

Microbiome Systems Biology for Human and Environmental Health

October 6, 2016



BU IBRO

**Boston University Interdisciplinary Biomedical
Research Office**

Dr. Katya Ravid, Director

www.bu.edu/research/ibro

**Pre- Affinity Research Collaborative (ARC)
Microbiome Systems Biology for Human and
Environmental Health**

Co-directors: Drs. Daniel Segrè and Evan Johnson

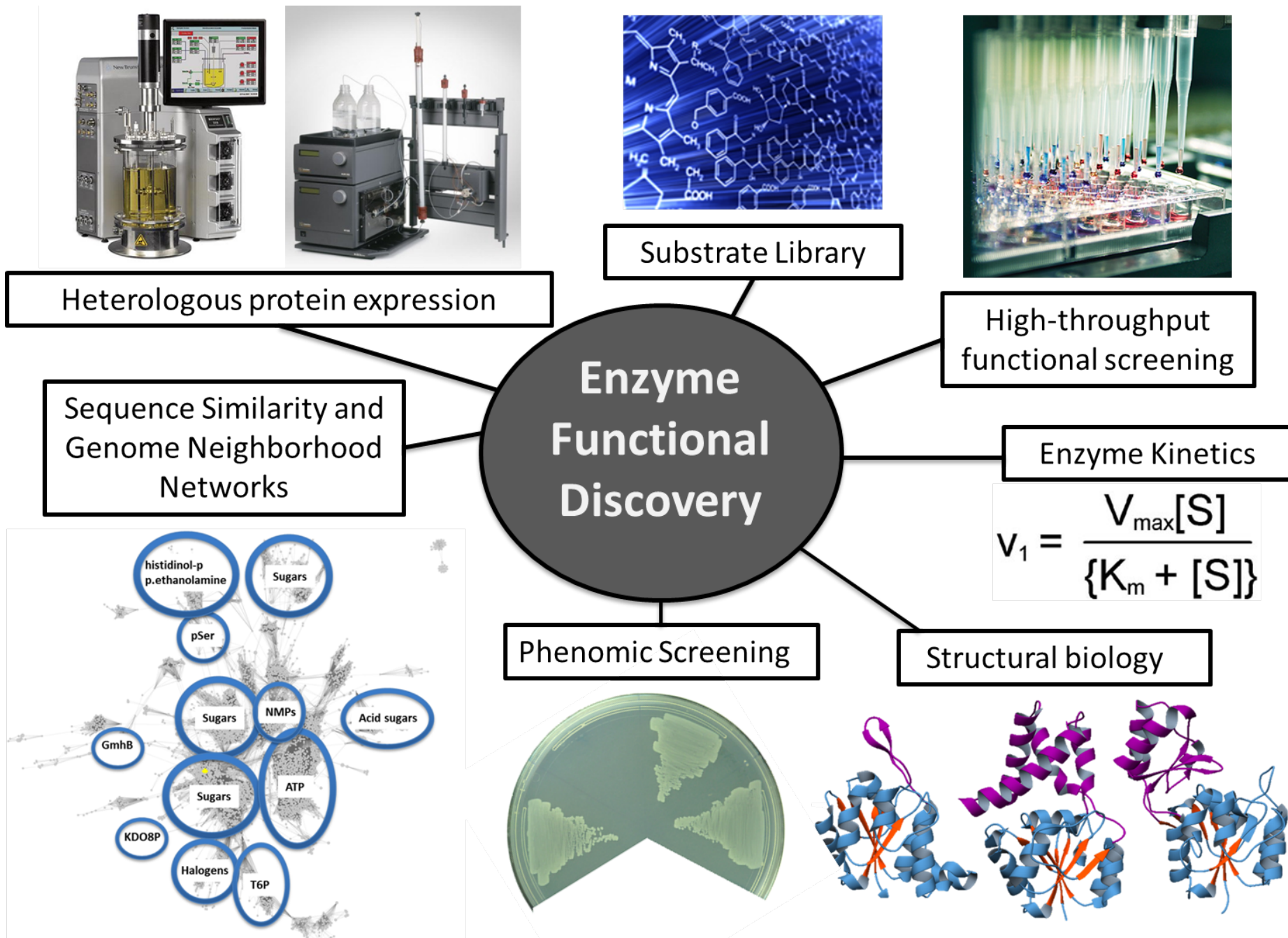
**Faculty participants across
Charles River & Medical Campuses**

3 min presentations

Karen Allen

*Professor
Department of Chemistry
College of Arts & Sciences*

Enzyme Profiling for Functional Discovery



Rama Bansil

Professor
Department of Physics
College of Arts & Sciences

Motility and colonization of *Helicobacter* in stomach mucosa

Rama Bansil
Physics Dept.

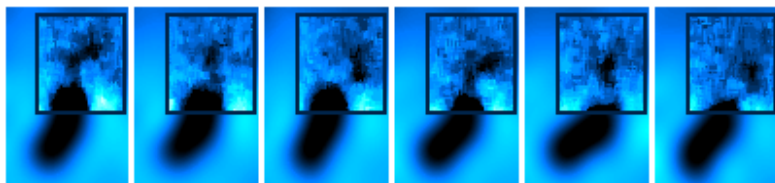
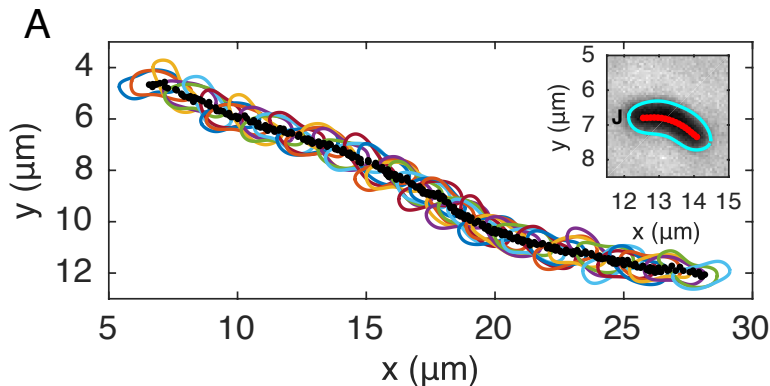
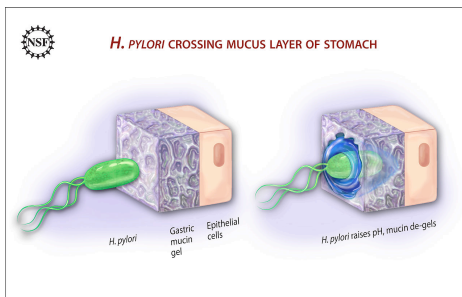
Current Focus:

- Motility across a gel or viscoelastic medium.
- Impact of helical shape and flagella distribution on motility and colonization?
- Chemotaxis in mucus: microfluidic geometries

Interest in Microbiome at BU:

- Access to stomach bacteria. Clinical isolates.
- Collaborate on broader issues of colonization in stomach or other mucosa

Adhesion to mucus



Pamela Templer

*Associate Professor
Department of Biology
College of Arts & Sciences*

Plant-Microbial Interactions in Natural and Managed Ecosystems

Climate Change



Reduced snowpack and increased soil freezing

- reduce water uptake & forest carbon storage
- increase N movement to waterways due to root damage and reduced N uptake by trees
- N losses offset by reductions in soil microbial biomass and exoenzyme activity

Plant-microbe interactions affected by climate change across seasons.

Urbanization



Atmospheric nitrogen deposition

- 4-times greater in Boston than rural areas
- Variation driven by ammonia fertilizer and vehicle emissions

CO₂ fluxes from soils

- 2-times greater in Boston than rural areas
- 77% CO₂ produced from fossil fuel combustion
- Fate of CO₂: vegetation vs. atmosphere

Need understanding of human activities & biological fluxes of carbon and nitrogen in cities.

