Do you have any strong views on journals and the peer review system? The peer review system isn't perfect, but I think it will continue to be better than the alternatives as long as we have hardworking and judicious editors. It worries me that an increasing number of action letters appear to have been written by someone who hasn't read the article, and just took a head count of reviewers in favour of and against publication. Along that path lies massive expansion of gee-whizz research — studies that don't annoy anyone because they don't have any theoretical content. Fortunately there are a lot of editors out there who are still selflessly giving up their time to read articles carefully and to make informed judgements about key issues. I'd like to see them receive more recognition and respect.

What do you think are the big questions to be answered next in your field? In my field, there's an urgent need to find the right kind of evolutionary thinking, and the right place for it, in psychology. 'Evolutionary Psychology', of the kind advocated by Cosmides and Tooby, did something important by combining evolutionary thinking with computationalism, but it needs updating in the light of recent discoveries about developmental systems and epigenetic inheritance, and, in my view, it was overstated. It is important to get a clear picture of how human and animal minds evolved, but it's not essential for every psychologist to couch their research questions in evolutionary terms.

I think the biggest challenge for the scientific community as a whole is to resist the business model of research. We're not like executives in an oil company. We're more like artisans in a workshop. We work hardest, and produce our best 'wealth-creating' craftsmanship, when we experience ownership of a project and the respect of our peers. Resisting the business model includes recognising the commonalities and interdependence between the sciences and the humanities; protecting early career lecturers from bean-counting policies that make it hard for them to establish their own research programmes; and resisting both the language and practices of business, such as 'self-promotion', 'line management' and endless, pointless 'restructuring'. Business is a wonderful thing, but it's not science.

What is your greatest ambition? When I went to Cambridge as a postdoc I was suddenly immersed in a completely unfamiliar academic environment. The lab where I worked was empiricist in both ways — good, hard experimental data were all-important, and the focus was on learning — especially associative learning — as the truly powerful force shaping behaviour. This came as quite a shock after five years, as a PhD student and during my first postdoc in the US, when everything I read and everyone I met was excited about 'ideas' (not necessarily testable theories), and interested in the evolution of behaviour. It felt like I was standing on the fault line between nature and nurture. To try and steady myself, at the end of each week I drew a pie chart representing how I felt about the likely outcome of this trauma. The first section, marked 'insanity', never occupied less than half the pie, and the second section, 'conversion' — the probability that I'd just abandon my earlier interests and go with the local flow — took up most of the rest. But at the end of a good week there'd be a little slice saying 'synthesis'. It was a glimmer of hope that I'd find ways to reconcile the two sets of methods and interests, of bringing experimental data and associative learning theory to bear on evolutionary ideas about the mind.

That hope of synthesis has got stronger over the ensuing 25 years and, although the word is a bit scary, I guess you could call it my ambition. I don't in my wildest dreams imagine that I can 'solve' the nature–nurture problem. Even the luckiest scientist doesn't do more than put a small brick in the wall. But that's the wall I want to contribute to building, and coming to All Souls as a Senior Research Fellow has given me a wonderful opportunity to work on it in earnest. The College likes to give people the chance to pursue worthwhile projects that it would be difficult or impossible to undertake elsewhere, and that certainly applies to my project. I can't think of another place in the world where I could do my kind of 'theoretical psychology'.

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Quick guide

ROS

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What are ROS? Reactive oxygen species (ROS) are intracellular chemical species that contain oxygen (O_2) and are reactive towards lipids, proteins and DNA. ROS include the superoxide anion (O_2^-), hydrogen peroxide (H_2O_2), as well as hydroxyl radicals (OH•). ROS are more chemically reactive than O_2 and are able to trigger various biological events. Each ROS has different intrinsic chemical properties, which dictate its reactivity and preferred biological targets. O_2^- is produced during oxidative metabolism by the one-electron reduction of molecular O_2. O_2^- is rapidly converted by superoxide dismutases (SODs) into H_2O_2, which can impinge on cellular signaling by interacting with thiols within proteins. The concentration of H_2O_2 associated with signaling is likely in the low nanomolar range. Unlike O_2^-, H_2O_2 can readily diffuse through membranes, making it an ideal intracellular signaling molecule. In the presence of ferrous or cuprous ions, H_2O_2 can become a hydroxyl radical, which is very reactive and causes oxidation of lipids, proteins and DNA, resulting in damage to the cell.

