

Longitudinal Analysis of Child Microbiomes and Brain Development

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- 1 Background
- 2 The RESONANCE cohort of child brain development
- 3 Methods for longitudinal analysis
- 4 The GP tool - GaPLAC

The microbiome develops rapidly in the first year of life

- No (or little) prenatal microbiome
- Perinatal microbiome strongly influenced by delivery, antibiotics, diet (breast milk vs formula)
- Gut microbiome is seeded by delivery (birth canal), skin of caregivers, and milk source
- Slowly increasing diversity, conversion to “adult-like” microbiome after transition to solid food

The brain develops rapidly in the first years of life

- By age 5, brain has reached 85% of adult size
- Gross patterns of axonal connections are established, and near-adult levels of myelination also achieved by 5 years of age
- Development driven in part by environmental exposures (care-giver attention, stress, diet, etc)

The gut-brain-microbiome axis

Evidence of microbiome from pathology

- esp autism
- Autism mouse models
- other behavioral outputs

Open questions

- effects of microbiome on normal brain development
- links between microbial metabolism, gut metabolites, and neurocognitive function

Background
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The RESONANCE cohort of child brain development
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Cohort design

Data Collection

- shotgun metagenomic sequencing
- neuroimaging
- cognitive assessments (IQ-like)
- sleep
- genetics
- Other clinical covariates

Early evidence for effects

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Functional analysis (FSEA)

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Limitations due to pandemic

Background on linear models

Application of linear models to longitudinal data (mixed effects models)

Challenges with microbiome data

- unevenly sampled timepoints
- non-uniform sparsity (eg kids)

Background on GPs

- HMPI-II
- other gp papers

Motivation for using GPs

- Example: irregular longitudinal sampling
- Example: Bugs that disappear or appear with age

(Ga)ussian (P)rocess for (L)ongitudinal (A)nalysis of (C)ommunities

- **Goal:** Make fitting GPs as easy as fitting LMs

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Model definition

Current Functionality - Sample

Current Functionality - MCMC

Current Functionality - Select

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Performance on simulated data

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An H2

Some other stuff

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- Item 1.
- Item 2.
- Item 3.