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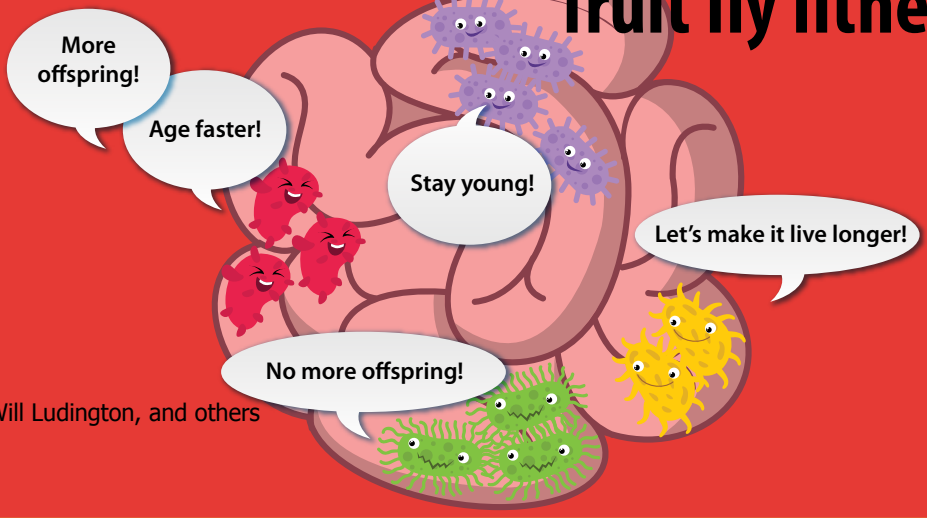
How do microbes shape fruit fly fitness?



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Abstract

Did you know that you are never alone in your own body? Like with all animals, your body provides a home for a community of *microbes*, making it a *microbiome*. Microbiomes impact their host's ability to survive, age, and produce offspring. An important question is how each bacterial species affects our health. But with hundreds of species in our gut, it is difficult to single out any one in particular. Any species could have a direct effect on us, or the effects could be due to interactions between species. How do we unravel this complexity?

To explore how microbes impact their host, we looked at the *Drosophila melanogaster* fruit fly. It has only five bacterial species in its gut making it much simpler to study than a human. We examined a fly without bacteria and with every possible combination of the five bacterial species. We found that the species present in the gut and the interactions between them both affect the fly. This finding suggests that humans might also be impacted by the complex microbe interactions in their gut.

Introduction

How would you describe fitness? Being big and strong? That might be so when we talk about physical fitness, but in biology, *fitness* is how good an organism is at passing its genes to the next generation.

Certain traits impact biological fitness:

- The ability to have more offspring (*fecundity*)
- Short *development time* (the organism reaches maturity quicker)
- Longer reproductive lifespan (the organism can produce offspring for longer)

Organisms that are a better fit to their environment produce more offspring than those who are not. Over time, these 'favorable' traits become more common in the population. We call this process *natural selection*.

Scientists believe that the gut microbiome — the community of microbes that live in animals' intestinal tract — has a critical role in its host's fitness, well-being, and even behavior (see Science Journal for Kids' paper *How do bacteria in the gut control the brain?*). Previous studies reported that *germ-free* flies live longer than those with a microbiome. Therefore, bacteria could decrease host fitness.

However, fitness is defined by how many offspring an organism has over its entire life rather than just how long it lives. So an organism can have the same fitness with a short life if it has its offspring faster. Also, the gut microbiome is a complex thing. It has a variety of bacterial species. These species interact with each other and respond to their surroundings. These interactions may create changes in a microbiome, which in turn can change the host.

These observations bring up some questions:

1. How much does the complex network of bacterial interactions in the gut affect the host?
2. How can we measure these interactions?
3. How does the microbiome shape host fitness by impacting lifespan and fecundity?

Methods

With more than one hundred bacterial species, the human gut microbiome is very complex and difficult to understand. So, we used a *model organism* with a fairly simple microbiome: *Drosophila melanogaster*, commonly known as the fruit fly (Fig. 1).

