

Stressed! How do animals cope with what life throws at them?

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Project summary

Animals face many environmental stresses, and this is only likely to get worse as we face an era of rapid climate change. This brings into sharp focus the need to understand what the responses to stressors are and what molecular mechanisms underpin the strategies animals use to cope with stress. In this way we can better predict what the consequences of environmental stress will be and whether animals will cope on ecological and evolutionary timescales. This project will investigate how stressors interact, whether they are general stress responses that are common across species and whether the epigenome is key to combatting stress.



Drosophila melanogaster fruit flies mating, as used by the Bretman lab. Mating is very stressful for females, they age and die quicker the more they interact and mate with males. Males and females also react to intrasexual interactions, males are more stressed by being with other males, females are more stressed by being held alone. This social stress also alters how they age and respond to other stresses like temperature and infection.

Background and project description

Animals face challenges of environmental stress from many sources, such as temperature, nutrition, toxins, disease and social interactions. These stresses can be variable and unpredictable, acute or long lasting. Their impact on the individual may reduce future lifespan, reproductive output or ability to fight disease. Alternatively a mild stress may

increase resilience to subsequent stress (known as hormeisis). To combat these stresses individuals can be plastic in their behaviour or physiology, but the mechanisms that underlie these processes are not well understood. The epigenome (marks on the genome that alter gene expression) is environmentally sensitive and so may be a mechanism that allows animals respond to the environment through gene regulation. Changes to the epigenome can be long lasting, so could hold the key to how a current stress alters resilience to future stress.



A *Plodia interpunctella* Indian meal moth, a pest of food stores but a great ecological model. The Sait lab investigates how it responds to the stress of unpredictable temperature variation, and how this alters interactions with its natural enemy a parasitoid wasp *Venturia canescens*.

The mechanisms that underlie responses to stress are not well understood. Certainly there is a genetic responses, for example some of our recent work shows that social stress alters expression of genes of the *Turandot* family that have been linked to other stressors (Mohorianu, Bretman et al 2017; Leech, Sait and Bretman in prep). It may be then that there is a general stress Responses pathway common across stressors. But how is this regulated and how is the environmental information integrated? Recently there has been rise in interest in the role played by the epigenome (chemical markers on DNA that do not change the sequence but determining how accessible genes are for expression). Information about the environment an animal experiences can affect gene expression and the epigenome (Duncan et al., 2014). This enables the epigenome to be environmentally sensitive, for example to maternal nutrition (Dolinoy et al., 2007), heat stress (Seong et al., 2011), amount of parental care (Roth et al., 2009), stressful confinement (Rodgers et al., 2015), and environmental toxins such as cigarette smoke (Qiu et al., 2015). Despite the fact that changes to the epigenome can be fast, occurring within hours (e.g. Kangaspeska et al., 2008), these changes states can have long lasting effects on the individual and even transgenerational effects as epigenetic information can be passed from parent to offspring (e.g. Roth et al., 2009). These processes may therefore play a critical role in determining which species survive this era of huge global environment change.

Key questions

How do animals cope with combinations of stress?

Are there sex differences in stress responses?

Are there common responses to stress across different species?

What molecular mechanisms enable animals to cope with stress?



The Duncan lab investigates how in social insects like bees control and separate who in the colony is allowed to reproduce. But this is also may be altered by stress, such as pesticides in the environment. The Duncan lab is currently investigating the role of neonicotinoids in reproductive behaviour and physiology.

To investigate these questions we will use a range of insect species. Insects are not only extremely ecologically important but are also superb laboratory models with which we can do large-scale experiments in a relatively short time. The standard lab model *Drosophila melanogaster* fruit flies will be our first pass system, as they are very easy to manipulate and have many genetic resources available that can help us to pin down mechanisms. We will then move to other *Drosophila* species and animals of direct agricultural importance such as Indian meal moths, bees, aphids, to find general patterns in responses. These experiments will involve life history assays of animals that undergo different stressors, to measure subsequent lifespan and reproductive output. We will then manipulate epigenetic marks chemically and genetically, and use sequencing to understand how stress alters the epigenome and gene expression.

