SHUTTERSTOCK

Trilobites disappeared from the fossil record during a mass extinction 252 million years ago.

and rebounds that have been hard to uncover because of gaps in the fossil record. An understanding of these processes could reveal parallels to the planet's current loss of biodiversity.

Patchy record

Most organisms in Earth's history didn't leave fossils, and scientists have identified only a tiny fraction of those that did. As a result, it can be hard to tell whether changes in the fossil record mark real shifts, such as mass extinctions, or are simply caused by a lack of fossil finds.

In the 1960s, palaeontologists began analysing the fossil record systematically, revealing multiple mass extinctions and periods during which life flourished. But these and later efforts could usually pinpoint biodiversity changes to within only about ten million years, because fossils were lumped into relatively long geological periods and analysed en masse.

To improve on this, a team led by palaeontologist Jun-xuan Fan at Nanjing University in China created and analysed a database of fossil marine invertebrates that were found in more than 3,000 layers of rock, mostly from China but representing geology around the planet during the early Palaeozoic. The group then used software to measure when individual species had emerged and gone extinct.

The program took advantage of the fact that species were usually found in multiple rock formations — each spanning hundreds of thousands to millions of years — and used this information to place upper and lower limits on the period in which the species actually existed. The effort revealed for how long, and in what order, all 11,000 species had existed. It took the supercomputer around seven million processor hours.

Using this approach, the team was able to learn extra details about events such as the end-Permian extinction, and the Cambrian explosion around 540 million years ago. The analysis showed, for instance, that species diversity declined in the 80,000 years leading up to the end-Permian mass extinction, which itself occurred over about 60,000 years.

The findings also cast doubt on the existence of a smaller-scale die-off known as the end-Guadalupian extinction, which is thought to have wiped out many marine species around 260 million years ago. That was the biggest surprise, says Mike Benton, a palaeontologist at the University of Bristol, UK, who has documented changes in vertebrate diversity during that period. The study, he adds, "represents a pretty amazing big-data endeavour".

Benton hopes to see the effort extended to later periods — particularly the past 100 million years. Palaeontologists disagree over whether an apparent increase in animal diversity in this period is the result of sampling bias.

Norman MacLeod, a palaeontologist at the University of Nanjing and a co-author of the study, says the team's work might help to reveal the underlying causes of changes in biodiversity, by charting ups and downs on a timescale that can be matched with environmental and climatic shifts.

Wagner adds that the team's approach will be most valuable in uncovering — and explaining — smaller-scale extinctions, not dissimilar to those occurring today. Such extinctions could turn out to be "a bad 100,000 years, or a bad week" for some groups of organisms but not others, he says. "When you get this resolution, it starts opening the doors to actually testing what the smaller-turnover events might be like."

STUDIES OF EMBRYO-LIKE STRUCTURES STRUGGLE TO WIN US GRANTS

Biologists say they need clearer guidelines on funding rules for this nascent field.

By Nidhi Subbaraman

Scientists can now create clumps of cells that resemble human embryos, raising hopes that they could study the elusive first stages of human development while avoiding the ethical concerns that make it difficult to study actual human embryos. But as these embryo models — in which human stem cells are transformed into embryo-like structures whose growth mirrors stages of embryonic development — grow in popularity, US researchers say that they are finding it increasingly difficult to obtain federal funding for such work.

The US National Institutes of Health (NIH) in Bethesda, Maryland, has funded and still does fund work on embryo-like structures. A spokesperson told *Nature* that the agency considers grant applications involving models that "could be considered an organism" on a "case-by-case basis", and cited a provision of federal law known as the Dickey–Wicker Amendment, which bars the government from funding research that creates or destroys human embryos.

But the ban, which dates back to 1996, was put in place before the advent of techniques that produce embryo-like structures from stem cells. Scientists working on such research say that they need clearer guidance on what is eligible for federal funding. "The writing on the wall is that synthetic embryos are out of bounds with the NIH. The next step in the science is not allowed," says Eric Siggia, a physicist who studies developmental systems

at the Rockefeller University in New York City.

Amid this growing criticism, the agency's Office of Science Policy asked the US National Academies of Sciences, Engineering, and Medicine (NASEM) to host a day-long workshop to lay out the latest developments in experiments with embryo-like structures. At the NIH's request, the meeting on 17 January in Washington DC did not include any presentations on ethics or regulations.

The NASEM meeting was intended to help people to "better understand some of the unknowns associated with this nascent field", Carrie Wolinetz, the NIH's acting chief of staff and associate director for science policy, wrote in a blogpost last year. "Can research involving various models of aspects of human embryo development be supported by NIH? The answer is 'it depends'," she added.

Sticky wicket

Embryo research in the United States has long been fraught. In addition to the Dickey–Wicker Amendment, US scientists are guided by an internationally acknowledged ethical guideline called the 14-day rule. This limits embryo research to the two-week period after fertilization. And last June, the US government halted fetal-tissue research by government scientists and began requiring that any grant application involving such material undergo an extra ethics review.

