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Greening the lab

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Making biological research more sustainable requires an accurate assessment of its environmental impact, both at the bench and on the computer.

By Caroline Seydel

Molecular biology is transforming our world in ways that only the wildest dreamers could have imagined fifty years ago. Babies with catastrophic genetic conditions can be diagnosed and treated within days thanks to rapid whole-genome sequencing. CRISPR gene editing has created new, effective treatments for sickle cell disease. When the COVID-19 pandemic arose, mRNA technology enabled the creation of a totally new kind of vaccine within months.

Yet all too often researchers pursue these advances single-mindedly, without consideration for the carbon footprint of the research laboratory. Sustainability advocates say there is still plenty of 'low-hanging fruit' where biology researchers can lessen their environmental impact without significantly altering their research goals and protocols. "There was this idea that we were doing such good in the world that the rules didn't really apply to us," says Star Scott, the Green Labs program manager at the University of Georgia. "We cannot keep practicing science as though we are exempt from the negative contributions we're making."

Massive increases in computing ability are also shaking up biology. For example, an artificial intelligence program called AlphaFold can predict the structures of nearly all known proteins. While working in silico doesn't generate the plastic trash or chemical waste that wet lab work does, today's energy-guzzling computers certainly contribute to climate change.

"We all sort of think that if it's on the computer, it's the green option," says Loïc Lannelongue, biomedical data scientist at the University of Cambridge, UK. "It turns out, when we're using massive algorithms and supercomputers, that they have very real environmental impact."

Lannelongue and others are working to raise awareness of the environmental toll of biological computing. "The field of computational science is lagging behind wet lab science for that kind of thing," he says. "Initiatives to make labs more sustainable have been going quite strong for a few years now, to reduce single-use plastic, reduce electricity

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usage for lab equipment, move freezers from −80 to −70."

Ultimately, funders will be key to driving cultural change in research. While funding bodies are warming to the idea of including sustainability assessments in their applications, it's been a challenge to accurately define and measure the sustainability of a given proposal. To that end, researchers are developing tools to calculate the environmental costs of their work, both at the bench and at the keyboard.

Principles of green computational science

Two major funders of research in the UK, Wellcome and UK Research and Innovation, recently published reports on reducing the carbon footprint of laboratory and computational science[1,2]. The Million Advocates for Sustainable Science letter-signing campaign, coordinated by My Green Lab and the International Institute for Sustainable Laboratories, urges funders around the world to set expectations for efficiency and sustainability in research methods. "Many funding agencies and institutions are incorporating sustainability criteria into grant applications and evaluation processes," says Namrata Jain, senior marketing manager for My Green Lab. "This shift in funding priorities contributes to the broader adoption of sustainability practices among researchers."

Yet, as Lannelongue points out, researchers often neglect the energy costs of their computational projects. Before funders can properly consider the relative environmental impact of projects, he says, there need to be accurate and easy-to-use tools to estimate those impacts. Realizing that there were no tools available to make those calculations, he and colleagues Jason Grealey of the Children's Medical Research Institute, Westmead, Australia, and Michael Inouye of the Baker Heart and Diabetes Institute, Melbourne, Australia, developed a tool called Green Algorithms[3].

"The idea behind this online calculator was to make something that someone can log in for half an hour and do the math," Lannelongue explains. "We can't expect researchers to spend weeks to learn about sustainability to be able to fill in a funding application."

While the main environmental consideration around computing is electricity use, Lannelongue says it can quickly get complicated to truly estimate the impact of a computing project on the planet's resources. "You need to figure out what is the carbon footprint of producing that electricity, which depends on where you are in the world and what's the energy mix of your country," he says. "Even within the US, depending on which state you are in, there are massive differences. Doing exactly the same task with exactly the same computer in two neighbor states might be completely different carbon footprints."

"It was never a scientific need for colder sample storage that drove us to the −80," says Star Scott of the University of Georgia. "It was the refrigeration industry, which figured out how to make a colder freezer." Keeping a freezer at −80 °C instead of −70 °C increases energy consumption by 30%, and most biological samples keep just fine at −70 °C.