- Five species of bacteria inhabit fruit flies' guts: *Lactobacillus plantarum (Lp), Lactobacillus brevis (Lb), Acetobacter pasteurianus (Ap), Acetobacter tropicalis (At),* and *Acetobacter orientalis (Ao)*. We isolated these species and put them into the guts of germ-free flies.
- With five species of bacteria, there are 32 possible microbiome combinations. We created germ-free flies and divided them into groups (ten males and ten females per group). We then put one microbiome combination into each group until we had a group for each possible combination. We kept one group of flies germ-free as a control case (Fig. 2).
- We measured the resulting fly traits for each group:

(i) development time: number of days from embryo to adult

(ii) fecundity: number of new live adults produced by a female in her lifespan

(iii) lifespan: length of a fly's life in days

Figure 1:
Have you ever dealt with fruit flies in your kitchen? They are small, seem to come out of nowhere, and easily reproduce. But the traits that make fruit flies a nuisance in the kitchen, make them a very popular organism in the science lab because they're so easy to grow. Scientists use fruit flies as a model organism to understand the human body.

Source: Martin Cooper on Wikimedia Commons

- We compared how the presence of particular bacteria impacted the fly measurements (if at all), and whether the amount of bacteria in the fly gut mattered.
- We used a mathematical *model* to calculate how the interactions between the bacterial species affected the fly (Fig.3). We considered interactions between two, three, four, and finally all five species.

