

# News & views

## Animal behaviour

# A bird's migration decoded

Simeon Lisovski & Miriam Liedvogel

Technological advances offer new ways to investigate the contribution that changing climate and genes have made in shaping past migrations by peregrine falcons. Can this help to predict the fate of future migrations? **See p.259**

Migration is a ubiquitous feature of the animal kingdom, and is arguably studied most comprehensively in birds. On page 259, Gu *et al.*<sup>1</sup> provide a range of insights into possible factors driving the evolution of migration in peregrine falcons (*Falco peregrinus*). These birds are probably best known for their record-breaking flight speed, which reaches more than 320 kilometres per hour when they dive for prey while hunting.

Humans have been endlessly fascinated and yet puzzled by the mysterious seasonal emergence and disappearance of birds. It is not all that long ago that we started to grasp this phenomenon better and refute imaginative speculations from the Middle Ages, which suggested that birds hibernate at the bottom of lakes during winter to emerge again in spring<sup>2</sup>. From the end of the nineteenth century, birds equipped with tiny metal rings on their legs have revealed secrets about their journeys, their whereabouts and the fate of individuals.

Thanks to technological advances on many different levels, we are now able to use lightweight tracking devices<sup>3</sup> to continuously follow these migrants across the globe. This has uncovered increasingly detailed evidence about this phenomenon. However, these advances are not just limited to providing a description of individuals' behaviour. The development of high-throughput DNA-sequencing technology has opened up the possibility of linking information about these enormous migratory movements with in-depth analyses of individual birds at the genome scale. Such efforts aim to identify the heritable components of migratory behaviour.

Progress that has been made has already produced major breakthroughs in our understanding of different aspects of migration. Yet

achieving a full appreciation of how this complex behavioural challenge is orchestrated remains a tough nut to crack. Nevertheless, it seems more crucial than ever to uncover this regulatory machinery, given that continuing global change, whether of climate or habitats, poses unprecedented challenges for migratory birds and also for the people trying to conserve threatened animal migrations<sup>4,5</sup>.

As with many of the grand challenges that society faces, investigating the regulatory architecture that governs bird migration requires the engagement and integration of

multiple disciplines. Gu and colleagues therefore used an impressive variety of complementary approaches to study the migration of the populations of peregrine falcon that breed far north in the Arctic and migrate south every year. The authors investigated how the migratory routes of these birds probably formed in the past, and how that influenced population dynamics and evolution up to the present. Gu *et al.* also looked at which genes might be key regulators of migratory behaviour, and how all these factors might jointly influence the future fate of the species.

Using satellite tracking devices strapped to the birds' backs (Fig. 1), Gu and colleagues followed 56 individuals over several years to determine a total of 150 complete migration routes originating from 6 different Arctic-breeding populations. The authors also sequenced the entire genomes of 35 birds. In addition, they reconstructed the past climate that birds encountered across their respective distribution ranges using pollen records since the Last Glacial Maximum (22,000 years ago). These predicted climate data provide remarkable insights into the probable historical formation of the different migration routes and the separation of the peregrine populations. The evidence suggests that these northern populations shrank in the past, because the size of their breeding ranges in tundra environments



**Figure 1** | A peregrine falcon (*Falco peregrinus*) fitted with a satellite tracking device. Gu *et al.*<sup>1</sup> used this equipment to map the migration routes of Arctic-breeding populations of this species.

ANDREW DIXON

diminished when ice caps retreated around 10,000–15,000 years ago.

Today, the annual journeys of the tracked populations happen within their own climate niches – individuals from the same population experience the same conditions, but conditions differ between the populations. This might be one reason why individuals seem to keep consistently to the same routes and use the same population-specific wintering grounds in temperate and tropical regions.

The authors' analysis suggests that the gene *ADCY8* might have a role in aiding the migratory behaviour of peregrine falcons. From the comparison of DNA sequences between the different bird populations, Gu and colleagues found that this particular gene is highly divergent between the different populations and is probably under some type of selection. This gene might also be functionally linked to aiding the long-term memory that could be particularly important for the populations that have to undertake longer-distance journeys. Learning probably has a role in successful migration, and Gu *et al.* focused on identifying inherited genetic components that might enable learning through memory formation. Other work<sup>6</sup> has also investigated the role of genes that are possibly linked to long-term memory in the context of bird migration.

Gu and colleagues' work provides a prime example of how interdisciplinary approaches and sophisticated statistics can be used to infer the evolutionary history of population sizes. Their research also shows how the timing of splits in divergent populations can be used to infer patterns in an ecological–evolutionary framework. Such insights enable the modelling of community dynamics across large time spans, including past and future scenarios. Gu *et al.* notably conclude that the Arctic-breeding populations that migrate to Europe will experience dramatic future changes as a consequence of global warming, and that this will require specific behavioural adjustments, including adaptations for shorter migratory distances.

