THIS WEEK

Fish have feelings too

Our obligation to keep the suffering of laboratory animals to a minimum — both in life and in death — does not apply only to mammals.

Former US President George W. Bush once cryptically remarked that he was sure that "the human being and fish can coexist peacefully". Fish might beg to differ. Humans continue to deplete ocean stocks for food and to stalk rivers in the name of sport. And then there are the millions of fish that die in scientific laboratories every year.

Much of the debate about the use of animals in research focuses on what happens while they are alive: the degree of pain and suffering inflicted on them, how this can be kept to a minimum, and the balance between this discomfort and the greater benefit it can and does bring to both people and animals. Less talked about — perhaps fortuitously, given the way emotion can drive such debates — is the fact that most of the animals lose more than their freedom and their comfort. The majority of laboratory animals are killed at the end of the work. Killing animals is an unpleasant thing to have to do, but unfortunately in some areas of science it is unavoidable. So it is important that the regulations scientists follow for animal euthanasia reflect the most humane options available. New research suggests that this might not always be the case for zebrafish.

A native of the southeastern Himalayas, zebrafish are one of the most commonly used model organisms in research. One reason for their popularity is that zebrafish embryos are transparent, making them an ideal organism in which to track development, as well as the influence that genes and other factors have on this process. As tools to exploit this unusual embryonic feature have grown, so has the use of zebrafish. Exact numbers are hard to find, but the total number of fish used in UK laboratories is second only to the number of mice.

Another factor that makes zebrafish attractive is that the creatures are relatively cheap to house. They need less space, less dedicated staff time and there are fewer regulations than for rodents on, say, habitat enrichment.

In the hierarchy of living things, fish are viewed by many as a lesser life form than mammals, but not everyone agrees. A small but committed number of animal-rights campaigners, for example, extend their attention to fish and related creatures. Certainly, whether hooked fish feel pain and what, if anything, lobsters experience when dropped live into boiling water are genuine scientific questions, and ones with the potential to stir feelings and change behaviour.

The questions raised this week concern the ways in which zebrafish used in laboratories are killed at the end of their useful lives. As we report on page 419, experimental work suggests that an approved anaesthetic commonly used in fish euthanasia causes the creatures distress.

Many researchers will rightly respond cautiously to calls to change regulations and long-standing experimental practice on the basis of just two papers, which are detailed in the News story. And it is not clear whether alternative options to the anaesthetic, MS-222, are more humane.

As animal-welfare researchers have probed the methods used in laboratory euthanasia, they have provoked sometimes fierce debate over which is the kindest option. The widespread use of carbon dioxide in rodent euthanasia has come under particular scrutiny, because evidence is growing that this method is more unpleasant for rats and mice than alternatives such as anaesthesia.

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At the very least, the work on the zebrafish should prompt reassessment of how much we know about some routine practices of animal research. Frequently, when researchers have probed the assumptions underpinning laboratory standards they have exposed flaws. And fixing these flaws — such as that revealed by the finding that rodents should not be picked up by their tails because this causes them stress, which could interfere with the results of some experiments — can produce better science.

Most laboratory animals are looked after by skilled and dedicated technicians and scientists who care deeply about the creatures' welfare. Their existence may not always be peaceful, but we can — and must — try to make it so, especially at the end. ■

Parallel lines

A collaborative online mathematics project holds lessons for other disciplines.

Crowd-sourcing has reached mathematics, and at first glance it might seem as if this stereotypically solitary discipline is finally catching up with what other sciences have been doing for years. But, as we explore on page 422, the maths project Polymath, which invites participants to pitch in with ideas and results that might help to solve whatever problem the coordinator has set, is in some ways ahead of the curve. Not all of Polymath's challenges — nine so far — have produced a successful solution. But even 'failures' can be productive, and all of these efforts represent genuine collaborations at the highest technical level.

It is in these respects that Polymath differs from the many other crowd-sourcing enterprises. Most commercial ventures are competitive: entrants vie to 'win' the challenge, and often to receive a financial prize as a result. As one researcher who has used these resources comments, this isn't necessarily the way to secure a truly useful solution: an extended period of post-competition development is often needed

to turn a winning entry into a practical approach. Entrants may not have the motivation or the time for that.

Other established crowd-sourcing efforts, such as Galaxy Zoo and Foldit, are all about weight of numbers, not expertise: they enlist lay volunteers to conduct repetitive tasks — such as classifying galaxy morphologies or predicting protein structures — for which human judgement still out-performs automated solutions. This is useful, but is not going to lead to the kind of conceptual novelty that drives science forwards.

So although all the various approaches to harnessing the 'wisdom' (or perhaps just the labour) of the crowd have a part to play, there are surely lessons that other disciplines could learn from Polymath. One is the value of openness. The system is fully democratic: anyone can propose and coordinate a project, and if it is deemed to be worth the effort, anyone can pitch in with answers or suggestions, however small, which are judged purely on merit. "Anybody who had anything whatsoever to say about the problem could chip in," Polymath's creator Timothy Gowers explains. "You would contribute ideas even if they were undeveloped and/or likely to be wrong." Although it is perhaps not surprising that the challenges so far have been instigated by senior researchers, an ethos of this sort means that, in principle, the barrier to participation of younger, less experienced people is low.