Expected outcomes

This project is using molecular and ecological tools to address fundamental and crucial questions relevant to climate change biology, conservation biology, evolution and adaptation. The project will produce several publishable papers, with at least one expected to be high impact as the questions being addressed are of wide scientific interest. The

candidate will also be expected to present their research at a both of national and international conferences.

Requirements

A strong undergraduate (and ideally Masters) degree in ecology, genetics, biology or zoology is expected. Experience in using insects in a lab and some statistics background would be helpful. However, training will be provided in all techniques relevant for the project. If you are not sure if you have the relevant background please feel free to contact the supervisors to discuss the project.

Training

This project will provide students with a broad range of training in a range of techniques associated with population monitoring, phenotypic measurements, life history measurements and molecular / genetic analysis. The work blends ecology and global change biology with genetics, providing a broad foundation for a future career. The PhD student will have access to a range of training courses designed to facilitate skills development and will be expected to present the outcomes of this project at both national and international conferences.

Research context and partners

The supervisory team have active research groups and strong records of relevant research in molecular mechanisms of phenotypic plasticity and population, community and evolutionary ecology respectively. The student will be involved in fortnightly team meetings, as well as having access to both formal (Faculty) and informal (Ecology & Evolution group) seminar series through the School of Biology. Co-supervision will involve meetings between all participants and the co-supervisors will provide guidance on the overall direction of the project. There are strong interactions between the research groups; Bretman and Sait have co-supervised two PhD students who completed in 2018, Bretman and Duncan have a current Leverhulme Trust funded project to understand the role of the

epigenome in plastic responses to sperm competition, and Duncan and Sait are co-Investigators in a NERC funded project to investigate pollinator ecology using radar. There is also the opportunity to link with other NERC funded projects that Bretman is currently co-supervising run by colleagues in Liverpool on thermal effects on fertility and in UEA on social effects on female reproduction. The student will therefore be integrated into the local and national biology community.

Bibliography

DOLINOY, D. C., HUANG, D. & JIRTLE, R. L. 2007. Maternal nutrient supplementation counteracts bisphenol A-induced DNA hypomethylation in early development. *Proceedings Of The National Academy Of Sciences Of The United States Of America*, 104, 13056-13061.

DUNCAN, E. J., GLUCKMAN, P. D. & DEARDEN, P. K. 2014. Epigenetics, Plasticity, and Evolution: How do We Link Epigenetic Change to Phenotype? *Journal of Experimental Zoology Part B-Molecular and Developmental Evolution*, 322, 208-220.

KANGASPESKA, S., STRIDE, B., METIVIER, R., POLYCARPOU-SCHWARZ, M., IBBERSON, D., CARMOUCHE, R. P., BENES, V., GANNON, F. & REID, G. 2008. Transient cyclical methylation of promoter DNA. *Nature*, 452, 112-115.

LEECH, T., SAIT, S. M. & BRETMAN, A. 2017. Sex-specific effects of social isolation on ageing in *Drosophila melanogaster*. *Journal of Insect Physiology*, 102, 12-17.

MOHORIANU, I., BRETMAN, A., SMITH, D., FOWLER, E., DALMAY, T. & CHAPMAN, T. 2017. Genomic responses to socio-sexual environment in male *Drosophila melanogaster* exposed to conspecific rivals. *RNA*, 23, 1048-1059.

QIU, W., WAN, E., MORROW, J., CHO, M. H., CRAPO, J. D., SILVERMAN, E. K. & DEMEO, D. L. 2015. The impact of genetic variation and cigarette smoke on DNA methylation in current and former smokers from the COPD Gene study. *Epigenetics*, 10, 1064-1073.

RODGERS, A. B., MORGAN, C. P., LEU, N. A. & BALE, T. L. 2015. Transgenerational epigenetic programming via sperm microRNA recapitulates effects of paternal stress. *Proceedings Of The National Academy Of Sciences Of The United States Of America*, 112, 13699-13704.

ROTH, T. L., LUBIN, F. D., FUNK, A. J. & SWEATT, J. D. 2009. Lasting epigenetic influence of early-life adversity on the BDNF gene. *Biological Psychiatry*, 65, 760-769.

SEONG, K. H., LI, D., SHIMIZU, H., NAKAMURA, R. & ISHII, S. 2011. Inheritance of stress-induced, ATF-2-dependent epigenetic change. *Cell*, 145, 1049-1061.