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Although an individual researcher can't have much impact on a country's electricity grid, there are ways to reduce carbon footprint, including a consideration for timing. "Sometimes just running your job 12 hours later has massive impacts," Lannelongue says. Collaborations can play an important role here as well: locating data centers in areas with greater reliance on sustainable sources of electricity and accessing them remotely can reduce the overall carbon footprint of a project, although this must be done with attention to concerns including equity of access, privacy of sensitive data, and the ecological impact of building data centers.

Aside from electricity usage, Lannelongue points out, there are other impacts, including extracting the raw material, fabricating the computers, shipping them across the world and eventually disposing of them. "So many other impacts don't get included," he says. "The ecological impact of a data center: if you take a big field and you put in a big data center, and suddenly you pump a lot of water for cooling, obviously, there are other impacts than just electricity usage."

Finally, Lannelongue says that it's important to balance the environmental cost of the work against its benefits, just the way that researchers already consider their monetary costs. "We don't start a research project with no idea what it will cost," he says. Similarly, investigators should ensure that the goals are worth the environmental cost. "I'm in the Heart and Lung Institute here in Cambridge," he says. "And if someone says, 'oh, you have a massive carbon footprint', it's easy to just say, 'Well, yes, but I'm trying to reduce the mortality of heart attack. Do you really want me to stop working on that?'" But he points out that at one time, medical researchers dismissed ethics concerns on similar grounds — that obtaining lifesaving data was more important than conducting ethical trials. Imposing ethical standards on clinical trials didn't end clinical trials; similarly, he says, taking environmental impact into consideration won't end research, but will reduce the overall carbon footprint of research and enable important work to continue more sustainably.

Sustainable method for whole-genome regression modeling

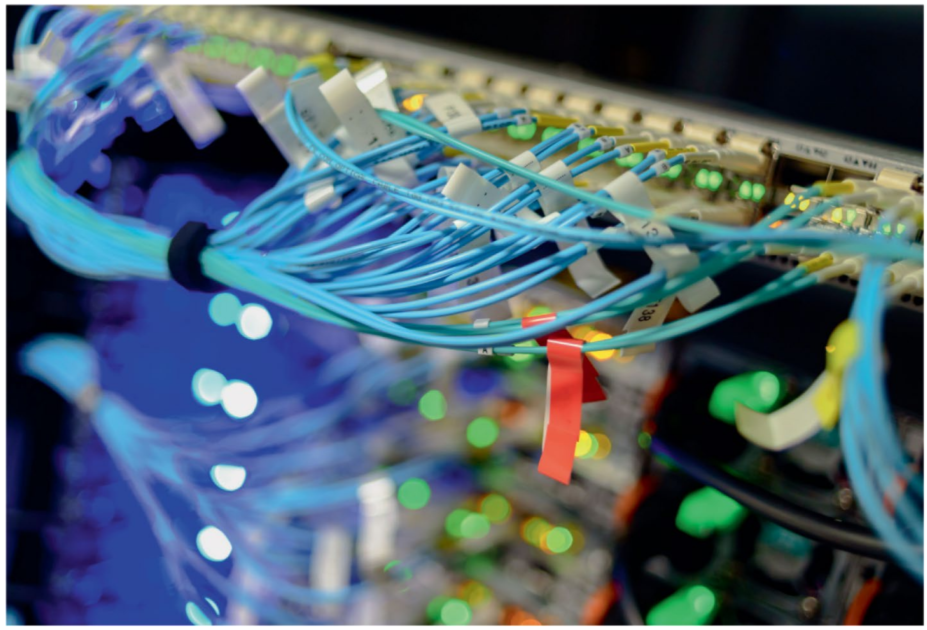
Genome-wide association studies are a method for identifying genetic variants that are statistically associated with a particular trait. These types of studies require large numbers of samples to get sufficient statistical power to separate the signal from the noise. As study sizes have ballooned to include millions of samples, new statistical methods have been developed to analyze the data. These methods often require massive amounts of computing power and time.