Where are ROS generated in the cell? The two main sources of ROS associated with cell signaling are mitochondria and the family of NADPH oxidases (NOXs) (Figure 1). There are eight sites in mitochondria that produce ROS. The three best characterized sites are complex I, II and III within the mitochondrial respiratory chain, which is located in the inner mitochondrial membrane. These complexes generate O_2^- by the one-electron reduction of molecular O_2. Complex I, II, and III release O_2^- into the mitochondrial matrix where SOD2 rapidly converts it into H_2O_2. Complex III can also release O_2^- into the intermembrane space. O_2^- traverses through voltage-dependent anion channels into the cytosol and is converted into H_2O_2 by SOD1. NOX proteins are primarily localized to the plasma membrane, although they can be found on other membranes, including the endoplasmic reticulum and mitochondria. NADPH

donates electrons to the center of the NOX catalytic subunit to generate O_2^- through the one-electron reduction of O_2. SOD1 in the cytosol converts NOX-generated O_2^- to H_2O_2.

How are ROS levels regulated in the cell? Given the reactivity and toxicity of ROS at high levels and given that specific quantities of ROS determine various cellular signaling events, spatial and temporal regulatory strategies must exist to regulate intracellular ROS levels. O_2^- can damage the iron-sulfur cluster of proteins. Cells have abundant SOD1 and SOD2 to rapidly detoxify O_2^- to H_2O_2. There are ample peroxiredoxins and glutathione peroxidases present in the cytosol and mitochondria that convert H_2O_2 to water. Catalase is primarily located in peroxisomes and removes intracellular H_2O_2 without cofactors.

What are the physiological roles of ROS signaling? ROS have been traditionally thought of as toxic metabolic byproducts that cause cellular damage. However, studies throughout the past decade have highlighted the role of ROS in cell signaling, with ROS being shown to play a causal role in cellular events such as proliferation, differentiation, metabolic adaptation and the regulation of adaptive and innate immunity.

How do ROS control cell signaling? ROS cause reversible post-translational modifications to proteins that regulate signaling pathways. Biological redox reactions catalyzed by H_2O_2, the most stable form of ROS, typically involve the oxidation of thiol groups on cysteines. Phosphatases, for example, which control protein kinase function in the cell, feature a common active-site motif, which causes the conserved catalytic cysteine to possess a low pKa, therefore existing as a thiolate anion with enhanced susceptibility to oxidation by H_2O_2. H_2O_2-induced cysteine modification can change the activity of the target protein and therefore signaling pathway function. Redox-sensitive phosphatases include PTP1B, PTEN and MAPK phosphatases, which can be reversibly oxidized by H_2O_2, inhibiting their dephosphorylation activity. Indirect ROS targets include transcription factors like hypoxia-inducible factor (HIF), and NFκB and kinases like Src, extracellular-signal-regulated kinases (ERKs), AMP-activated protein kinase (AMPK) and phosphatidylinositol 3-kinases (PI3Ks).