Adrien Finzi

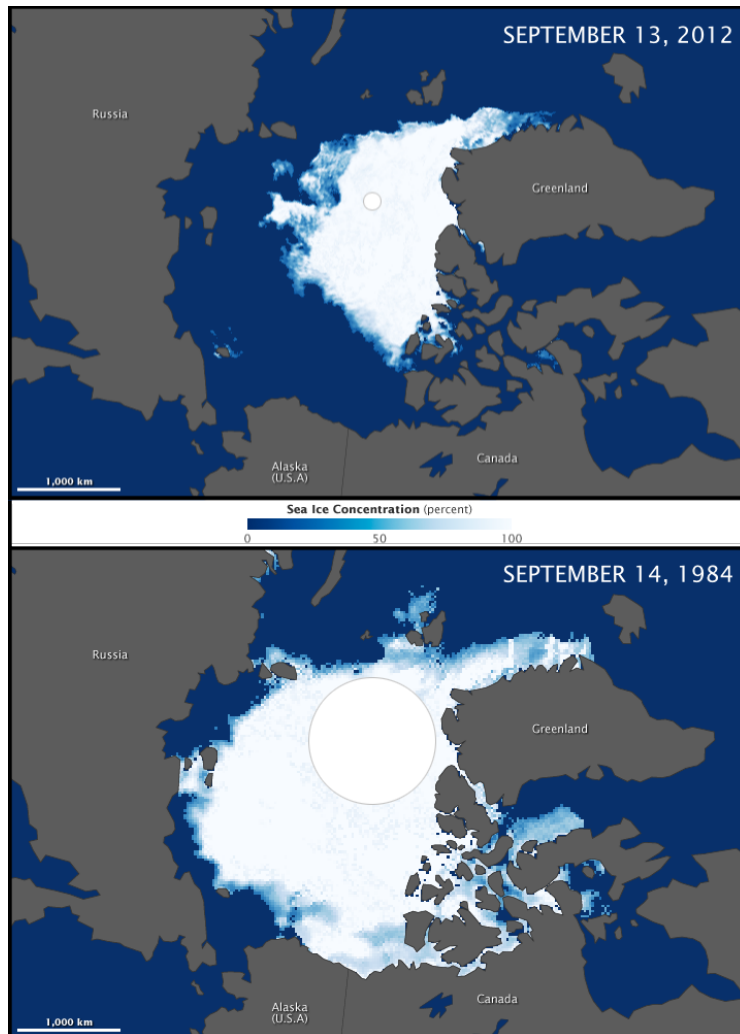
*Professor
Department of Biology
College of Arts & Sciences*

Microbes Gate Keep the Global Carbon Cycle & Regulate Climate

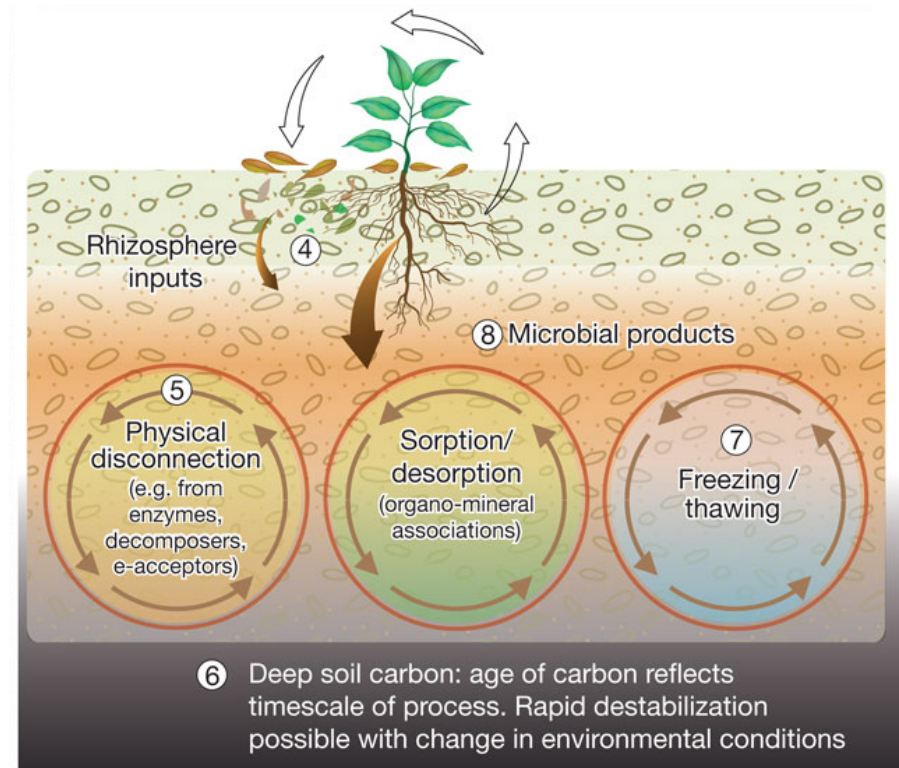
Grand Challenges

Scaling: systems biology to global biogeochemical cycles
microns to soil profiles to soil C inventories
seconds to years to millenia

Separating microbial signals [e.g., decomposition] from noise
[e.g., diversity]



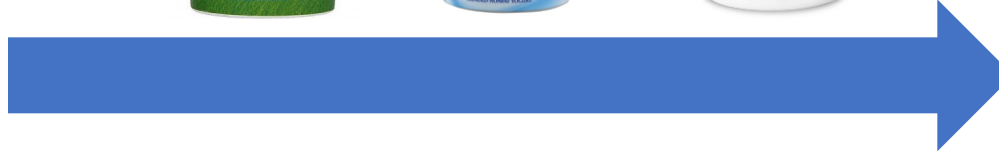
Schmidt *et al.* *Nature* (2011) doi:10.1038/nature10386



Horacio Frydman

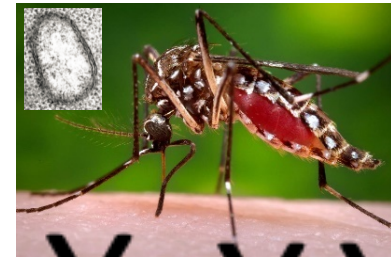
*Associate Professor
Department of Biology
College of Arts & Sciences
and National Infectious Diseases Laboratories (NEIDL)*

Insect probiotics: are *Wolbachia* in mosquitos good for human health?