"The computation starts to rack up," says Jonathan Marchini, the head of statistical genomics at the Regeneron Genetics Center. "We were thinking about what we could do from a statistical methods point of view to speed that up."

In 2021, Marchini and colleagues published a method of whole-genome regression they call regenie[4]. "There were some really great methods out at the time," he says. "But there were a few key steps in those methods that were hard to parallelize. Every time you analyze a new trait, you have to start from scratch." Also, with the existing methods, the entire dataset needed to be loaded into RAM on a single machine before running the analysis. Marchini and colleagues thought they could work out a way to fit the models to data that were stored in a distributed way, rather than on one large computer.

"We've got data across the whole genome — let's say a million positions in the genome — and then 100,000 individuals," Marchini says. "We had this idea that we'd load the data in small chunks, maybe 1,000 positions at once, and effectively compress down that data into the most meaningful parts of it." That step creates 'predictors' for each trait being studied. By moving across the genome, analyzing the data in chunks and creating predictors, the method yields a compressed dataset that requires far less RAM to load onto the computer. The other big advance was that the same calculations could be reused for each phenotype. "Let's say you have 50 different continuous traits. We could analyze all 50 of those in the first pass in a very computation-efficient way," explains Marchini. "I think it's a pretty substantial impact on the field." Regenie speeds up the analysis by one to two orders of magnitude, Marchini says, which means it uses less electricity, both saving money and reducing the environmental impact. According to the Green Algorithms calculator, the new method reduces the carbon footprint of the analysis tenfold: the equivalent of driving a car 1,000 kilometers, compared with 10,000 kilometers under the previous method.

Regeneron has made regenie publicly available online under an MIT license, and the original paper has been cited a few hundred times in the two years it's been available. Marchini also says that they receive lots of feedback from users that helps the team keep improving the system and develop new features. Joelle Mbatchou, the key developer, recently introduced some improvements that speed up the analysis for case–control traits. "We're probably not going to get another order of magnitude, but we're chipping away," Marchini says. "Making 10 to 20% improvements, that can be a lot of money when you have quite a big compute budget."



As high-powered computing plays a larger role in biological research, computer scientists are developing more efficient algorithms that reduce the energy costs of computing and save time.

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Green DNA synthesis

As humanity generates massive amounts of data, storing all those documents, photos and TikToks requires ever-increasing energy, materials and space. Synthetic biology may one day pave the way to greener data storage using DNA. DNA storage allows remarkably dense information storage: it's estimated that all the digital data on the planet, encoded in DNA, could be stored in a shoebox.

For now, though, manufacturing DNA is still too costly, and the most efficient method involves hazardous organic chemicals. Now, several companies are working on a more environmentally friendly method of making template-free DNA using enzymes. In addition to eliminating organic chemical waste, scaling up enzymatic synthesis methods to produce commercial quantities of DNA could lead to a higher-quality end product while sidestepping supply chain issues.

"Many of the past downturns economically have had a huge impact on DNA synthesis because the organic solvents that are used are also used for the automotive industry," says biophysicist Scott Fraser of the University of Southern California. "Each time there's been a downturn in the economy, there's been a near crisis in DNA and RNA synthesis because those solvents that are being made mostly for automotive and other applications become harder to get."

Fraser is an advisor to a company called Camena Bioscience, Cambridge, UK, which is commercializing enzymatic DNA synthesis. Camena joins a growing field of companies working to develop this method, including Molecular Assemblies, Ansa Biotechnologies, Touchlight Genetics and DNA Script.

Since the 1980s, the only practical way to synthesize DNA has been by the phosphoramidite chemical method[5]. "The estimates that are out there are that for every kilogram of DNA you make with phosphoramidites, you generate over 10 tonnes of waste," says Steve Harvey, Camena's CEO. "A lot of people don't really know that it generates so much waste."

Inside a living cell, however, DNA is assembled using enzymes in an aqueous process. For the past 10 years or so, companies have been trying to make enzymatic de novo synthesis of DNA as fast, accurate and inexpensive as chemical synthesis — and they're getting close.

