

field, such as memory for food stores in tits, making the crucial links with fitness has been difficult and at times controversial.

Why are there not more women in science? As an undergraduate, I was told by an ageing male lecturer that women who 'got on' in science had blonde hair, blue eyes and A grades. Usefully, back then I could tick all those boxes! However, when I finally looked at who had jobs in the department I realized that women did not stay on in zoology in spite of making up half of the undergraduate contingent. Now, I number amongst the older women at the conferences I attend, even though men of my age are still considered 'mid-career'. There are multiple explanations for this gender bias, and the more I research sex differences myself, the more comfortable I am that some of those differences exist. After all, from the neck down there is little dispute or concern over differences between males and females. However, the idea that a CV with a woman's name on it will be viewed less positively than the same CV bearing a man's name shames us all. We need to reach a state where gender does not contribute to decision making in any context. Women as well as men must play a role in this. For example, the comment that 'I don't want to get a job just because I am a woman' is one that women should be wary of producing. After all, at least some of the men surrounding us got their jobs because they were men! Whilst most of my 'insights' into this issue are best kept for sharing over a glass of wine, one point I would stress concerns confidence. In my own career, I will be forever grateful to people like Nicola Grimmond and Alison Mercer at Otago, who gave me the confidence to consider myself good enough to do the job. Unfortunately, confidence is not easily taught. However, I do make an attempt on a more local level to encourage my students' self-confidence. I look forward to seeing the young women I know being able to make confident career decisions on their own, rather than just because they were lucky enough to have the right people encourage them just at the right time.

Schools of Biology and Psychology, University of St Andrews, St Andrews KY16 9JP, UK.
E-mail: susan.healy@st-andrews.ac.uk

Quick guide

Stress

Carl Procko and Shai Shaham

Why do organisms respond to environmental stress? Organisms are adapted to particular environments; however, the environment in which an organism finds itself is rarely static, and may exhibit daily and seasonal fluctuations. Without the benefit of an air-conditioned home or a well-stocked refrigerator, most organisms must sense environmental changes and respond accordingly to optimize metabolism and growth. Environmental stressors, such as

temperature extremes or nutrient limitations, pose an additional problem: how to survive and maximize reproductive success in unfavorable conditions that may otherwise be lethal.

Can development be altered by stress? Many organisms have evolved developmental strategies to persist under high stress conditions. For example, some organisms enter a specialized, stress-resistant state that permits both the temporal avoidance of the environmental insult and also the dispersal of the organism from one environment to another. Bacteria are a good example: in response to nutrient depletion, some species become endospores (Figure 1A), metabolically-inactive cellular structures, with a thick, multi-layered protein coat and a dehydrated core. Specialized proteins,

