responded to a magnetic field in a way that could only result from the FQAHE. Zeng *et al.* supported this conclusion with measurements of the local electronic compressibility. Park *et al.* and Xu *et al.* took a different route — creating electrical contacts of sufficient quality to enable measurement of the transverse electrical conductance that is the smoking-gun signature of the FQAHE.

The observation of the FQAHE is much anticipated in condensed-matter physics — a fundamental achievement that could have important consequences for technological applications. But there's a long road ahead to reach the next goal: controlling anyons to facilitate quantum computation[8]. Manipulating anyons generically results in a change to the quantum state of a solid, which could be used to store information. But the type of FQAHE observed so far supports only the simplest type of anyon, known as abelian anyons, and the change required to alter the quantum state is large enough only in non-abelian anyons, which are even more elusive than those observed in these four studies.

One of the paths towards generating non-abelian anyons is to connect a material containing abelian anyons to a superconductor (a material with zero electrical resistance)[9–11]. This is because superconductors can convert the edge currents of abelian anyons into non-abelian anyons. But magnetic fields tend to interfere with a material's ability to superconduct, so the revelation that abelian anyons emerge in twisted $MoTe_2$ without a magnetic field could be crucial to efforts in this direction. Creating a hybrid device comprising twisted $MoTe_2$ and a superconductor will undoubtedly generate a new set of experimental obstacles, but the creative and tireless community of condensed-matter physicists should be up to the challenge.

Cécile Repellin is in the Laboratory of Physics and Modeling of Condensed Matter, 38000 Grenoble, France.
e-mail: cecile.repellin@lpmmc.cnrs.fr

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Developmental physiology

Coordinating the first heartbeat

Joshua Bloomekatz & Neil C. Chi

An impressive combination of computational modelling and experimental techniques in live zebrafish embryos reveals how the heart initiates its organized and rhythmic beating. **See p.149**

The human heart beats more than 2.5 billion times during a lifetime. But what makes it tick for the very first time? From studies of chick embryos more than a century ago through to more recent investigations in mice[1], it has become clear that the first heartbeat occurs even before formation of the primitive heart tube (the first functional structure formed during heart development). It is also known to be preceded by transient releases of calcium ions (Ca^{2+}), which initially present as spontaneous asynchronous oscillations of Ca^{2+} concentrations[2–4]. Now, on page 149, Jia *et al.*[5] exploit the unique attributes of zebrafish embryos (*Danio rerio*) — including their external fertilization, optical transparency and tractability to genetic modification — to investigate *in vivo* how Ca^{2+} waves organize and propagate across the developing heart to trigger the first heartbeats.

To capture the developmental events that lead to the first heartbeat, Jia *et al.* studied the early zebrafish heart in live embryos using a technique known as all-optical electrophysiology. In many organisms, populations of early cardiac muscle cells (cardiomyocytes) are known to develop bilaterally and migrate towards the midline (Fig. 1), and the authors observed sparse, transient bursts of Ca^{2+} in these cells in their experiments — similar to findings in mice[4].

As these cardiomyocytes merge and form

From the archive

The danger of scientific names getting lost in translation, and frog mysteries come into focus.

100 years ago

It is difficult ... to preserve orthography in scientific names derived from the Greek. A good example of the confusion which has been allowed to become inevitable occurs in the similarity of the generic title of two very dissimilar shrubs. *Chionanthus Virginica* has been named from *χιών* — snow — because of the masses of white blossom it bears at midsummer; while *Chimonanthus fragrans*, flowering in midwinter, ought to be written *Cheimonanthus*, from *χειμών*, winter. To each of these Greek generic names a Latin adjective has been tacked, which serves to distinguish the species, but may offend the scholar.

From *Nature* 6 October 1923

150 years ago

What is a Frog? At first, almost all persons will think, on meeting with this question, that they can answer it readily and easily. Second thoughts, however, will show to most that such is by no means the case ... "The Frog is a small saltatory Reptile" will probably be the reply of the majority. But *is* it a Reptile? At any rate it begins life (in its Tadpole stage) like *a Fish!* By the great Cuvier, however, as by very many naturalists since, it has been regarded as a Reptile and classed with Lizards, Crocodiles, and Serpents; and yet it may be a question whether the murine affinity connubially assigned to it in the Nursery tale, be not the lesser error of the two ... The number and nature of both the closer and the more remote allies of the Frog; its distribution both as to space and as to time; ... its bony frame-work; its muscles and nerves; its brain and sense-organs; its respiratory and excretory structures; its various changes from the egg to maturity, together with peculiarities of habit in allied forms; are all matters which will well repay a little attentive consideration. Indeed it is probable that no other existing animal is more replete with scientific interest of the highest kind, than is the Frog.

