University of Leicester
BBSRC MIBTP Studentship Project 2025-6 entry.

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Section 2 – *Project Information*

Project Title	A gut feeling for a sleepy season? Roles of gut microbiota in seasonality of sleep

Project Summary

Sleep is conventionally thought to be “by the brain and for the brain”. Yet, recent laboratory studies suggest sleep, immune system, and gut health regulate each other. This interaction between gut/immunity and sleep is less well understood in the wild. Seasonal and ecological variation exists for *Drosophila* immune genes[1], gut microbiota[2], and ecological traits such as body colour[3,4]. Experiments using the genetic workhorse *Drosophila melanogaster* have further tied sleep to immune function and microbe control[5]. Importantly, sleep in the wild requires temporal alignment to annual transitions in photoperiod and temperature, which correlates with seasonal variation in immunity, the microbiota, and body colour. Whether genetic or microbiota variation contributes to seasonal sleep profile, or vice versa, is unclear.

Temperate *Drosophila* fly species encounter seasonal transitions of photoperiod and temperature across generations, providing an ideal model for understanding the temporal regulatory mechanisms underlying seasonal adaptation of sleep. Unlike *D. melanogaster, D. testacea* is a temperate mushroom-breeding fly occurring primarily in the late summer & fall, with different colour morphs showing seasonal[3,4] and geographic[3] patterns (Fig.1).

We have isolated wild-caught *D. testacea* lines with heritable colour variation, suggesting this seasonal body colour involves a genetic component. Recently, Hanson *et al* showed that *D. testacea* has lost a crucial immune gene, Diptericin B (DptB), which evolved to supress *Acetobacter* infection in fruit-feeding *Drosophila*. This loss may reflect the dietary switch to fungi since *Acetobacter* is abundant in gut microbiota of fruit-feeders, but almost non-existent in mushroom-feeding *Drosophila*[2]. Increased gut *Acetobacter* is associated with reduced sleep in *D. melanogaster*. Intriguingly, we have found that *DptB* mutation in *D. melanogaster* also causes reduced sleep, and *D. testacea* sleep profile differs markedly from *D. melanogaster*.

Taken together, the *Drosophila* system boasts the powerful genetic tools of *D. melanogaster*, as well as natural variation in immune genes, gut microbes, seasonal photoperiod and temporal sleep profile. Using these tools, we will test if the sleep-controlling role of gut microbes relies on interactions with host immune genes and/or other factors.

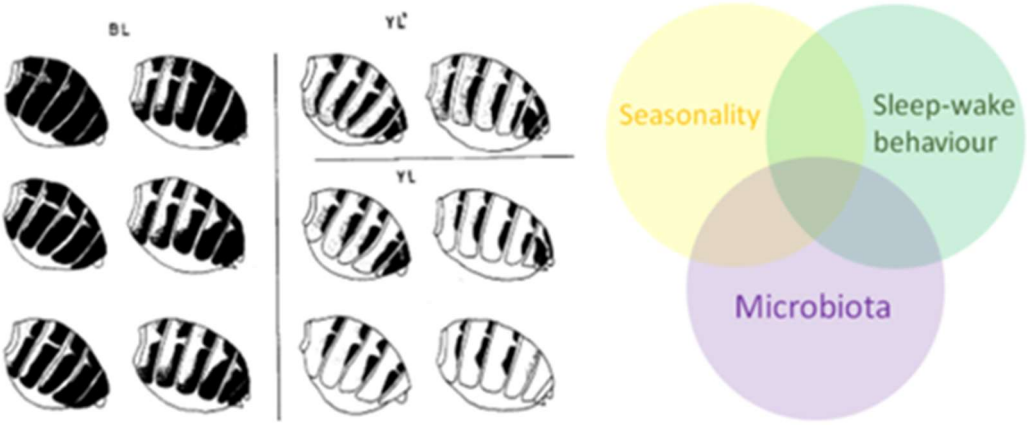

Fig. 1. Left: *D. testacea* colour morphs (BL vs YL, taken from[4]). **Right**: project themes

To address the knowledge gap, this collaborative PhD project aims to apply behaviour assays, and manipulations of the microbiota and host genetics in *D. melanogaster* and *D. testacea*. There are three research aims:

1. **Identifying the role of microbiota in DptB-mediated sleep.** This objective focuses on *D. melanogaster*. The student will use the available versatile *D. melanogaster* tools to clarify the neurophysiological and molecular mechanism underlying DptB-mediated sleep.
2. **Establishing the sleep-wake profile in *D. testacea*.** The student will apply video and infra-red based tracking systems[6] to assay adult *D. testacea* sleep across genetically distinct isolines exposed to seasonally-relevant photoperiods and ambient temperatures during development.
3. **Establishing the relationship between the microbiota and sleep.** Gnotobiotic experiments manipulating the presence/absence of different bacteria will establish these species' microbiome profiles & measure how key microbes affect *D. melanogaster* and *D. testacea* sleep. Available *D. melanogaster* transgenic lines, and even novel *D. testacea* transgenic lines, can further verify the effect of DptB on the gut microbiota and sleep.

In summary, this PhD project will be the first of its kind to explore the mechanistic interaction of seasonality, sleep-wake behaviour and the microbiota (Fig.1) using a predominantly genetic approach.

Techniques that will be undertaken during the project
The project will be conducted in two sites: At the Chen and Kyriacou laboratories (Leicester), the student will apply state-of-art infra-red and video-based **behaviour tracking and analysis** (DAM, DART and Ethoscope), as well as a **versatile toolkit of *Drosophila* genetics**. At the Hanson laboratory (Penryn), the student will conduct **microbiome collections, bioinformatic analyses, and gnotobiotic experiments.** The student may also have opportunity to conduct **novel transgenesis in *D. testacea***.

References

1. Proc B *285*, doi:10.1098/rspb.2017.2599 **2.** Science *381*, doi:10.1126/science.adg5725 **3.** An. ESA *85*, 671-685, doi:10.1093/aesa/85.6.671 **4.** Jour. Fac. Sci. Hokkaido Univ.VI, Zool. 21 (1),1977. 21-30 **5.** Science *363*, doi:10.1126/science.aat1650 **6.** eLife, 8, e38114