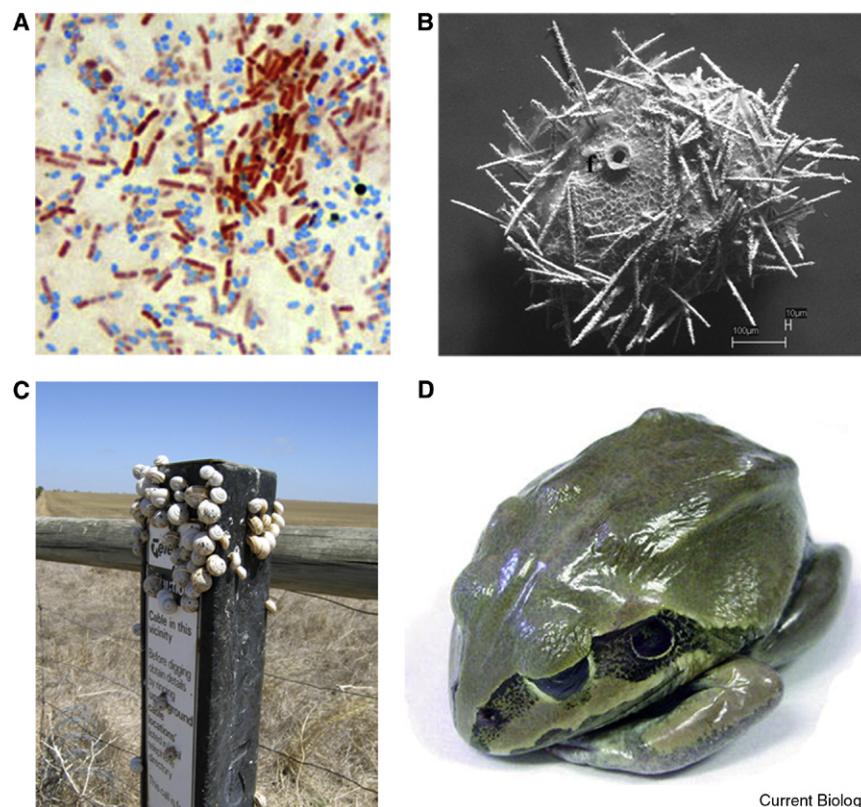


Figure 1. Coping with stress: from bacteria to vertebrates.

(A) Bacterial endospores of the *Bacillus* genus (blue) derived from vegetative cells (red) in response to nutrient depletion. Reproduced with permission from Zayaitz, A., and Hussey, M.A. (2007). (B) Scanning electron micrograph of a sponge gemmule (*Duosclera mackayi*). Gemmules are protected from environmental insults by a collagenous coat, sometimes containing glass spicules. Reproduced with permission from Annesley, J. *et al.* (2007). (C) In periods of high heat and low water, some species of land snail such as *Theba pisana* (pictured) avoid desiccation by entering a state of dormancy, termed estivation. Estivating snails are frequently found atop posts and vegetation, where the temperature is cooler than the soil surface. Port Vincent, Australia; photo: M.R. Procko. (D) The frog *Cyclorana australis* also estivates during periods of low water availability. In addition to lowering its metabolic rate, the animal burrows underground and produces a hardened cocoon from shed layers of epithelial cells (pictured) to avoid desiccation. Reproduced with permission from Withers, P.C., and Cooper, C.E. (2010).

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called small acid soluble spore proteins (SASPs), are synthesized during sporulation and bind to the DNA, generating a protective conformational change. These developmental changes in the bacterium confer resistance to environmental stressors, including high temperature, DNA-damaging ultraviolet radiation, and noxious chemicals. These developmental changes are reversible: upon return to a favorable environment the endospore will germinate and return to vegetative growth. Endospores have incredible longevity; indeed, by one account viable endospores of a *Bacillus* species have been recovered from an extinct symbiotic bee host preserved in amber over 25 million years ago!

What other developmental strategies can be used to escape stress?

Another strategy employed by organisms to escape a temporal period of stress is the generation of stress-resistant offspring. For example, in response to changes in water temperature many fresh and saltwater sponges reproduce asexually to generate gemmules (Figure 1B). Gemmules are composed of metabolically-repressed cells that are packaged into collagenous glass capsules. These packages are resistant to environmental insults such as freezing and desiccation. In gemmules of the sponge species *Eunapius fragilis*, the synthesis of sorbitol may serve as a cryoprotectant and also to generate a high osmotic pressure, which represses germination. The return to a favorable environment triggers the synthesis of sorbitol dehydrogenase, in turn relieving osmotic pressure and permitting germination and the differentiation of the encapsulated cells into a new sponge. This strategy ensures the genetic success of the species during freezing winters and summer droughts.

And if the weather forecast is hot and dry...? In response to high temperature and low water availability, many animals enter a developmental period of metabolic arrest known as estivation. Many land snails, for example, have evolved annual cycles of estivation (Figure 1C), which even allows some snail species to survive in arid environments that might not see rainfall within a given year. Estivation is marked by a dramatic reduction in metabolic rate and the generation of

