CellPress

airing their opinions on it. Actions have consequences, and social media makes things happen faster; this sometimes means that people can't get away with saying ill-advised things that in the past would have fallen on only a few ears. I think it remains enormously important for scientists — especially young ones, like PhD students and postdocs — to be able to have their balanced and respectful say without fear of reprisal.

Did those recent events have anything good fall out of them? Well, it was pretty amazing to see the issues of gender parity in science be front-page news for several weeks on end. People were talking openly and passionately about a topic that still touches a nerve — and the reason it does is because it's still such a problem. Any PhD or postdoc in the life sciences today will still wonder why, considering initial cohorts composed equally of men and women, fewer than 20% of professors are female. We have seen gender parity at the time that scientists embark on their research careers since about the late 1980s/early 1990s, but women continue to hemorrhage out of the system at an alarming rate. There are many reasons why and it's horribly complicated — but we as a community need to keep having this discussion until the problem is solved.

Which aspect of science, your field or in general, would you wish the general public knew more about? I wish more people knew what science was really like — that scientists are real people, not stereotypes, and that science is not black and white. A fundamental misunderstanding of how science works breeds a lot of mistrust and pseudoscientific thinking. Scientists need to be open about what they're doing and how they do it if they want their messages to be trusted. As long as people suspect we're evil geniuses working in secret labs to build a clone army, there will always be a lack of trust.

Centre for Nephrology, Division of Medicine, University College London, Royal Free Hospital Campus, Rowland Hill Street, London NW3 2PF, UK.
E-mail: j.rohn@ucl.ac.uk

Quick guide

Turquoise killifish

Martin Reichard[1,*], Alessandro Cellerino[2,3], and Dario R. Valenzano[4]

What is a killifish? Killifishes are a diverse group of small, mainly freshwater fishes that are often found in marginal habitats not occupied by other fish species — from tropical mangrove tidal zones inhabited by the amphibious and self-fertilizing hermaphroditic *Kryptolebias marmoratus*, to cold lakes on the Andean plateau occupied by the endemic *Orestias* species flock. As adaptations to these marginal habitats, killifish possess some unusual reproductive strategies.

What is so special about the turquoise killifish? The turquoise killifish (*Nothobranchius furzeri*), along with over 60 other species in the genus *Nothobranchius*, inhabits temporary pools on the African savannah. Here, the killifish have pushed adaptation to marginal habitats to the extreme. They have evolved special adaptations that allow them to survive the complete annual desiccation of their habitat. While adults die during dry periods, developing embryos survive, encased in dry mud in a dormant state, termed 'diapause', where development is completely arrested.

Is embryonic diapause unique to killifish? For a vertebrate, diapause is extremely unusual but not unique. By contrast, many non-vertebrates and plants have diapause stages, forming seed or egg banks in the soil. In killifishes it is still unclear whether diapause is an ancestral feature of this lineage or if it has repeatedly evolved. Potentially is has independently evolved on at least six occasions across two continents — three times in Africa and three times in South America. There are three different forms of diapause, each occurring at distinct embryonic stages. Importantly, in all six killifish lineages with diapause, developmental arrest takes place at the same stage.

Is diapause relevant to humans? Apart from the fact that it is a fascinating evolutionary adaptation, the biological mechanisms underlying diapause may be associated with those that control longevity. In the roundworm *Caenorabditis elegans*, the genetic pathways that control diapause and ageing overlap. Some of these genes are evolutionarily conserved and associated with longevity in humans. The study of killifish diapause has potential to reveal novel longevity-associated genes.

What happens when the rains come? As you might expect, the fish hatch. However, the timing is critical. Initial bouts of rainfall seal the dried bottom of the pond, and there is a delay before the substrate reliably retains rainwater. During this phase some embryos start to develop, but not all. A 'bet-hedging' strategy, comparable to that seen in plant seed banks, is observed, whereby the trigger to emerge from diapause is highly variable. Rapid hatching is risky, because after the initial rains, pools may again desiccate. In this scenario, undeveloped embryos would be the only survivors, outcompeting the fast-developing embryos. The highly unpredictable environment maintains variation for the trigger to emerge from diapause.

As their habitat is ephemeral, do they need to grow and mature quickly? Yes, annual killifishes live incredibly fast lives. Among them, the turquoise killifish has taken the 'live fast, die young' strategy to an extreme (Figure 1). Turquoise killifish females start laying eggs as soon as 18 days after hatching, but then die from ageing-associated deterioration in just a few months, even in captivity. A full generation cycle (from adult to adult in the next generation) can take as little as 5 weeks if they skip all diapauses. Skipping diapause happens regularly in captivity if embryos are incubated at high temperatures. In nature, however, the typical life cycle takes one year.

