

Nature Podcast

Introduction

This is a transcript of the 17th May 2018 edition of the weekly *Nature Podcast*. Audio files for the current show and archive episodes can be accessed from the *Nature Podcast* index page (<http://www.nature.com/nature/podcast>), which also contains details on how to subscribe to the *Nature Podcast* for FREE, and has troubleshooting top-tips. Send us your feedback to podcast@nature.com.

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Interviewer: Benjamin Thompson

Welcome back to the *Nature Podcast*. This week on the show, we're probing protons and learning how to maintain a healthy lab environment.

Interviewer: Shamini Bundell

Plus, we'll be finding out how to make sense of mystery microbe genes. This is the *Nature Podcast* for the 17th May 2018. I'm Shamini Bundell.

Interviewer: Benjamin Thompson

And I'm Benjamin Thompson.

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Interviewer: Benjamin Thompson

First up this week, reporter Lizzie Gibney is peering into the heart of matter.

Interviewer: Lizzie Gibney

Here at *Nature*, we talk a fair amount about dark matter. But what about boring old ordinary matter? It may account for just 15% of material in the Universe, but it's a pretty important part. After all, it makes up everything we can see, from stars to us. And even though it's visible, it still hides plenty of mysteries. The bulk of the matter in the Universe is made up of protons. But what makes up the proton? That's where things get a little fuzzy. Protons are far too small to see under a microscope – around 100,000 times smaller than an atom. So instead, physicists study protons by pinging high-energy electrons off them. These experiments show that each proton must consist of more fundamental particles: three quarks, which are held together by the strong nuclear force. But scientists haven't known much about how the quarks are arranged in 3D or anything about the proton's mechanical properties. Only now are physicists developing techniques that allow them to probe inside the proton: the particle that's crucial to anything being here at all. To hear how, I spoke to physicist Latifa Elouadrhiri, who explained how techniques to study the proton have evolved.

Interviewee: Latifa Elouadrhiri

Prior to the 90s, the only thing we could study is one-dimensional structure of the proton. And in the 90s there were developments of new formalism that enabled us to connect

electromagnetic processes to do three-dimensional structure of the proton. Let me just make simple analogy – so what we have we been doing prior to the 90s and 00s, is like we want to study the heart, and we are studying it through electrography, which is the process of just recording electrical activity of the heart that give us one-dimensional structure that tells us lots about the heart, but not everything. Now with the heart, we have the medical 3D imaging technology that now allow the doctors to learn more in non-invasive manner, the structure of the heart. And this is what we want to do with the new generation of experiments.

Interviewer: Lizzie Gibney

And how do you go about doing those experiments then?

Interviewee: Latifa Elouadrhiri

We are firing high-energy electrons at our protons with very precise measurements. But in order to understand the structure, we want to be able to understand the energy and the momentum that is transferred to the quark so that you acquire both the developments in the theory to interpret results, but also developments in the technology to perform the measurements.

Interviewer: Lizzie Gibney

So, new kinds of theory can connect how electrons bounce off the protons with what's actually going on inside the proton, things like the forces on the quarks?

Interviewee: Latifa Elouadrhiri

Exactly, and it's only able to do this interpretation if from the experiment, we have measured all the necessary observables.

Interviewer: Lizzie Gibney

So, what do you actually do then? You fire your electron at the proton, and what happens?

Interviewee: Latifa Elouadrhiri

So, we fire a high-energy electron because by increasing the energy, the wavelength is smaller so we can see deeper into the object. We measure the light that is emitted by the quark, together with the scattered electron, then we also measure the proton. So, we leave the proton intact, we measure it, we measure the produced photon, the light, and the scattered electron. We need to detect all these particles in the final state in order to use the formalism and understand the structure, and that was, this is what was not possible in earlier experiments with electron scattering.

Interviewer: Lizzie Gibney

And what is it then, what did you see, what did you discover about the structure inside the proton?

Interviewee: Latifa Elouadrhiri

So, this is our, the first measurement of the pressure distribution experienced by the quark inside the proton. So, what we found is that there is this extreme outward pressure, but if there was only this pressure in the centre, the proton would explode. But there is another

pressure that is going in the other direction, that balances this pressure at the centre that makes the proton stable.