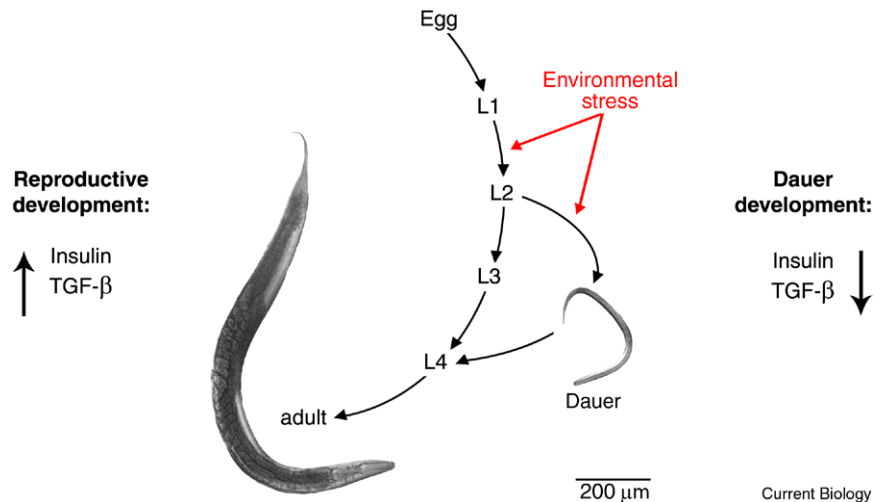


Figure 2. The roundworm *C. elegans* responds to stress by becoming a dauer larva. During reproductive development, *C. elegans* progresses through four larval stages, L1 to L4, before becoming an egg-laying adult. In an unfavorable environment, *C. elegans* will instead enter a diapause state, termed dauer, after the second molt. The environmental signals that regulate dauer entry are sensed during the first and second larval stages, marked in red. When environmental conditions become favorable, *C. elegans* will exit the dauer state and become a fertile adult. Dauer development is triggered by systemic changes in insulin/insulin-like growth factor and transforming growth factor- β (TGF- β) hormone levels.

an epiphragm, a protective membrane that seals off the inside of the shell to the environment. Estivating land snails are resistant to desiccation and high temperatures, and can survive prolonged periods of stress.

Do vertebrates respond to stress?

Vertebrates, including mammals, are also known to enter periods of estivation when food is limiting and when challenged with a hot, dry environment. Most species of lungfish undergo seasonal estivation when the water level of their environment is reduced. The African lungfish *Protopterus annectens* excavates a burrow in the mud and secretes mucus from epithelial mucous glands to generate a protective cocoon that prevents water loss from the dormant animal. Amphibians also reduce metabolism to increase survival time on endogenous energy stores when estivating, and, like the lungfish, some species will generate a cocoon to prevent desiccation (Figure 1D). These animals can survive many months at a time waiting for water levels to return. Hibernating and estivating mammals also reduce metabolism to conserve energy, and switch from carbohydrate to lipid metabolism during dormancy.

What laboratory models can be used to study developmental responses to stress? The roundworm *Caenorhabditis*

elegans is a striking example of an animal that enters an alternative developmental program in response to environmental stressors. Under favorable conditions, the worm grows rapidly, progressing through four larval stages in only a few days to become an egg-laying adult. But in an unfavorable environment, it enters a protective, developmentally-arrested larval stage after the second larval transition, termed dauer, from the German for 'enduring' larva (Figure 2). Dauer larvae have an altered cuticle, movement is suppressed, and metabolism is altered for long-term survival. These changes confer on the animal extreme longevity and increased resistance to stressors. Not unlike a bacterial endospore, when conditions improve the animal resumes feeding and development to become a fertile adult. The ease of *C. elegans* cultivation in the laboratory and its facile genetics makes it an excellent model for studying stress-induced developmental changes.

What molecular pathways control dauer development? Dauer development of *C. elegans* is promoted through two major neuroendocrine hormone pathways: insulin/insulin-like growth factor (IGF) and transforming growth factor- β (TGF- β). In both pathways, when hormone levels are high, animals proceed with rapid

development to adults. When either hormone is low, the dauer state is promoted. Insulin/IGF and TGF- β are expressed by sensory neurons in *C. elegans*, which couple transcription of both hormones to the environment. By contrast, downstream hormone receptors are broadly expressed, allowing for organism-wide developmental changes. Interestingly, the insulin pathway has also been linked to longevity, both in *C. elegans* and mammals, suggesting a link between stress-responses and aging, and that this 'lowly' worm can perhaps teach us something about human longevity as well.

