One day in May 2014, while visiting his parents in Bulgaria, biologist Nikolai Slavov sat at his laptop and called up a free online archive of scientific papers called bioRxiv. Then, with a click of an “upload” button, he submitted the draft of a paper he’d written about his postdoctoral work at the Massachusetts Institute of Technology in Cambridge on the unexpectedly diverse structure of ribosomes, the cell’s protein-making factories. “I was mostly excited, but a little bit nervous” about sharing findings that hadn’t been scrutinized by peer reviewers, he says.

He didn’t worry for long. In a few hours, the manuscript appeared online for all the world to see. Within weeks, it had drawn hundreds of downloads, two dozen tweets, and a trickle of online comments. It also brought job offers. And in July 2015, months before a final peer-reviewed version of his paper appeared in the journal Cell Reports, Slavov accepted a tenure-track position at Northeastern University in Boston.

Posting that first-draft manuscript, or preprint, “clearly expedited and helped with my job search,” Slavov says. And he thinks the half-dozen preprints he’s posted since have helped turbocharge his career. Science journalists have covered his work, colleagues have proposed collaborations, and journal editors have invited him to submit papers.

Slavov represents the promise of a movement that is sweeping across the life sciences. Although physicists have been posting preprints for nearly 3 decades, many biologists have only just begun to widely share their unreviewed papers. The shift has been catalyzed, in part, by endorsements of preprint publishing from high-profile scientists, as well as the 2013 launch of the nonprofit bioRxiv by Cold Spring Harbor Laboratory (CSHL) in New York; bioRxiv now holds more than 15,000 papers. But in contrast to physics, where preprints took off without much fanfare or controversy, the leap into preprints...
is stirring strong passions in the hyper-competitive world of the life sciences.

Proponents of biology preprints argue they will accelerate the pace of science—and improve its quality—by publicizing findings long before they reach journals, helping researchers get rapid feedback on their work, and giving a leg up to young researchers who don’t yet have many publications. Some see little difference between posting a preprint and presenting unpublished findings at a meeting, except that the preprint audience can be far larger.

Many biologists remain wary, however. Some worry that competitors will steal their data or ideas, or rush to publish similar work. Others predict that preprint servers will become a time sink, as scientists spend hours trying to sift through an immense mishmash of papers of various quality. And some researchers fear that easy, rapid publication could foster preprint wars—in which the findings in one preprint are quickly attacked in another, sometimes within hours. Such online squabbles could leave the public bewildered and erode trust in scientists.

Like it or not, however, the rough and tumble new world of biology preprints has arrived. For those debating whether to take the plunge, *Science* offers this guide.

**Why are biology preprints taking off now?**

Today’s boom was long in the making. In the 1960s, the National Institutes of Health (NIH) in Bethesda, Maryland, mailed photocopied copies of draft manuscripts to groups of biologists (see sidebar, p. 1348); the short-lived project was followed in 1991 by arXiv, a nonprofit preprint server for physics now at Cornell University. In 1999, Nobel laureate Harold Varmus, then-director of NIH, proposed a similar server for biology, but journal publishers saw it as a threat. In 2003, however, arXiv opened a quantitative biology section. And in 2007, Nature Publishing launched a server called Nature Precedings, which collated more than 2000 manuscripts, mostly in biology, before folding in 2012.

The concept really gained traction in November 2013, when CSHL launched bioRxiv as a way to promote scientific communication. It had the weight of CSHL behind it, along with commitments from scores of volunteers to post their own preprints and help screen submissions. Recently, bioRxiv has drawn support from a deep-pocketed source, the Chan Zuckerberg Initiative (CZI) funded by Facebook Co-Founder Mark Zuckerberg and his wife, pediatrician Priscilla Chan.

CSHL isn’t alone in promoting preprints. Other servers have sprung up, and early last year, a nonprofit called ASAPbio, incorporated in San Francisco, California, began deploying preprint “ambassadors,” enthusiasts who evangelize to their colleagues, and holding meetings on such topics as how funders and journals view preprints.

Major research funders have also moved to legitimize preprints. The U.K. Medical Research Council and the Wellcome Trust in London, as well as NIH and the Howard Hughes Medical Institute in Chevy Chase, Maryland, now encourage grantees to cite preprints—not just peer-reviewed papers—in grant proposals. CZI has even made posting a preprint (at the same time as the paper is submitted to a journal) a requirement for its grantees. Preprints have also gotten some indirect, but highly placed, endorsements. “I’ve yet to see any instance where somebody was harmed by that early reveal of the work that they’re doing,” NIH Director Francis Collins says.
Who is posting biology preprints?