And the process is a conversation, not a competition. It's not just, or even primarily, about cracking a problem, but about sharing ideas. "One strength is in gathering literature and connections with other fields that a traditional small collaboration might not be aware of without a fortuitous conversation with the right colleague," says Terence Tao, another of Polymath's coordinators. And participants are learning the effort's limits. "Projects that seem to require a genuinely new idea have so far not been terribly successful," says Gil Kalai of the Hebrew University of Jerusalem in Israel. That's one reason why he feels "it will be nice to have a Polymath devoted to theory-building rather than to specific problem-solving".

Preconceptions aside, it is perhaps not surprising that mathematicians are the first to approach crowd-sourcing in this way. Their field is relatively small and well connected, and not nearly as competitive as some might think. It has an active blogging community. And it faces problems that can be tackled online with digital pen and paper. It is less obvious how, say, a chemistry challenge that demands lab work could be solved in this manner.

"Sometimes it is not market forces that achieve efficiencies, but cooperatives."

But is that really the case? Some of the successful Polymath problems have been those that could be broken down into smaller parts that individuals could work on independently. An organic chemical synthesis is rather like that: a series of distinct steps between intermediates. The total synthesis of quinine was famously — and controversially — claimed in 1944 on that basis, when, rather than making the compound itself, Robert Woodward and William Doering bridged the last gap in a multi-stage process that had been largely completed by others. Might not these feats of synthesis be more systematically apportioned between several groups, swapping ideas, tips and techniques along the way? That could be much more efficient than the herculean efforts often doggedly pursued in single labs today, not least because there is less chance of going down blind alleys when many minds are involved. But it would require a change in the prevailing mentality of competition and victory that was evident, for example, in the total synthesis of taxol that was reported in 1994.

This is just one way in which crowd-sourcing need not be about letting a thousand flowers bloom and then throwing away all but the most fragrant, nor putting all hands to the pump. Sometimes it is not market forces that achieve efficiencies, but cooperatives. ■

Virgin territory

Putting a private craft into space requires vision, hard work and a big dose of optimism.

Last week, *Nature* painted a pessimistic picture of the Google Lunar X Prize challenge in space exploration — which asks firms to land a robot explorer on the Moon by the end of next year. The technical hurdles are too high, critics say, and the financial incentives too low. A halfway house has been announced to offer encouragement: US$6 million for groups that can demonstrate that their lander works on Earth by September this year (see *Nature* **506,** 278; 2014).

By then, the X Prize model to encourage scientific progress could have launched its most successful venture yet. The word 'could' is pertinent, for the man talking up the chances of the venture is Richard Branson, the business tycoon with an ear for a catchy and ambitious sound bite. This is a man who does not do pessimism.

Branson said in the British newspaper *The Guardian* last week that the maiden flight of his private suborbital space-plane will blast off later this year — and that he and his family will be on board. We have been here before. Branson first promised that his company Virgin Galactic would start its space rides for paying customers in 2007, and it has been selling tickets for a decade.

He now says that work to launch the vehicle, *SpaceShipTwo*, is almost done. It is the successor to *SpaceShipOne*, which won the $10-million Ansari X Prize for repeatable space flight with a manned craft in 2004, and for which Virgin bought the rights. And Branson is typically bullish about the craft's prospects. The re-entry technology, always the most risky part, is foolproof, he claims: "The pilot could be sound asleep on re-entry." Branson wants *SpaceShipTwo* to fly to the edge of space "100 times, maybe 1,000 times", he said.

SpaceShipOne hangs from the ceiling of the Smithsonian National Air and Space Museum in Washington DC, alongside the *Spirit of St. Louis* monoplane. *SpaceShipTwo* will have large windows, and white and silver seats. Engineers will customize those seats to the rears of the wealthy guests, to minimize the effects of *g* force and to allow them to get the most of their estimated five minutes of weightlessness.

The Guardian spoke to astronaut Chris Hadfield, veteran of the NASA space shuttle and former commander of the International Space Station, who was sceptical of Branson's guarantees that nothing could go wrong. "To come into any programme with any vehicle and think you're somehow immune from what everybody else has always experienced with every machine in history is unrealistic," he said. "They don't know everything yet."

One thing that Branson does know (almost) everything about is how to keep a jumbo jet flying. As we report on page 420, that is more difficult than it sounds, particularly when the jet has a 2.5-metre infrared telescope sticking out of a hole in its fuselage. More than $1 billion has so far gone into the modified Boeing 747, formally called the Stratospheric Observatory for Infrared Astronomy. After years of delays (sound familiar?) it is now fully operational, and could do some valuable science. And with annual running costs of $78 million, it needs to.

There is something brilliantly simple about sticking a telescope on an aircraft as a way to beat atmospheric interference. But in 2014, doesn't such a solution seem a bit, well, twentieth century?

Back in the mid-1980s, Branson was invited by then Soviet leader Mikhail Gorbachev to become the first civilian in space. The ticket would have cost $50 million. "I thought," Branson said, "wouldn't it be better to spend that $50 million building a spaceship company instead?" Optimism is not for everyone, but it has its benefits. ■

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