Ecological Modeling from Time-Series Inference: Insight into Dynamics and Stability of Intestinal Microbiota (2013)

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Outline

- Microbial effects on human health
- Previously shown methods and their shortcomings
- Overview of new method
- Results
- Discussion

Intestinal microbiome: Friend or foe

Diseases. 2018 Sep; 6(3): 56.
Published online 2018 Jun 29. doi: 10.3390/diseases6030056
PMCID: PMC6164700
PMID: 29966270

Gut Microbiome and Cardiovascular Diseases

Naofumi Yoshida, Tomoya Yamashita,* and Ken-ichi Hirata

Luis Vitetta, Academic Editor

Analysis of the relationship between the gut microbiome and dementia: a cross-sectional study conducted in Japan

Naoki Saji, Shumpei Niida, Kenta Murotani, Takayoshi Hisada, Tsuyoshi Tsuduki, Taiki Sugimoto, Ai Kimura, Kenji Toba & Takashi Sakurai

Review Article | Published: 06 March 2019

The microbiome, cancer, and cancer therapy

Beth A. Helmink, M. A. Wadud Khan, Amanda Hermann, Vancheswaran Gopalakrishnan & Jennifer A. Wargo

Nature Medicine **25**, 377–388 (2019) | Download Citation

of Deaths by Cause

World) (2016)

Gut Microbes. 2015; 6(2): 85–92.
Published online 2015 Apr 22. doi: 10.1080/19490976.2015.1024918
PMCID: PMC4615359
PMID: 25901889

Type 2 diabetes and gut microbiome: at the intersection of known and unknown

Smitha Upadhyaya* and Gautam Banerjee

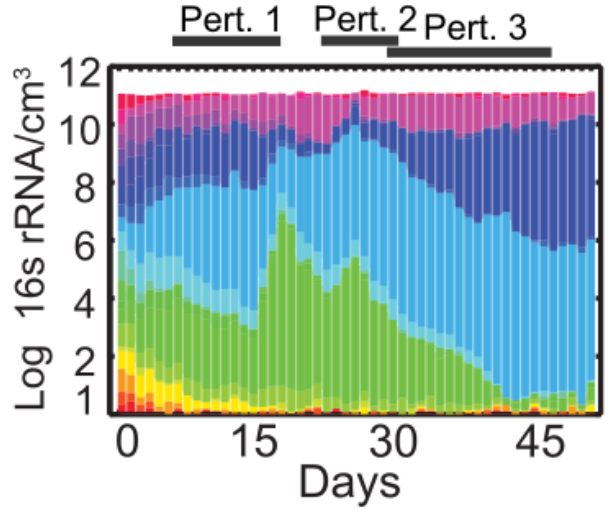
Front Microbiol. 2018; 9: 2147.
Published online 2018 Sep 19. doi: 10.3389/fmicb.2018.02147
PMCID: PMC615652
PMID: 3028341

Diet, Microbiota and Gut-Lung Connection

Swadha Anand and Sharmila S. Mande*

The methods discussed thus far

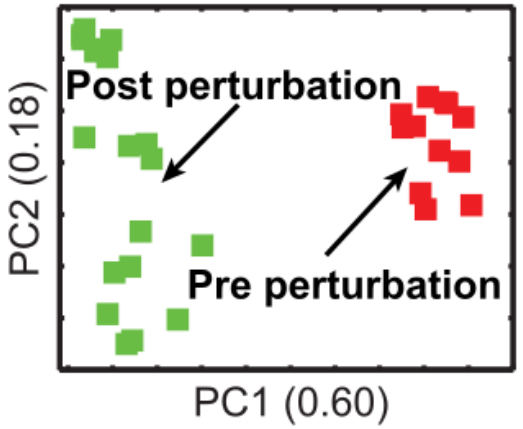
High-throughput community data and perturbation profiles



