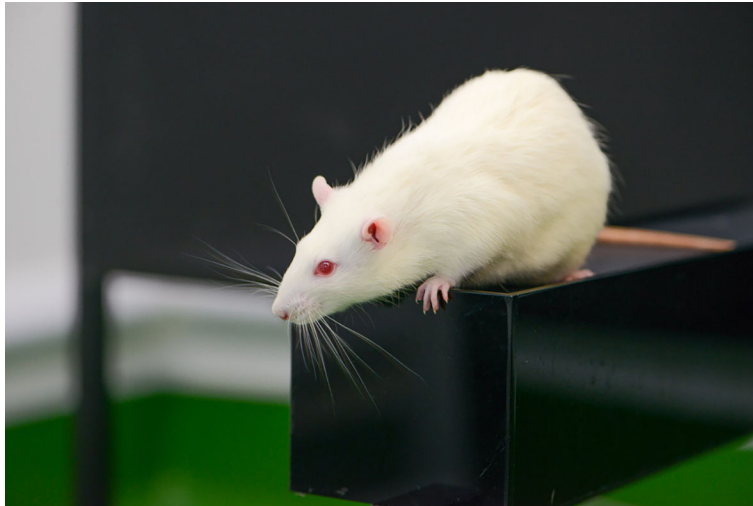


Biology through the lens of development: from gestation to evolution



A rat on an open arm of the elevated plus maze used to assess anxiety-like behaviour. Photo credit: Norman Russell.

From the instant of conception, a cascade of developmental processes is unleashed that drives the cell to divide, multiply and differentiate, creating organs, tissues and more complex structures. However, throughout the process, each creature experiences a range of environmental conditions, some of which impact directly, while others are mediated through the experiences of their mothers, to influence and mould the course of their development. ‘As comparative animal physiologists, we are fascinated with how animals cope with environmental change and, therefore, how early development can be shaped by environmental variation is a natural question’, says Pat Wright (University of Guelph, Canada), who has focused on the impact of temperature and oxygen availability on development through her own research. More recently, researchers have begun unravelling the molecular mechanisms that underpin the developmental responses of organisms to changes in their environment, potentially offering a lifeline to creatures threatened by climate change. Given the pivotal role that developmental plasticity may play in

the evolutionary process, Katie Gilmour (University of Ottawa, Canada) says, ‘We wanted to consider developmental plasticity broadly and from different perspectives’. Guided by this goal, Gilmour and Wright invited leaders in the field to review and discuss the impact of factors such as maternal stress and environmental factors on developmental trajectories, hormone and epigenetic effects mediating physiological responses to stress, and the role of developmental plasticity in evolution.

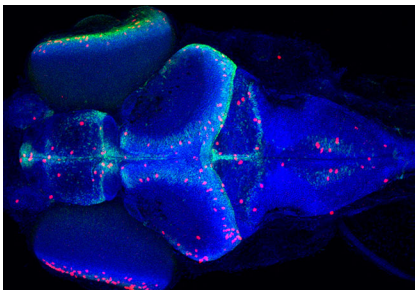
How the environment impacts development

Given that adverse environmental factors during gestation have a disproportionate effect on the future of developing embryos, Ying Sze and Paula Brunton (University of Edinburgh, UK) review our understanding of how maternal stresses, such as malnourishment and anxiety, are transmitted to fetuses ([jeb246073](#)). The experience of stress is communicated through the body by a cascade of hormones, triggered by the hypothalamus, which ultimately releases glucocorticoid hormones that trigger

energy release. However, this communication network is hyperactivated in the offspring of stressed mothers, as the mechanisms that usually keep the network in check are less active, raising their anxiety levels. The mechanisms by which maternal stress is communicated to offspring are less clear. Although the placenta usually protects the fetus from glucocorticoids circulating in their mother’s blood, it is unclear whether this barrier functions in highly stressed mothers and whether maternal glucocorticoids reprogramme the fetus’s stress response by altering the placenta or triggering other mechanisms that signal stress. However, most of the stress hormones circulating in the fetus’s blood are produced by the fetus itself, not the mother. The placentas of stressed mothers may also contribute to the physiological stress experienced by the fetus, by limiting the nutrient supply as well as exposing the fetus to oxidative stress and releasing microRNAs that could alter the expression of key genes in the developing brain, resulting in high levels of anxiety in offspring. ‘We propose that fetal programming is probably not the consequence of a single factor but rather is more likely mediated by multiple mechanisms’, says Sze and Brunton.

