Editorial

What is stress?

Figure 1. Adaptations and tradeoffs.
The theory of allocation predicts that the evolution of adaptations to a particular environment necessitates a loss in fitness in other environments. This prediction has been explored by testing the running speed of lizards at various temperatures. Interestingly, while critical maximum temperatures are positively correlated with the animals' normal temperature in the field, consistent with adaptation, lizards that are optimized for performance at high temperature do not necessarily have compromised function at low temperatures, at odds with allocation theory [2]. (Image: Wikipedia.)

As is readily evident in this special issue, the concept of 'stress' is pervasive in biology, and the responses to stress can be appreciated at various timescales. The term also has both positive and negative connotations. If talking about physical strain, i.e. mechanical stress, then stress can be intertwined with normal developmental processes. In plants, for example, we see that the internal pressures generated inside cells provide the driving force behind growth, and these expanding cells in turn squeeze their neighbors, which can sense this and alter their own growth accordingly. These interactions create a complex set of feedbacks between cells that together help determine the final form of mature plant organs. So it is clear that stress can be a normal, even essential, part of the life cycle.

But, of course, stress can also be a negative, as in the psychological stress that comes with writing an editorial under a tight deadline. Ecologists usually describe stress as any perturbation, such as a change in moisture or temperature, that reduces the fitness of the individual if left unattended. In response to stress, organisms may develop strategies to mitigate the harmful effects. One option is to curl up into a ball, shield yourself from outside elements, and hope for better times. This is seen in many organisms that undergo diapause or dauer transitions. Yet another option is to simply run away. For example, it is clear that animals can migrate to more favorable locales, and we can see this as the ranges of various species become altered by climate change.

dispause = suspension of growth

Escape is not an option for sessile organisms like plants, so in response to stressful conditions, such as intermittent periods of heat or drought, mechanisms may evolve that allow rapid physiological changes that help 'move' the individual back into its comfort zone. The evolution of these homeostatic mechanisms will inevitably depend on the strength of natural selection, determined by the magnitude of the stress and its frequency, as well as the cost of building up these defences.

It's often useful to first examine an exaggerated, special case before moving on to generalities, and there may not be a more extreme form of stress response than that seen in the bacterium *Deinococcus radiodurans*. This microbe was first discovered living in meat that had been zapped by high doses of radiation, typically an effective method to sterilize food. Impressively, the bacterium can survive exposures of up to 20,000 Gy, which shatter its genome into many fragments. For a typical bacterium, radiation levels far below this would sound the death knell, but *D. radiodurans* has evolved an exotic DNA repair mechanism that depends on the bacterium keeping multiple copies of its genome on hand [1]. Using the undamaged templates, *D. radiodurans* is able to stitch chromosome fragments back together, restoring its genome. The bacterium also possesses a battery of other defences, such as pigments that block radiation and a host of enzymes that can repair damaged nucleotides. So *D. radiodurans* has invested heavily in a supercharged DNA damage response, which is well suited to the arid environments in which it finds itself, conditions that promote extensive DNA damage.

The case of *D. radiodurans* serves as an excellent example of a response that can contend with the worst that the environment can throw at an organism. But similar homeostatic processes exist everywhere in nature, though these deal with perhaps less severe insults. A classic example is the heat shock response, which is thrown into action by thermal stress to deal with the unfolded proteins and aggregates that ensue. In these pathways, pervasive in both prokaryotes and eukaryotes, sensors that respond to heat induce the expression of genes whose products help mitigate the