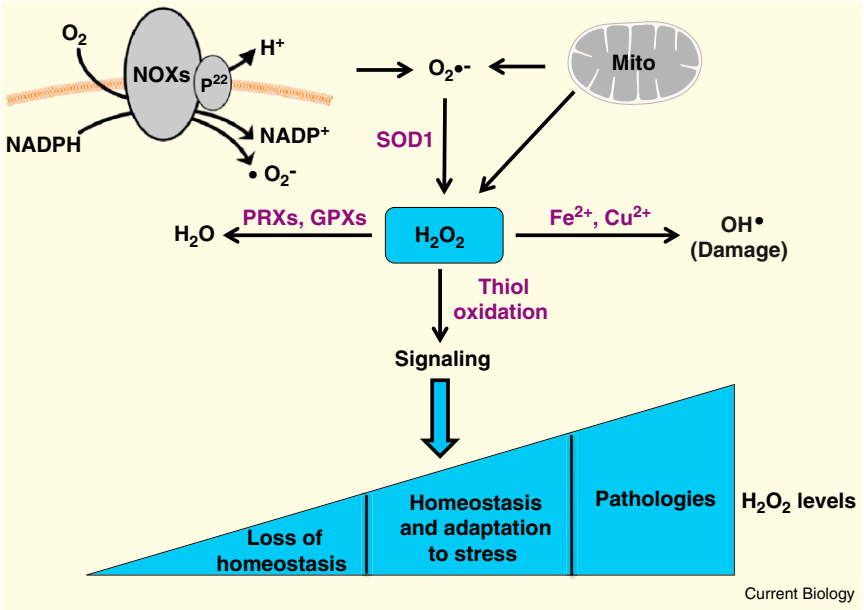

Figure 1. ROS signaling is essential for homeostasis and adaptation to stress.
Mitochondria can release either O_2^- or H_2O_2. In the cytosol O_2^- is converted to H_2O_2 by SOD1. NADPH oxidases can also generate O_2^- in the cytosol. Glutathione peroxidases (GPXs) and peroxiredoxins (PRXs) can convert H_2O_2 to water. Upon reaction with ferrous or cuprous ions, H_2O_2 forms reactive OH• radicals that are damaging to DNA, proteins and lipids. H_2O_2 controls cell signaling through the oxidation of thiols on proteins. Different levels of H_2O_2 lead to different cellular outcomes. Intracellular H_2O_2 concentrations in the low nanomolar range provide a permissive oxidative environment for cellular signaling which is ideal to maintain homeostasis (e.g. differentiation and proliferation) and to adapt to stress (e.g. metabolic and infection). H_2O_2 levels below this optimal range lead to a disruption of cell signaling resulting in loss of homeostasis. H_2O_2 levels above the optimal range cause oxidative damage and aberrant cell signaling resulting in pathologies, including cancer, cardiovascular and neurodegenerative disease and diabetes.

What is the free radical theory of aging? In the 1950s, Denham Harman proposed the 'free radical theory of aging', which postulated that the accumulation of oxidative damage results in aging. A simple test of this theory would be to administer antioxidants and observe whether they ameliorate aging or age-associated diseases. However, the data to support a detrimental causal effect of ROS on aging and age-related diseases has not been convincing. It is important to note that ROS are required for normal homeostasis and serve as mediators of cellular stress adaptation. Thus, dampening ROS may not be beneficial to an organism. Moreover, recent data in model organisms suggest that low levels of ROS activate stress responses that extend lifespan. Presently, it remains unresolved whether the increase in ROS cause or are a consequence of aging.

What are the roles of ROS in disease? Aberrant intracellular ROS levels and the cell's inability to clear the oxidants have been implicated in various diseases, including cancer, neurodegenerative disease, cardiovascular disease, diabetes and gastrointestinal disease. A key question is whether ROS have a causal role or are just a marker of these pathologies. Accumulating evidence in mouse models indicates that ROS-driven signaling contributes to cancer and diabetes. Furthermore, in mouse models ROS contributes to damage of neurons and cardiac cells resulting in Parkinson's and ischemia-reperfusion injury, respectively.

What are the experimental techniques of measuring ROS in the cell? The (patho)physiological roles of ROS mean that it is essential to be able to measure intracellular ROS concentrations and also to distinguish the different species like O_2^- and H_2O_2. Cell-permeable, redox-sensitive fluorescent dyes are commonly used to measure ROS levels. Dichlorodihydrofluorescein (DCFH) oxidation to the fluorescent dichlorofluorescein (DCF) has been

widely utilized to examine ROS levels. However, measurements based on redox-sensitive dyes such as DCFH can be problematic because they depend on dye uptake and lack any specificity towards a particular type of ROS. The advent of protein-based redox sensors like redox-sensitive GFP (roGFP) have improved specificity to particular ROS and can be targeted to different compartments within the cells to gather spatial resolution of ROS levels.