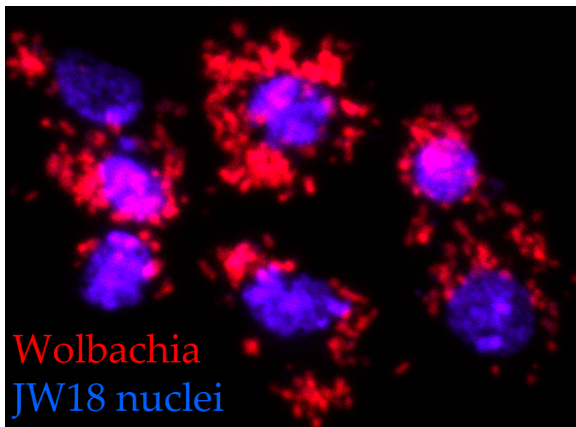
Enterobacter - Gut

Wolbachia - Ovary

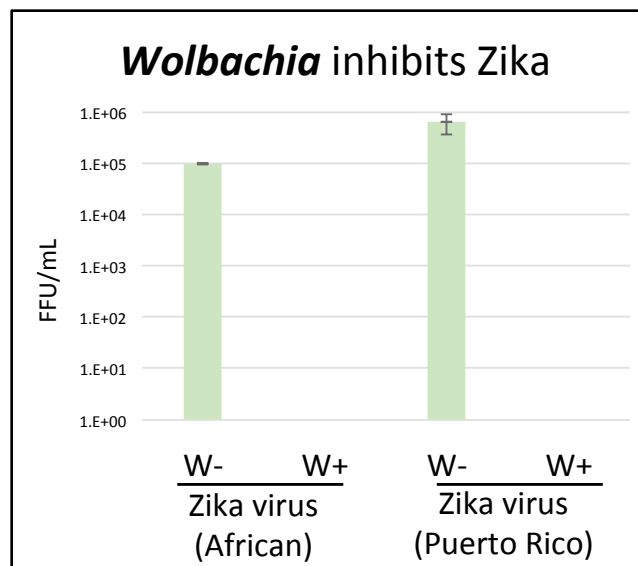


Malaria Dengue Zika

~~Malaria~~ ~~Dengue~~ ~~Zika~~



Frydman Lab, unpublished



Acknowledgements

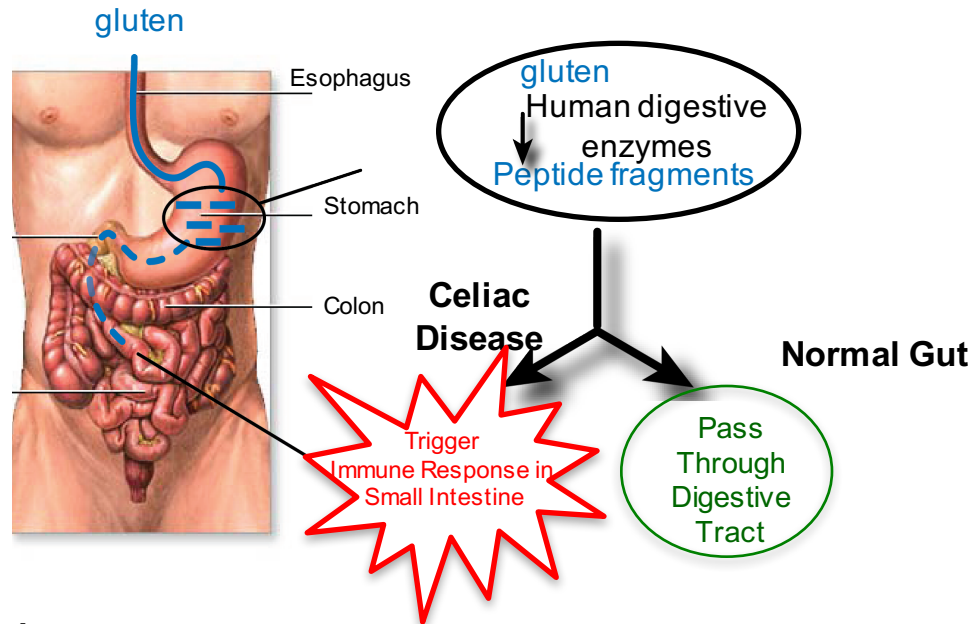
- Michaela Smith
PhD student
- John Connor
Colaborator
- Ron Corley
Support at the NEIDL

Eva Helmerhorst

*Associate Professor
Department of Molecular & Cell Biology
School of Dental Medicine*

Gluten-Degrading Bacteria and Enzymes: Novel Therapeutics for Celiac Disease

Helmerhorst Lab



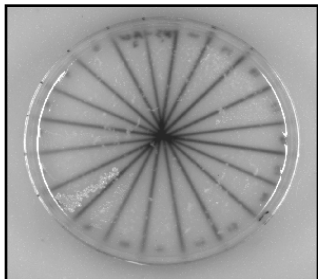
Only approach is gluten-free diet:

Difficult to maintain
Inadequate ingredient labeling
Cross contamination

Therapeutic strategy:

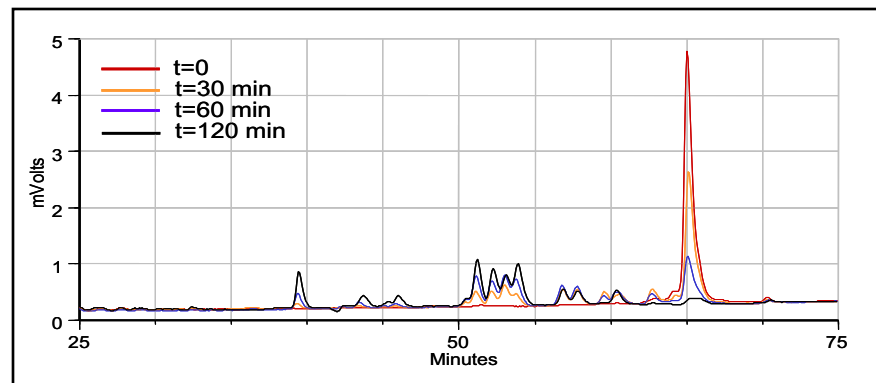
Elimination of immunogenic epitopes by exogenous enzymes with correct cleavage specificities

Dental plaque



Gluten-limited agar

33-mer + *Rothia aeria*



- ◆ *Rothia* bacteria
- ◆ Gluten-degrading enzymes
- ◆ Food-grade enzyme candidates

Complete degradation

Novel natural therapeutics for CD

Probiotics:

Safety/efficacy assessment
in vivo in mouse models for digestion and CD

Enzymes:

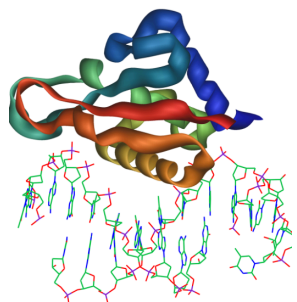
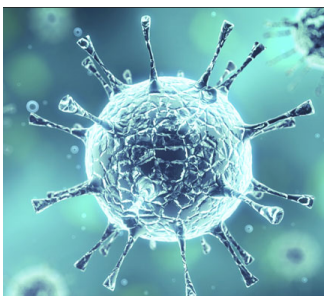
Dietary supplement
Structural modifications to increase retention/activity in GI tract

R01 AI087803, K02 AI101067
BU Ignition Award, CTSI Award

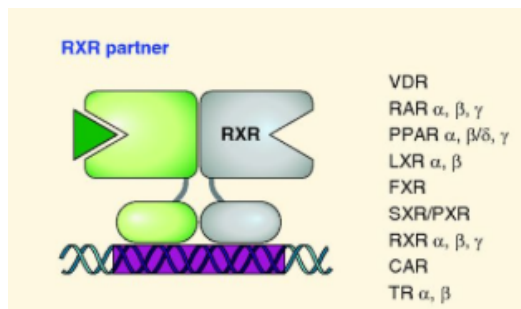
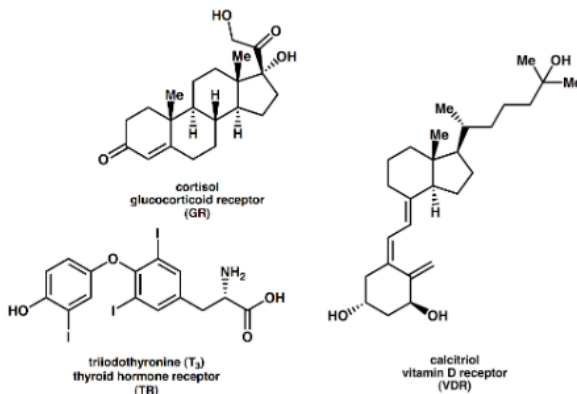
Trevor Siggers

*Assistant Professor
Department of Biology
College of Arts & Sciences*

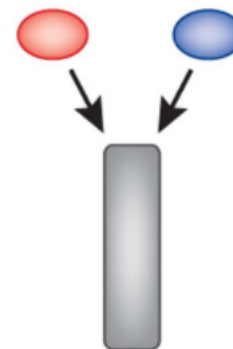
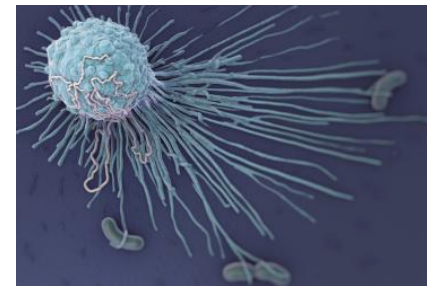
Siggers lab (Dept. of Biology)