A wide array of scientists. BioRxiv counts more than 11,000 corresponding authors and 63,000 unique authors in total, 56% from outside the United States. Hundreds of life scientists have posted on other free nonprofit and commercial servers, such as PeerJ Preprints. Researchers in computational fields such as bioinformatics and genomics were early adopters of bioRxiv. Neuroscientists were slower to embrace the service, but the field is now one of bioRxiv’s largest categories, making up 15% of all papers.

Some preprint authors are prominent researchers with large followings, including genomics/gr/Eric Lander of the Broad Institute in Cambridge, Massachusetts, as well as synthetic biologist George Church and ancient DNA researcher David Reich, both of Harvard University. Also preprint fans: two leaders of research into the CRISPR gene-editing tool, Feng Zhang of the Broad Institute and Jennifer Doudna of the University of California (UC), Berkeley. But plenty are less known, including many from institutions in China. One prolific bioRxiv author—with seven preprints—is a self-described independent bioinformatics researcher in India and (according to one paper) a Buddhist monk.

Neuroscientist Leslie Vosshall of The Rockefeller University in New York City, who describes herself as a “Fidel Castro” spreading the preprint revolution, sees two main groups embracing preprints: midcareer, established scientists who “can afford to take the risk” and millennials, “who share everything. They get it right away.”

Preprint servers have also become a go-to outlet for researchers seeking to air critiques of controversial findings. Journals may not be interested in publishing such contrarian studies, which bioRxiv users can label as “contradictory results,” says bioRxiv co-founder John Inglis of CSHL. And the online world can enable very rapid responses: After genomics pioneer J. Craig Venter’s Human Longevity Institute in San Diego, California, published a paper last month claiming it could predict faces from DNA, critics responded within a day with a bioRxiv preprint slamming the study. Venter soon parried—with another bioRxiv preprint.

Who is not on board?

The vast majority of biologists. Although bioRxiv has grown rapidly, the more than 1200 preprints deposited in it in August still represented just 1.3% of the 93,000 papers added to PubMed, the NIH-run database of biomedical abstracts, during that month.

“It’s not obvious to me yet that there is any advantage” to preprints, says stem cell researcher Sean Morrison of the University of Texas Southwestern Medical Center in Dallas, who shares his latest work at meetings.

For others, the reluctance reflects concern that journals will reject a study that was already posted as a preprint. Until recently, many banned releasing papers to the public before formal publication.

Now, most basic science journals (including Science) say they will accept papers posted as preprints (see Editorial, p. 1331), and many will even accept submissions directly through an interface on bioRxiv. But some major medical journals, including The New England Journal of Medicine, still discourage preprint posting.

Ant biologist Terry McGlynn of California State University in Dominguez Hills prefers waiting a few months so that the public can see a polished paper in a journal, not a draft that could have errors. And he thinks that rushing to post preprints adds to the pressures on researchers. “Preprint advocates might think that they are a prescription to fix the rat race, but I think it just puts the rats in a more convoluted maze,” he wrote in July on the blog Small Pond Science.

Some researchers avoid posting to preprint archives because they believe that the screening and sorting performed by traditional journals serves readers well. “For the nonexpert, such archives are very difficult to navigate, and the filter of peer review is essential,” says cancer geneticist Bert Vogelstein of Johns Hopkins University in Baltimore, Maryland, who has posted only a few preprints.

Researchers who conduct complex lab experiments also appear to be more reluctant to post. Within some bioRxiv categories that have begun to take off, such as plant science and cancer biology, papers still skew toward computational and theoretical work. That may reflect the fact that lab experiments can “take a long time—there’s a whole lot invested in creating some of those data,” says cancer modeler Jacob Scott of the Cleveland Clinic in Ohio, a bioRxiv enthusiast. And they may involve novel compounds and therapies that have commercial potential, discouraging authors from early publication.

How polished should your preprint be?

Some scientists say the preprints they post are almost identical to what ends up in a journal. Neuroscientist Leslie Vosshall says that the papers she sees on bioRxiv are of “significantly higher quality” than the typical journal submission, because the authors can’t lean on editors to fix typos, clarify prose, and ask for more experiments. “I have seen very few, but not zero, examples of poorly put together preprints,” cancer modeler Jacob Scott says. “Sometimes someone’s afraid that they’re about to be scooped or needs something for a grant application,” leading them to rush out a sloppy preprint. “But in general, people take their preprints seriously.”

