Modeling recovery of Crohn's disease, by simulating microbial community dynamics under perturbations

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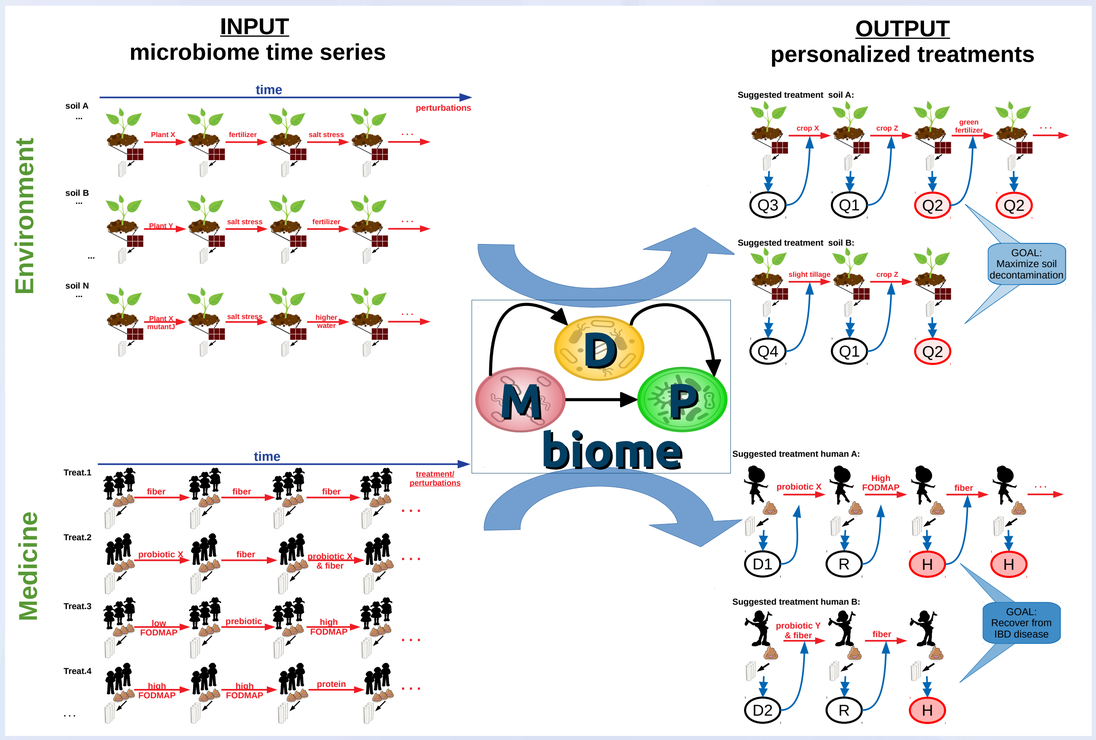
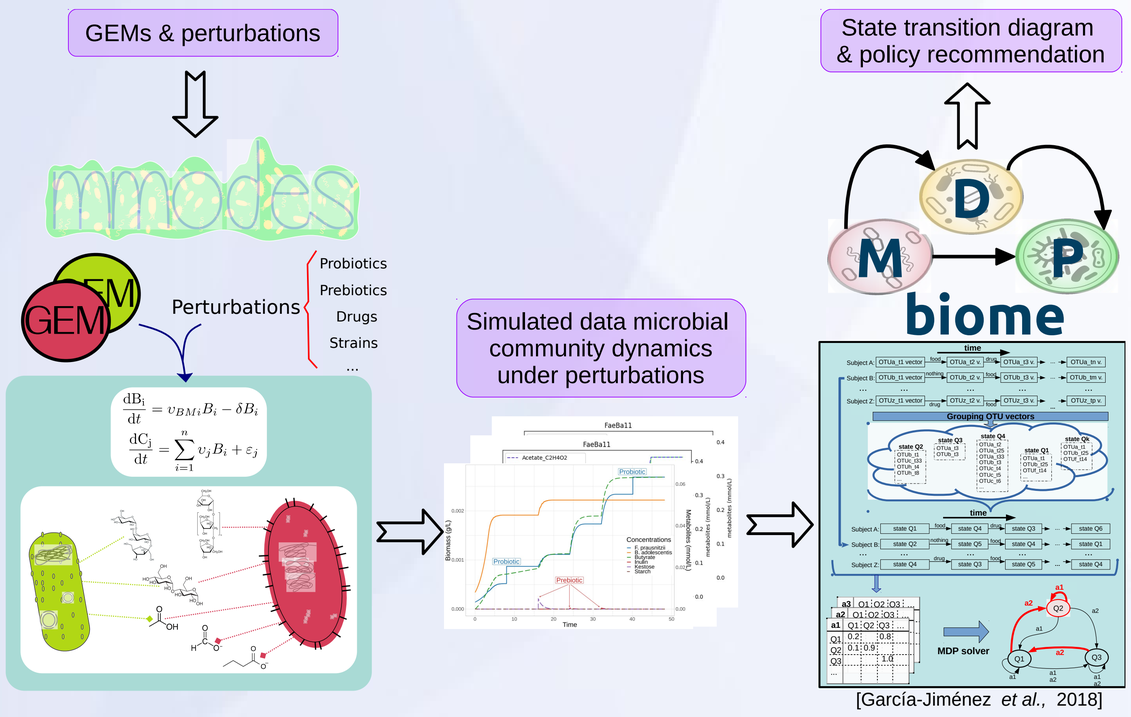
TALK Monday 12:20h SysMod

