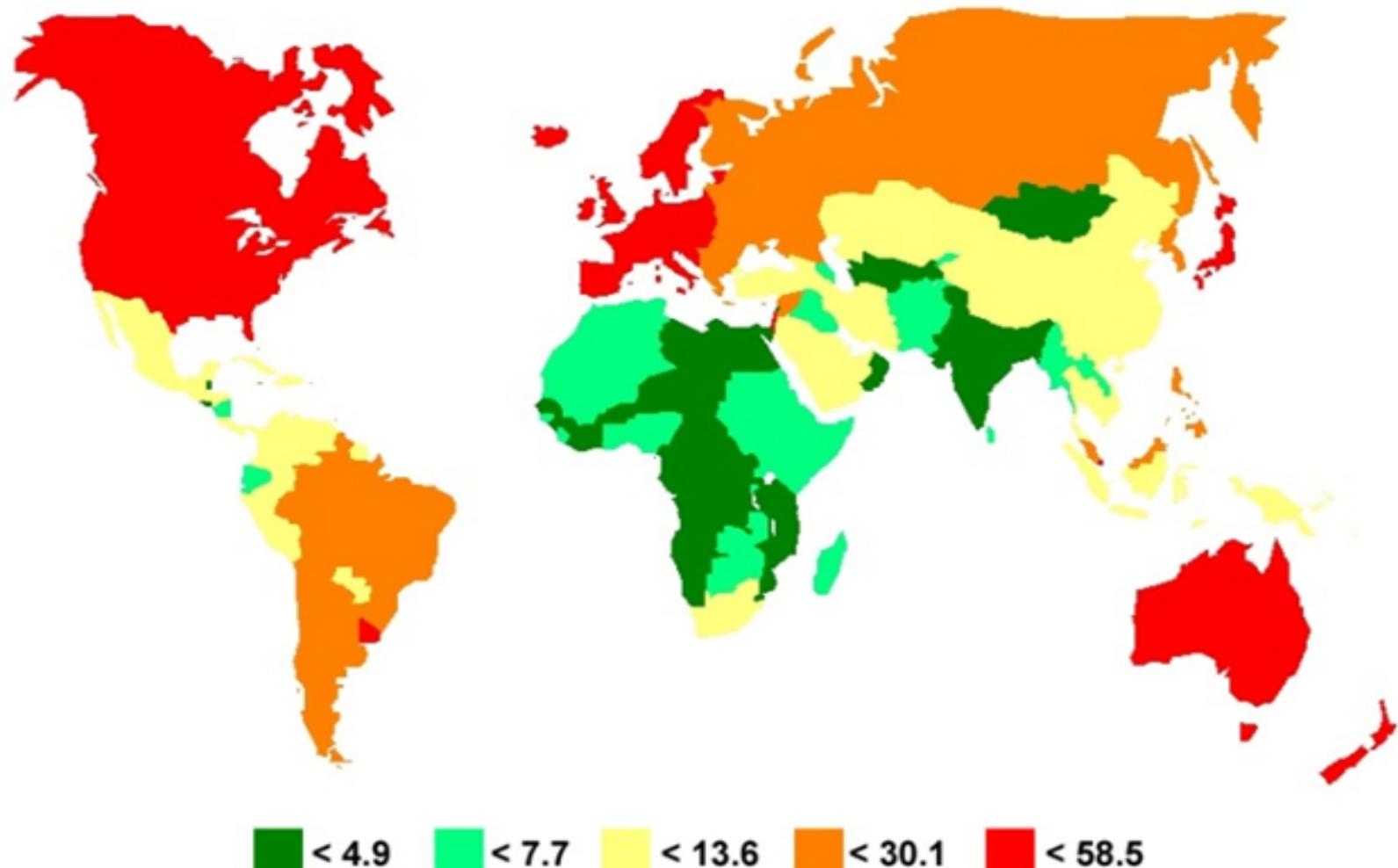
Microbiota composition

Colon cancer rates:
-Africans: <10:100,000
-African Americans: >65:100,000

Ou et al. Am J Clin Nutr.