From *Nature* 2 October 1873

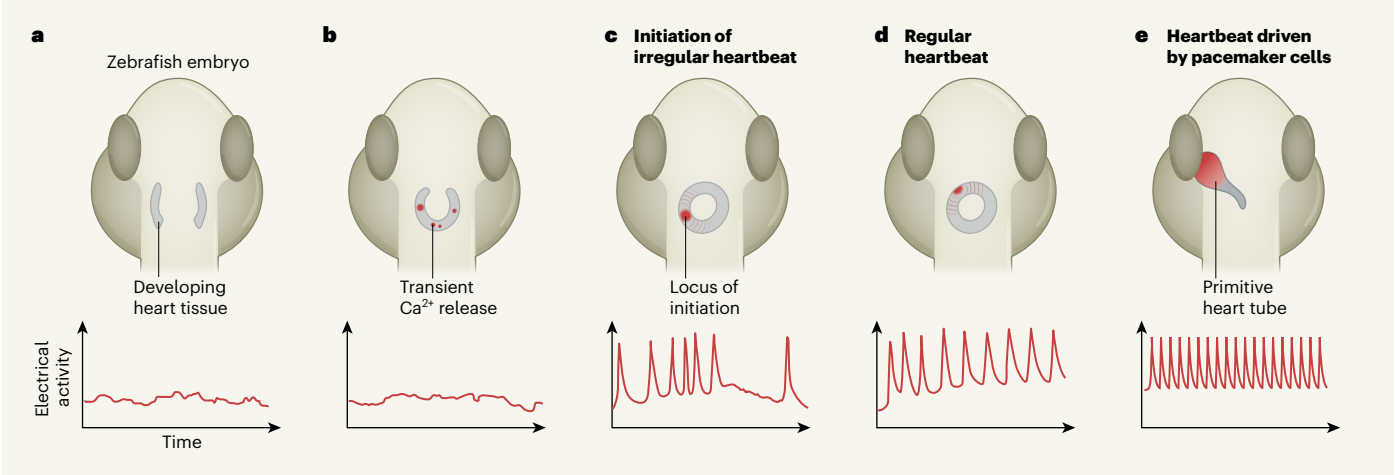

Figure 1 | Calcium bursts and the first heartbeat. From their studies of zebrafish embryos (*Danio rerio*), Jia *et al.*[5] identified changes in the cellular release of calcium ions (Ca^{2+}) — and in the heartbeat (bottom traces) — that accompany the stages of heart development. **a**, **b**, Populations of cells known as cardiomyocytes develop bilaterally and migrate towards the midline of the embryo, with accompanying sparse, transient releases of Ca^{2+}. **c**, As the cardiomyocytes form a circular structure (the cardiac ring), larger and more frequent waves of Ca^{2+} develop and propagate across the ring, beginning at a single locus of initiation (LOI). **d**, **e**, The LOI can migrate around the cardiac ring, eventually overlapping with pacemaker cells in the primitive heart tube (the first functional heart structure to form in the embryo).

a ring at the midline at 20 hours after fertilization there is an abrupt bioelectrical transition to larger, more frequent Ca^{2+} waves that propagate across most of this cardiomyocyte ring. Irregularly timed at first, these large Ca^{2+} waves gradually become periodic, leading eventually to mechanical contractions of the cardiomyocytes. Several classes of quiescent-to-oscillatory phase transitions have been described mathematically; Jia *et al.* found that only one of these — the 'saddle-node on invariant circle' (SNIC) bifurcation — matched the trajectory of the initial Ca^{2+} waves as they became periodic.

The authors used this mathematical model as a framework to shed light on the electrophysiological mechanisms that underlie the initiation of the first large Ca^{2+} wave through the developing heart. Specifically, they investigated whether intracellular Ca^{2+} release is triggered by voltage-dependent or voltage-independent mechanisms: in other words, does initiation rely on electrical depolarization of the plasma membrane of cardiomyocytes, or not? Using a 'reporter' gene that enables voltage and calcium dynamics to be monitored simultaneously, the authors observed a voltage wave immediately before the Ca^{2+} wave, suggesting that voltage triggers Ca^{2+} release.