Interviewer: Lizzie Gibney

Which is something we're very grateful for.

Interviewee: Latifa Elouadrhiri

Yes!

Interviewer: Lizzie Gibney

And can you give me an idea of the scale of the forces that we are talking about, or the pressure at the heart of the proton?

Interviewee: Latifa Elouadrhiri

So, the pressure that we measured is 10 to 35 pascal. This is 10 times larger than, for example, the pressure inside the neutron star.

Interviewer: Lizzie Gibney

Wow, and that's pretty much the densest matter that we know of, right?

Interviewee: Latifa Elouadrhiri

Exactly.

Interviewer: Lizzie Gibney

And does that match with what theorists predicted?

Interviewee: Latifa Elouadrhiri

That matches some of them. There was a model that were theoretical prediction before this experiment, but this is the first observation, yeah.

Interviewer: Lizzie Gibney

And are you going to be able to use this technique to find out anything else about what's going on inside a proton?

Interviewee: Latifa Elouadrhiri

This measurement now is just the beginning of a new field of research. So, the paper we published is related to the pressure distributions inside the proton, but next will be to calculate forces, and then move on and understand the 3D imaging of the proton, the spatial distribution of the quark inside the proton, and also the motion of the quark inside the proton.

Interviewer: Lizzie Gibney

Gosh, so the proton might not be so much of a mystery anymore.

Interviewee: Latifa Elouadrhiri

That's the beginning of solving the mysteries.

Interviewer: Benjamin Thomsson

That was Latifa Elouadrhiri who's based at the Jefferson Lab in the United States, speaking with reporter Lizzie Gibney. You can find her paper over at nature.com/nature.

Interviewer: Shamini Bundell

This week, *Nature* is publishing a special on maintaining a healthy, happy and productive lab. A good environment promotes good research, but sometimes things can go wrong. Research misconduct not only degrades the reliability of research findings, but in the most extreme cases can end a career. Tina Gunsalus is Director of the National Center for Professional and Research Ethics, and she's co-authored a Comment piece outlining the pitfalls of misconduct that can plague departments. She's also come up with a mnemonic, to help researchers identify the causes. Reporter Geoff Marsh gave her a call.

Interviewer: Geoff Marsh

You've worked with troubled departments as part of your job. Could you share some anecdotes of research misconduct that you see coming up time and time again?

Interviewee: Tina Gunsalus

I think what happens is that people with power get cross, they want results, they feel pressured themselves, where are the data, where are the data, why aren't you doing this right? And the person with no power doesn't know how to respond effectively, and doesn't know how to account for themselves, so they start to pretty the data up and make it look like what's expected, as opposed to hewing to the actual results that the actual research provided. So, I think that that's a place that things really go wrong - when people are so afraid and don't have the tools to interact, that they start cutting corners.

Interviewer: Geoff Marsh

Right, so in an effort to help researchers spot the most common pitfalls associated with misconduct, you've created a suitably alarming mnemonic which is TRAGEDIES. Could you break that down for us?

Interviewee: Tina Gunsalus

So, it starts with temptation, rationalisation, ambition, group and authority pressure, entitlement, deception, incrementalism, embarrassment and stupid systems. Most of them you'll see are feelings. Temptation is a feeling. Rationalisation is something entirely internal, you know, and it's always possible to rationalise any scummy thing you want to do. Entitlement is a feeling. Embarrassment is a feeling. Stupid systems is something that we all exist within, all the time, and if you don't know how to deal with the mixed messages and mixed incentives, and sometimes perverse incentives in an environment, you can really easily end up in a career tragedy.

Interviewer: Geoff Marsh

And who do you think that the separate elements of the TRAGEDIES mnemonic kind of relate to? Because it sounds almost like it's mainly focused at maybe the newer scientists who are feeling pressure from above, you know the people at the lower end of the power dynamic. Is that who you're sort of talking to here?