How can they manage to mature so fast? Not by a developmental trick. Killifish are not paedomorphic (sexually mature larvae possessing functional gonads), as some neotenic salamanders or fish can be. Instead, they become sexually mature by greatly speeding up the normal process of organ development.

Figure 1. Turquoise killifish and its habitat.
Seasonal savannah pools retain water for only a few months (top left), giving turquoise killifish limited time to complete their life cycle. In less than three weeks, females (top right) develop ripe eggs. Males exist in two discrete colour morphs, with a red (bottom right) or yellow (bottom left) caudal fin. Photo credits: Martin Reichard (top left), and Radim Blažek.

Do they also age faster? Certainly. In the few months that they live, they display cellular and molecular changes comparable to those observed in ageing humans over several decades, developing learning impairments, heart lesions, pigment change and even tumours. For these reasons, they have been used to test the effects of diet and drugs on ageing and longevity.

Are there any resources available to experimental biologists?
Despite being a recently adopted model taxon, there are already many resources for genetic studies on turquoise killifish. There is an inbred strain and a number of wild-derived strains that differ in their lifespan and other phenotypic traits. The genome has recently been sequenced, assembled and annotated, and some chromosomal regions responsible for phenotypic differences among strains identified. Transgenesis has been developed, permitting the manipulation of the killifish genome, and genome-editing techniques have even introduced human point mutations into its genes. With growing understanding of the ecology of wild populations on one hand, and of the biological mechanisms associated with short lifespan and rapid ageing on the other, the turquoise killifish offers a tractable system for integrating conceptual and methodological insights from ecological and biomedical research.

Where can I find out more?

Blažek, R., Polačik, M., and Reichard, M. (2013). Rapid growth, early maturation and short generation time in African annual fishes. EvoDevo *4*, 24.

Cellerino, A., Valenzano, D.R., and Reichard, M. (2015). From the bush to the bench: the annual *Nothobranchius* fishes as a new model system in biology. Biol. Rev. http://dx.doi.org/10.1111/brv.12183.

Furness, A.I., Reznick, D.N., Springer, M.S., and Meredith, R.W. (2015). Convergent evolution of alternative developmental trajectories associated with diapause in African and South American killifish. Proc. R. Soc. Lond. B *282*, 20142189.

Harel, I., Benayoun, B.A., Machado, B., Singh, P.P., Hu, C.K., Pech, M.F., Valenzano, D.R., *et al*. (2015). A platform for rapid exploration of aging and diseases in a naturally short-lived vertebrate. Cell *160*, 1013–1026.

[1]Institute of Vertebrate Biology, Academy of Sciences of the Czech Republic, Květná 8, Brno, Czech Republic. [2]Scuola Normale Superiore, Piazza dei Cavalieri 7, Pisa, Italy. [3]Fritz Lipmann Institute for Age Research, Leibniz Institute, Beutenbergstr. 11, Jena, Germany. [4]Max Planck Institute for Biology of Ageing, Joseph-Stelzmann-Str. 9b, Cologne, Germany.
*E-mail: reichard@ivb.cz

Primer

Epilepsy

Vikram R. Rao*
and Daniel H. Lowenstein

Our cognitive abilities emerge from the coordinated activity of neurons in the brain. The average human brain contains 86 billion neurons that are richly interconnected through synapses, contact points for electrochemical communication. Patterns of synaptic connectivity create functional ensembles of neurons, called neural circuits, which mediate information processing in the brain. Neural circuits can be deconstructed further into basic motifs ('microcircuits') involving feedforward and feedback connections between different types of neurons that exert excitatory or inhibitory influence. At each level of neural circuitry, the opposing forces of excitation and inhibition are normally held in balance through a variety of homeostatic mechanisms.

Epileptic seizures — the paroxysmal symptoms and signs related to excessive electrical activity in the brain — are a common clinical expression of neural circuit dysfunction. Seizures can result from myriad brain pathologies, and the protean manifestations of seizures relate to the fact that they can arise from any region of the cerebral cortex. Epilepsy is the clinical condition characterized by a chronic predisposition to spontaneous seizures. Affecting 0.5–1% of the world's population, epilepsy is associated with considerable somatic and psychosocial morbidity as well as increased mortality. Despite the global burden of epilepsy, however, the pathogenesis of seizures remains poorly understood.

Hypersynchrony

A canonical view holds that seizures result when an imbalance between excitation and inhibition produces runaway excitation and 'hypersynchrony' within neural circuits. Synchrony in this context is loosely defined as large numbers of neurons firing action potentials in unison. Conceptualization of seizures as a homogeneous, unbridled alliance of