What remains to be explored? Four big challenges face ROS biology: (1) The intracellular targets of ROS are not well defined; these targets are likely to be context dependent. (2) The measurement of ROS continues to be challenging especially *in vivo*. (3) The use of rigorous genetics in mammalian model organisms is essential to further elucidate the physiological role of ROS. (4) The development of selective pharmacological scavengers against different types of ROS is needed to test whether ROS are a cause or consequence of pathological conditions. Understanding ROS biology is paramount especially from a public health point of view. Antioxidants are the most widely used or abused drugs worldwide. However, a large number of clinical trials have uniformly failed to demonstrate beneficial effects of antioxidants on a variety of pathologies. We must understand the importance of ROS in normal physiological processes and rationally design antioxidants that do not undermine normal physiology but might be effective under pathological conditions.

Where can I find out more?

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Adaptive aerial righting during the escape dropping of wingless pea aphids

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Pea aphids (*Acyrthosiphon pisum*) are small sap-sucking insects that live on plants in colonies containing mostly wingless individuals. They often escape predators, parasitoids and grazing mammalian herbivores by dropping off the plant [1,2], avoiding immediate danger but exposing themselves to ground predators, starvation and desiccation [3]. We show here that dropping pea aphids land on their legs, regardless of their initial orientation on the plant (like a defenestrated cat), by rotating their body during the fall. This righting ability is intriguing, as wingless aphids have no specialized structures for maneuvering in mid-air. Instead, they assume a stereotypic posture which is aerodynamically stable only when the aphids fall right-side up. Consequently, the body passively rotates to the stable upright orientation, improving the chance of clinging to leaves encountered on the way down and lowering the danger of reaching the ground.

We evoked dropping behavior in aphids situated on a fava bean (*Vicia faba*) stem by introducing a predator (ladybug, *Coccinella septempunctata*). The stem was positioned at different heights above a viscous substrate (petroleum jelly) that captured the landing posture. We found that up to 95% of the aphids landed upright after dropping 20 cm (Figure 1A). The aphid's body appendages play an important role in aerial righting: when dropped upside-down from delicate tweezers, live aphids (n = 20), dead aphids (random appendage posture, n = 23) and aphids with amputated appendages (n = 25) landed on their ventral side in 95%, 52% and 28% of the trials, respectively (Fisher Exact, $p < 0.001$). High-speed video visualization of the fall revealed that aphids do not jump off the plant, but rather release their hold, allowing gravity to accelerate them downwards. The aphids start rotating after falling a few body lengths (Supplemental movies S1 and S2) reaching a final right-side up orientation within the first 13.7 cm of the fall (~170 ms) in 90% of the trials (n = 45). Early during the fall aphids assumed a stereotypic posture and maintained it throughout. The aphids moved their antennae forward and up and the hind tibiae backward above the body. In that posture, the aphids reached the ground with the long axis of the body tilted upward so that their ventral-caudal end touched the ground first (Figure 1A,B).

The stereotypic posture was used to construct a mathematical-physical 'model aphid' using mean mass, volume and mass-moment of inertia, measured from five aphids (Supplemental information). Using the model, we simulated body rotations due to air resistance acting on the appendages during the free fall. The simulations show that the stereotypic posture provides static longitudinal stability; i.e., at any starting orientation, the air resistance on the appendages works to return the body to a balanced (zero net aerodynamic torque) orientation, such that the ventral side faces downwards and the longitudinal axis of the body is tilted at 32.6° upwards (Figure 1B). This aerodynamic mechanism is based on the anisotropic drag of a slender (length/diameter >10) cylinder, where the drag of a cylinder aligned normal to the flow is greater than the drag of the same cylinder in axial flow [4]. By orienting the different segments of the appendages at specific angles at a distance from the center of mass, the falling aphids create a pitching torque imbalance that works to rotate the body to the stable orientation. The stable orientation obtained in the model is only 0.6 standard deviations higher than the mean orientation angle (23.9 ± 14.4°) observed in falling aphids.

Controlled descent and gliding are not uncommon in wingless arboreal arthropods [5–7] and aerial righting has been demonstrated in larval stick insects [8]. Controlled descent and righting reflexes may have been primordial precursors for the development of insect flight [6,7] as they improve the fitness of arboreal species trying to avoid reaching the ground [6]. We therefore hypothesized that aphids falling upright would be more successful in stopping the fall on a lower part of their host plant by clinging