Jul 2013; 98(1): 111–120



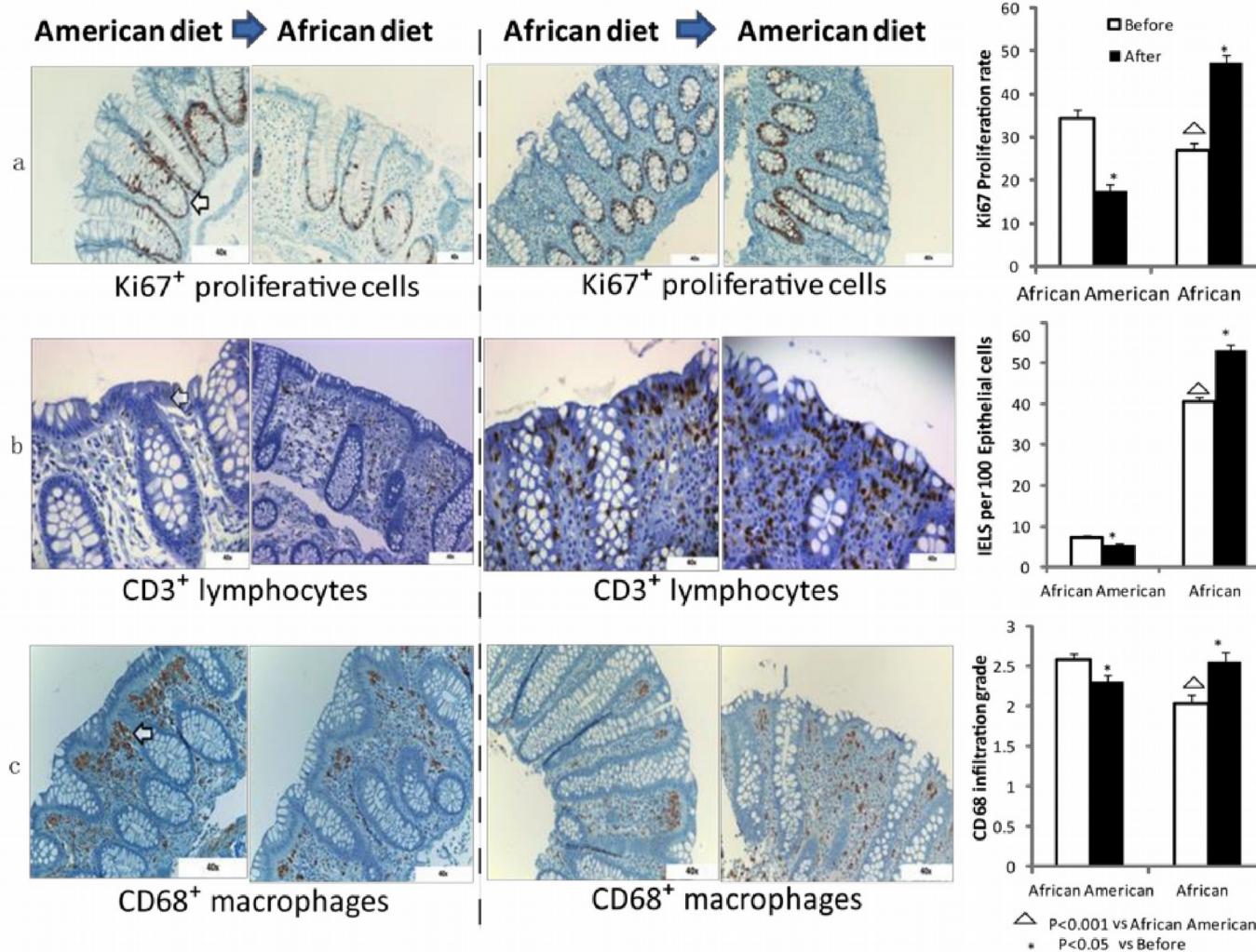
Colon cancer prevalence



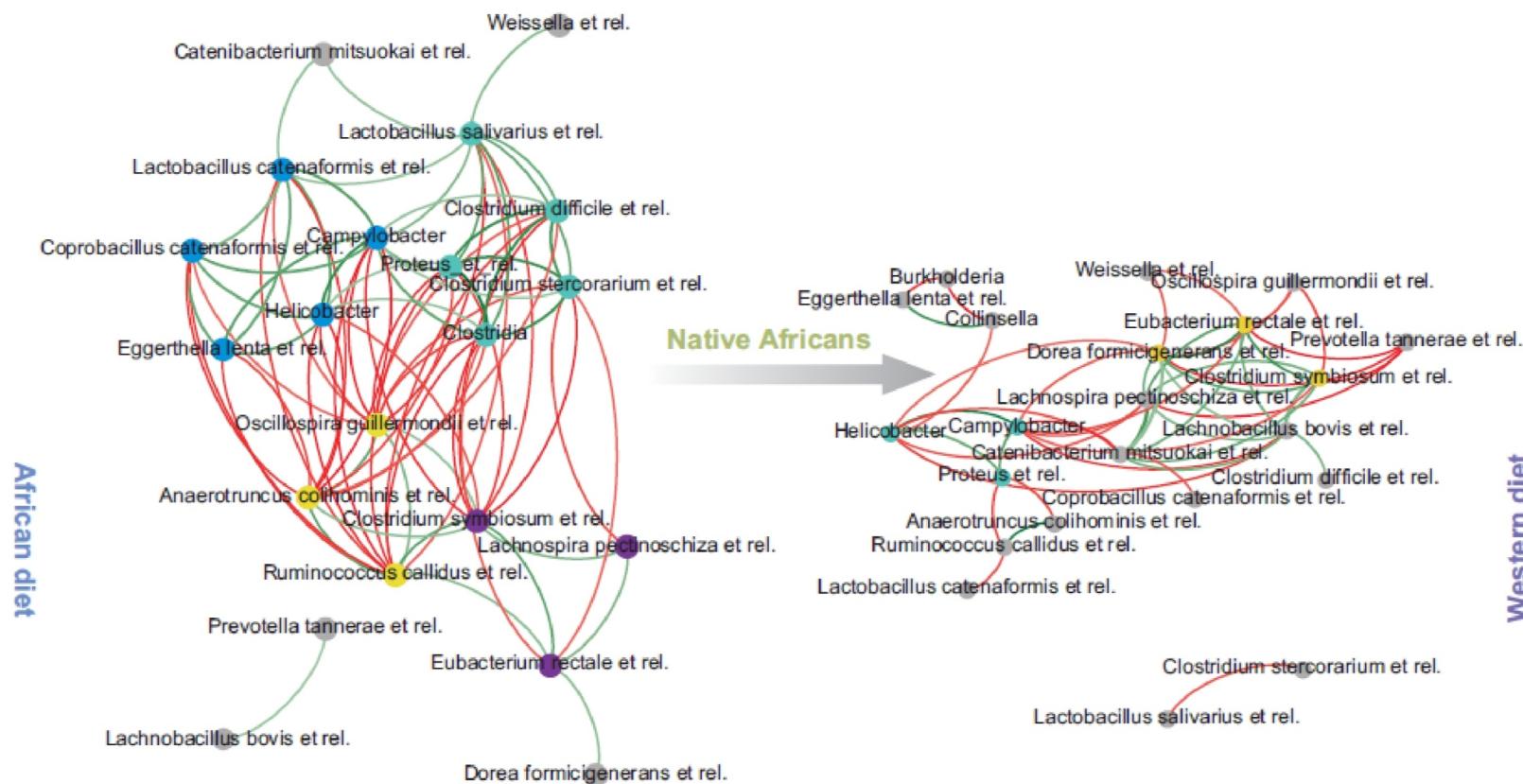
Colon cancer rates per country

Diet swap (2 weeks) and colon cancer risk

Reciprocal impact on epithelial biomarkers for colon cancer risk seen already after two weeks !



