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.

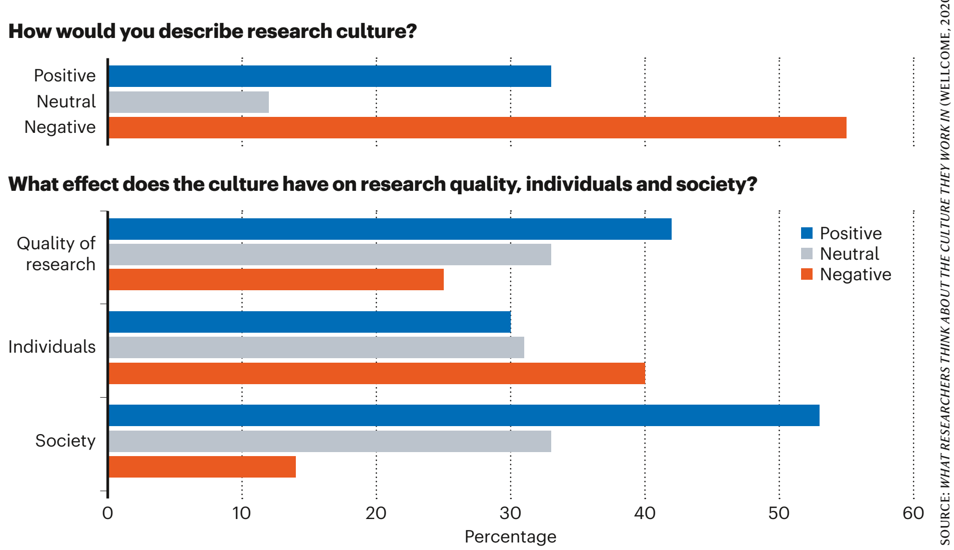
By Alison Abbott

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.



"These results paint a shocking portrait of the research environment – and one we must all help change," says Jeremy Farrar, director of Wellcome, a major research funder in London that conducted the study with market-research agency Shift Learning. "A poor research culture ultimately leads to poor research."

Farrar says that Wellcome – which supports some 15,000 people working in science worldwide – is committed to addressing the issues highlighted by the survey, and he calls on the entire research system to get on board. "The pressures of working in research must be recognized and acted upon by all, from funders to leaders of research and to heads of universities and institutions," he says.

Unsustainable environment

Wellcome conducted the survey, published on 15 January, as part of a broader drive to improve working environments in science. It says the push for excellence has created a troubling culture. "It's more than clear that our current research practice is not sustainable," says Beth Thompson, who leads Wellcome's research-culture initiatives. "We knew things were not right, from our own discussions with scientists, from high-profile bullying cases, reports of misconduct and irreproducibility."

The results come from an online survey open to all researchers, which was answered by around 4,300 people across career stages and disciplines. Respondents hailed from 87 countries; three-quarters were in the United Kingdom. Workshops with 36 UK-based researchers and in-depth interviews with 94 also informed the findings.

Most researchers reported having pride in their institutions and passion for their work, but spoke of the high personal toll of their environment (see 'Cost of the culture'). Many accepted that pressure and long hours came with the territory – two-thirds of respondents said they worked for more than 40 hours a week. But researchers said that the situation was worsening and that the negative aspects were no longer offset by job security and the ability to work autonomously, flexibly and creatively. Barely 30% of respondents felt that there was job security in research careers.

Many blamed funders and institutes that emphasize performance indicators and metrics such as number of publications and the impact factors of journals in which researchers publish. They said that the importance of these metrics is often stressed in ways that reduce morale and encourage researchers to game the system. Some said that good management could shelter scientists from such distorting pressures, but that it was too seldom applied.

One-quarter of respondents thought that the quality of research suffered in the unsupportive environments. The same proportion had felt pressured by their supervisors to produce a particular result.