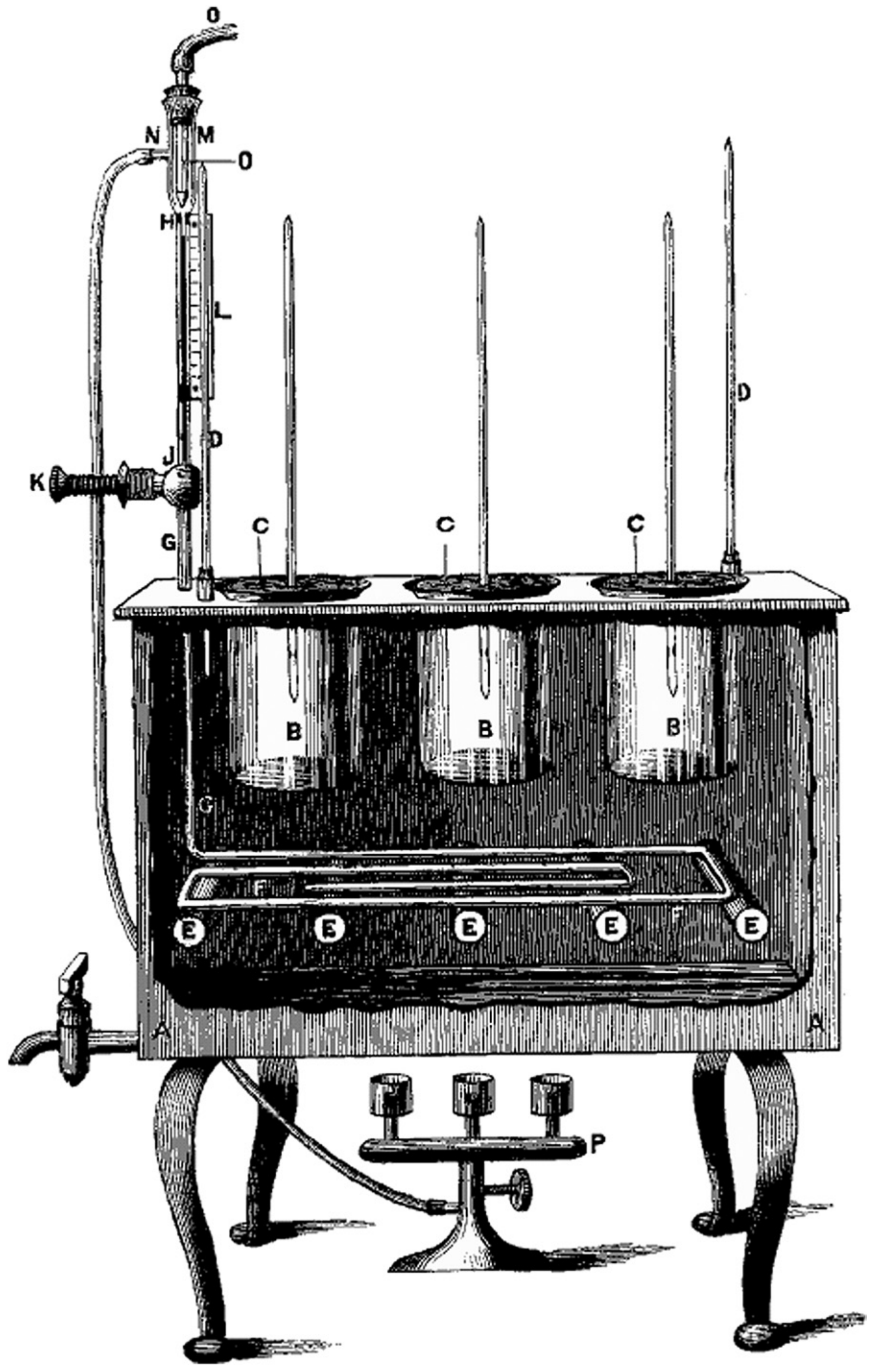

Figure 2. Evolution in the laboratory.
There has been a long tradition of studying evolution in the laboratory, probably starting with the work of William H. Dallinger who was able to show that protozoa could adapt to ever increasing temperatures, an important demonstration of Darwin's theory of natural selection. To accomplish this work, Dallinger had to build an incubator allowing precise temperature control. The experiment lasted 7 years before an accident ended the work. (Image: Wikipedia.)

damage, quickly bringing the system back to a normal state. If we move to longer timescales, we can see slower physiological adaptations taking place, such as the acclimatization that occurs when alpine climbers move up to high-altitude base camps. In this case, exposure to the thin air — hypoxic stress — stimulates an increase in red blood cells and blood volume, allowing a higher oxygen-carrying capacity.

While acclimatization responses occur over the scale of weeks and months, we can go still one step further and examine stress responses on an evolutionary timescale. Indeed, a wide swathe of research in evolutionary biology is devoted to understanding the adaptation of species to changing environments, and the question becomes increasingly important as scientists try to predict the effects of global warming. As mentioned in the specific case of *D. radiodurans,* there is an assumed cost of developing a trait suited to a particular environment, such as the resources necessary to produce enzymes that repair DNA. Conversely, those traits that were adaptive in an organism's old environment might be useless, or even counterproductive, in its new environment. We can, for example, imagine an enzyme active site evolving mutations that stabilize it at high temperature but which would compromise function at lower temperatures. Thus, in general, we might expect a tradeoff in one set of adaptations for another. This is better known as the principle of allocation.

tradeoff = allocation (of resources)

The principle of allocation seems reasonable enough at face value, but what happens when we move from theory to observations in nature and actual experiments? One popular route to investigating the evolutionary responses of species to the environment is the comparative approach. In a well-known series of studies, for example, Raymond Huey and colleagues examined the relationship between body temperature and running speed in a clade of iguanid lizards [2] (Figure 1). As one might expect, the optimal temperature for running, which varied among the lizard species, closely matched the body temperatures of the animals in the field, suggesting adaptation. Likewise, the maximum temperature at which a given species could run was positively correlated with optimum running temperature. This makes sense. However, and in contrast to the principle of allocation, there was no relationship between the minimum temperature at which lizards would still run and their optimum running temperature. That is, according to the principle, lizards that run fast at high temperatures should have traded off ability at lower temperatures, but this was not necessarily the case.