None of these laws and guidelines specifically deals with the increasingly complex collections of cells that mimic the early stages of human embryonic development, and can shed light on processes that are otherwise difficult to study. Crucially, embryo-like structures are not formed from an egg and sperm, as real embryos are. Scientists say that it is unclear whether or how existing guidelines are being applied to research that uses the structures.

Siggia and a colleague at Rockefeller, developmental biologist Ali Brivanlou, submitted a progress report to the NIH in 2018 on their grant to study the mechanisms by which colonies of embryonic stem cells organize themselves. Siggia says that they were told by NIH staff to cut plans for research in which synthetic embryonic cells would interact with "extra-embryonic" cells — tissue that grows into the placenta and other structures that nourish an embryo. "The mix of extra-embryonic and embryonic cells could get what someone would construe to be an embryo — and they didn't want to go anywhere near that," Siggia says. But he argues that the work would be the next logical step in experimental design.

He and Brivanlou resubmitted their plans for the next year after altering the original text. "Then it moved forward," he says.

The Rockefeller group is not the only one adapting its plans so that it can continue its work. Aryeh Warmflash, a stem-cell biologist at Rice University in Houston, Texas, says he isn't applying for federal funding for work that uses embryo-like structures to study the phase of development known as gastrulation. "It doesn't seem to me to be worth the effort," Warmflash says. He is turning to private funders.

And Fu Jianping, a bioengineer at the University of Michigan in Ann Arbor, says that he submitted a grant application to the NIH to study the origin of cells that are precursors to eggs and sperm using embryo-like structures. The agency reviewed and scored it last June, and a programme officer e-mailed Fu a list of questions, including one that asked whether his experiments would involve extra-embryonic tissue. Several months later, Fu says he hasn't received any funding. "The uncertainty from the funding agencies is definitely going to be a roadblock to continued progress," he says.

An NIH spokesperson told *Nature* that scientists with questions about any grant application or award could contact the relevant agency official, and that the agency does not comment on unfunded grant applications.

The International Society for Stem Cell Research in Skokie, Illinois, said on 16 January that it would release updated guidelines in early 2021 to address the complexity of research with embryo-like structures. It also released a series of recommendations for researchers to follow until then.

"The NIH of course is struggling with the question when is an embryo not an embryo," says Janet Rossant, a developmental biologist at the Hospital for Sick Children in Toronto, Canada, and an organizer of the NASEM workshop. "I would also absolutely say we're not close to a line that should not be crossed."

HUGE SURVEY REVEALS PRESSURES OF SCIENTISTS' LIVES

Global study highlights long hours, poor job security and mental-health struggles.

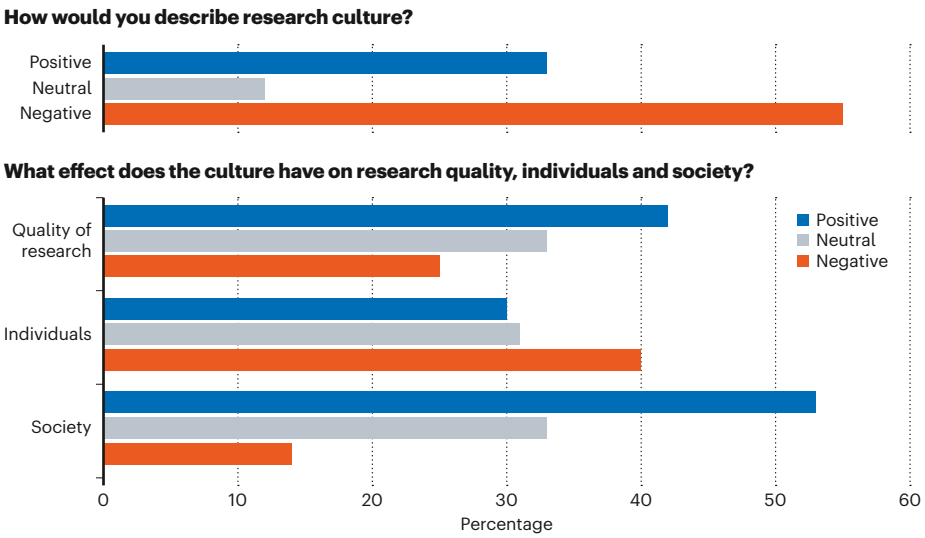
By Alison Abbott

A survey of more than 4,000 scientists has painted a damning picture of the culture in which they work, suggesting that highly competitive and often hostile environments are damaging the quality of research.

Around 80% of the survey's participants — mostly academic researchers in the United Kingdom — believed that competition had fostered mean or aggressive working conditions, and half described struggles with depression or anxiety. Nearly two-thirds of respondents reported witnessing bullying or harassment and 43% said they had experienced it.

COST OF THE CULTURE

In a global survey of around 4,000 researchers, 55% said that they had a negative impression of scientific working cultures. One-quarter said that the culture damaged the quality of research.



SOURCE: *WHAT RESEARCHERS THINK ABOUT THE CULTURE THEY WORK IN* (WELLCOME, 2020)