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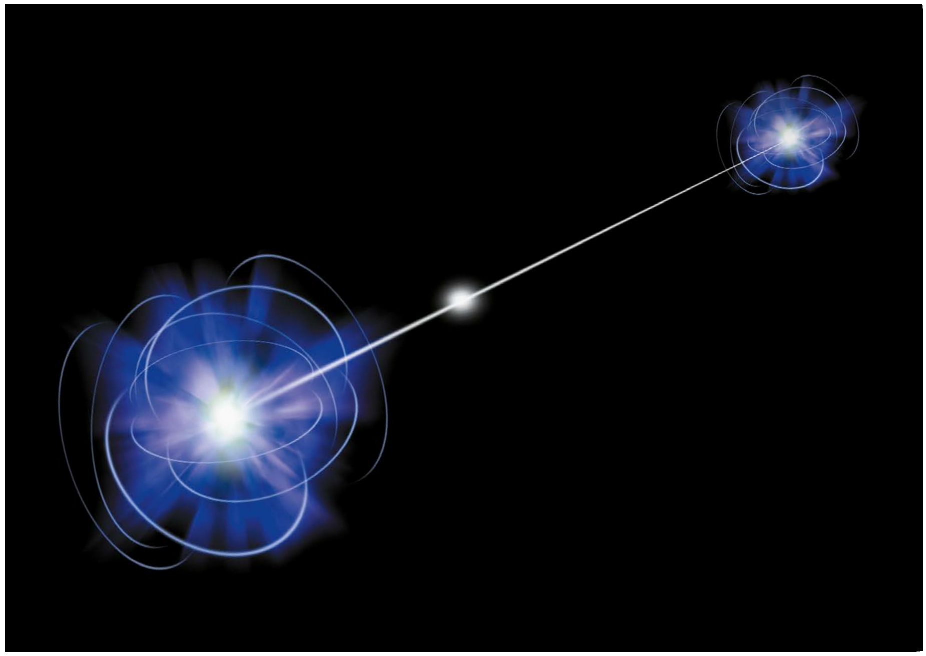

Quantum entanglement is at the centre of a new mathematical proof.

THE 'SPOOKINESS' OF QUANTUM PHYSICS COULD BE INCALCULABLE

Proof at the nexus of pure mathematics and algorithms puts 'quantum weirdness' on a new level.

By Davide Castelvecchi

Albert Einstein famously said that quantum mechanics should allow two objects to affect each other's behaviour instantly across vast distances, something he dubbed "spooky action at a distance"[1]. Decades after his death, experiments confirmed this. But, to this day, it remains unclear exactly how much coordination nature allows between distant objects. Now, five researchers say that they have solved a theoretical problem that shows that the answer is, in principle, unknowable.

The team's proof[2], presented in a 165-page paper, was posted on the arXiv preprint repository on 14 January, and has yet to be peer reviewed. If it holds up, it will solve in one fell swoop a number of related problems in pure mathematics, quantum mechanics and a branch of computer science known as complexity theory. In particular, it will answer a mathematical question that has gone unsolved for more than 40 years.

If their proof checks out, "it's a super-beautiful result" says Stephanie Wehner, a theoretical quantum physicist at Delft University of Technology in the Netherlands.

At the heart of the paper is proof of a theorem in complexity theory, which is concerned with efficiency of algorithms. Earlier studies had shown this problem to be mathematically equivalent to the question of spooky action at a distance – also known as quantum entanglement[3].

Quantum game theory

The theorem concerns a game-theory problem, with a team of two players who are able to coordinate their actions through quantum entanglement, even though they are not allowed to talk to each other. This allows both players to 'win' much more often than they would without quantum entanglement. But it is intrinsically impossible for the two players to calculate an optimal strategy, the authors show. This implies that it is impossible to calculate how much coordination they could theoretically achieve. "There is no algorithm that is going to tell you what is the maximal violation you can get in quantum mechanics," says co-author Thomas Vidick at the California Institute of Technology in Pasadena.

"What's amazing is that quantum