A: Current Analysis

Cross-sectional analysis

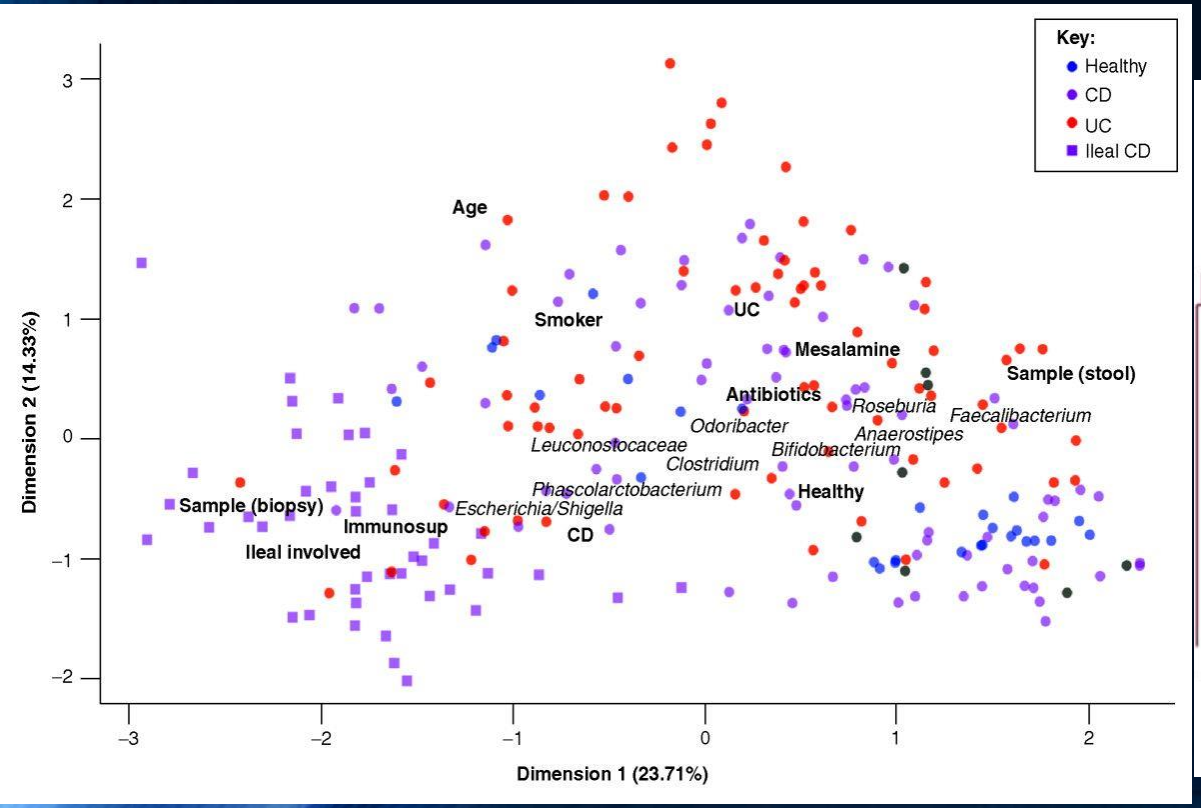
Correspondence analysis

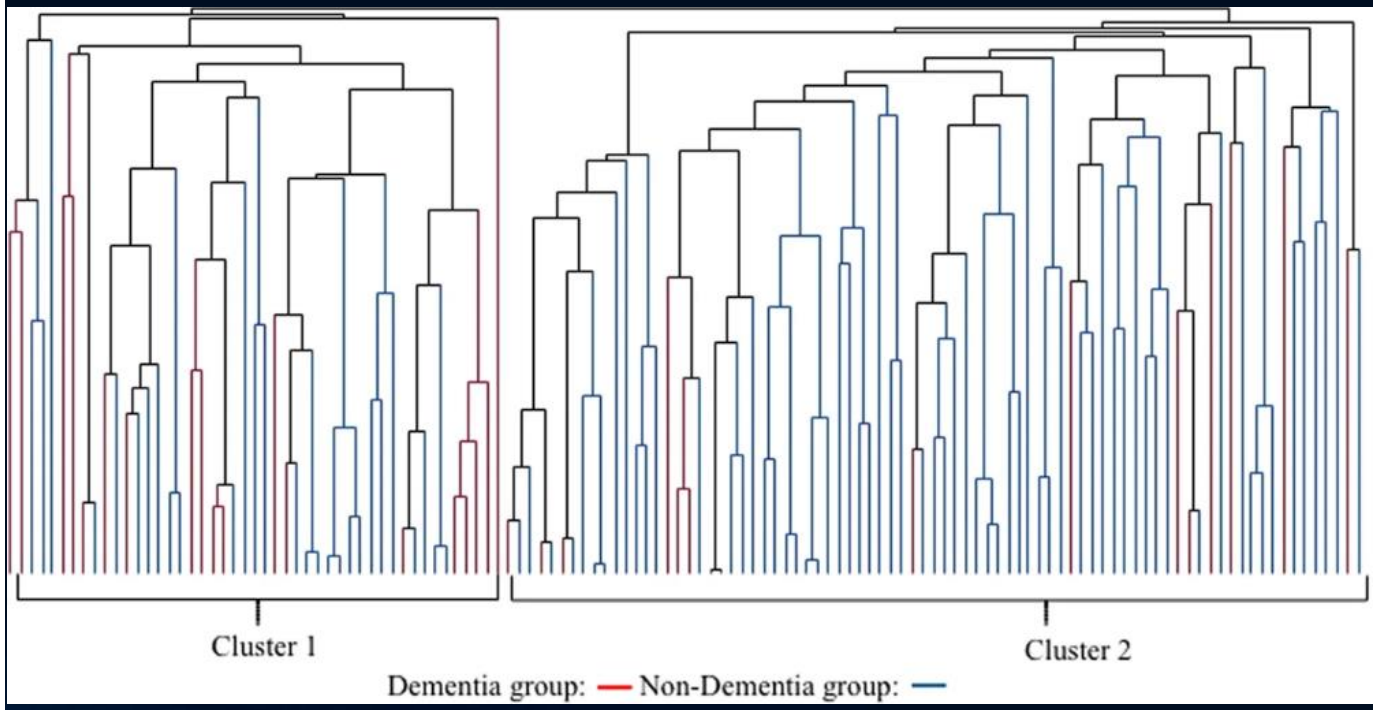


+ Statistical Tests
  (Kruskall–Wallis, Wilcoxon,…)
+ PCoA/NMDS
  (Unifrac, Bray–Curtis, Euclidean)
+ Diversity Indices
  (Shannon, Chao,…)
+ Community Similarity Time Decay
+ Co-occurance (correlation) networks

- Exclusively correlative (non-directional) inference of interaction
- No predictive power
- Limited to a single time-frame

Static analyses



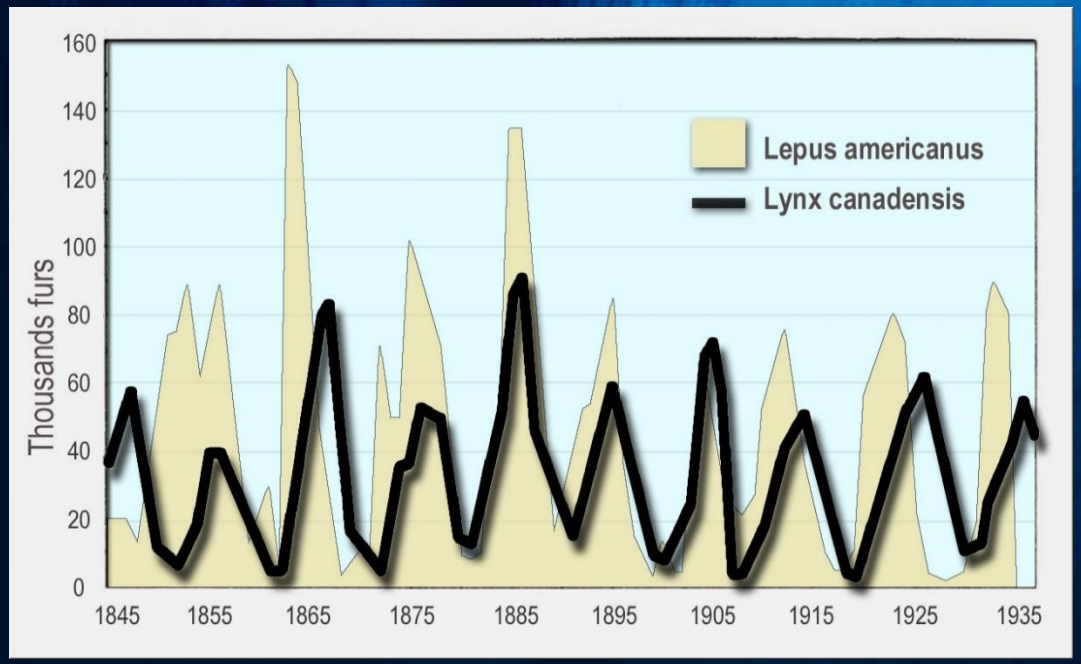


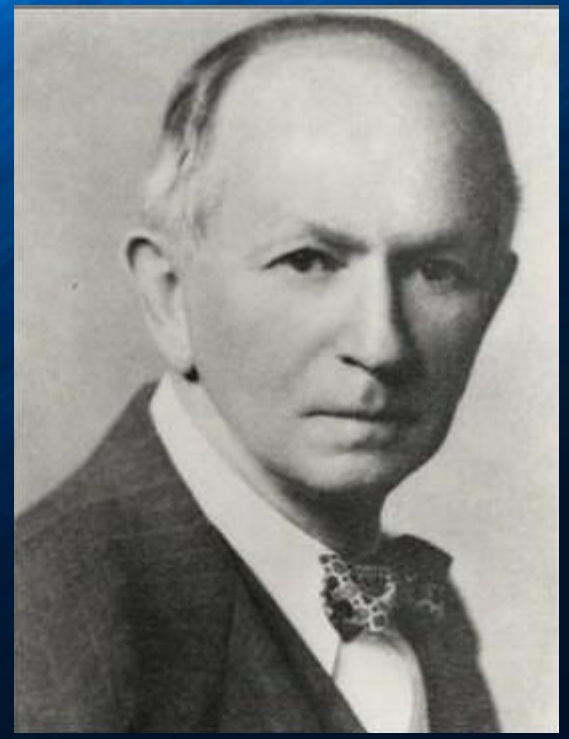
Microbes are alive

The microbiome is highly dynamic, effected by various factors:

- Diet
- Competition
- Drugs
- Infections

Lotka-Volterra Predator-prey model (1910)