Enzymatic synthesis has other advantages over phosphoramidite synthesis as well. The chemical synthesis process damages the DNA a little bit each time a base is added, which functionally imposes a maximum length constraint of about 200 bases on the synthetic molecule because the accuracy declines as the length increases. In March 2023, Ansa Biotechnologies, Emeryville, CA, announced that they'd made the longest ever de novo DNA molecule created in a single synthesis, a 1,005-base oligonucleotide. Enzymatic synthesis methods also perform better on complex sequences, including G+C-rich regions and hairpins, which are difficult to make using conventional methods.

Camena's method uses a proprietary mix of enzymes and highly pure reagents to bring down their error rate. Many synthetic biology applications require gene-length fragments, and enzymatic synthesis could turn out to be a faster and more environmentally friendly method for making these longer constructs. Still, Harvey points out, there are steps that could be improved. "There's a little bit of a problem that synthetic biology has at the moment where some things are marketed as a very 'green' or environmentally very favorable solution, but actually the people that market it stop counting at a certain point," says Harvey. "That's greenwashing, right? It's not telling people the whole picture." For instance, he says, while the enzymatic DNA synthesis process doesn't generate organic chemical waste, certain processes for making the nucleotide building blocks requires a large amount of acetonitrile. "You've got to be completely transparent when you're talking to scientists and provide numbers that support what you're doing," he says. "We're on a bit of a journey at the moment, as a company, of how we can tell everyone our whole pipeline."

Plenty of 'low-hanging fruit' remains

Back in 2014, when Martin Farley first created a sustainable science program at the University of Edinburgh, "there weren't a lot of us working in green labs," he says. Farley and other like-minded scientists formed LEAN, the Laboratory Efficiency Action Network, and they entered discussions with funders about how to encourage researchers to go green. "The goal was to get conditions within grants that would drive sustainability," says Farley. They soon realized that, to make this happen, there would need to be some metric by which different labs could be fairly compared on their level of sustainability.

"It was tricky with labs, because they're not all doing the same things," says Farley, who is now the sustainable research manager at University College London. "How do you create something that pushes sustainability but doesn't necessarily penalize somebody for the type of science they're doing? That was the thought behind creating LEAF."

LEAF is the Laboratory Efficiency Assessment Framework, an online tool that researchers can use to estimate the environmental impact of their labs. The program provides actions users can take to reduce their consumption of plastic, water, energy and other resources in their laboratory and includes a calculator to measure the carbon impact of the laboratory and track improvements. Labs can get LEAF-accredited at three different levels — Bronze, Silver, or Gold — depending on the actions they take. Launched in 2021, it has now been adopted by more than 95 institutions in 15 countries.

Similarly, My Green Lab, a private certification company based in San Diego, California, provides assessments and recommendations for changes in lab practices to improve sustainability. "A majority of these guidelines are simple adjustments in lab users' daily habits that have a significant impact," says Jain. "For instance, shutting the fume hoods when not in use and improving lab cold storage management practices can yield substantial savings and foster a greener research environment." My Green Lab has helped over 1,700 labs adopt more sustainable practices.

The University of Southern California's Keck School of Medicine is piloting a program to recycle latex and nitrile gloves through TerraCycle, a company that specializes in difficult-to-recycle materials.

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While My Green Lab enrolls individual labs to make these adjustments, LEAF engages at the level of the institution. "If you can sign up an institution, it might take a little bit more up-front administration, but you get better buy-in long term," Farley says. "The idea was for these programs to have continuity and to last." By working with administration, LEAF adapts to whatever governance structure the institution has in place and sidesteps a common objection to adopting sustainability measures, which is costs. "One of the issues I've seen is that it's not the cost, it's who holds the different budgets," Farley explains. For instance, a new piece of equipment or reusable labware might come out of a faculty budget, while the institution pays the energy bill. "The classic example is that if a lab has to pay for a more efficient freezer, that costs more and they won't see the energy savings, so how do we incentivize that?"