To validate these findings, the authors used synthetic nucleic acids called morpholinos to reduce the expression of the *cacna1c* gene — which encodes a subunit of a voltage-dependent Ca^{2+} channel — and observed that this inhibited the initiation of both voltage waves and large Ca^{2+} waves. But the role of the *ncx1* gene (also known as *slc8a1a*), which encodes a sodium–calcium exchanger, another type of ion channel, remains less clear: Jia and colleagues found that morpholino-mediated reduction of its expression in zebrafish slowed the decay of the earliest cardiac Ca^{2+} transients, whereas another study in mice reported that chemical inhibition of the NCX1 protein led to a complete loss of transients[4]. So, further genetic studies of *ncx1*, or of its counterparts in other species, at this early stage of heart development will be helpful.

Next, Jia *et al.* investigated whether the timing of the initial Ca^{2+} wave was due to the timing of a voltage-inducing event, or to changes in the ability of cardiomyocytes to respond to such an event. Using a technique known as optogenetics to induce membrane depolarization only in part of the myocardium (the tissue formed by the cardiomyocytes), they found that they could trigger a large Ca^{2+} wave before the natural Ca^{2+} wave began. This suggests that the cells of the myocardium are electrically coupled to each other — possibly through intercellular connections known as gap junctions — and that the myocardium is able to conduct a Ca^{2+} wave before the first wave is induced naturally. Together these results reveal that, after the myocardium reaches this point, the first Ca^{2+} wave in the heart is triggered by spontaneous, voltage-dependent release of Ca^{2+}, which sets off an ever-continuing oscillatory system that gradually becomes periodic.

The authors then turned their attention to determining where in the myocardial ring the Ca^{2+} waves might begin — the locus of initiation (LOI). Pacemaker cardiomyocytes (specialized cells that pace the beating of the mature heart) become specified on the distal edges of the cardiac ring during the same developmental window as that in which myocardial Ca^{2+} waves initiate[6,7]. But Jia *et al.* found that, although the location of the first LOI varied between embryos, as reported previously[8], it was most often observed in a central region of the cardiac ring, suggesting that the LOI is distinct from the pacemaker cells. The authors also noticed that each embryo had only one LOI. It remained stable for long periods of time (more than ten minutes), but could shift suddenly and drift outwards as development proceeded, eventually overlapping with pacemaker cells in the primitive heart tube[9].

Why is there only one LOI? To find out, the authors silenced the LOI region optogenetically, which led to the emergence of a new LOI, elsewhere in the cardiac ring. This seems to be stage-specific: in previous work, silencing pacemaker cells later in zebrafish development resulted in cardiac arrest (no detectable heart contraction) rather than the emergence of a new pacing region[9], possibly because more-mature cardiomyocytes are less likely to create periodic Ca^{2+} transients spontaneously. Jia *et al.* also found that inducing pacing in a different region of the cardiac ring could establish a new LOI — but only when this region was paced at a frequency higher than that of the spontaneous LOI. This supports the idea that overdrive suppression, an electrophysiological phenomenon in which higher-frequency pulses in the heart can dominate pacing[10], could explain why there is just one LOI.

Jia *et al.*[5] have used an array of complementary electrophysiological and optogenetic studies of live zebrafish, as well as computational modelling, to show how early cardiac electrical activity self-organizes to regulate the transition from a dormant to a mechanically beating heart. Their research builds on studies of the first heartbeats in mice, chicks and rats[1], and suggests that the underlying mechanisms are conserved across vertebrates.

What remains to be learnt? One question is how spontaneous asynchronous Ca^{2+} oscillations are connected to the establishment of the synchronous Ca^{2+} wave. Another is how exactly this bioelectrical synchronization

translates molecularly into the rhythmic contractility that is needed to propel blood around the body. It will be exciting to use genetic models to identify the roles of specific ion channels and calcium-handling proteins in initiating the first heartbeat. Such models might also help to reveal the molecular underpinnings of the parameters of the SNIC bifurcation, including how the thresholds for induction and amplification of the Ca^{2+} waves are determined and coordinated. Finally, investigating the molecular basis for periodicity dynamics and LOI drift could provide insight into the pathology of cardiac arrhythmias in adult humans: many of the same genes and biophysical phenomena might function in the adult heart.