- Motivation: There are few large longitudinal microbiome studies with planned interventions over time and, thus, few opportunities to employ data-driven systems to analyze microbial communities dynamics under perturbations
- Methods: Our novel tool, MMODES, simulates the dynamics of microbial communities under perturbations (such as pre-/pro-biotics) using genome-scale metabolic models (GEM); generating sufficient data to be analyzed by MDPbiome, an Artificial Intelligence system that suggests interventional microbiome engineering strategies
- Results: Simulated data, analyzed by MDPbiome, recommended Inulin (a fiber source) consumption to recover the human gut from Crohn's-related dysbiosis. Inulin promotes butyrate production to reach bowel homeostasis

Motivation / Goal

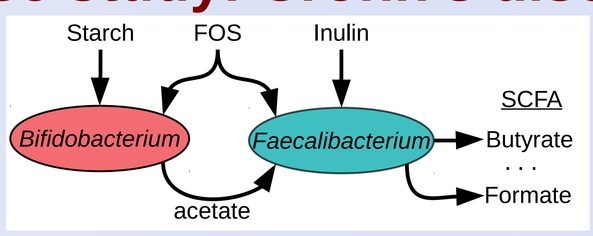


Method: MDPbiomeGEM



[García-Jiménez *et al.*, 2018]

Case study: Crohn's disease



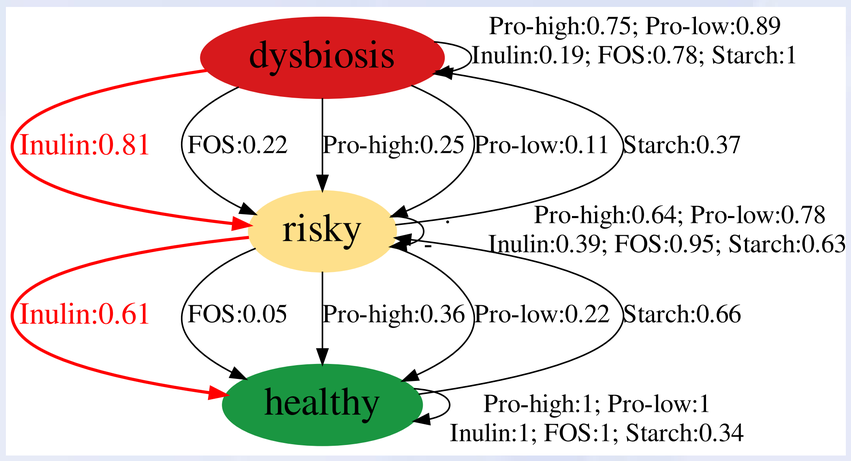
GEM community dynamics methods comparison

Method	Kinetics		Integrator	Space	Perturbations	Reference
	FBA	*Michaelis-Menten*				
MMODES	✔	Fine-tuning	Variable and fixed		✔	This work
DAPHNE	✔	Fine-tuning	Variable			Succurro et al, 2019
BacArena	✔		Agent Based Modeling	✔		Bauer et al., 2017
MCM	✔		Forward Euler Approach			Louca and Doebeli, 2015
COMETS	✔	Global	Forward Euler Approach	✔		Harcombe et al., 2014
DMMM	✔		Forward Euler Approach			Zhuang et al., 2012