Other scientists, however, say part of their motivation for posting is to get feedback, and they are comfortable posting a rough draft that they update with revisions. Scott says he sometimes posts two or three versions. Feedback rarely comes directly through bioRxiv: Just 10% of articles draw comments. Instead, reaction tends to arrive through Twitter or email. To stimulate more feedback, ASAPbio is encouraging labs to form journal clubs to discuss only preprints.

But because scientists are already “saturated” with formally reviewing papers for journals, it may take a cultural change for them to devote the same attention to preprints, says plant pathologist Sophie Kamoun of The Sainsbury Laboratory in Norwich, U.K. One incentive for journal peer reviewers—a chance to see an early draft of a paper before anyone else—“doesn’t apply to preprints,” he says.
What will you get out of it?

One advantage, preprint advocates say, is that you will be able to share your paper with colleagues months or years before it wends its way into a peer-reviewed journal. And that rapidity can help a researcher maintain enthusiasm, says cell biologist Stephen Royle of the University of Warwick in Coventry, U.K. “Publishing can be such a long process that all the excitement is usually sucked out of your work by the time it appears,” he says. “Getting the paper out when you are still excited about it is an amazing feeling.” The early attention to a finding can pay off later: Preprints that do end up in journals appear to be cited more quickly, according to a study of arXiv submissions.

Getting a time stamp for a new finding is also part of the appeal. Servers such as bioRxiv and PeerJ Preprints give submissions a posting date and digital object identifier, in essence planting a flag that establishes priority. At the same time, “there is some confusion about this because we don’t really have standards for deciding who should get priority for a discovery,” plant pathologist Sophien Kamoun says. “Some people hang on to the notion that publishing first in a peer-reviewed journal is what matters.”

Because preprints can be cited, they can help young scientists quickly build a scholarly track record. That can benefit people who are seeking funding or a job. Preprint authors may hear from journal editors who become intrigued by their preprint: Some editors are browsing bioRxiv for papers.

Sometimes, preprints can promote healthy competition. Neuroscientist Leslie Vosshall cites a group that posted a preprint on the first genetically modified ants; another group doing similar work saw the paper and soon posted its own preprint. The two teams submitted their papers to Cell, which published them together last month.

Preprints can also catalyze collaboration. Three groups studying the same cellular protein agreed to time their preprints so they all appeared on bioRxiv within a day or two of one another. The groups had learned about one another at a meeting, says biochemist Adam Frost of UC San Francisco, and decided simultaneous posting “would be fair. ... It was really positive because it kept us on very good terms and communicating freely.”

A long time coming

Physicists have posted unreviewed preprints of their work for decades, but the practice is only just taking off among biologists. Many reckon that the 2013 launch of bioRxiv marked the tipping point. But even now, just 1.3% of biology papers first appear as preprints.

Quick studies

Some areas of biology have embraced preprints faster than others. Fields that do time-intensive experiments have been hesitant.

Preprint poster children

Preprint enthusiasts include established scientists and junior researchers accustomed to online sharing. Here are the six most prolific corresponding authors on bioRxiv.

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<td>1 Yaniv Erlich</td>
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<td>2 Thierry Mora</td>
<td>École Normale Superieure</td>
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<td>3 Suresh Neethirajan</td>
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<td>Indian Institute of Science Education and Research, Pune</td>
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<td>5 Antonio Benitez-Burraco</td>
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<td>6 Sophien Kamoun</td>
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Can you talk to reporters about your preprint?

The answer is “no” for some high-impact journals that promote papers to the media. These journals discourage authors who have papers in press, and even those who simply plan to submit, from discussing the preprint version with the media. (Science warns authors that “the editors may also take into account comprehensive media coverage while on preprint when considering the novelty of the paper,” a journal spokesperson says.) Many journalists will report on a preprint regardless of whether its authors are free to talk, however. The result is news stories that quote other scientists about the work, but not the authors.

The rules seem fluid, however. The Rockefeller University’s Daniel Kronauer says he felt that talking to journalists about his February preprint on genetically modified ants “wasn’t an issue” because he had not yet submitted it to Cell. Some journals also make an exception for preprints that are presented at a public meeting, providing the news coverage doesn’t include more detail than the presentation itself. One downside to talking to reporters about a preprint, however, is that early news coverage can mean that the study gets less attention from the media when it is published.