Please see Figure 3 Page 3

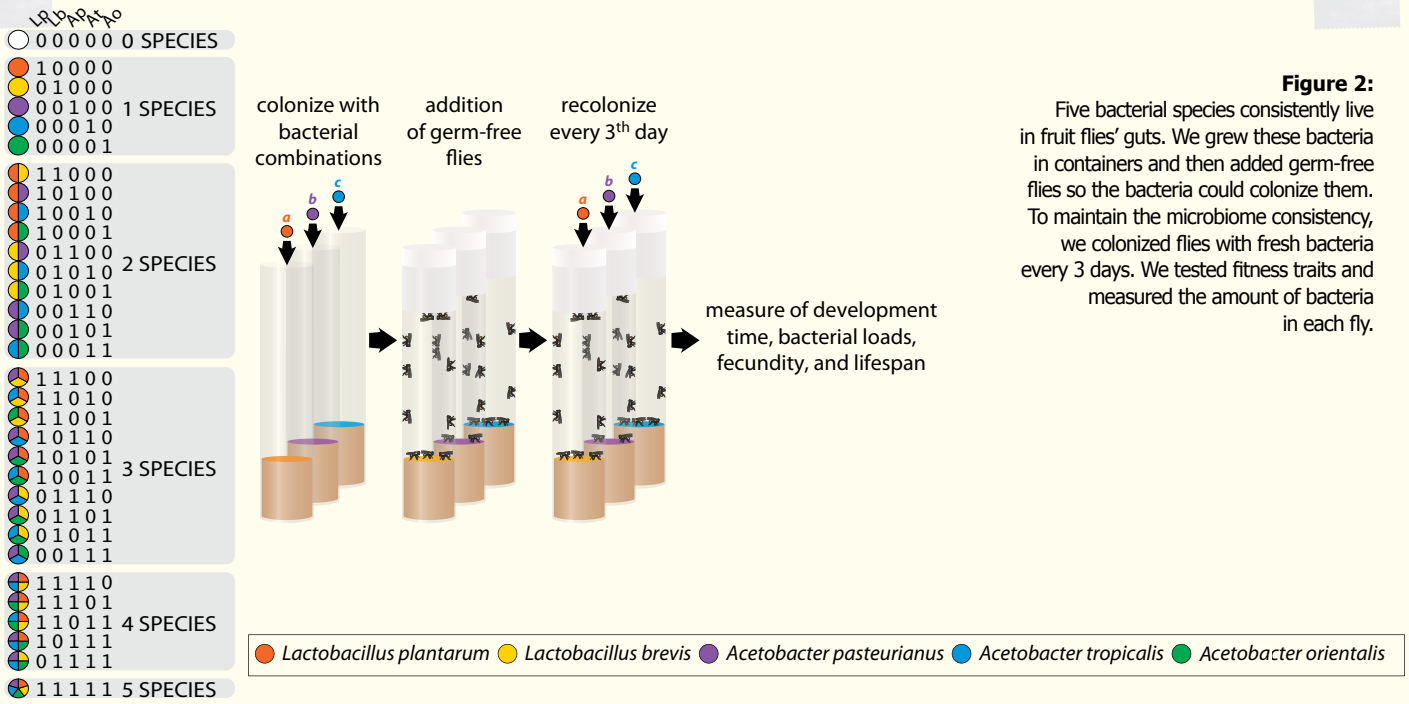


Figure 2:
Five bacterial species consistently live in fruit flies' guts. We grew these bacteria in containers and then added germ-free flies so the bacteria could colonize them. To maintain the microbiome consistency, we colonized flies with fresh bacteria every 3 days. We tested fitness traits and measured the amount of bacteria in each fly.

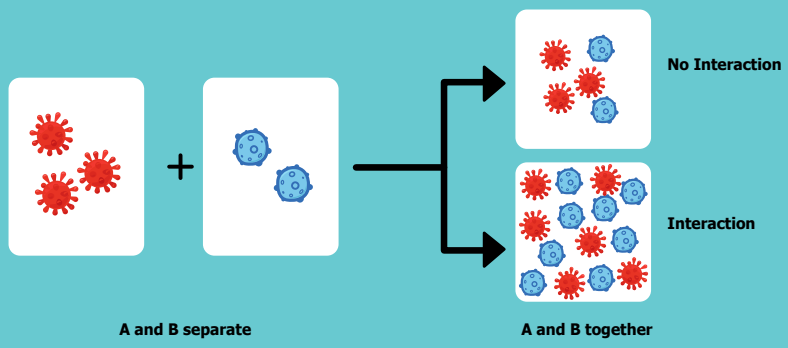
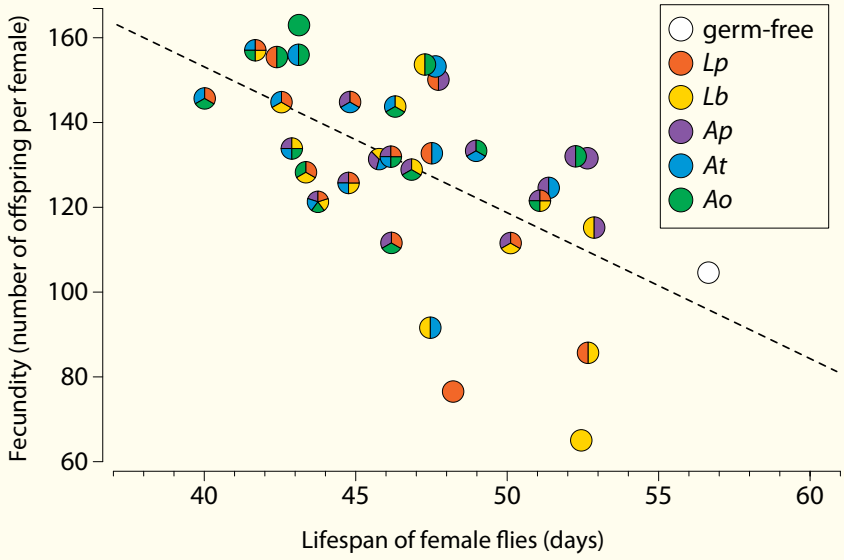


Figure 3:
We know an interaction between the different types of bacteria has occurred in a fly's gut because we observe a change. Our model quantifies that change. This diagram shows a made-up example where two bacteria, A and B can either interact or not. When A and B are separate, they produce 3 and 2 cells respectively. If there is no interaction, then A and B would still produce 3 and 2 cells when they are mixed together. However, if they do have an interaction, they produce a different number of cells, 6 and 8 cells respectively in this example. Our model calculates this interaction as the difference in the number of cells when grown separately versus together, i.e. 14-5=9. Here, the interaction is positive because overall more cells were produced, but we also saw examples of negative interactions. We applied our model not just to numbers of bacteria but also to fly lifespan and reproduction.