Results

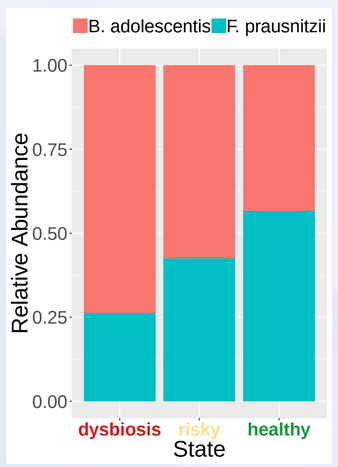
Markov Decision Process diagram with optimal policy

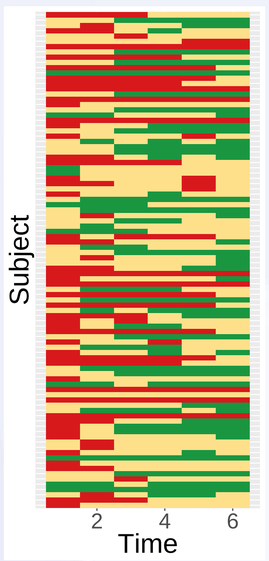
MDPbiomeGEM recommends Inulin as a fiber source to recover the human gut microbiome from Crohn's disease



Microbial community states

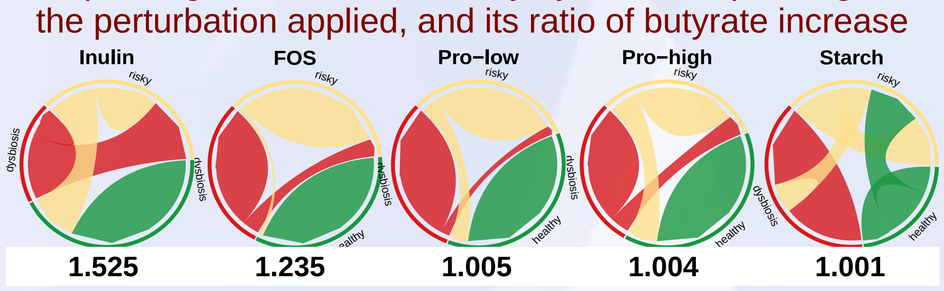
Microbial composition of distinct states and time series of those states in simulated subjects



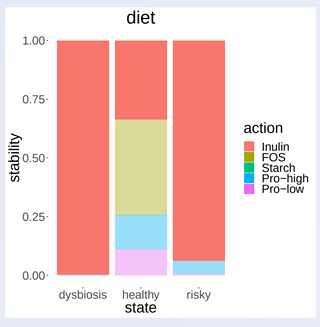


Transition diagrams

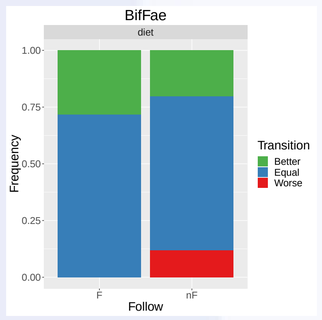
Explaining microbial community dynamics depending on the perturbation applied, and its ratio of butyrate increase



Assessment of the recommendation



- Highly stable recommendation of Inulin to recover from dysbiosis/risky states
  - Higher frequency to move to a better/equal state when following (F) than not following (nF) our policy of Inulin as fiber source



Contributions:

- MMODES simulates various perturbations in microbial community dynamics (such as prebiotics or probiotics)
- MDPbiomeGEM generates predictive personalized intervention plans in the absence of sufficient experimentally-derived metagenomics data
- Empowering microbiome engineering, by data-driven hypotheses
- Design (perturbed) microbial community dynamics experiments, saving resources, in natural and *in-vitro* culture

Limitations: limited to available GEMs, non-standardized nomenclature, non-curated models

https://github.com/beatrizgj/MDPbiome
https://github.com/carrascomj/mmodes
https://doi.org/10.13140/RG.2.2.33350.63049