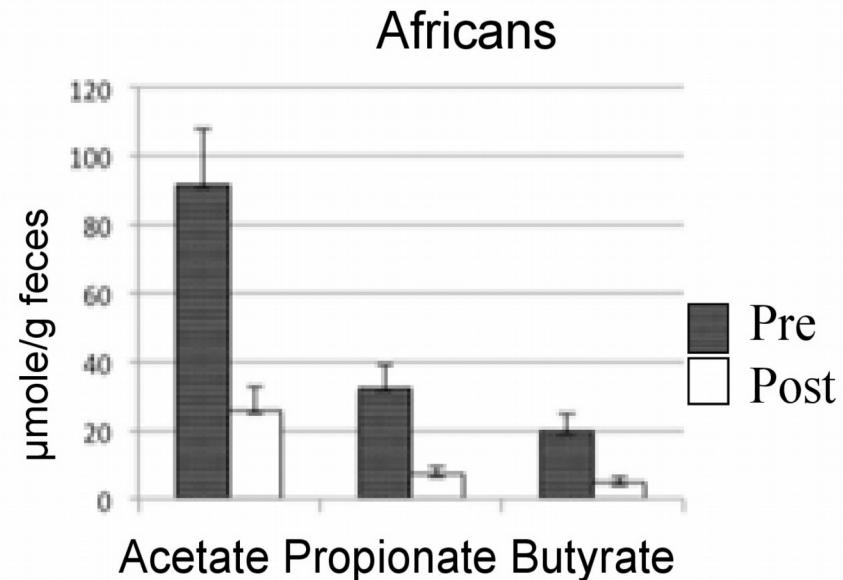
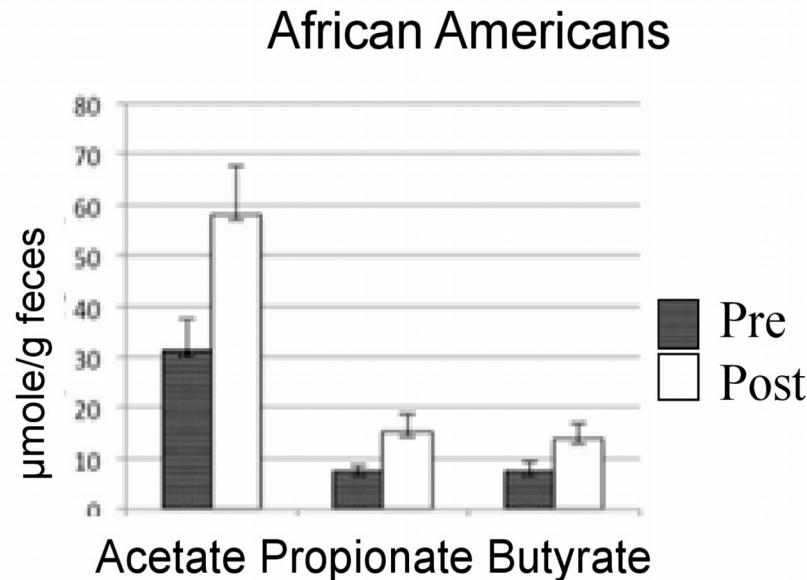
Westernization of African communities?



Short-term diet shift

- > Limited impact on microbiota composition
- > Large impact on microbiota activity
- > Can microbiota interactions explain the differences ?

Impact diet exchange on SCFA

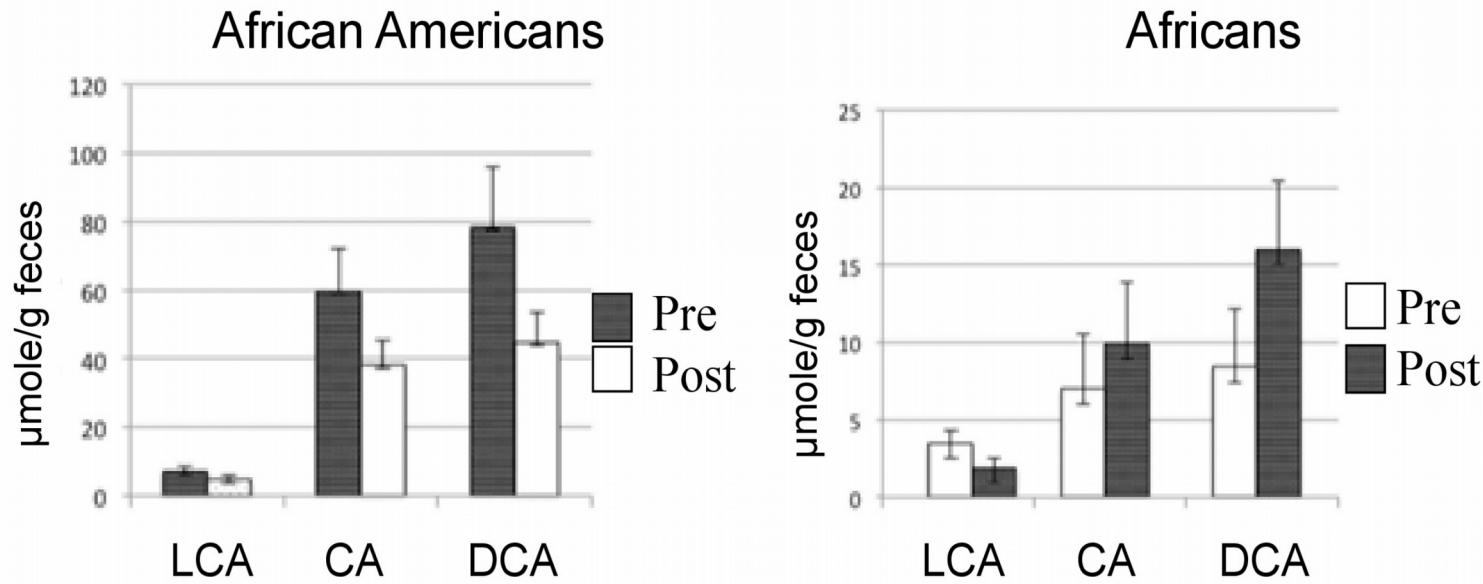


Reciprocally increased SCFA production with African diet: reported anti-inflammatory and anti-carcinogenic properties !