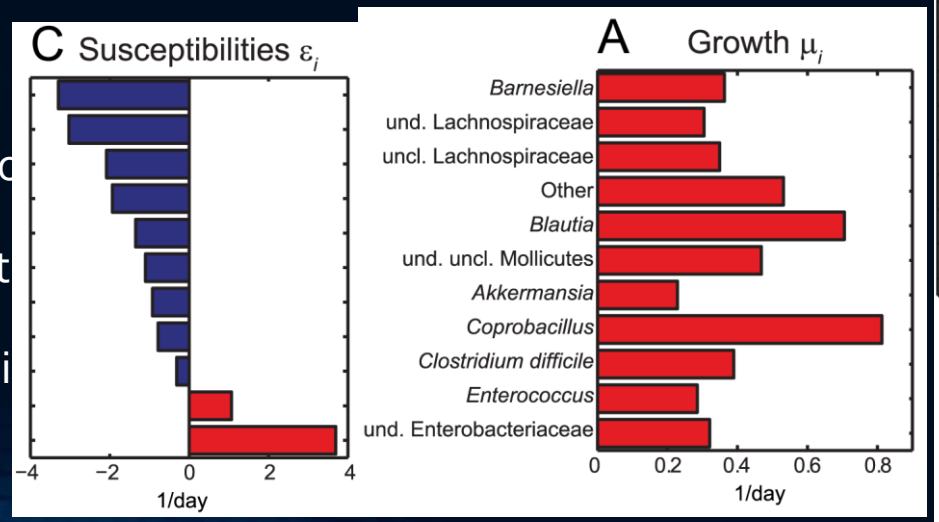


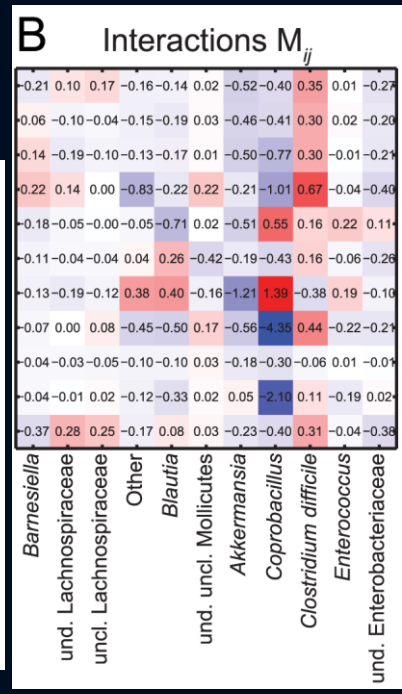


Modelling an ecological community

$$\frac{d}{dt}x_i(t) = \mu_i x_i(t) + x_i(t)\sum_{j=1}^{L} M_{ij}x_j(t) + x_i(t)\sum_{l=1}^{P} \varepsilon_{il}\upsilon_l(t)$$

$i = 1, \ldots, L$	Species of interest
$x_i(t)$	Concentration of i at time point t
μ_i	Growth rate of i
M_{ij}	Effect of j on i during interacti
ε_{il}	Susceptibility of i to perturbat
$\upsilon_l(t)$	Susceptibility of i to perturbati





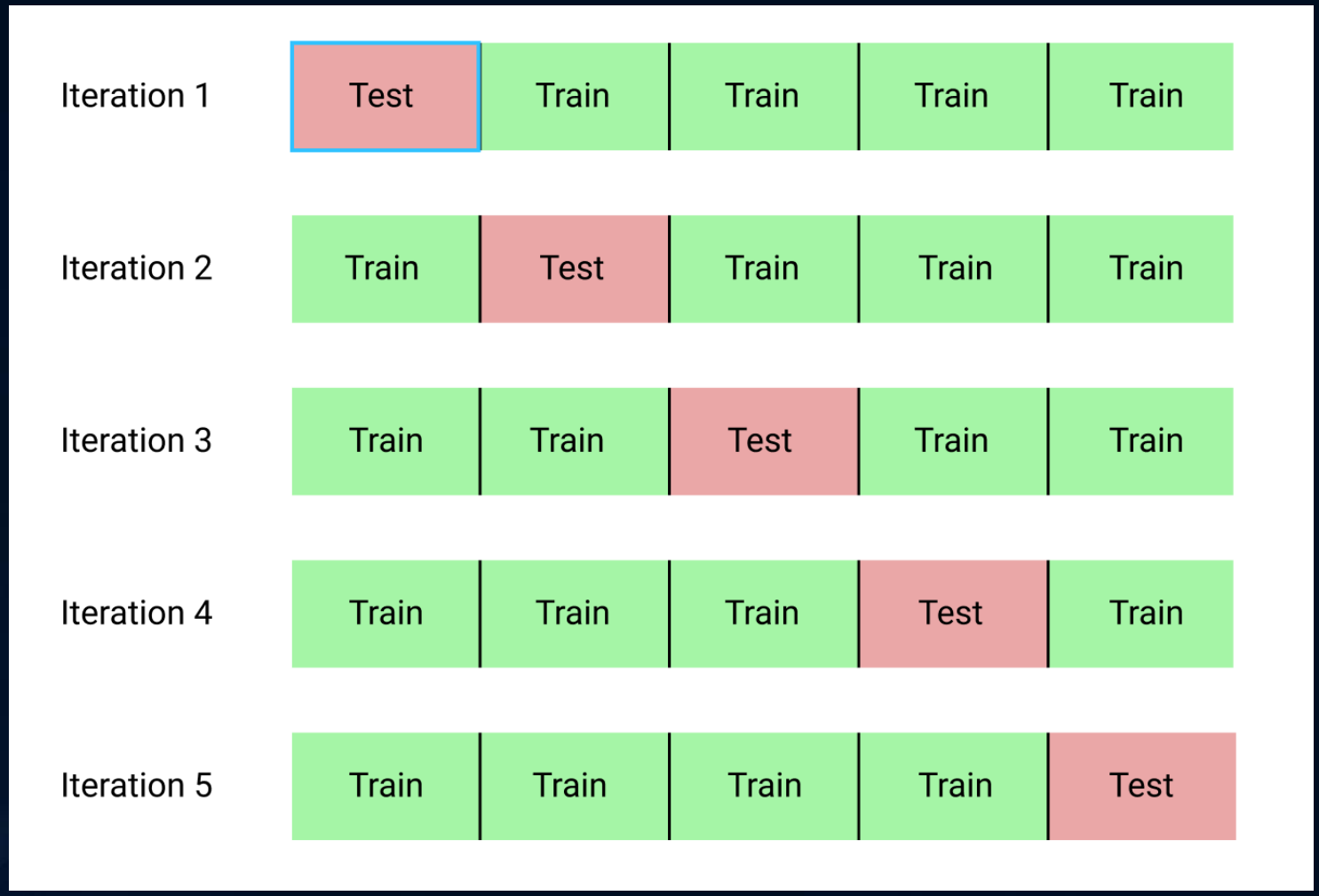
Converting continuous to discrete

$$\frac{\Delta \ln x_i(t_k)}{\Delta t_k} = \mu_i + \sum_{j=1}^{L} M_{ij} x_j(t_k) + \sum_{l=1}^{P} \varepsilon_{il} \upsilon_l(t_k)$$

Estimating parameters with regularized regression

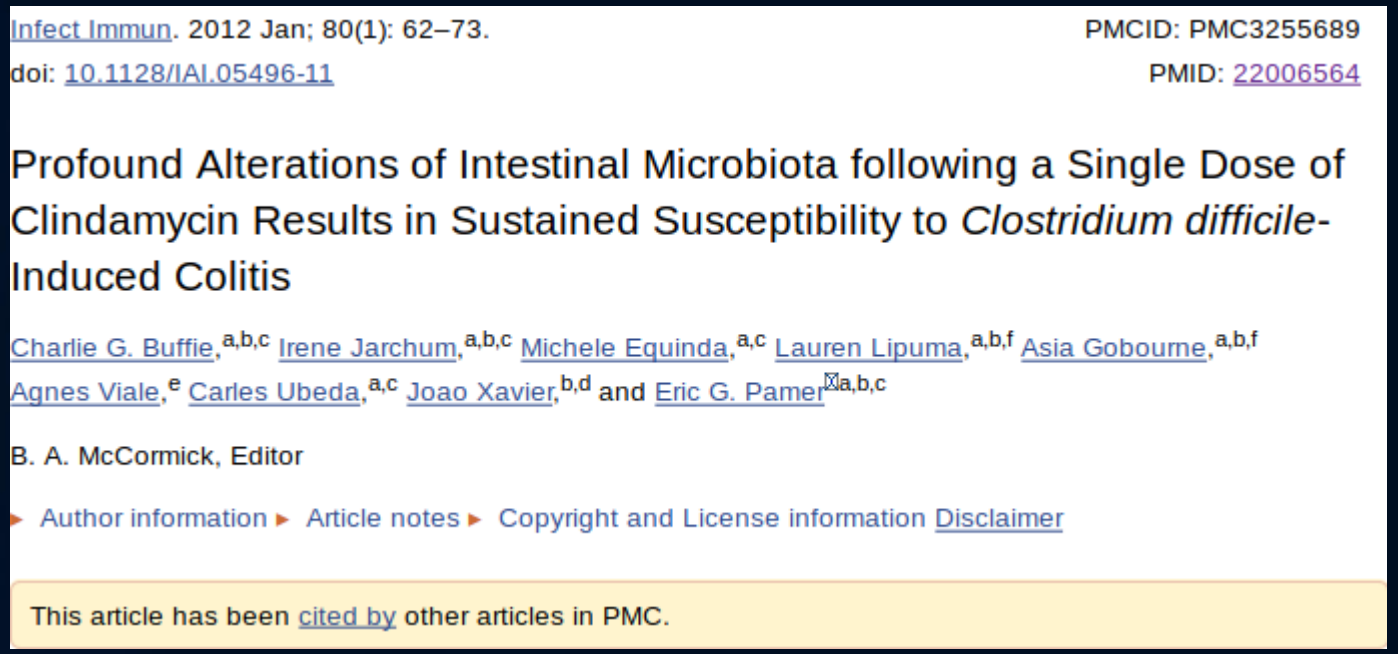
$$\min \left\| (M\ \mu\ E)Y - F \right\|_2^2 + \lambda_M \left\| M \right\|_2^2 + \lambda_\mu \left\| \mu \right\|_2^2 + \lambda_E \left\| E \right\|_2^2$$