The allocation principle has also been tested using more direct approaches, involving natural selection in the laboratory. Such experiments have a rich history, probably beginning with the experiments of Reverend William H. Dallinger, a contemporary of Darwin who was likely best known for his detailed accounts of protozoan life cycles, which helped dispel a widely held view at the time that life arose *de novo*, from nothing.

Encouraged by Darwin, Dallinger sought to test the theory of evolution via natural selection by subjecting protozoa to increasingly higher temperatures to see if they would adapt to the new conditions. To do this, Dallinger had to construct an incubation apparatus that allowed precise control of temperature (Figure 2). In an experiment that lasted seven years, Dallinger was able to show that an organism originating from an environment where the temperature is 60°F could, amazingly, become adapted to 158°F. Darwin's own reaction on hearing about the work speaks to its importance: "I did not know that you were attending to the mutation of the lower organisms under changed conditions of life; and your results, I have no doubt, will be extremely curious and valuable. The fact which you mention about their being adapted to certain temperatures, but becoming gradually accustomed to much higher ones, is very remarkable. It explains the existence of algae in hot springs." Interestingly, when Dallinger placed the adapted protozoa back at 60°F, this proved lethal, an observation that would seem consistent with the allocation principle.

cases where there is no tradeoff -- the organism performs just as well in extreme temperature!

The tradition of experimental evolution continued into the 20^{th} century with work on a number of other organisms chosen in part for their relatively short generation times, such as *Drosophila*. But the Dallinger experiment has a particularly close corollary in a fruitful line of research initiated by Richard Lenski and colleagues, who have been performing a long-term evolution experiment on bacteria exposed to different, sometimes varying conditions. Initiated in 1988, the experiment has now crossed the 50,000 generation mark. The work has addressed a number of questions, but, of relevance to Dallinger and allocation theory, Bennett and Lenski placed 20 different lines of *Escherichia coli* at 20°C for 2,000 generations and then asked how they fared at 40°C [3]. In general, while fitness increased at 20°C, it became reduced at 40°C, consistent with allocation theory. But the effect was not universal as several lines showed no loss of fitness at the higher temperature and, in one case, even greater fitness.

What we can take away from these studies is that we are starting to see patterns that in some cases are consistent with tradeoffs occurring over the course of evolution, but this is certainly not a given. In some cases, there is apparently no penalty for maintaining adaptations that are no longer of use. It will be interesting to continue to gather data from more species using different stresses and selection regimes to see if these patterns hold up. And, of course, we'll want to better understand the genetic basis of adaptation to stress so that we can start to understand the mechanisms and why, in some cases, a tradeoff may be necessary as organisms adapt to stressful environments.

Coming full circle then, we can see that the term 'stress' can be broadly construed, functioning as an integral part of the life cycle but more often manifesting as an environmental insult, in response to which homeostatic mechanisms arise. Stress responses also operate at various scales, from rapid millisecond responses that restore homeostasis, to the adaptation of organisms over evolutionary timescales. The reach of stress into so many facets of biology is such that we almost take it for granted. It seems appropriate then that we devote this special issue to the topic and explore stress in its various forms. Enjoy!

References

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Feature

Chronic stress means we're always on the hunt

Stress responses that evolved for occasional dangerous situations can make us ill when they become chronic. But why do we perceive our relatively safe lives as stressful and what can we do to avoid the associated dangers? **Michael Gross** investigates.

Life for many mammalian species is a long string of happy days spent grazing in the savannah — brutally interrupted by short moments when a predator shows up and they have to run for their lives. Herbivores, like the horses and their relatives, have evolved a range of characteristics especially for these short moments of flight, from their fast-running legs through to the ability to keep cool by abundant sweating (shared with humans but otherwise rare in the animal kingdom).

The situation is similar for the hunters, albeit reversed. Lions spend much of their day sleeping and digesting, interrupted by short periods of hunting fleet-footed prey. Their survival also depends on this short period of exertion, as they would starve if they failed to hunt successfully.

In both cases, two systems are activated. The sympathetic nervous system prepares the body's organs for 'fight or flight' responses, increasing oxygen intake, blood pressure, heart rate, and muscle activity, while shutting down the digestive system. Additionally, a general hormone response is activated that makes extra energy available for the short-term use and sharpens the senses. Specifically, the HPA axis (hypothalamus, pituitary gland, and adrenal cortex) releases hormones including corticosteroids and the catecholamines adrenaline (epinephrine) and noradrenaline, which enhance metabolic activity (increasing blood sugar), and improve alertness and attention. These two processes, nervous and endocrine (hormonal), work together to form the physiological stress response.