See also
Louis et al. Nat. Rev.
Microbiol Sept 2014

O'Keefe et al. Nat. Comm. 6:6342, 2015

Impact diet exchange on bile acids



LCA: Lithocholic Acid, CA: Cholic Acid, DCA: Deoxycholic Acid

Primary and secondary bile acids
reciprocally increased with American diet:
reported pro-inflammatory and
carcinogenic properties !

See also
Louis et al. Nat. Rev.
Microbiol Sept 2014



Fiber rich vegetarian food



Finnish Savo
people?



African Zulu
(< 5:100,000)



African
americans
(65:100,000)

Meat and fat



Alaska Yupiks
>100:100,000



Stephen O'Keefe

"African" vegetarian diet – Two weeks

- + Inflammation-reducing microbes
- + Short-chain fatty acids
- Inflammation-promoting microbes
- Bile acids
- Cancer biomarkers (inflammation, cell proliferation)

Challenge for manipulation:
- individual responses !

Responders vs.
non-responders
- personalized treatment ?

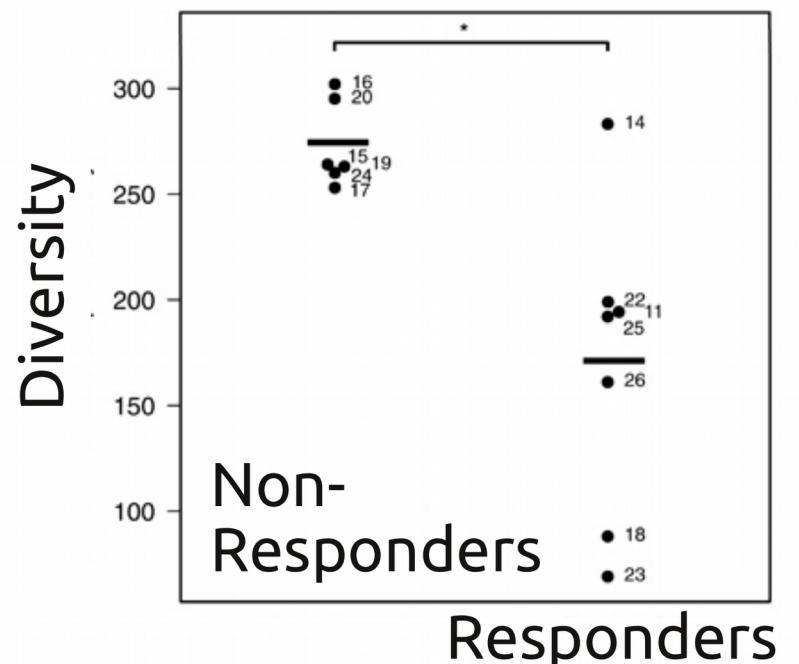
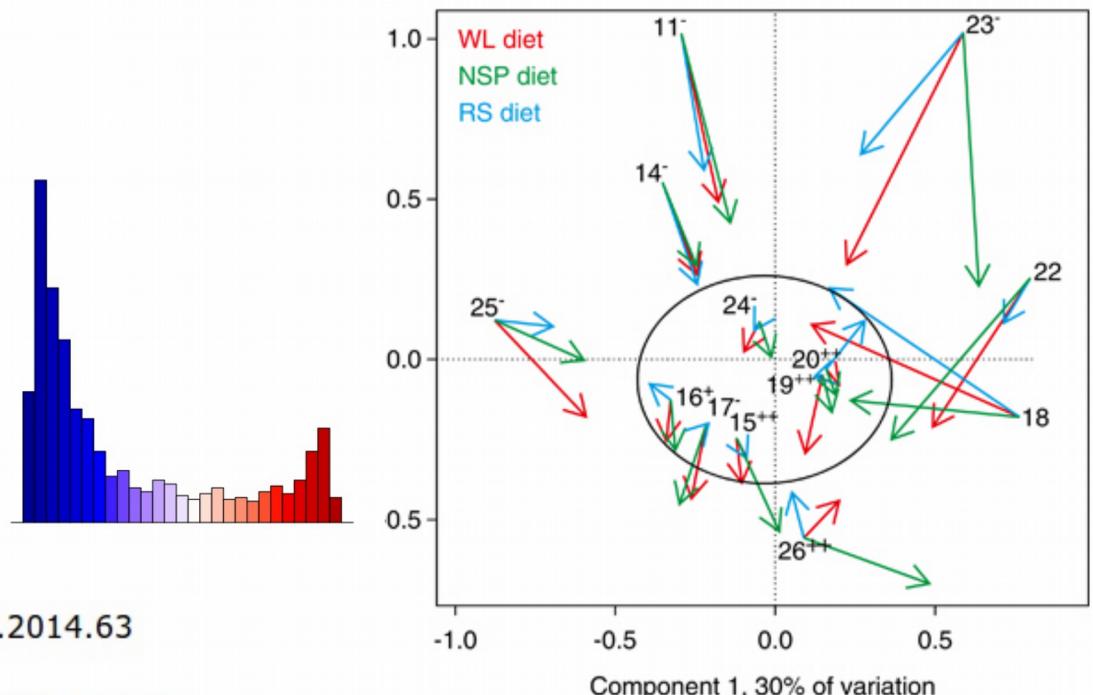
The ISME Journal , (24 April 2014) | doi:10.1038/ismej.2014.63