What remains to be explored? We are only beginning to understand the molecular pathways that link development to environmental changes. While many of the molecular players may be organism-specific, some common themes may exist; for example, in metazoans, dedicated sensory cells may detect environmental stressors and alter systemic hormone pathways, as occurs in *C. elegans*. In addition, it remains unclear if these same developmental pathways are also linked to mechanisms controlling changes in animal behavior. It seems that in a worm eat worm world, coping with environmental stress by altering development can be the best way for some organisms to maximize genetic success.

Where can I find out more?

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Laboratory of Developmental Genetics,
Rockefeller University, 1230 York Avenue,
New York, NY 10065, USA.
E-mail: shaham@rockefeller.edu

Correspondences

Reduced perceptual sensitivity for biological motion in paraplegia patients

Roberto Arrighi¹, Giulia Cartocci¹, and David Burr^{1,2}

Many physiological and psychophysical studies suggest that the perception and execution of movement may be linked [1–4]. Here we ask whether severe impairment of locomotion could impact on the capacity to perceive human locomotion. We measured sensitivity for the perception of point-light walkers — animation sequences of human biological motion portrayed by only the joints — in patients with severe spinal injury. These patients showed a huge (nearly three-fold) reduction of sensitivity for detecting and for discriminating the direction of biological motion compared with healthy controls, and also a smaller (~40%) reduction in sensitivity to simple translational motion. However, they showed no statistically significant reduction in contrast sensitivity for discriminating the orientation of static gratings. The results point to a strong interaction between perceiving and producing motion, implicating shared algorithms and neural mechanisms.

We measured sensitivity for discriminating the direction of ambulation of a 'point-light' walker (an animation sequence showing only the joints) in 16 patients with total lower-limb paralysis (with no concomitant head-injury) caused by adult spinal trauma at least nine months prior to testing, and also in 15 healthy controls. Random noise dots were added to the display, and sensitivity defined as the number of dots to yield 75% correct responses (see [5] and the Supplemental Movie). In ten patients, we also measured contrast sensitivity for discriminating the orientation or direction of a sinusoidal grating.

Figure 1A shows sensitivity for biological motion against orientation contrast-sensitivity, separately for patients (blue symbols) and controls

(red). While contrast sensitivity was clearly similar for the two groups (showing that there are no generalized perceptual impairments), sensitivity to biological motion was much reduced, by a factor of nearly three. Figure 1B plots average sensitivities for these and three other tasks: coherence sensitivity for detection of the point-light walker (choosing between a walker and an adjacent scrambled walker); coherence sensitivity for discriminating the direction of translation of a single frame of walker; and contrast sensitivity for discriminating the direction of motion of a 0.5 cycle/deg grating drifting at 8 Hz (16 deg/sec).

In both biological motion tasks (detection and direction-discrimination), average sensitivity for the patient group was greatly reduced compared with healthy controls, both by a factor of 2.8, which is highly statistically significant (one-tailed unpaired t-tests: detection $t(29) = 3.63$, $p = 0.0005$; direction discrimination $t(29) = 3.79$, $p = 0.0003$). Coherence sensitivity for translation of silhouette and the dynamic contrast sensitivity were also lower in patient than in controls, by about 40%, again statistically significant (coherence: $t(29) = 1.80$, $p = 0.04$; dynamic contrast sensitivity: $t = 1.90$, $p = 0.04$). This suggests that sensitivity to motion in general may be reduced in these patients, but less so than for biological motion. Static contrast sensitivity, on the other hand, showed no statistically significant impairment ($t(18) = 0.81$, $p = 0.21$), confirming that the reduced sensitivity for motion did not result from a generalised perceptual or cognitive deficit, or from reduced capacity to perform psychophysical tasks.

We also analysed the data by bootstrap sign-test, an assumption-free technique that takes into account the intra-subject variance (see Supplemental Information). For the two biological motion tasks, the significance level was $p < 10^{-4}$, meaning that on 10,000 independent samplings of the data, not one yielded higher average sensitivity for the patient group than the control. The difference in sensitivity of the translating walker was also significant ($p = 0.009$), as was dynamic contrast sensitivity ($p = 0.014$). Static contrast sensitivity, however,