K-Fold cross validation



Shown with k=5, authors used k=3

Mouse experiment



Infect Immun. 2012 Jan; 80(1): 62–73.
PMCID: PMC3255689
doi: 10.1128/IAI.05496-11
PMID: 22006564

Profound Alterations of Intestinal Microbiota following a Single Dose of Clindamycin Results in Sustained Susceptibility to *Clostridium difficile*-Induced Colitis

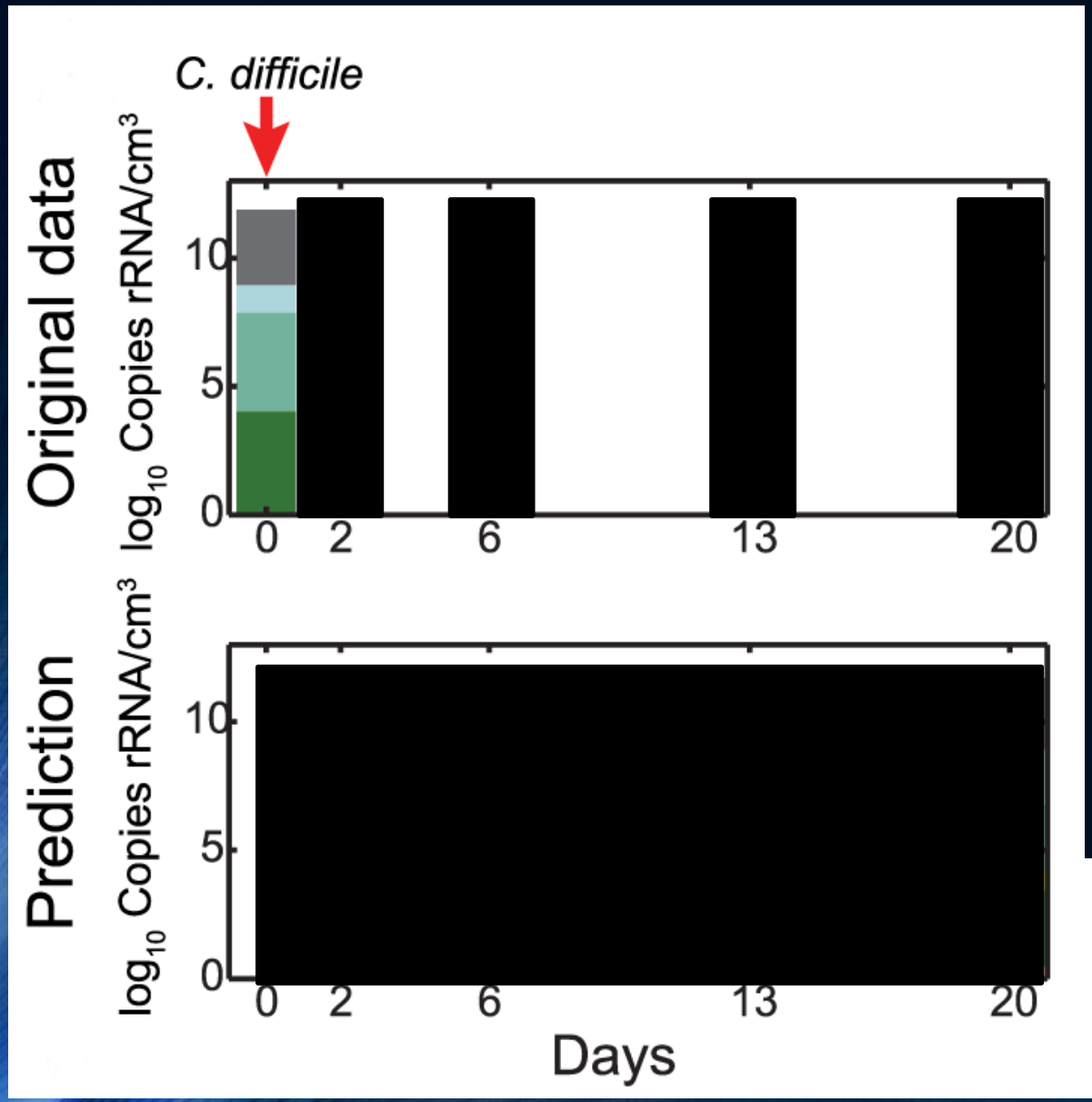
Charlie G. Buffie,[a,b,c] Irene Jarchum,[a,b,c] Michele Equinda,[a,c] Lauren Lipuma,[a,b,f] Asia Gobourne,[a,b,f] Agnes Viale,[e] Carles Ubeda,[a,c] Joao Xavier,[b,d] and Eric G. Pamer[a,b,c]

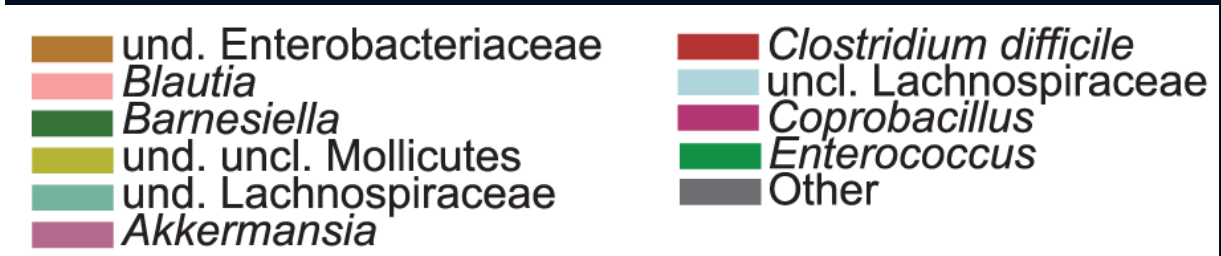
B. A. McCormick, Editor

3 mice groups:

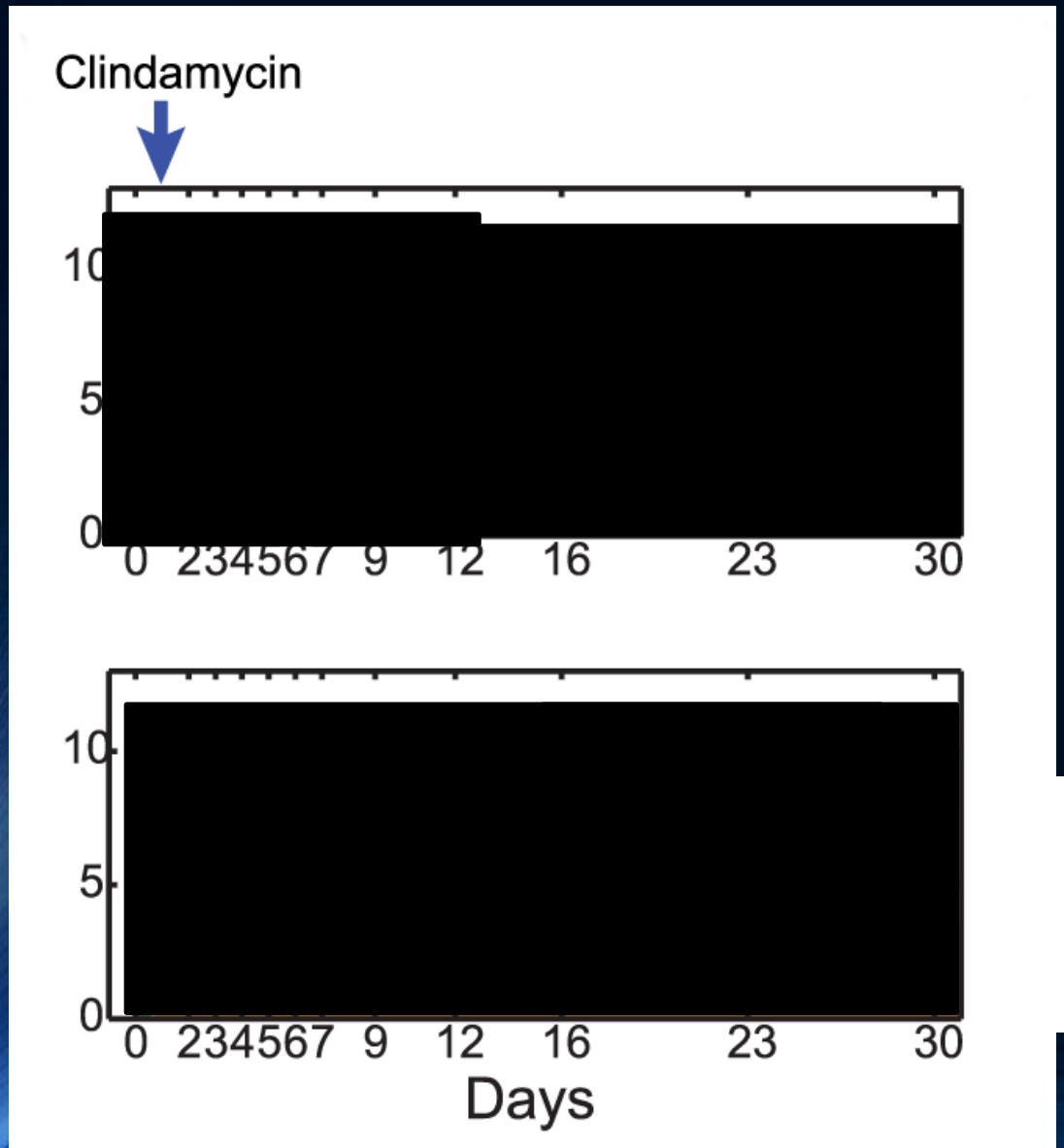
- Administration of Clostridium difficile, a bacterial pathogen.
- Administration of Clindamycin, an antibiotic.
- Administration of Clindamycin, followed by an administration of C. difficile the day after.