Interviewee: Tina Gunsalus

Actually, I think it's pretty universal. I mean, one of the things I did for several decades of my career was, I was the Research Integrity Officer, and I did, led internal investigations for my university. And that included things that weren't about research, sometimes they were about human subjects, sometimes they were financial, sometimes they were policy violations. And I spent a lot of time investigating very highly-educated, very smart people who had ended up in a situation where they were facing some sort of reputational disaster, shambles. I never met anyone who said, yeah, you know, that was the day I woke up and decided to you know, put my career at risk, potentially go to jail, embarrass my family, lose my job. Organisations are shaped by their leaders, and they're shaped by the human beings within them, and human beings are susceptible to these pitfalls.

Interviewer: Geoff Marsh

Yeah, and so, individually these can actually be quite small occurrences. They kind of ironically don't tend to look like actual tragedies themselves. The point is that they, if you spot them early, hopefully you'll avoid an actual tragedy.

Interviewee: Tina Gunsalus

Sure, I mean I think people don't know what they don't know about how really smart individuals get into trouble. And so, if you learn about the TRAGEDIES, and learn to be aware of them in yourself, and how each one of them feels individually, and how they interact, you have more tools for building other professional skills for having the career that you want to have.

Interviewer: Geoff Marsh

In terms of learning, you mention in the article that training alone, formal training, won't necessarily be as effective for changing attitudes as the informal curriculum, how we see the other people around us working.

Interviewee: Tina Gunsalus

Well, I think that it takes attention both to intentional professional development where people teach practical professional skills, that include how to have disputes and how to raise questions, and it includes attention to the informal environment and the informal curriculum. What happens when someone makes a mistake here? How do we treat them? Is it educational or is it shaming and blaming? So, there's a whole series of things and they interlock. There's not one magic bullet, it's being aware of and taking responsibility for our professional conduct and our professional environments.

Interviewer: Geoff Marsh

What advice would you give to a young PhD student, who did spot some ethically dubious behaviour going on from above?

Interviewee: Tina Gunsalus

Well, I think there are two parts to it, and the most cited paper I ever wrote is called 'How to blow the whistle and still have a career afterwards', and the first six steps are all about how to assure that you're actually in a situation that requires that, because it's very easy at the bottom of the power curve when you are working so hard, to get tunnel vision and not see

the bigger picture. And then, and only then, do you follow the steps for actually blowing the whistle, and there are effective ways to do it. So, there are things that work and things that don't work, and you have to know that. You don't know what you don't know when you start out, and that's what intentional professional development is about, and that's why learning about the TRAGEDIES is important.

Interviewer: Geoff Marsh

How do you think research departments should be sort of assessing their own conduct health?

Interviewee: Tina Gunsalus

Well I think there are two very time-effective ways to do it. One of them is the Survey of Organizational Research Climate, the SOuRCe, which can be done in under fifteen minutes. We also have an informal, very quick self-assessment called the Academic Unit Diagnostic Tool available on our website that just gives you a place to start having conversations.

Interviewer: Shamini Bundell

That was Tina Gunsalus talking with Geoff Marsh. You can read more about TRAGEDIES and how to avoid them in her co-authored Comment over at nature.com/news, along with the rest of the special issue, filled with tips and advice for keeping lab culture healthy.

Interviewer: Benjamin Thompson

Still to come in the show, we'll be taking a look at the most cited science on Wikipedia. That's coming up in the News Chat. Right now though, Noah Baker's here, and he's bought the Research Highlights with him.

[Jingle]

Interviewer: Noah Baker

Flesh-eating bacteria have an excruciating trick up their sleeves. *Streptococcus pyogenes* destroys skin and soft tissue. But before these symptoms even show up, the infection is extremely painful. Now, researchers have found out why. The bacteria actually release a toxin, which cause pain-sensing neurons in the brain to fire. This sends signals to the immune system to hold back its response. When researchers blocked the neuron signals in mice, the immune system could fight off the infection. The hope is that this could help treat this gruesome disease. Find that paper in *Cell*.

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Interviewer: Noah Baker

Holidays are heating up the planet. Researchers used an in-depth model to unpick the impact of tourism, and found that worldwide, it's responsible for 8% of greenhouse gas emissions. That's quadruple what scientists had previously thought. Plus, this carbon footprint is increasing over time. According to the researchers, American tourists have the biggest footprint, but the impact varies from destination to destination. A holiday in the Maldives has the biggest carbon cost, which puts the country in a tricky situation. Tourism is the largest contributor to the Maldivian economy, but as a low-lying island nation, it's also

one of the countries most threatened by sea level rise. Find out more in *Nature Climate Change*.

