# Nutritional roles of beneficial bacteria associated with insects revealed by metabolic modeling

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## Background

- Many animals depend on symbiotic associations with nutrient-overproducing bacteria for survival
- Net nutrient production by bacteria is dictated by competitive and cooperative interactions among multiple bacterial taxa and by the metabolites derived from the animal host
- Elucidating the mechanistic details of the multi-way metabolic interactions will:
  - aid in understanding the metabolic basis of animal-microbial coevolutionary interactions
  - provide the basis to identify specific gene targets for novel control strategies against major insect pests
- We reconstructed integrated multi-compartment genome-scale metabolic models of insect-bacterial associations to investigate the processes shaping metabolic interactions between the partners

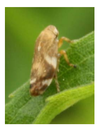
Our model systems

Phloem feeders

Whitefly (*Bemisia tabaci*)

Aphid (*Acyrthosiphon pisum*)

Xylem feeders



Spittlebug (*Philaenus spumarius*)

Sharpshooter (*Graphocephala coccinea*)

Cicada (*Neotibicen canicularis*)

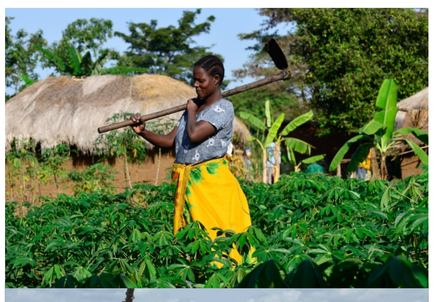
Images not to scale

Image credit: Alex Wilson, Bessem Chouaia

## Whitefly case study

### Introduction

*Bemisia tabaci* (whitefly) important agricultural pest with very broad range of plant hosts



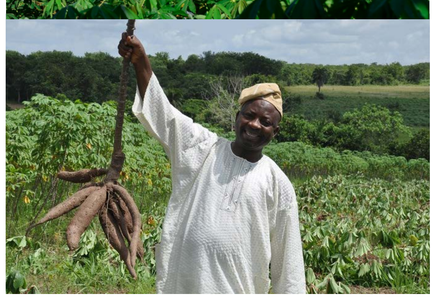


Photo credit: Natural Resources Institute

Whitefly causes severe reductions in crop yield and acts as a vector for numerous plant viruses

Billions of dollars in crop damage attributed to whitefly infestation worldwide annually

Evolutionary and reproductive success of whitefly relies on essential amino acid (EAA ) production by endosymbionts to meet shortfalls in diet

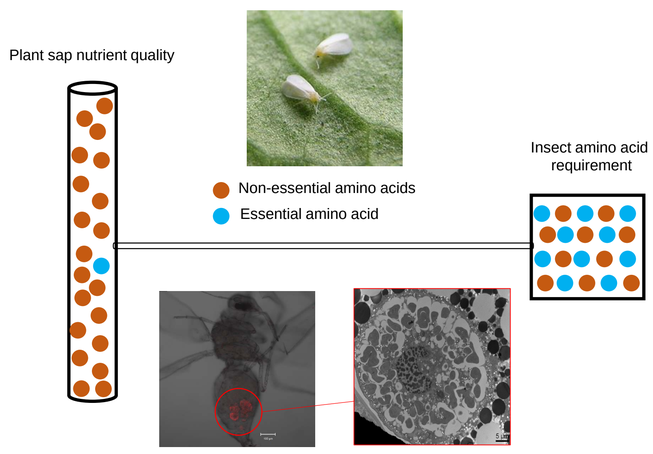
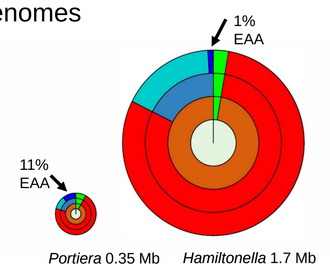



Image credit: Junbo Luan, Hong-Wei Shan

Whitefly endosymbionts have highly reduced genomes

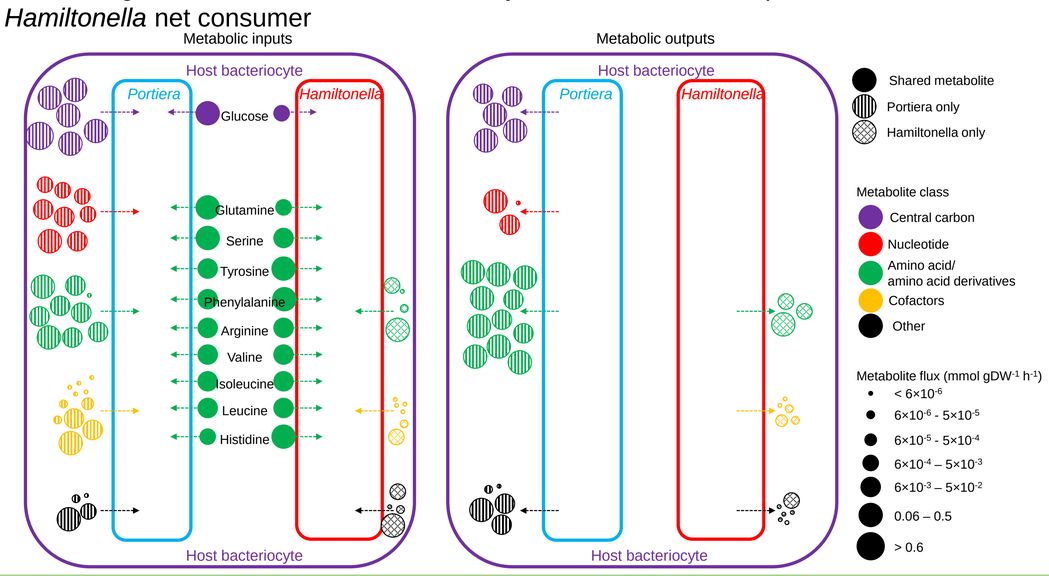
| | *Portiera* | *Hamiltonella* |
|---|---|---|
| Total ORFs | (448, 100%) | (1,962, 100%) |
| CDS | (412, 92%) | (1,910, 97%) |
| Non-Coding | (36, 8%) | (52, 3%) |
| Non-metabolic | (318, 71%) | (1,564, 80%) |
| Metabolic | (94, 21%) | (346, 18%) |
| EAA | (48, 11%) | (20, 1%) |
| Other | (46, 10%) | (326, 17%) |