Microbes &
Inflammation



Metabolism &
Inflammation



Engineering
Macrophages

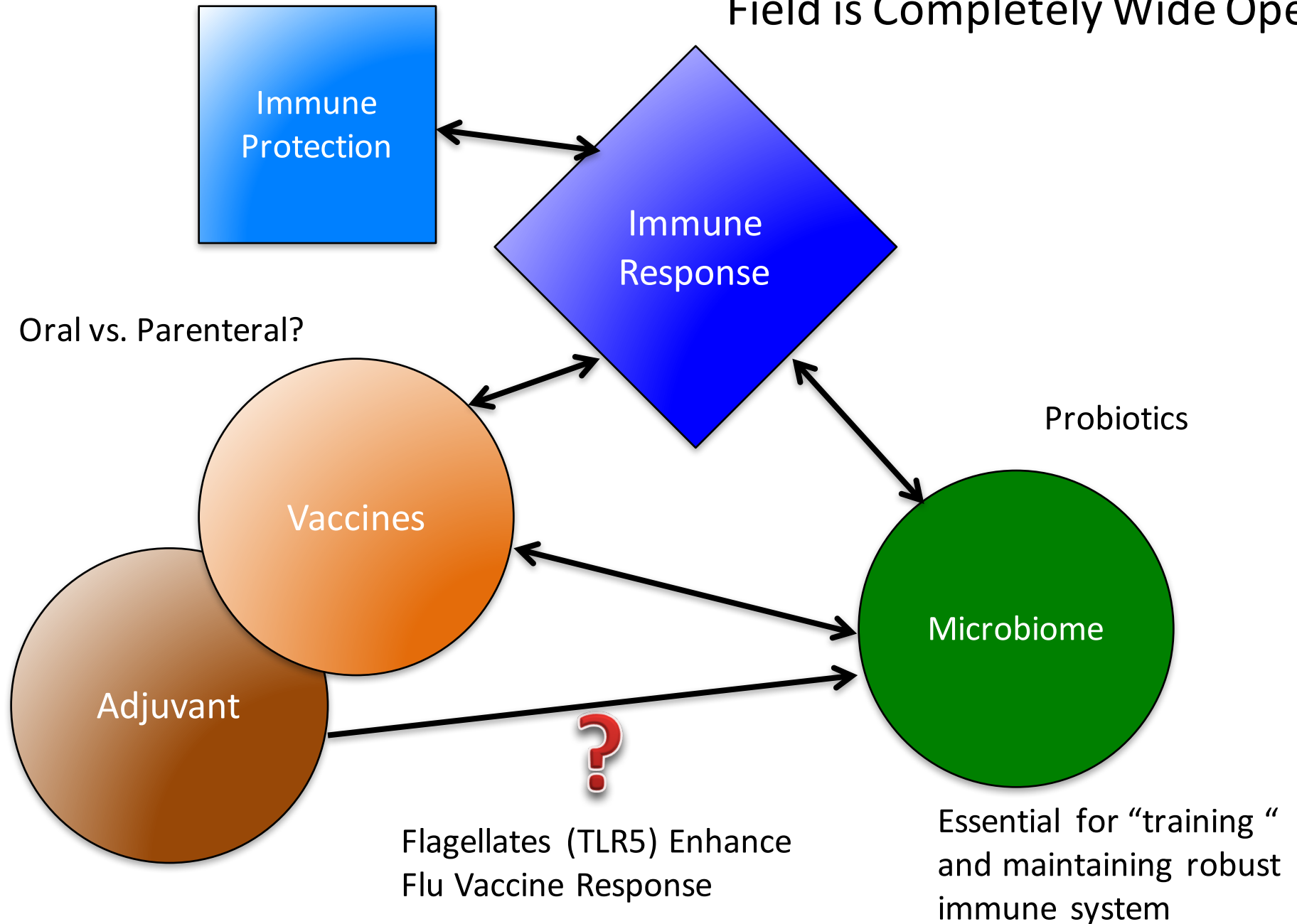
Lee Wetzler

*Professor
Department of Microbiology
School of Medicine*

Vaccines, Adjuvants and the Microbiome

Lee Wetzler, M.D.

Not Much is Known,
Field is Completely Wide Open



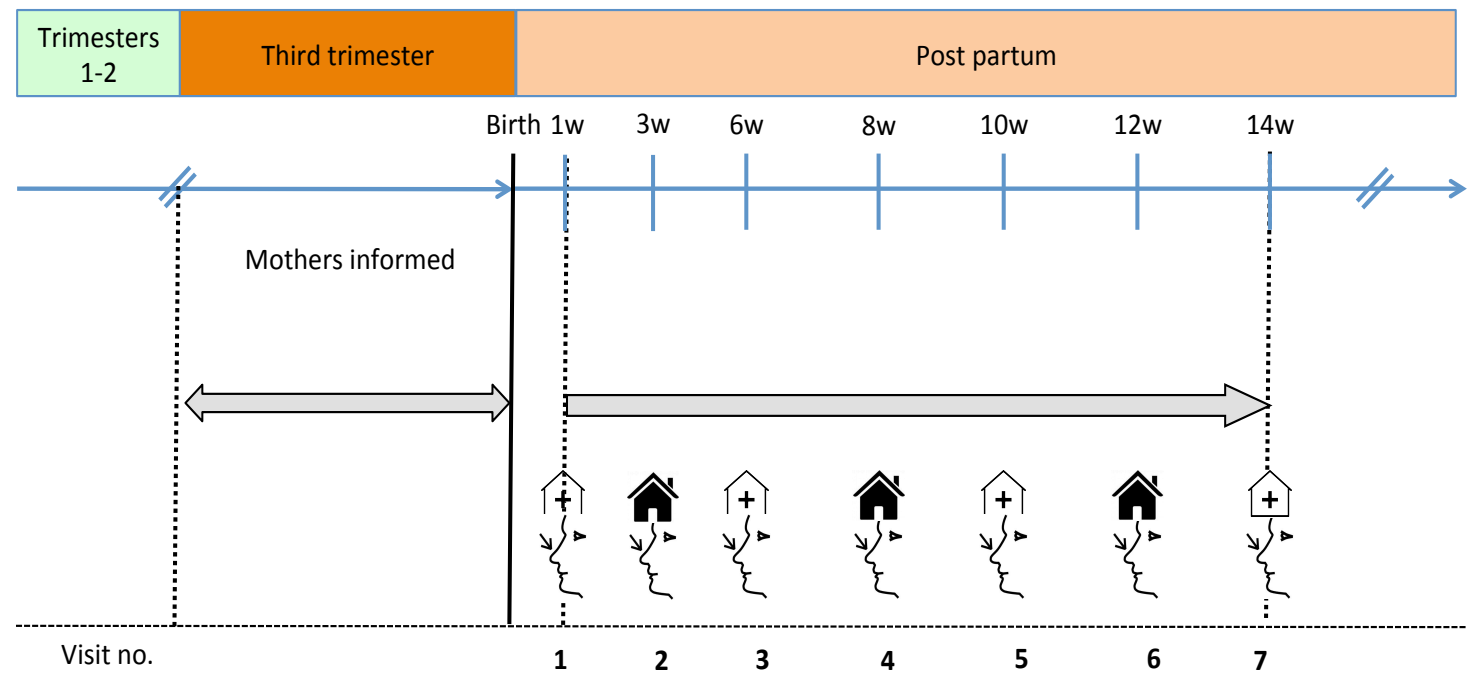
Chris Gill

*Associate Professor
Department of Global Health
School of Public Health*

C. Gill: Southern Africa Mother Infant Pertussis Study

- Mother infant pair seen at 1 week post partum then every 2-3 weeks to 14 weeks
- At each visit, NP swabs obtained from both irrespective of symptoms
- Result: ~10,000 maternal and 10,000 infant NP swabs obtained for longitudinal analyses
- Proposal: Characterize the evolution of infant respiratory microbiome with stratification by:
 - Maternal HIV status (positive vs. negative)
 - Infant vaccination status (pre/post)