Joshua Bloomekatz is in the Department of Biology, University of Mississippi, University, Mississippi 38677, USA. **Neil C. Chi** is in the Division of Cardiology, Department of Medicine, University of California, San Diego, La Jolla, California 92093, USA.
e-mails: josh@olemiss.edu; nchi@ucsd.edu

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Ecology

Measuring the benefits of protected areas

Ana S. L. Rodrigues & Marie-Morgane Rouyer

Are protected areas slowing down global biodiversity declines? A global analysis provides evidence that they are, although effects vary across groups of species, and what happens outside protected areas matters, too. **See p.101**

Protected areas — defined, recognized geographical spaces that are managed to try to achieve the long-term conservation of nature — are the cornerstones of national and global efforts to slow biodiversity loss[1]. They already occupy nearly 17% of the planet's land and inland water surface and 8% of the oceans[1], and most nations have committed to expanding their protected-area coverage to 30% by 2030, under the Kunming–Montreal Global Biodiversity Framework of the United Nations Convention on Biological Diversity[2]. For such a fundamental conservation tool, the amount of evidence available to assess whether protected areas are effective at limiting biodiversity declines is surprisingly scant[3]. On page 101, Nowakowski *et al.*[4] address some of this shortfall through a global-scale analysis that shows that populations of terrestrial vertebrates inside protected areas decline more slowly than do those in comparable unprotected sites. However, the authors found wide variation in the mitigating effects of protected areas, raising questions about the factors that explain the effectiveness of this conservation tool and the uncertainties associated with quantifying this effectiveness.

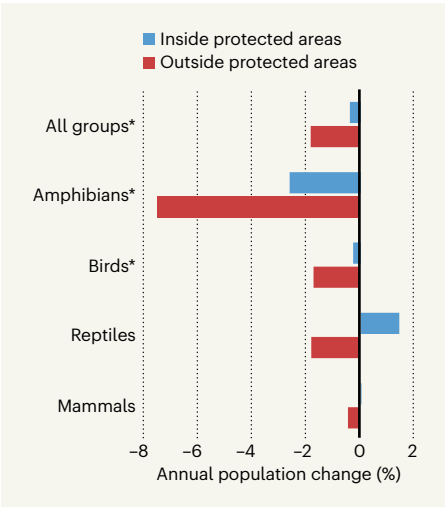

Figure 1 | Assessing the effectiveness of protected areas for vertebrate species. Nowakowski *et al.*[4] analysed data for 1,032 vertebrate species from around the globe to determine whether protected areas affected population trends. Asterisks indicate groups of species for which there was a statistically significant lower rate of change in the number of individuals inside protected areas than outside such areas.

If effectively implemented through appropriate regulation and management, protected areas work by buffering the biodiversity inside their boundaries against human-driven pressures, such as habitat destruction and the overexploitation of species. In practice, it is challenging to demonstrate formally that such protective effects do take place, because it is seldom possible to carry out controlled experiments on the scale of protected areas. Instead, studies contrast protected versus comparable unprotected areas in terms of either the intensity of pressures or the state of biodiversity[3]. Analyses of the effects of protection on the state of biodiversity are particularly rare, because they require large biodiversity data sets. For their study, Nowakowski *et al.* combined the two largest global data sets on wildlife population trends — Living Planet[5] and BioTIME[6] — to obtain data consisting of 2,239 population trends for 1,032 bird, mammal, amphibian and reptile species at more than 1,000 protected areas and at a similar number of comparable unprotected sites.

The results are both reassuring and puzzling. Nowakowski and colleagues found that, on average, the populations declined significantly faster outside protected areas (−1.8% per year across all studied species groups) than inside them (−0.4%; Fig. 1), indicating that area protection substantially mitigates population losses. Furthermore, average declines in protected areas were statistically indistinguishable from zero, suggesting that protected areas almost completely offset the drivers of population declines outside those areas.

This mitigation effect varied, however, across different taxonomic groups. It was strongest for amphibians (−2.6% inside protected areas, compared with −7.5% outside them) and birds (−0.3 versus −1.7%). It was positive, but non-statistically significant, for mammals (0.0% versus −0.4%) and reptiles (1.4% versus −1.8% per year). With much conservation attention focused on birds, it is unsurprising that they are benefiting from such efforts, as was also found in a previous analysis of the effect of conservation on species' risks of extinction[7].

It was less predictable that the effects of protection would be so strong for amphibians, although it is consistent with the authors' finding that this group is particularly sensitive to changes in land use. A previous study[8] found that conservation of wetland habitats under the United Nations' Ramsar Convention has been effective at slowing down declines in bird populations[8], and amphibians, too, might have benefited from this international treaty.

It is less easy to explain why no measurable effect of area protection was found for mammals, given their popularity as conservation targets. Even more puzzlingly, Nowakowski *et al.* found no evidence of significant population