The interdisciplinary nature of Gu and colleagues' research could provide a blueprint to motivate similarly holistic approaches. Migratory species that have a wide diversity of migratory strategies are ideal model systems to consider for such efforts. For example, some subspecies of the white crowned sparrow (*Zonotrichia leucophrys*) in North America undergo a long-distance migration, whereas others are non-migratory<sup>7</sup>. The Eurasian blackcap (*Sylvia atricapilla*) has large migratory variations, particularly regarding the orientation and routes taken by members of this species<sup>8</sup>.

Furthermore, and particularly in the context of investigating memory formation in relation to migrations, it is probably inevitable

that studies similar to that carried out by Gu *et al.* will be undertaken to compare the first migration of juvenile birds with the routes they take as experienced adults. Species in which routes are taught to the juveniles by adults, such as in crane families<sup>9</sup>, should also be investigated. The data should then be compared with analysis of some of the many shorebird or passerine species in which juveniles on their first migratory journey either manage migration on their own or even choose different routes from those of the adults<sup>10</sup>. Such comparative approaches and the complementary strengths of various study systems might pave the way to characterizing the genetic architecture of migratory behaviour and provide proof of causal factors.

There is arguably a thin line that separates oversimplifications within one discipline from the combining power provided by interdisciplinary research. However, Gu and colleagues' study is yet another example of the value of taking an interdisciplinary path that places the evidence from different fields in context to offer new insights and push scientific boundaries. More of this will be needed to understand complex behavioural processes such as migration. It will also provide the toolbox necessary for effective conservation work

to preserve a natural phenomenon that awes and inspires us, and that is integral to many of Earth's ecosystems.

**Simeon Lisovski** is at the Alfred Wegener Institute Helmholtz Centre for Polar and Marine Research, Polar Terrestrial Environmental Systems, 14473 Potsdam, Germany. **Miriam Liedvogel** is at the the Institute of Avian Research, 26386 Wilhelmshaven, Germany, and also at the Max Planck Institute for Evolutionary Biology, Plön, Germany.  
e-mails: simeon.lisovski@awi.de; liedvogel@evolbio.mpg.de

1. Gu, Z. *et al.* *Nature* **591**, 259–264 (2021).
2. Magnus, O. *Historia de Gentibus Septentrionalibus* (Giovanni Maria Viotto, 1555).
3. Bridge, E. S. *et al.* *BioScience* **61**, 689–698 (2011).
4. Bay, R. A. *et al.* *Science* **359**, 83–86 (2018).
5. Wilcove, D. S. & Wikelski, M. *PLoS Biol.* **6**, e188 (2008).
6. Delmore, K. E. *et al.* *eLife* **9**, e54462 (2020).
7. Ramenofsky, M., Campion, A. W., Pérez, J. H., Krause, J. S. & Németh, Z. J. *J. Exp. Biol.* **220**, 1330–1340 (2017).
8. Delmore, K. E. *et al.* *Proc. R. Soc. B* **287**, 20201339 (2020).
9. Mueller, T., O'Hara, R. B., Converse, S. J., Urbanek, R. P. & Fagan, W. F. *Science* **341**, 999–1002 (2013).
10. Grönroos, J., Muheim, R. & Åkesson, S. *J. Exp. Biol.* **213**, 1829–1835 (2010).

This article was published online on 3 March 2021.

### Immunology

# Cancer aided by greasy traitors

Caroline Perry & Ulf H. Beier

Cancer can evade destruction by the immune system if aided by immunosuppressive regulatory T cells. These cells depend on a lipid-production pathway in the tumour environment, a vulnerability that might be used to target them. **See p.306**

Immune cells called regulatory T cells ( $T_{reg}$  cells) are a subset of T cells that selectively dampen immune responses. They do this by suppressing the activation of inflammation-promoting T cells, and also by secreting anti-inflammatory factors<sup>1</sup>. Such blunting of an immune response is valuable because it prevents the immune system from turning on a person's own body – a type of malfunction that occurs in autoimmune disease. However,  $T_{reg}$  cells can benefit tumours by suppressing cancer-attacking immune cells, such as CD8 T cells (also known as killer T cells). On page 306, Lim *et al.*<sup>2</sup> identify a metabolic dependency of  $T_{reg}$  cells in the tumour microenvironment, a finding that reveals how the cells operate there.

Immunotherapy is used in the clinic to overcome a tumour's evasion of killer T cells.

The approach can include treatments such as antibodies that target  $T_{reg}$  cells<sup>3</sup>. Although such therapy boosts anticancer immune responses, it can have a negative effect on  $T_{reg}$  cells elsewhere in the body that help to keep the immune system in balance. As a result, people receiving such treatments often develop autoimmune disease<sup>4</sup>. A major unmet need is therefore immunotherapy that targets only the 'bad'  $T_{reg}$  cells in the tumour vicinity while leaving the beneficial  $T_{reg}$  cells untouched.

To find a way to single out the unwanted  $T_{reg}$  cells, Lim and colleagues used mice that had a type of tumour called melanoma. They compared the gene-expression profiles of  $T_{reg}$  cells extracted from the tumour vicinity with those taken from elsewhere in