SAMIPS data/sample collection schedule



Ad hoc sick visits were also conducted in between scheduled visits as needed



Additional study visits



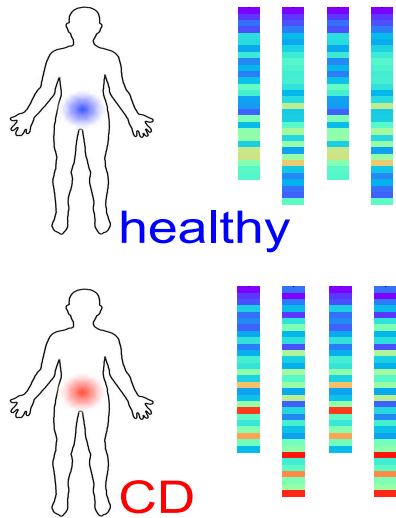
Routine well-child visits

Kirill Korolev

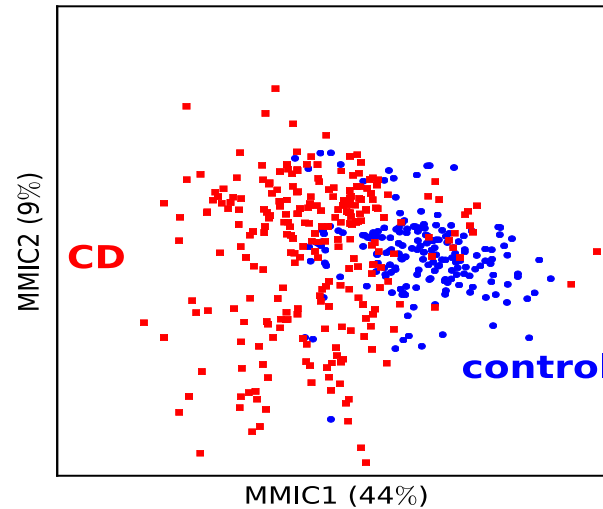
*Assistant Professor
Department of Physics
College of Arts & Sciences*

Microbiome: from Data to Models

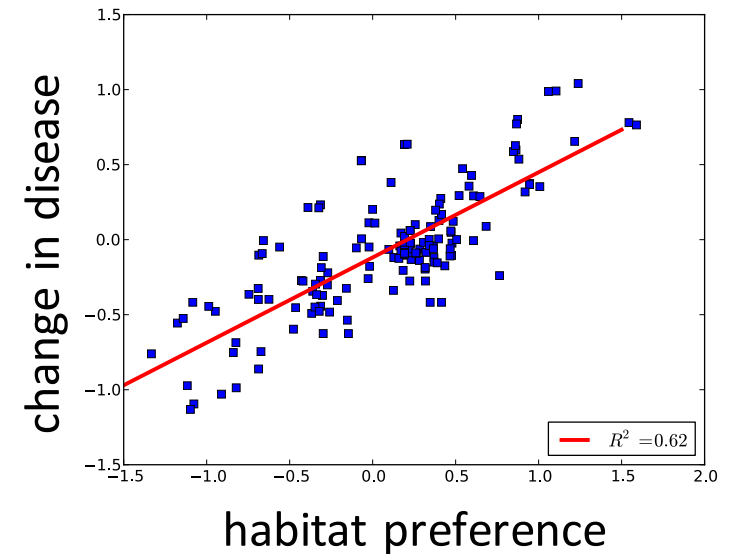
data



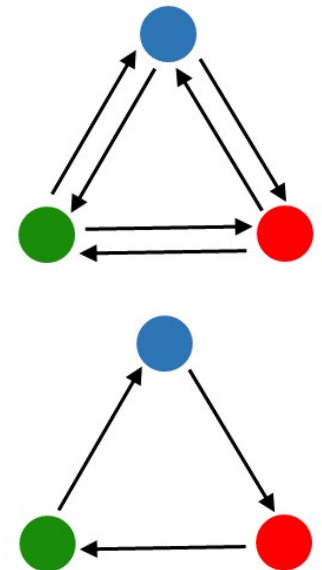
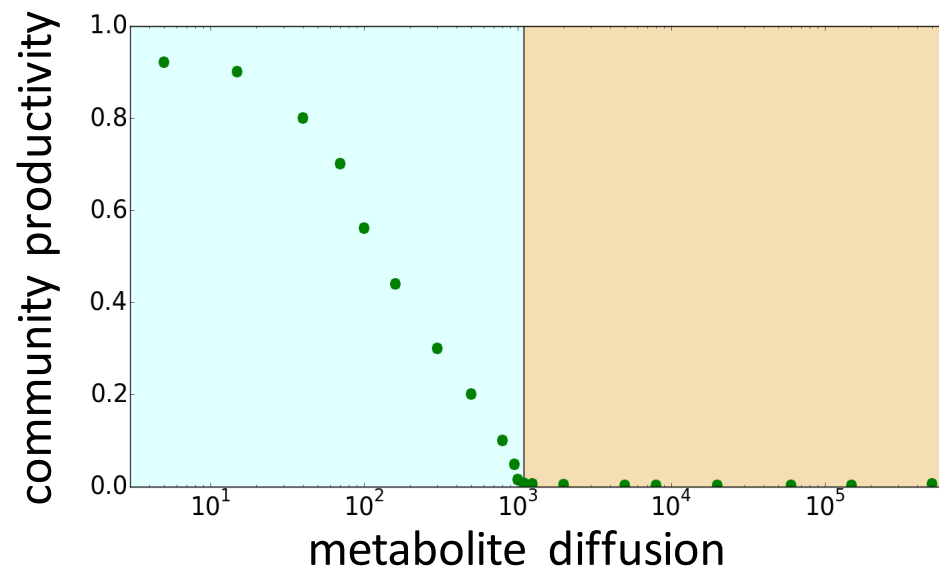
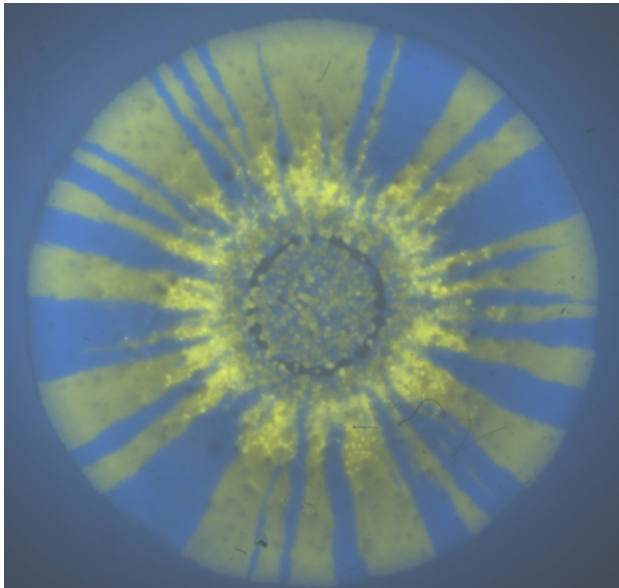
diagnosis