Effects of Clostridium difficile

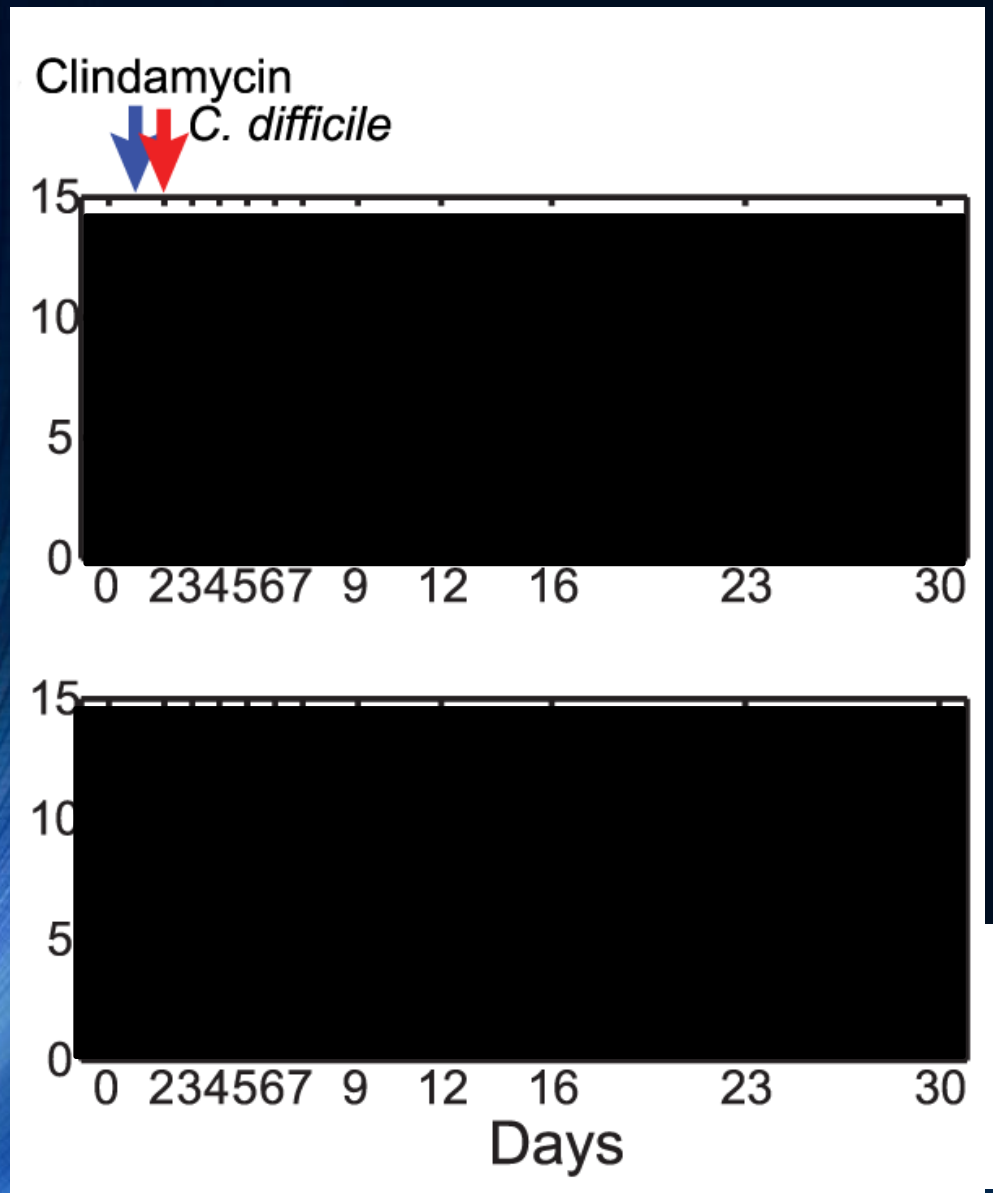




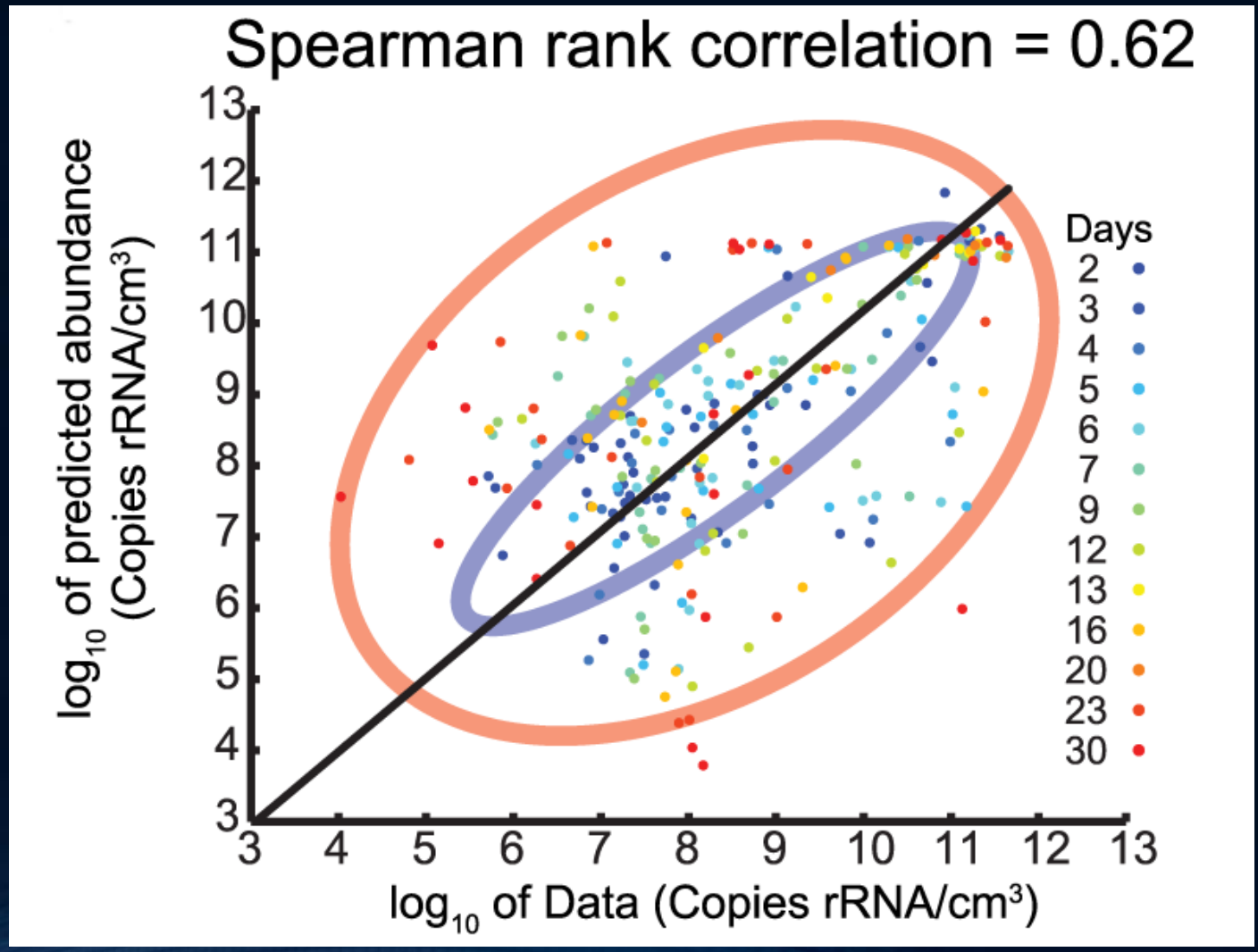
Effects of Clindamycin



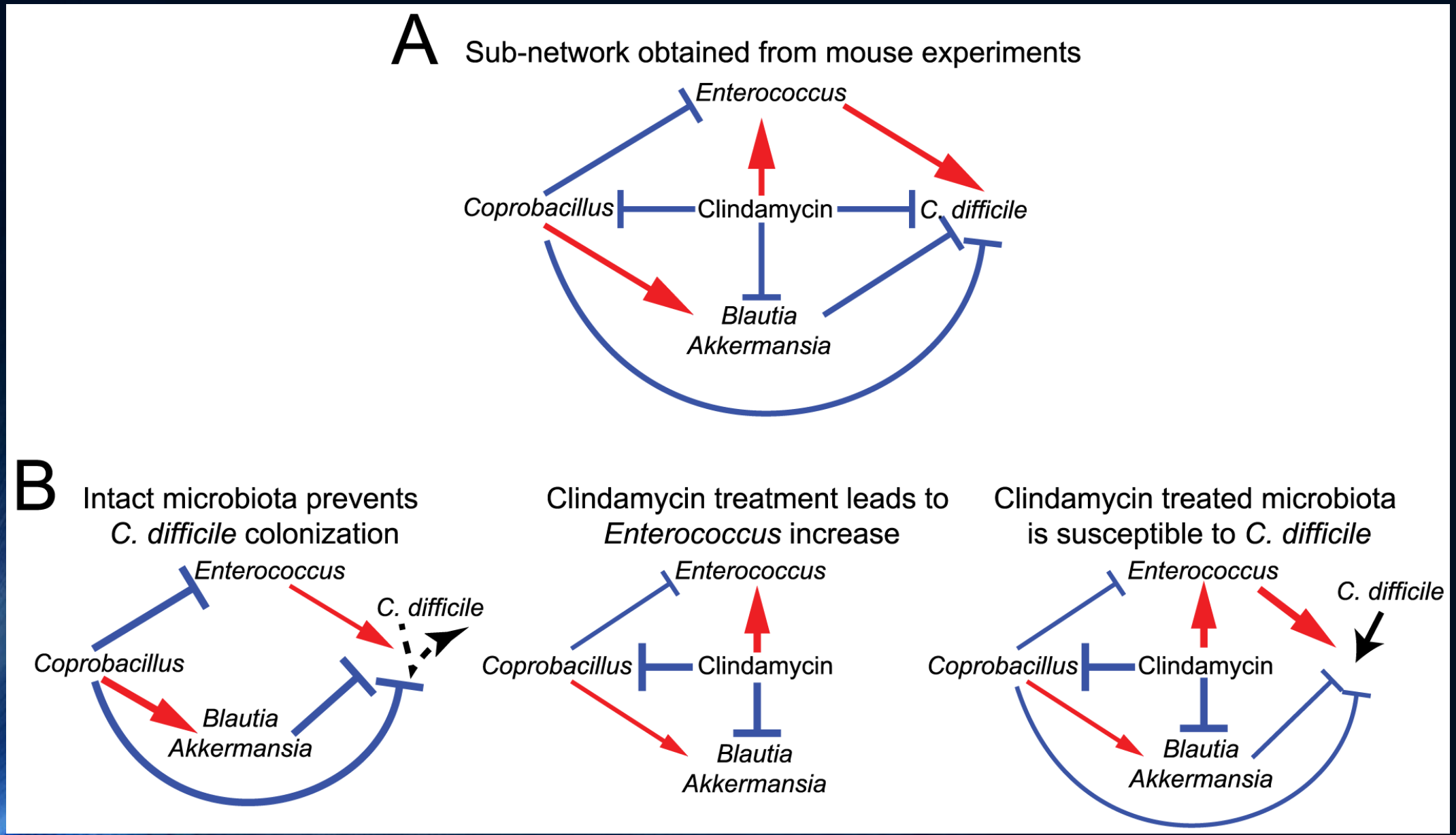
Effects of Clindamycin + Clostridium difficile