While the environment experienced by parents impacts their offspring, and subsequent generations, mothers also modify their offspring’s physiology in preparation for predictable environmental variations, such as seasonal temperatures variations. However, Matthew Walsh and colleagues from the University of Texas at Arlington, USA, suggest that the impact that parents have on the next generation can be more nuanced. They discuss how the conditions experienced by parents during their own development in turn impacts the development of their offspring and future generations, effectively transferring their physical condition across the generations to produce either stronger or weaker offspring ([jeb246094](#)). After an extensive literature

search, Walsh and colleagues identified 55 research articles reporting studies investigating the impact of the environment on the offspring of parents reared in contrasting environments. In more than 50% of the studies (29/55), the offspring benefited from parental transfer, with the offspring of fit and healthy parents developing better in poor and plentiful circumstances. However, the team also identified situations where lizard hatchlings benefited by being prepared for predictable variations in the environment, in addition to benefiting from their parents' rearing conditions. In that case, the hatchlings produced by mothers that had developed when food was scarce grew faster, benefiting from their ability to anticipate environmental conditions, while the youngsters produced by well-fed mothers were better sprinters when food was scarce, benefiting from their parent's better start in life. 'Condition transfer effects are indeed more widespread than is currently appreciated', say Walsh and colleagues.



Neurogenesis in the larval zebrafish brain. Photo credit: Helen Eachus.

Returning to the role of glucocorticoid hormones – released in response to stress – this time in brain development, Helen Eachus and Soojin Ryu review how the hormones impact dendritic spine remodelling in the rodent brain, facilitating the formation of new nerve spines in the sensory brain region, which are essential for learning and memory (jeb246128). Elevated levels of the hormones may lead to faster brain development, which could be 'advantageous in a high stress environment', say Eachus and Ryu. Yet, despite the apparent benefits of accelerated brain development in early life, the long-term implications of prolonged stress exposure can be harmful, leading to the accumulation of bodily wear-and-tear. Eachus and Ryu

also discuss the specific impact of early and prolonged exposure to glucocorticoid hormone on the brain in later life; depleting neural stem cells, which affects the brain's structure and function and can lead to disease in later life. 'Further understanding of how stress and glucocorticoid exposure can alter developmental trajectories at the molecular and cellular level is of critical importance to reduce the burden of mental and physical ill health across the life course', say Eachus and Ryu.

Focusing on development in birds, Suvi Ruuskanen from the University of Jyväskylä, Finland, reviews the life-long physiological effects of the environment experienced by chicks in the egg and after hatching, mediated through epigenetic changes and the gut microbiome (jeb246024). Early changes in one epigenetic marker (DNA methylation) in response to changes in the environment can significantly alter chick development. Changes in the gut microbiome in early life can have later implications for the animal's digestion – from the ability to remove toxins from the body, to the synthesis of key metabolites – in addition to affecting behaviour and cognition, and the ability to fight infection. The early social environment – including competition with siblings – and the physical environment – from the temperatures experienced to human pollution, noise and light – all impact DNA methylation and likely affect chick development. Although the long-term implications of these changes on the future health of birds is unclear, it is probable that changes in the epigenome and microbiome caused by early life stress will impact later health.



A zebra finch hatchling emerging from the egg, after being exposed to prenatal acoustic playback. Photo credit: Mylene Mariette.

Sound is a pervasive element of the natural world, from wind to familiar voices, and in her Review, Mylene Mariette (Doñana Biological Station, Spain) discusses how exposure to sound during development shapes the auditory system and how the effects are modulated by hormones (jeb246696). Intriguingly, the impact of sound on development extends beyond the sound-processing centres, to include the region of the brain involved in memory and spatial learning (the hippocampus), the region of the brain involved in emotional regulation (the amygdala) and the hypothalamus, which regulates the endocrine system. Outlining the impact of sound on these brain regions and its implications for development, Mariette also discusses how organisms sense vibrations prior to maturation of their hearing organs through neuromast cells and the balance-sensing vestibular system. Plants and single-cell organisms, such as yeast, also detect and respond to vibrations. She concludes that sound experienced before birth is capable of altering development and says that there is a 'fascinating capacity for sound to plastically modulate the brain'.