community dynamics



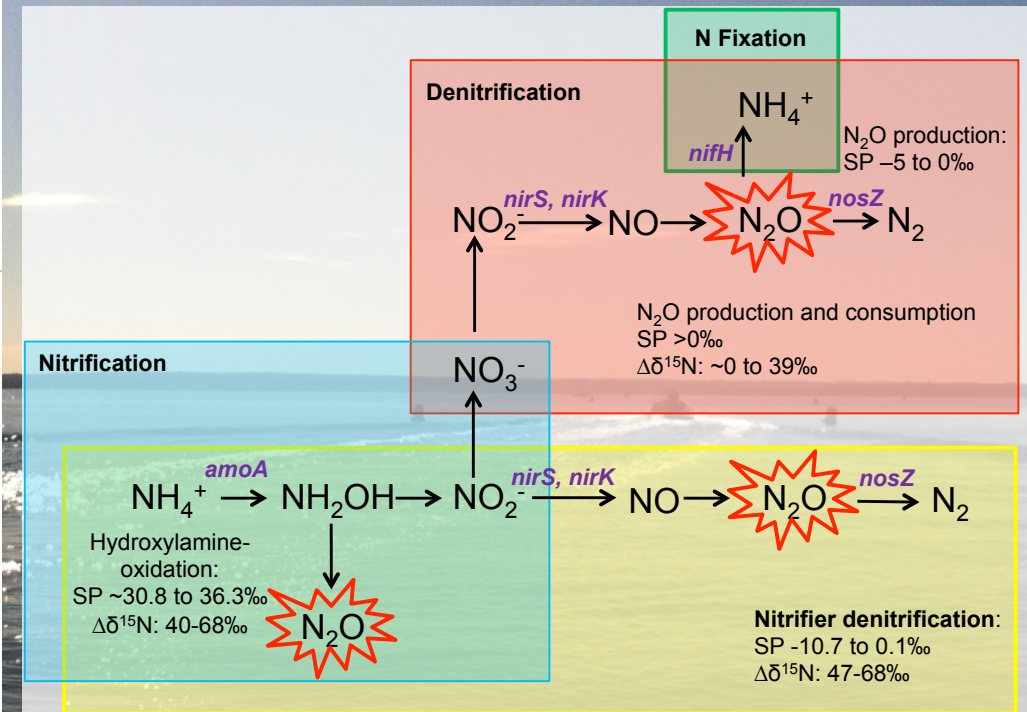
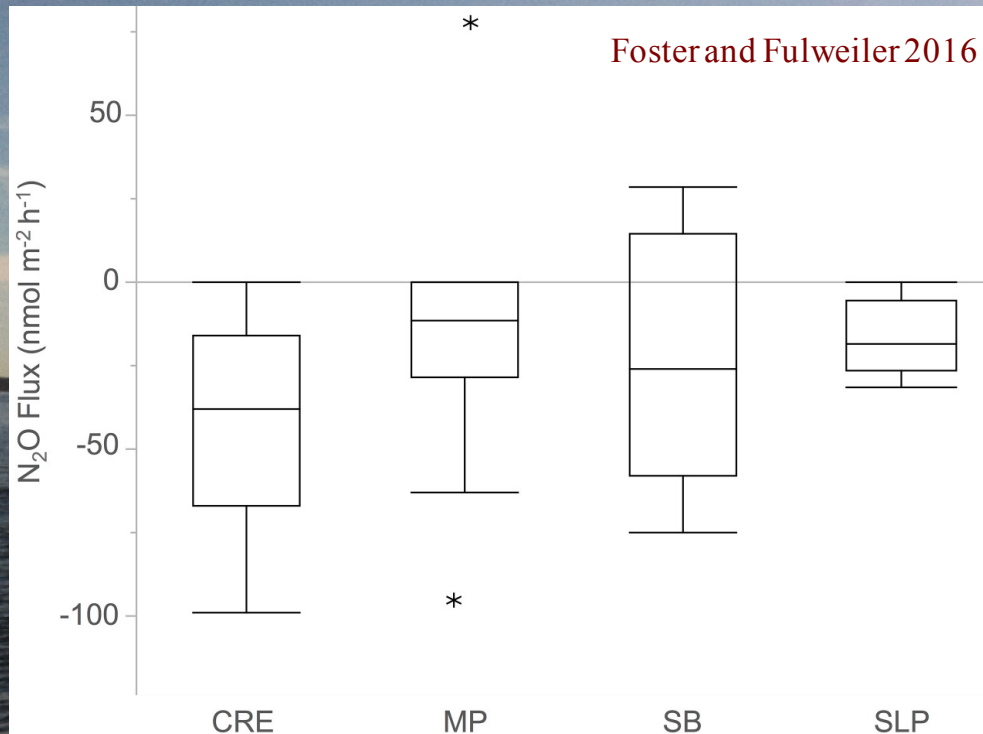
Models with physical constraints



Wally Fulweiler

*Associate Professor
Departments of Earth & Environment and
Biology
College of Arts & Sciences*

Marine Microbiomes – Linking Ecosystem Function to Microbial Community Dynamics



Robinson W. Fulweiler • Boston University • Department of Earth and Environment • Department of Biology

• Email: rwf@bu.edu Website: www.fulweilerlab.com • Twitter: @FulweilerLab • Facebook: FulweilerLab

Jennifer Talbot

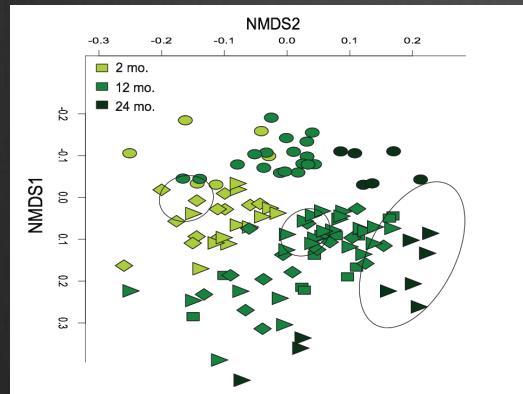
*Assistant Professor
Department of Biology
College of Arts & Sciences*