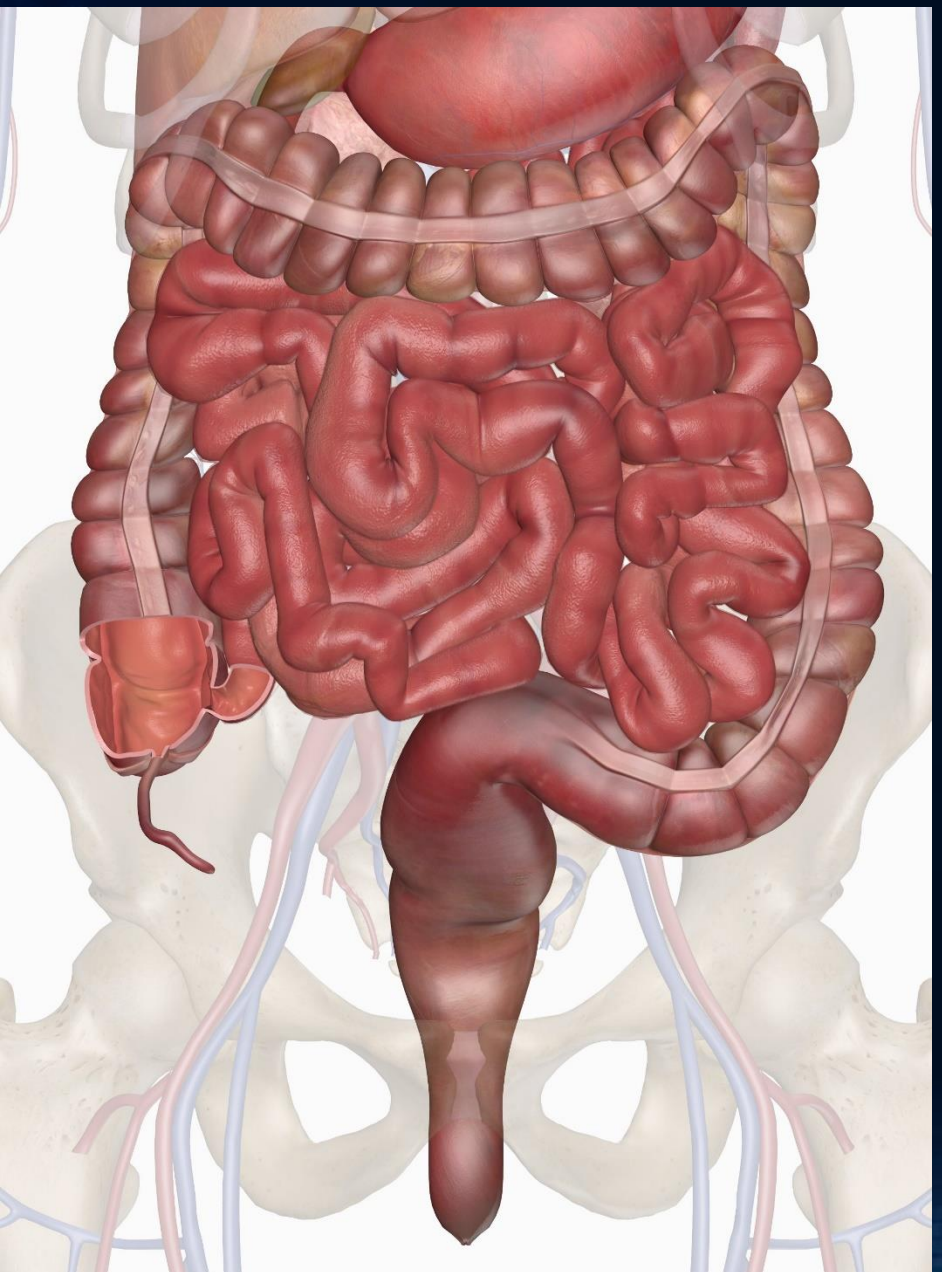
Predictive power



The interplay between microbial taxa



The microbial drama unfolds



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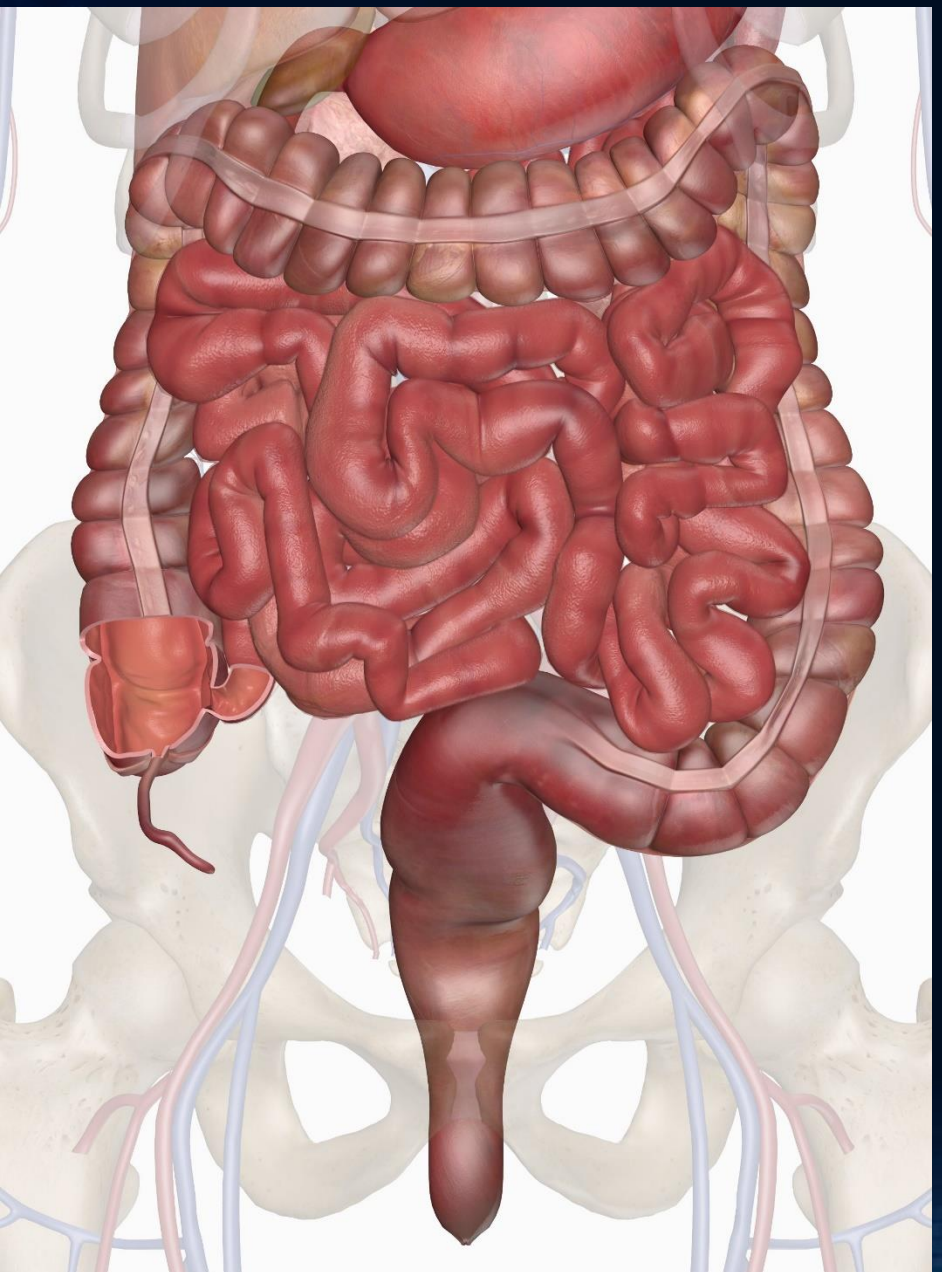