Farley envisions a sustainability model similar to that of health and safety, where these practices are seamlessly integrated into the operations of the institution, and that integration depends on bringing facilities and technical staff on board, not just individual scientists. "Once we get over the hump of understanding how to integrate this, it becomes less cumbersome because it's just naturally within the system," he says.

Scott's Green Labs program at Georgia is working on its own sustainability certification, in which researchers can select the measures they are taking from an online menu. "At that point, the Green Labs professionals meet with them and audit that," Scott says. By starting with the least disruptive interventions, she says, Green Labs can bring researchers on board without adding to their already substantial burden. "These initiatives should not interrupt your research process," she says. "We pick the low-hanging fruit, the things that are going to be easiest for the labs to engage with." Rather than start with purchasing new equipment, she points out how behavioral modifications can not only improve efficiency but also improve the quality of science. Shutting down water baths overnight, Scott says, can save up to $400 per bath per year. Keeping freezer door seals free of icy buildup can not only save energy, but also extend the life of the freezer and prevents temperature pockets from forming. "Now you have better sample storage," she says. "So there's a direct benefit to our researchers from engaging in our program."

Recycling has long been synonymous with community environmentalism, but lab consumables present a challenge. For instance, Scott says that the University of Georgia is unique in their ability to recycle used pipette tips. Ordinarily, recycling facilities can't handle tiny plastic items like pipette tips because they clog up the machinery. "We have a triad partnership that's happening," she explains. "There's a private sector business that part of their waste stream is large polypropylene drums." By filling these drums with lab plastics, including microcentrifuge tubes, Falcon tubes, pipette tips and tip boxes, the recycler can process the entire drum full of lab plastics together.

Used latex and nitrile gloves also make up a large source of waste, but it's not always simple to recycle them. Sarah Hamm-Alvarez, associate dean of basic and translational research at Keck School of Medicine at the University of Southern California, is piloting a glove recycling program in select labs. Glove recycling seemed like a natural place to start because it could be implemented without disrupting established lab protocols while significantly reducing trash. Participating labs receive a collection container from TerraCycle at a cost of $150 each, and the company breaks them down to resell to manufacturing companies. At the end of the 3-month pilot program, Hamm-Alvarez says, data will be collected on how much waste was diverted from the landfill compared with the cost per lab. Right now, a university fund for sustainability pilots covers the program, she says, but it's unclear whether recycling is an allowable use of research grant funding in the long term or if separate funding will need to be found.

In all of these efforts, an important principle is engaging researchers as stakeholders so they feel invested in the outcomes of their efforts. Jeroen Dobbelaere, sustainability manager at the Institute of Science and Technology Austria (ISTA), says that a common flaw he's noticed in institutional settings is the attempt to manage sustainability separately from research. "The researchers have an important role in monitoring what's happening," he says. Even if a policy sounds great in theory, he says, it's important to measure the real-world results and make sure it is working as implemented. "This is something I'm trying to develop now at ISTA: to have a clear monitoring structure," he says. A feedback loop, where people can see the effect that their actions have, helps people stay engaged, he says.

Dobbelaere says the key to successful sustainability management is striking the right balance between top-down and bottom-up initiatives. "Some things need to come from the bottom up," he says. Lab protocols, for instance, need to work well for the particular project and on the right timeline. "But many other things, definitely infrastructure or travel policy, need to be guided from the top down."

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References

1. UK Research and Innovation. *UKRI Environmental Sustainability Strategy* https://www.ukri.org/wp-content/uploads/2020/10/UKRI-050920-SustainabilityStrategy.pdf (2020).
2. Smith, P. et al. *Advancing Environmentally Sustainable Health Research* https://cms.wellcome.org/sites/default/files/2023-08/Research_Sustainability_Report_RAND_Europe_August_2023.pdf (2023).
3. Lannelongue, L., Grealey, J. & Inouye, M. *Adv. Sci.* **8**, 2100707 (2021).
4. Mbatchou, J. et al. *Nat. Genet.* **53**, 1097–1103 (2021).
5. Matteucci, M. D. & Caruthers, M. H. *J. Am. Chem. Soc.* **103**, 3185–3191 (1981).