Because of the uncertainty about press interactions, Harvard evolutionary biologist Hopi Hoekstra, a bioRxiv advocate, holds back some papers that she plans to submit to a top journal. But, she says, “My guess is over the next couple years we’ll just post everything as people become more comfortable with the process.”

What could go wrong?

Scooping is the No. 1 worry. A competing team could see your preprint and rush a similar study into a journal. Editors might then reject your final paper. “I get that fear,” cancer mod-uler Jacob Scott says. “But I look at it in the opposite way. Preprints are my defense ... really a flag in the sand and proof that it’s mine.”

Still, this year EMBO Press’s four journals announced “scooping protection”: If an author submits a manuscript within 4 months of posting a preprint, EMBO will consider the work novel even if a competitor publishes similar work during that time.

Another concern is that a competing group could grab your data or ideas from a preprint before you can publish in a journal. Developmental biologist Alberto Stolfi of the Georgia Institute of Technology in Atlanta recently recounted on Twitter that another lab, without warning, published a paper that included preprint data from his postdoctoral research on using CRISPR to modify a sea squirt. He was surprised, but decided the preprint data were “fair game.” And it ended well: “We knew the author, liked him,” and they ended up collaborat- ing on a final, published version of that first preprint. Some say such borrowing is no different from the cross-pollination that comes from seeing another group’s talk or poster at a meeting.

For the broader scientific community, a common fear is that substandard work, which would not have survived peer review, will become widely available. “The danger for bioRxiv is being hijacked by pseudoscience chasing a veneer of respectability,” geneticist Barry Thompson of The Francis Crick Institute in London tweeted recently. Although bioRxiv staff do a plagiarism check and the project’s volunteers check for scientific validity, bioRxiv accepts 95% of submissions.

John Inglis defends bioRxiv’s process and notes that about 60% of preprints end up in journals, indicating they are scientifically worthy. And preprint advocates like to note that even peer-reviewed journals publish flawed work. “Junk is already out there,” neuroscientist Leslie Vosshall says. “BioRxiv isn’t going to have any impact on that.”

For preprint fans, one nightmare would be a faulty preprint with health implications. To guard against the possibility, bioRxiv does not currently accept any clinical research except epidemiology and certain trial results. Yale University researchers this month announced plans for a new server, MedArXiv, for clinical research preprints; it might be built with bioRxiv’s infrastructure but would have separate, tighter standards for screening papers, Inglis says. Yale cardiologist Harlan Krumholz says he hopes the project will win over medical journals that now reject preprints: “It’s our job to show that [preprints are] not as scary as they think,” he says.

Another worrisome scenario is that authors will post incomplete papers simply to stake a claim, without sharing details of their work. This past July, a Twitter storm erupted over two papers on a technique for sequencing RNA that were posted without methods sections. Both teams apologized (one co-author said her group was in a rush) and posted full manuscripts.

The episode has fueled calls for stricter common standards for preprints—covering issues such as screening submissions and retracting those that turn out to be seriously flawed or fraudulent. That’s a task ASAPbio expects to take on. Posting a preprint is “so easy and quick, it is very attractive,” says Johanna McEntyre of the European Bioinformatics Institute in Hinxton, U.K. “But if key elements of rigor are missed, it could potentially damage uptake. So it is a balancing act of ease versus rigor—which is not easy.”

Will preprints replace journals?

Some proponents predict that preprint servers will become the favored venue for publishing and critiquing findings, and will eventually replace peer-reviewed journals altogether. For the moment, that appears to be a minority view. Even PLOS, which has shaken up scientific publishing with its pio- neering open-access journals, has stood up for traditional journals. “Preprints do not diminish the need for reputable peer-reviewed journals,” Sheryl Denker, communica-tions editor at PLOS in San Francisco, wrote last year. She argued that preprint servers can’t provide the ethics and quality checks carried out by journals. And more than 2 decades after arXiv was founded, most physicists still send their preprints to journals, even though that final step often amounts to a formality.

Whatever the future holds for traditional journals, biology pre-prints are likely to be more than a fad. “Preprints will percolate slower in some communities,” biologist Nikolai Slavov says, “but I am confident that they will continue to spread fast and eventually will be adopted by all.”

[Sciencemag.org](http://science.sciencemag.org/)
The preprint dilemma
Jocelyn Kaiser

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