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Interviewer: Shamini Bundell

Sequencing the first human genome took scientists around the world 13 years. Today, that time has been reduced to days, if not hours. But while science may be able to tell you the sequences of genes in your body, in many cases it can't tell you what the proteins that the genes code for actually do. The same is true for bacteria – you can sequence a bacterial genome, but how do you work out what all those genes are for? I rang up Adam Deutschbauer, to find out how his research is trying to keep up with advances in gene sequencing.

Interviewee: Adam Deutschbauer

The ability to sequence genomes and genes is just extraordinary. It's really, really easy, right, so we have just in databases, we have millions and millions of different gene sequences, and virtually none of those genes have been studied experimentally.

Interviewer: Shamini Bundell

Why is it hard to figure out what all these genes are doing?

Interviewee: Adam Deutschbauer

The reason why it's hard to figure out the function of a gene, is that there's actually not that much data beyond genome sequence in microbiology. And so, the best that we can do, because we have the sequences of so many genes, is there's basically servers that will try to predict the functions or annotate the functions of genes using automated approaches.

Interviewer: Shamini Bundell

And how are these, like, databases making these predictions about function, just based on a gene sequence?

Interviewee: Adam Deutschbauer

All of the existing servers do it based on the sequence similarity, the something that they have in their database, right? So, they will say, well your, you know, your protein that you sequenced is 40% identical to some characterised protein family. The issue is that we know that even for a closely related genes and proteins that have a high sequence similarity, they can perform very different functions within the physiology of a different bacterium.

Interviewer: Shamini Bundell

And there are people out there doing studies on particular proteins, and obviously it takes a lot of time and effort. And as you've said, we're sequencing more and more bacterial genomes every day, we have more and more data and we can't keep up with the, sort of identifying the protein functions, or annotating the protein functions. So that's where you and your colleagues have sort of taken a slightly different approach to solving this problem.

Interviewee: Adam Deutschbauer

The approach that we take is large-scale genetics. So, I'm trained with a geneticist, right, Genetics 101 is that you make mutations in an organism, and then you ask what are the consequences of making the mutation. So, the consequences, what you can measure, and the organism that we call the phenotype. And, that's basically exactly what we did in our story. We made and measured lots and lots of phenotypes of mutants in bacteria across many, many conditions.

Interviewer: Shamini Bundell

And how difficult was it to do something like that at scale, because I can imagine you could take a particular gene, introduce a mutation, and you look at the outcome for that bacterium, but how do you do that for multiple genes?

Interviewee: Adam Deutschbauer

We actually make a large population of mutants in a given bacterium, and we mix together say 100,000 different mutations of an organism, and we mix them all together in the tube and we let them compete against each other under different growth conditions. And so, as they're competing in different growth conditions, we can measure which genes when knocked out were the winners, and which ones were the losers, across many, many conditions.

Interviewer: Shamini Bundell

So, if you're growing bacteria in conditions where they need to, for example, get carbon from a particular food source, or be able to resist an antibiotic, you can then find out based on which bacteria do well, which mutations are beneficial or harmful to those processes.

Interviewee: Adam Deutschbauer

So, if you take a population of 100,000 mutants, and many of those mutants are in say, a gene involved in eating sucrose, right, as a carbon substrate. If I grow that population, that population of mutants, and I let them compete against each other in a condition where the only food is sucrose, then those mutants won't grow.

Interviewer: Shamini Bundell

And then that's how you know that that gene has something to do with sucrose metabolism. But then you didn't want to target specific genes for mutations, you actually created a whole load of mutations, tested them all, and then just sort of looked at what came out.

Interviewee: Adam Deutschbauer

Yeah, we tried to develop an approach that was scalable enough, and cheap enough, that we can measure at least genetically, sort of like measure everything for all genes.