The ability of an animal's immune system to respond rapidly and strongly to a previously experienced infectious agent, such as a parasite – known as immune memory – was thought to be the domain of vertebrates, but evidence accumulated over recent decades indicates that some invertebrates also benefit from plastic immune memory. Jorge Contreras-Garduño (National Autonomous University of Mexico) with colleagues from Mexico and Panama discusses different factors – including developmental rate and stage, temperature and mutualist infections – that impact invertebrate immune memory (jeb246158). In addition, it is clear that the two-stage expression of immune memory in invertebrates is highly plastic, differing greatly between species, and is currently poorly understood. 'One possible explanation [for the plasticity of the invertebrate immune system] is that different immune response parameters are traded-off, meaning that not all parameters may increase simultaneously after the second [immune] challenge', says Contreras-Garduño, who hopes that the mechanisms underpinning this remarkably plastic system will soon be resolved.



Patterns of ageing in zebra finches may depend on developmental trajectories early in life. Photo credit: Paul Jerem.

However, the long-term outcome of a developmental response to changes in the environment can be achieved by organisms taking alternative developmental routes, ultimately altering an animal's physiology with consequences later in life. 'The organism that has reached the original target but through an altered trajectory is "built" differently', explains Neil Metcalfe from the University of Glasgow, UK ([jeb246010](#)). Metcalfe points out that alternative development trajectories are likely to incur physiological costs that must be borne by the animal. For example, fish that experienced an accelerated growth rate after a limited food supply suffered lower fertility as adults than fish that had achieved the same body size while developing at a more even rate. 'It is necessary to look beyond the final phenotype when studying and quantifying developmental plasticity: the route by which that phenotype was reached is also relevant', Metcalfe says.

Developmental responses to food insecurity and starvation

Unpredictable access to food is a major factor with implications for developing organisms, with human food insecurity – caused by conflict, wealth inequality and climate change – raising specific concern for babies, children and adolescents across the globe. 'The experience of food insecurity... may have very different effects on development and plasticity when compared with sustained malnutrition and starvation', says Linda Wilbrecht from the University of California, Berkeley, USA, writing with a team of international collaborators ([jeb246215](#)). Turning to the literature of investigations studying the impact of food insecurity in birds and rodents, Wilbrecht and colleagues discuss how unreliable access to food generally leads birds and rodents to gain weight when access to food is restored, especially if the food

restriction occurred in early life. Food insecurity also alters rats' motivational networks and dopamine neurons (involved in reinforcing behaviours), potentially making them more vulnerable to addiction and impacting the rodents' ability to learn. Explaining how the nutrition-related hormones leptin and ghrelin programme the metabolic circuitry in early life, Wilbrecht speculates how food insecurity might alter gene expression in the bodies of young animals through these hormones, potentially reprogramming their physiology through life, with 'lasting impacts on feeding and other motivated behaviour, as well as learning and cognitive function', she says.



Adult and larvae of *C. elegans* worms moving on an agar plate seeded with *E. coli*. Photo credit: Christelle Gally.

To learn in more detail about the impact of food availability on the physiology of animals, Sophie Jarriault and Christelle Gally, both from Université de Strasbourg, France, turned to the workhorse of the developmental biology world, nematodes – including *Caenorhabditis elegans* and *Pristionchus pacificus*. The duo describes how the availability of food can impact the whole organism, triggering the animal to enter a form of suspended animation, where the animal stops developing, known as dauer ([jeb246546](#)). Starvation can also impact the development of specific organs, such as the vulva in *C. elegans*, and switch the mouth form (with one or two teeth) in developing *P. pacificus* larvae. Reviewing the sensory network that allows *C. elegans* to detect food, they also describe how the nematodes alter their foraging strategy depending on food availability in response to changes in the associated neuronal networks. The impact of starvation can also be passed down the generations, with the third-generation descendants of starved nematodes that resorted to dauer coping better when

deprived of nutrition than the descendants of well-fed third-generation ancestors. '*Caenorhabditis elegans* has provided a powerful model to address the impact of the environment on the development of the organism and specific structures', say Jarriault and Gally.