Systems Biology of the Earth Microbiome

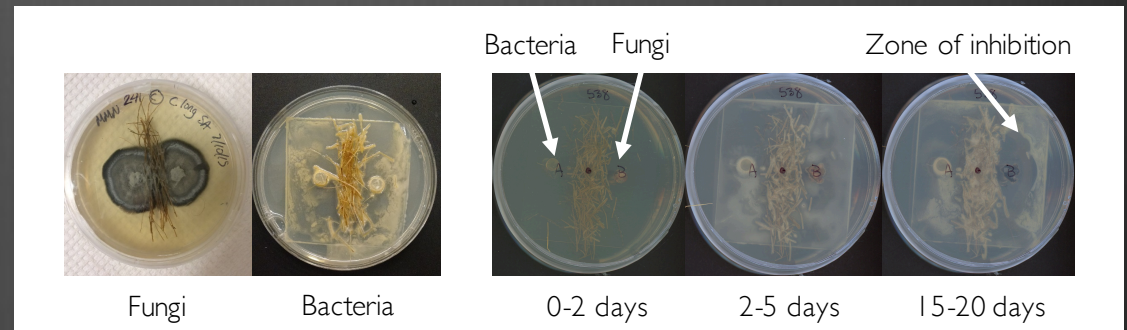
Jennifer Talbot

Boston University
Biology

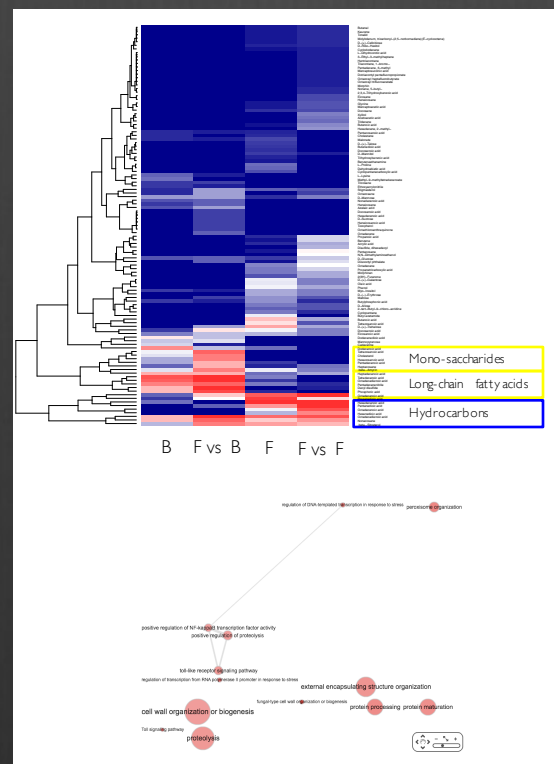
Field systems



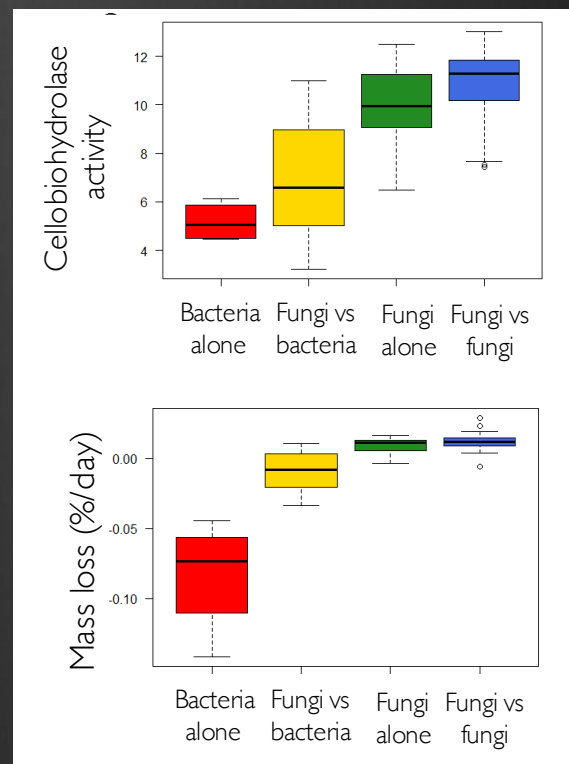
Experimental systems



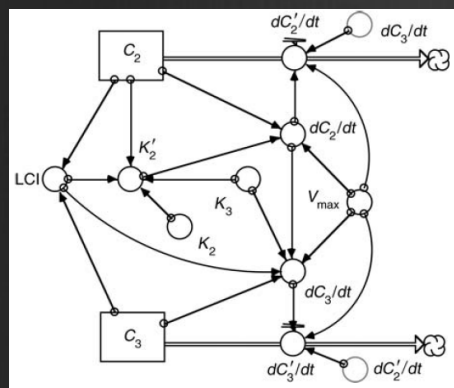
-omics



Ecosystem function



Modelin

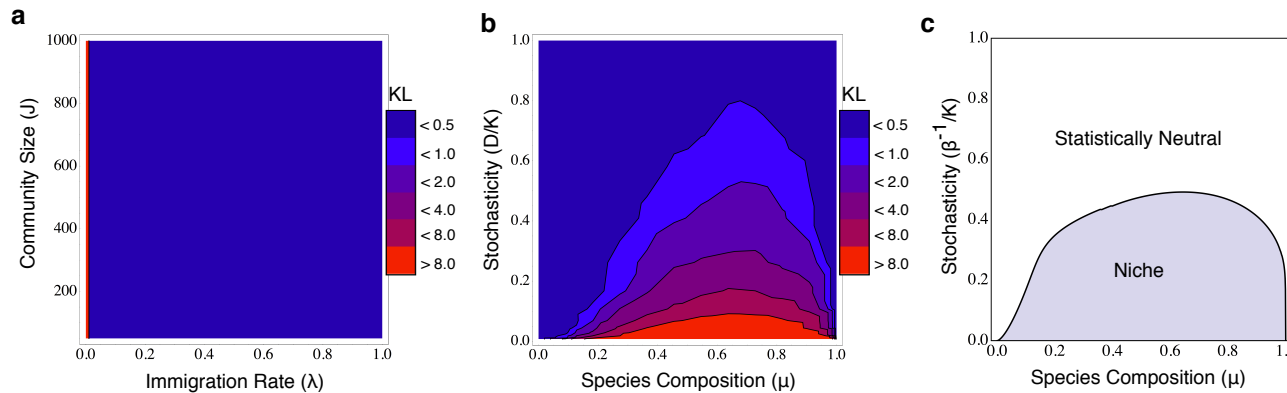


Pankaj Mehta

*Associate Professor
Department Physics
College of Arts & Sciences*

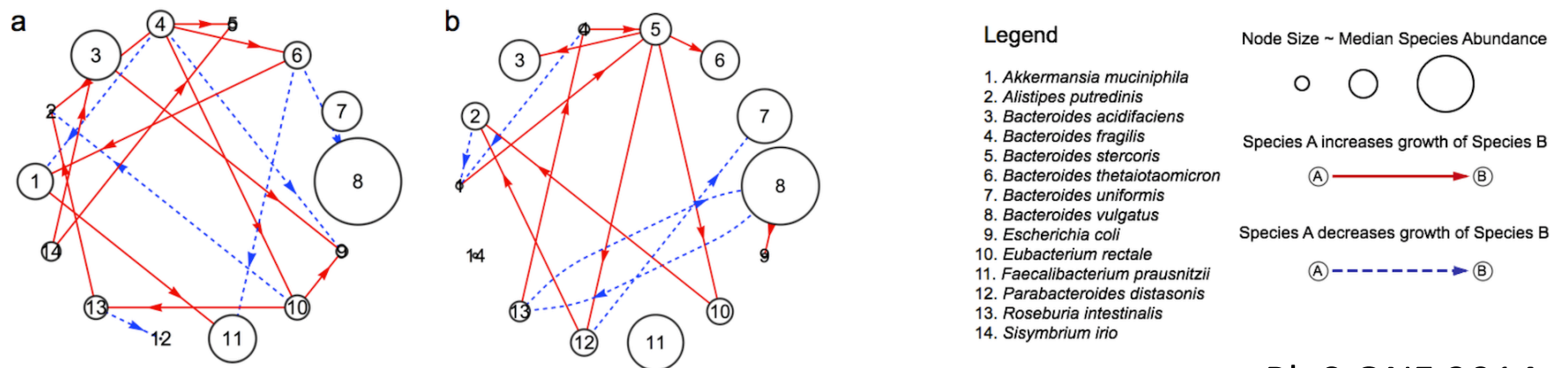
Two approaches to uncovering ecological principles

Top-down systems approach— understand theoretical models, in particular role of ecological selection (niche) and ecological drift (neutral), selection using ideas from statistical mechanics



PNAS 2014
PRE 2016

Bottom-up approach—infer how species interactions to try to understand community assembly from microbiome data (ideas from ML/Statistics)



PloS ONE 2014

Evan Johnson

*Associate Professor
Departments of Medicine and
Biostatistics
School of Medicine*



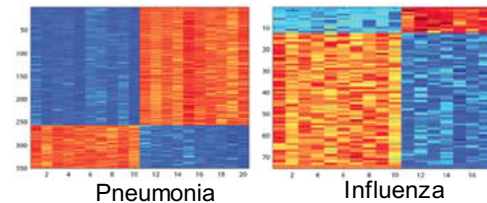
Collect specimen



DNA/RNA Sequencing



Host Response Pathways



PathoScope Analysis

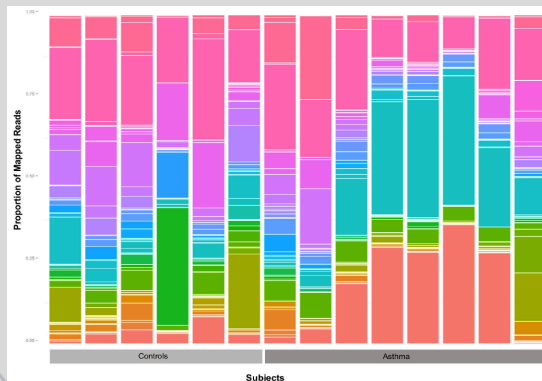
Align to Microbial Genomes



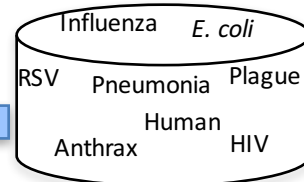
Bayesian Mixture Modeling

$$\mathcal{L}(\pi, \theta, \eta) = \prod_{i=1}^R \prod_{j=1}^G q_{ij} \pi_j^{x_{ij}} \theta_j^{(1-y_i)x_{ij}}$$