Impact of diet and individual variation on
intestinal microbiota composition and
fermentation products in obese men

Anne Salonen, Leo Lahti, Jarkko Salojärvi, Grietje Holtrop, Katri Korpela,
Sylvia H Duncan, Priya Date, Freda Farquharson, Alexandra M Johnstone,
Gerald E Loble, Petra Louis, Harry J Flint and Willem M de Vos

Lahti et al. Nat. Comm. 5:4344, 2014

Korpela et al. PLoS ONE 9(3): e90702, 2014



Summary

Individuality and temporal dynamics best understood in the context of larger populations

Majority (>80%) of total variation in healthy microbiome composition still not explained

Standardization, study design and confounder analysis remain essential yet easily overlooked

Open data, analysis & visualization tools:
<http://microbiome.github.io>



Wednesday outline

- Network pharmacology modelling to predict personalized drug combinations (Jing Tang)
- Tipping points in ecological networks (Vasilis Dakos)
- Evolving web of antagonistic interactions among digital organisms (Miguel A Fortuna)
- Tutorial: human gut microbiome population-level analysis (Leo Lahti & Karoline Faust):
<http://microbiome.github.io/microbiome/Tutorial.html>

Thank You !

Materials at: <http://www.iki.fi/Leo.Lahti>

Jeroen Raes

Willem M de Vos

Sudarshan Shetty

Anna Sorjamaa

Justus Reunanen

Karoline Faust

Didier Gonze

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Wageningen University, Lab.

Of Microbiology, Netherlands

VIB/KU Leuven, Center for

Biol. Of Disease, Belgium

Intestinal microbiome landscaping: Insight into community assemblage and implications for microbial modulation strategies. Shetty, SA et al. *FEMS Microbiology Reviews* 2017, fuw045

Population-level analysis of gut microbiome variation. Falony et al. *Science* 352(6285):560-4, 2016

Metagenomics meets time series analysis: unraveling microbial community dynamics. Faust, Lahti et al. *Current Opinion in Microbiology* 15:56-66 2015

Improved taxonomic assignment of human intestinal 16S rRNA sequences by a dedicated reference database Ritari et al. *BMC Genomics* 16:1056, 2015.

Fat, Fiber and Cancer Risk in African, Americans and Rural Africans. O'Keefe et al. *Nat. Comm.* 6:6342, 2015

Impact of diet and individual variation on intestinal microbiota composition and fermentation products in obese men. Salonen et al. *ISME Journal* 8:2218-30, 2014

Tipping elements in the human intestinal ecosystem. Lahti et al. *Nat. Comm.* 5:4344, 2014

PhD position open for applications !

- Contact: Leo Lahti leo.lahti@iki.fi
- Belgium (Leuven) & Finland (Turku)
- Microbial bioinformatics, ecology, computational science



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