Results

- Germ-free flies survived the longest. As microbiome diversity increased, the flies' lifespans decreased. Germ-free flies survived about 20% longer than flies with all five bacteria.
- Germ-free flies had low fecundity. Increasing the number of bacterial species in the fly microbiome usually increased its fecundity. As female flies' fecundity increased, their lifespan decreased (Fig. 4).
- We hypothesized that high fecundity causes short lifespan. Like humans, flies reproduce the most before they are middle-aged (21 days old). We raised flies with a microbiome until 21 days old. When we removed the microbiome (using *antibiotics*), lifespan increased by about 15%. This suggests that the microbiome, rather than high fecundity, causes the decrease in lifespan.
- Our knowledge about how individual bacterial species impact fly lifespan was insufficient to tell us what the individual species do when another species is present.



Do flies that produce more offspring tend to have longer or shorter lifespan?

Figure 4:
The circles represent all 32 possible combinations of microbiomes. Each color represents a bacterial species. Here we compare how these different microbiomes impact fly lifespan and fly fecundity.

Discussion

Our results clearly show that the microbiome affects host fitness. As we changed the mixture of bacterial species in the fly gut, we saw changes in how flies developed, aged, and reproduced. However, even as these fly characteristics changed, the overall fly fitness stayed relatively constant since flies that reproduced more died sooner.

More interestingly, our mathematical model captured the interactions between the bacterial species. We compared flies with one type of bacteria in the gut to flies with many types of bacteria in the gut. We saw that the latter lived shorter than the former. However, we could not predict the lifespan of flies with a variety of bacteria in their gut based on the lifespans of flies with only one type of bacteria. This shows that interactions between different bacteria can be as important as the type of bacteria for fly fitness.

Conclusion

But why does this matter for us? Our results can guide future studies in solving the mystery of human gut microbiome. Humans and plants have very high-diversity microbiomes with a complex network of bacterial species interactions. Examining the simple fruit fly microbiome can provide clues about these complex microbiomes.

You may not realize it but you are a walking *ecosystem*. Just like the ecosystems in nature, our microbes interact with each other and respond to changes in their environment. Take good care of your microbiome by eating a diverse and balanced diet.

Check your understanding

1. What is biological fitness? Why is it important?

2. Why did the scientists use a model organism to study the impact of the gut microbiome on its host's fitness traits?

3. How did germ-free flies compare to those with a microbiome?

4. How do we know that bacteria in the microbiome interact with each other and their host?

Glossary of Key Terms

Antibiotic – a chemical substance that kills bacteria.

Bacteria – microscopic single-celled organisms.

Development time – the time it takes adult flies to complete their metamorphosis and emerge from their pupal phase, reaching their mature adult form.

Ecosystem – a biological community of interacting organisms and their physical environment.

Fecundity – fertility or ability to reproduce. Animals with higher fertility produce more offspring.

[Biological] fitness – the ability to survive to reproductive age, find a mate, and produce offspring. For example, in a desert ecosystem, sand color lizards have a greater biological fitness than green lizards because they can hide from their predators better, and therefore survive for longer and have the opportunity to reproduce more.

Germ-free fruit fly – flies that are sterile, have no bacteria in their guts.

Microbes – are organisms that are so small that you have to use a microscope to see them. They can either consist of a single cell, or several cells. They are bacteria, archaea, fungi or other tiny organisms.

Microbiome – the ecological community of microorganisms that live in and on animal or human bodies. These microorganisms can either be beneficial for their host, neutral for the host, or they can harm their host. One site of the microbiome is in the digestive tract or gut.

[Mathematical] Model – A mathematical description of a phenomenon (event). Such descriptions might involve graphs, equations, diagrams.

Model organism – a species that has been widely studied, usually because it is easy to maintain and breed in a laboratory. Scientific discoveries in model organisms often tell us a lot about the workings of many other organisms, too. Some common model organisms, besides fruit flies, are mice, zebrafish, and the bacteria *Escherichia coli*.

Natural selection – a process in nature in which organisms possessing favorable traits are more likely to survive and reproduce.

Phenotype – the set of observable, physical characteristics of an individual. Lifespan, development time, fertility, hair color, eye color, and height are all examples of phenotypes.

Pupa – life stage of some insects undergoing the transformation between immature to mature stages.

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