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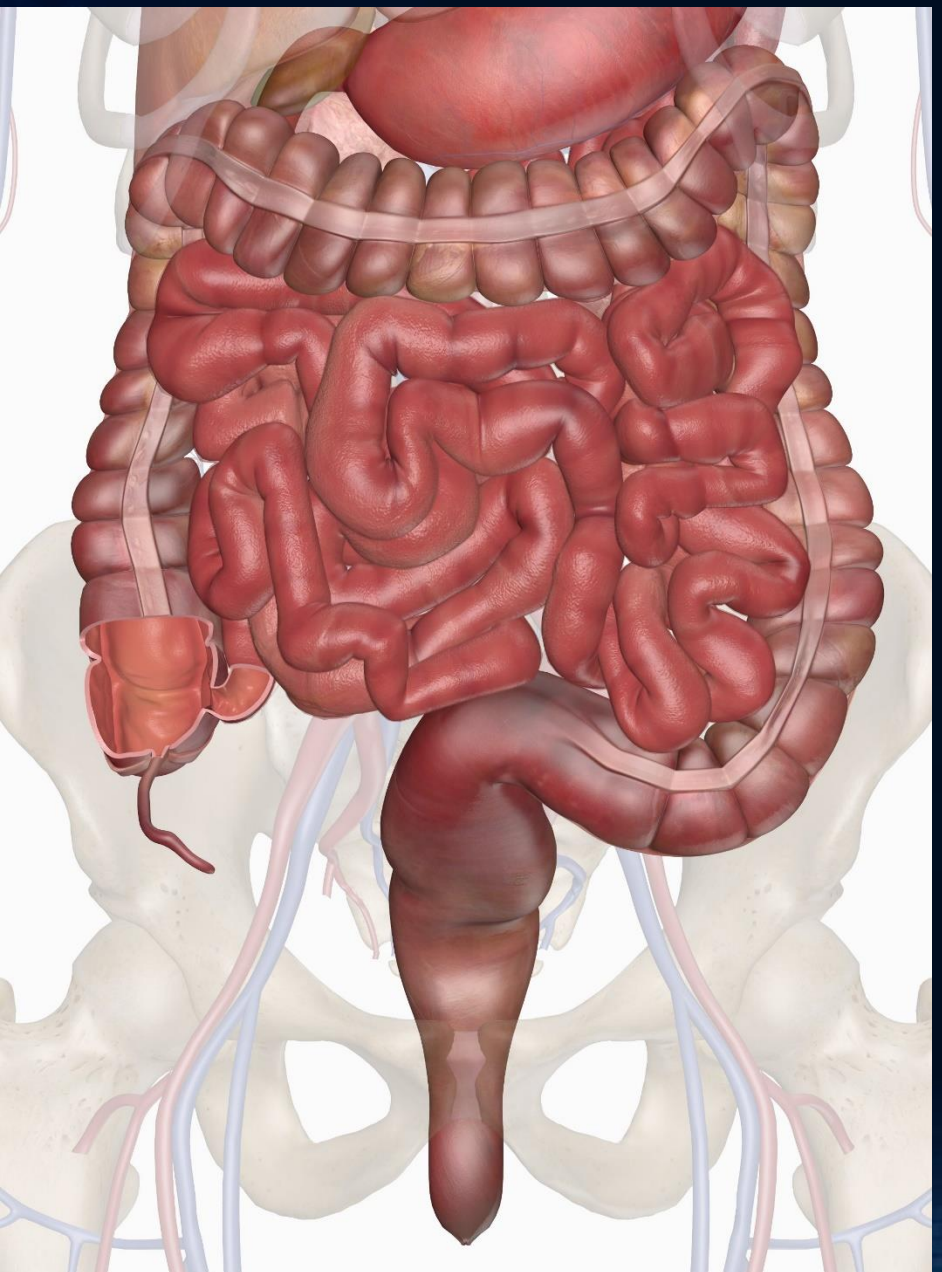
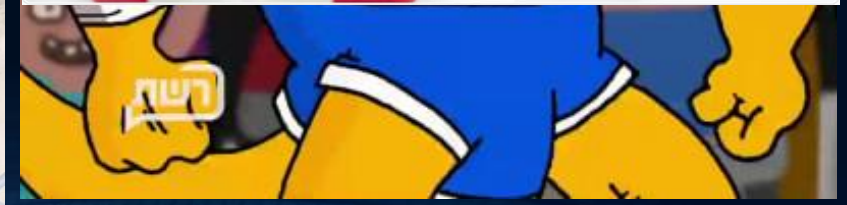
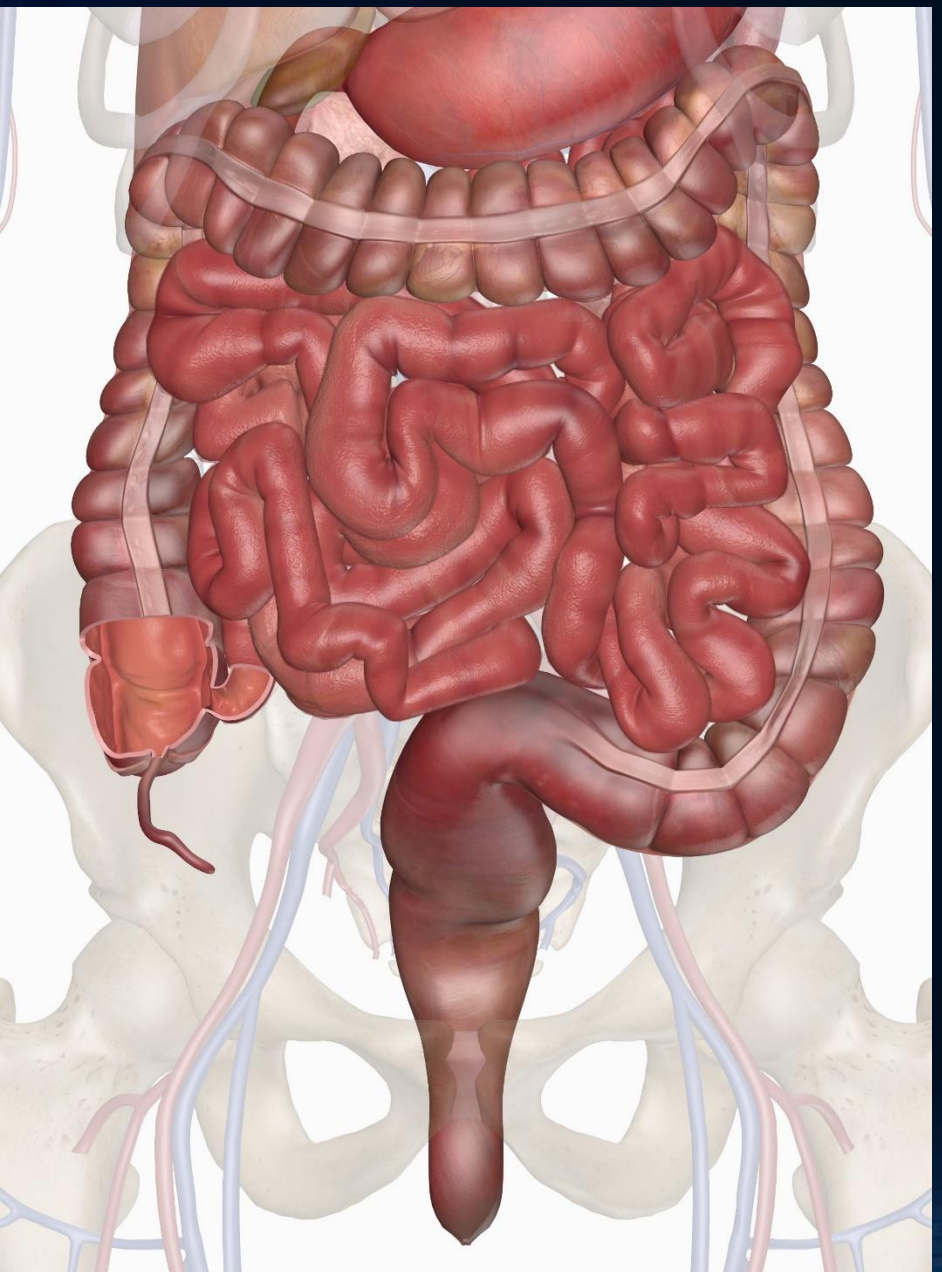




The microbial drama unfolds



Current shortcomings and possibilities for improvement

- Currently tested with absolute data only (antibiotically treated to extinction).
- Only supports with pairwise, second order interactions.
- Currently only works with roughly estimated and transformed count data
- Works in a rough genus-level resolution and includes only the most common of those
- More specific and gradual experimental data for empirical modeling of specific effects

Discussion

- What is the best possible way to improve the current method (whether it's a model improvement, addition, data consideration)?
- Are you more averse to antibiotic treatment after seeing the results of the experiment