Microbial Abundance

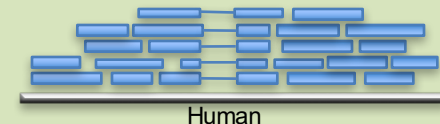


Genome Sequence Library

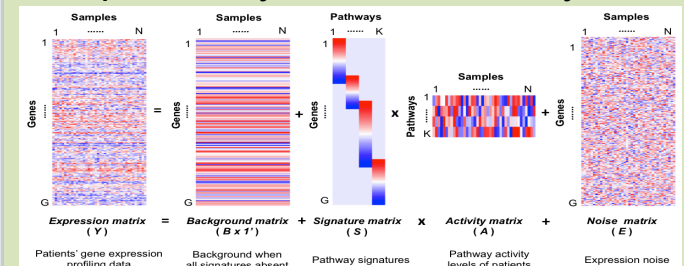


ASSIGN Profiling

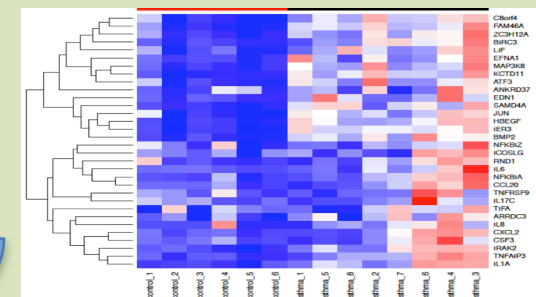
Align to Human Genome



Sparse Bayesian Factor Analysis

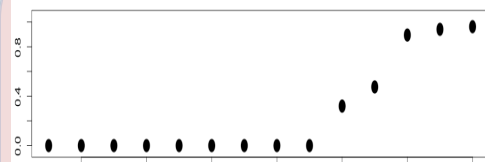


Immune Pathway Activity

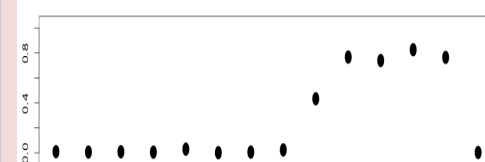


Integrate Results

Pathway Activation



Pathogen Abundance



Control

Asthma

Daniel Segre

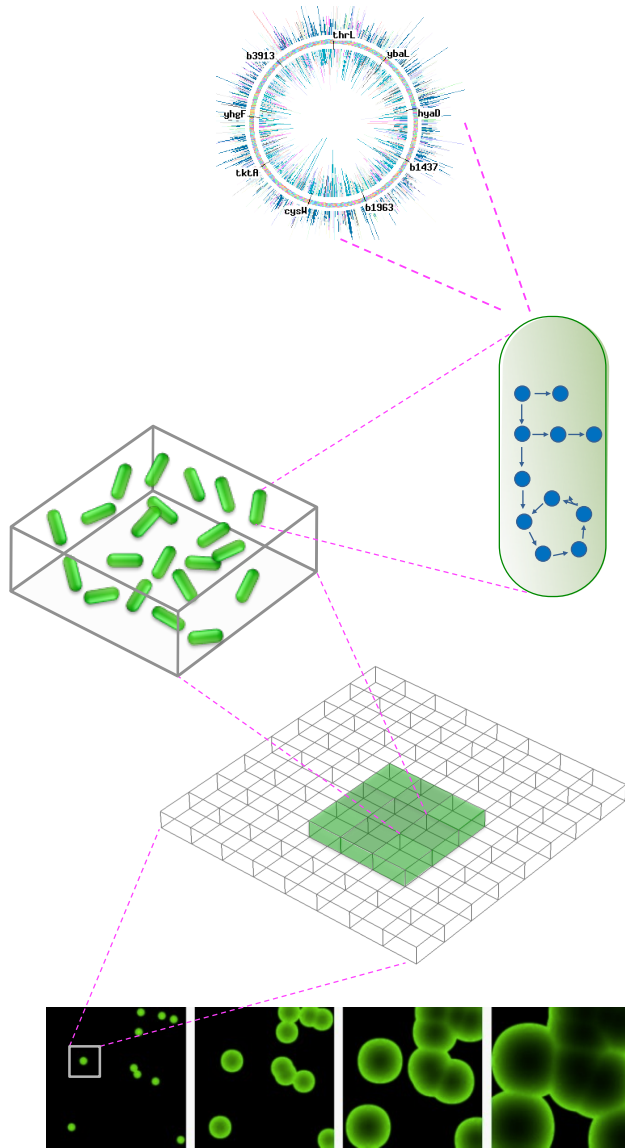
Professor

*Departments of Biology and
Physics*

*College of Arts & Sciences;
Department of Biomedical
Engineering*

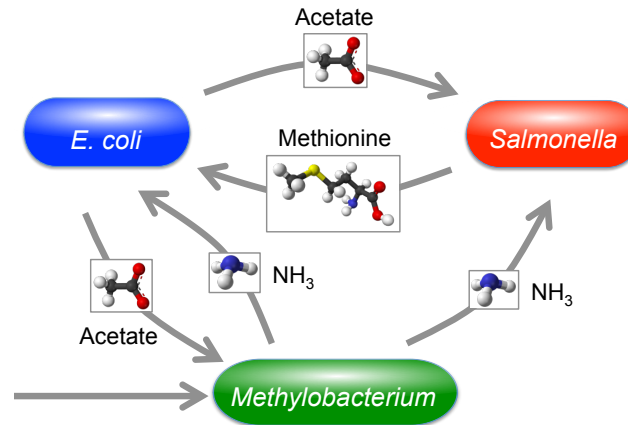
*College of Engineering; and
Bioinformatics Program*

From intracellular wiring to cell and community behavior

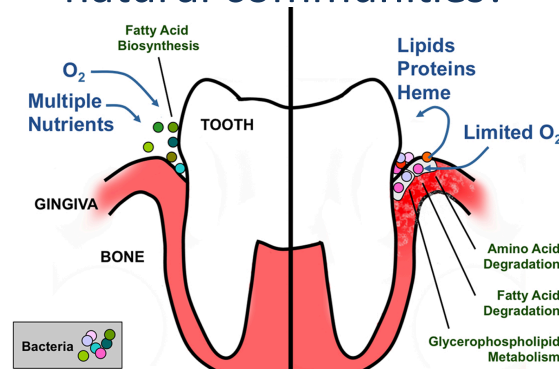


A “virtual Petri dish”

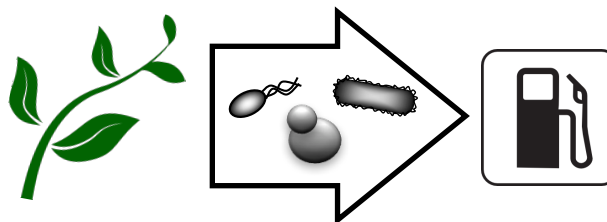
Metabolism mediates competition and cooperation



Can models scale up to natural communities?

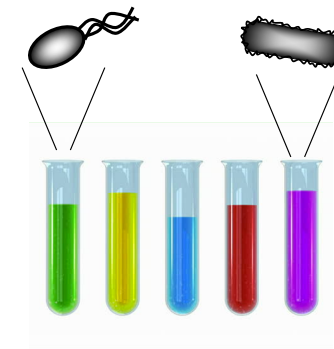
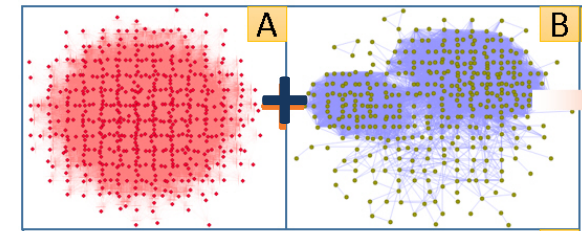


Engineering task-specific communities



What is needed?

Network integration



Ecological building blocks and real-time detection

Multiscale models