*Portiera* 0.35 Mb *Hamiltonella* 1.7 Mb

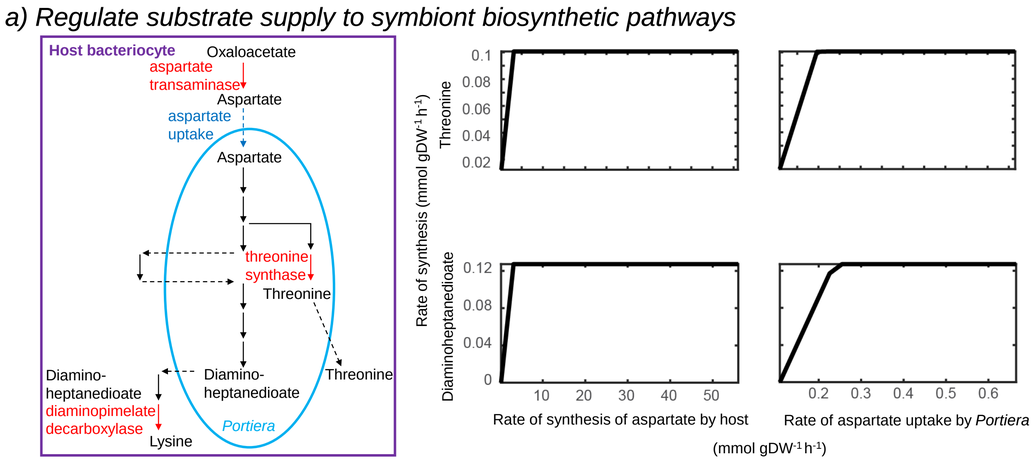
### Results

1) Partitioning of metabolic function between symbionts: *Portiera* net producer of EAAs, *Hamiltonella* net consumer

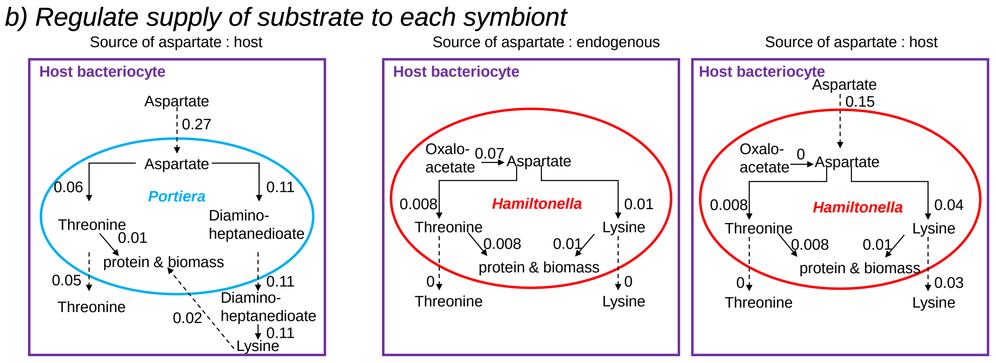



2) Host control of symbiont nutrient production:

*a) Regulate substrate supply to symbiont biosynthetic pathways*




*b) Regulate supply of substrate to each symbiont*




3) Host-symbiont mediated assimilation and recycling of N

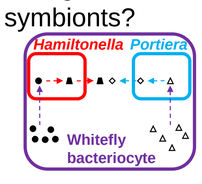



### Conclusion

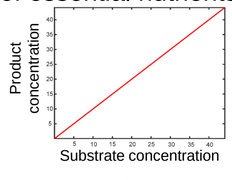
- Metabolic networks of bacteria are restructured to promote cooperative cross-feeding of metabolites and minimize competition for host-derived substrates
- Host regulates bacterial overproduction of essential nutrients by precise controls over the concentrations of substrate metabolites in essential nutrient biosynthetic pathways
- Bacteria utilize host waste nitrogen, enhancing the efficiency of dietary nitrogen utilization by the association

### Research questions

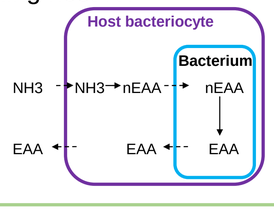
1) What is the degree of metabolic overlap between symbionts?




2) How does the host regulate symbiont supply of essential nutrients?




3) What is the role of each symbiont in recycling host N?




### Research approach

Collect biological data

*Sequence genomes* *Measure transcript* *Measure metabolites*

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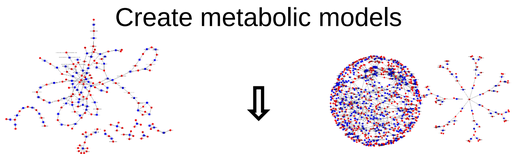
Create metabolic models



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Analyze metabolic models to understand how nutrient exchange is structured in insect-bacterial symbiosis

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Validate models with empirical data

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