Interviewer: Shamini Bundell

So, your experiment obviously couldn't measure everything, but you got quite a big dataset. How many genes were you then able to predict or guess functions for?

Interviewee: Adam Deutschbauer

You know, we created lots and lots of genetic data across 32 different bacteria, and we have phenotypes for thousands and thousands of genes. The number of genes though that we can make really specific inferences about in their function, is probably in the order of like 600 or so.

Interviewer: Shamini Bundell

And so, if you've only got, well 600 is still quite a lot, but those are the ones you're more confident in, but are the other data, this massive dataset, is that still going to be useful for you or other researchers?

Interviewee: Adam Deutschbauer

We hope so. My colleague Morgan Price created an interactive website for the comparative analysis of all of this data.

Interviewer: Shamini Bundell

And that anyone could go to, and find information about their specific protein that they're looking in, or their particular species, or a particular pathway?

Interviewee: Adam Deutschbauer

Yes, so you can go to our site now and you can enter a sequence of your favourite protein, and basically do a search against all of our data, and find if we have data for any relatives of your favourite protein. You know, I think long term, right, because we can only mine the data so much ourselves, my hope is that ultimately there's going to be multiple large databases of experimental data across many, many bacteria, that can be used to augment the existing annotation servers.

Interviewer: Shamini Bundell

That was Adam Deutschbauer of the Lawrence Berkeley National Laboratory. You can find his paper online in the usual place: nature.com/nature.

Interviewer: Benjamin Thompson

Right then listeners, it's time for this week's News Chat, and I'm joined here in the studio by Nisha Gaid, one of the News Editors here at *Nature*. Hi Nisha.

Interviewee: Nisha Gaid

Hi Ben.

Interviewer: Benjamin Thompson

Thanks for joining us. Two stories today, and our first one, we're going to be delving into some, well, some metrics from Wikipedia, and I don't think I need to explain to listeners what Wikipedia is, but what's the story about?

Interviewee: Nisha Gaid

This is a really interesting story, a little data story that shows what are the most cited journal articles on Wikipedia.

Interviewer: Benjamin Thompson

Okay well who's been doing this data diving then, and what specifically have they been looking at?

Interviewee: Nisha Gaid

So, the Wikimedia Foundation, which runs Wikipedia, released loads of its citation data, and a data scientist called Matt Miller looked at the data to see what the top-cited articles which had DOIs, which I'm sure lots of listeners will know are identifiers for scientific articles, looked at what the top ten most-cited DOI articles are.

Interviewer: Benjamin Thompson

Alright then Nisha, well lot's not muck about – what's the number one article then?

Interviewee: Nisha Gaid

The most-cited article on the English language version of Wikipedia is a collection of human and mouse genes, and in fact there are lots of DNA sequence collections and gene collections throughout the top ten most-cited DOI journal articles.

Interviewer: Benjamin Thompson

Hmm, and how many citations does the number one spot have then?

Interviewee: Nisha Gaid

So, across all of English Wikipedia it's got 4,700 citations, and what's interesting about that is that that's a lot more than it has even in the scientific literature.

Interviewer: Benjamin Thompson

Well listeners, back in 2014 we had a Feature article that looked at the top 100 citations in academic papers, and that was according to the Web of Science. Nisha, many of the top papers in that study were methods papers, which seem a lot more sparse in the Wikipedia citation list.

Interviewee: Nisha Gaid

Yeah, so what's interesting about this, and maybe expected, is that lots of the most-cited articles are collections, reference collections, and really interestingly one of the papers which is the third most-cited paper, is a collection of the nomenclature of lunar craters.

Interviewer: Benjamin Thompson

Oh really? So space is always in there, everyone loves space.

Interviewee: Nisha Gaid

It's always in there. Published in 1971, has thousands of citations on Wikipedia, but just 16 in the scientific literature.

Interviewer: Benjamin Thompson

Okay, and I guess that makes sense then, because I suppose each of these craters presumably has its own Wikipedia page, and each of them referenced this paper.

Interviewee: Nisha Gaid

Exactly, so lots of individual craters will have a page, and the same goes for genes, and they all tend to reference reliable collections that have this information.