Developmental plasticity: evolution and adaptation

While developmental plasticity is key for survival in ever-fluctuating environments, developmental responses to environmental change also have the potential to drive adaptive evolution. Establishing how developmental responses contribute to evolution has been a long-term challenge, addressed by Mary-Jane West-Eberhard in her 2003 book, *Developmental Plasticity and Evolution*, where she argued that the 'developmental mechanisms that enable organisms to respond to their environment are fundamental causes of adaptation'. Tobias Uller and colleagues from Lund University, Sweden, explain this standpoint had been hotly debated, because of the lack of testable theories for the role of developmental plasticity in evolution. However, in their review, Uller and associates provide an overview of the evolutionary process, in which development influences the distribution of phenotypes upon which selection may act, while selection, in turn, acts upon developmental processes, resulting in phenotypic diversity ([jeb246375](#)). Outlining a framework to identify developmental causes of adaptive evolution, the team says, 'Organisms that evolve environmental regulation of development may become intrinsically better at evolving if plasticity allows them to track the adaptive landscape associated with environmental change'.

Reviewing a spectacular example of developmental plasticity, Patrick Rohner (University of California San Diego, USA) with Joshua Jones and Armin Moczek (Indiana University Bloomington, USA) discuss how recently introduced tunnel-burrowing *Onthophagus taurus* dung beetles from the Mediterranean have colonised North America, migrating over a 40-year period (80–100 beetle generations) across a 1600 km range from Florida to the Canadian border. By comparing the modern Mediterranean dung beetle population with introduced beetles from North America, the team reveals that the

population at the northern-most extreme now develops faster, to compensate for the shorter growing season ([jeb245976](#)).



Nutritional polyphenism in dung beetles separating large horned males (left) from smaller hornless males (right). Photo credit: Patrick Rohner.

However, instead of evolving a reduced size at which the beetles develop their impressive horns, in order to maintain the balance between long- and short-horned forms of beetle in the population, the northern population shifted to higher threshold sizes, altering the relative proportions of the long- and short-horned beetles to unexpectedly reduce the number of long-horned males in the population. Rohner and colleagues also discuss how the beetle larvae modify their environment by chewing and digesting the ball of dung in which they develop, and how the act of modifying their local environment may suppress the expression of genetic variability that will only become apparent if the

environment-altering behaviours change to permit previously inhibited developmental plasticity. ‘This work documents the power and versatility of the horned dung beetles as a study system in which to explore the varied mechanisms and consequences of plasticity in development and evolution’, says Rohner.

Given that populations diverge genetically over time, Simon Blanchet and colleagues from the Station d’Ecologie Théorique et Expérimentale, France, investigated the epigenetic variation across plant and animal populations with the hope of determining whether knowledge of population epigenetic marker distributions could aid conservation management ([jeb246009](#)). Although genetic differentiation between populations was stronger than the measured epigenetic differentiation when populations are distantly related, the team show that epigenetic markers in recently differentiated and closely related populations can reveal local and contemporary adaption of populations. They say, ‘Our results suggest that epigenetic information is particularly relevant in populations that have recently diverged genetically and are connected by gene flow’. However, the epigenetic differentiation of plant populations was not that dissimilar from that of animals, despite their prediction that plant populations would show more epigenetic differentiation, as plants are immobile

organisms that should depend on epigenetic modification, rather than relocation, to respond to environmental change.

To conclude

Having considered the role and impact of developmental plasticity from the perspective of the rearing environment and parental condition to developmental plasticity in evolution, we hope that this Review collection will inspire comparative physiologists to consider the profound impact that early life conditions can have later on and as populations adapt and evolve. ‘Understanding developmental plasticity will facilitate deeper investigations of the range of responses in animal populations, leading us to a closer understanding of the natural world’, says Wright. Gilmour adds that she hopes that ‘comparative physiologists will think about developmental plasticity as something that they may incorporate into their research’, to cement the power of the developmental approach within the context of comparative physiology. ‘We hope that JEB readers will learn from the diverse taxa covered in these articles that the comparative approach highlighted in this Special Issue will allow us to learn of the common and unique mechanisms and responses to early life variation’, says Wright.

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Kathryn Knight
kathryn.knight@biologists.com