Interviewer: Benjamin Thompson

So that's the top ten of sort of English language Wikipedia then, but of course Wikipedia is a lot more than that. Have people been looking at sort of different languages as well?

Interviewee: Nisha Gaid

Yeah, so the initial release from the Wikimedia Foundation contained information about citations across all of its language editions, and there are nearly 300 of them. So, someone else has looked at the top DOI citations for the whole of Wikipedia, and it's got a really different paper in the number one slot, which has been cited almost 3,000,000 times. So, this article is a climate paper that looks at how the climate varies around the globe, and the reason that it's been cited so many times is because it's cited on lots of articles that are created by a bot, which is an automated computer programme that just creates articles and automatically cites this article.

Interviewer: Benjamin Thompson

Well that's obviously kind of a heck of a data dive then, but to what end though? What value does this data have?

Interviewee: Nisha Gaid

Citations are really important, whether in Wikipedia or in the scientific literature, because they enable people to trust the information. And what's really interesting about this study is that we can actually get at this citation data, and do these sorts of comparisons, which is actually quite difficult to do if you're comparing it to the scientific literature because lots of that information is behind paywall services.

Interviewer: Benjamin Thompson

Alright then Nisha, well let's move on to our second story then this week, and this is about dams and their effects on ecology. Often, I guess when we think about dams being built, we think about how this might negatively affect sort of wildlife in the area, but this new story perhaps is a little bit different.

Interviewee: Nisha Gaid

Yeah, so this story is about dam removal rather than dam building, which we don't often talk about much. And the story is about a very large dam in Spain, which is about to be removed, and it's going to be the biggest dam removal project in the European Union.

Interviewer: Benjamin Thompson

Well why are scientists interested in this then?

Interviewee: Nisha Gaid

So, dams and dam removal is quite important for the ecology of an ecosystem. And the removal of this large dam in western Spain is being hailed as a milestone by ecologists for river restoration efforts. It could help to revive some of the rivers ecosystems.

Interviewer: Benjamin Thompson

And are there any examples where sort of a dam removal has made a difference in the past?

Interviewee: Nisha Gaid

Yeah, absolutely. In the United States, more than a thousand barriers have been removed in recent decades, and they've generally had very positive effects on local ecosystems. For example, they've improved the habitats of species including certain types of salmon.

Interviewer: Benjamin Thompson

And is this endeavour in Spain part of a sort of wider trend then?

Interviewee: Nisha Gaid

Yeah, it looks as though dam removal is actually on the up around the European Union, after a piece of legislation was introduced in 2000. Now this legislation requires member states to improve ecological protection of rivers and lakes, and because there are hundreds of thousands of dams, some small, some large, many are no longer used, but their presence threatens the habitat of fish and wildlife.

Interviewer: Benjamin Thompson

I guess that some, many perhaps, of these dams were put up without necessarily thinking about local ecosystems. If this is a work in progress, how can we make sure that nothing bad happens?

Interviewee: Nisha Gaid

These projects do absolutely have to be monitored for negative effects as well. Dams are often huge structures, and their removal could damage the surrounding environment. They might allow invasive species to come into freshwater ecosystems, or they might move toxic sediment. So, experts are saying that even though dams might have been built with little regard for the impacts they might have on the ecosystem, we shouldn't be making the same mistake when they're then being removed.

Interviewer: Benjamin Thompson

Well finally from me then this week Nisha, what happens next?

Interviewee: Nisha Gaid

So, there are a number of small dams that are scheduled for removal later this year, in countries including the Netherlands, Denmark and Spain. But next year, French scientists are planning to monitor the removal of two massive hydropower dams, one of them 35 metres tall and the other 15 metres tall.

Interviewer: Benjamin Thompson

Oh my goodness, right, well, watch this space then – we'll see how that goes next year. Nisha, thanks for joining us, and listeners for all the latest science news head over to nature.com/news.

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Interviewer: Shamini Bundell

That's it for this week's show. Don't forget to follow the podcast on Twitter, we're @NaturePodcast. And if you'd like to get in touch, you can do so on email: podcast@nature.com. I'm Shamini Bundell.

Interviewer: Benjamin Thompson

And I'm Benjamin Thompson, thanks for listening.

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