Nature Podcast

Introduction

This is a transcript of the 18th January 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: Adam Levy
Welcome to this week's *Nature Podcast*. In the show, we're asking when babies get their first bacteria, and how sensitive the climate is to carbon-dioxide.

Interviewer: Shamini Bundell
Plus super-fast photography and peckish penguins… I'm Shamini Bundell.

Interviewer: Adam Levy
And I'm Adam Levy.

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Interviewer: Adam Levy
When did you first come into contact with bacteria? Of course, everyday we're practically swimming with microbes. But what about before we enter the world, while we're still in our mothers' wombs? For a long time the womb has been thought of as a pristine environment.

Interviewee: Marcus de Goffau
At first it started off that people all thought it was sterile, more or less. If bacteria start multiplying over there then things are going wrong.

Interviewer: Adam Levy
This is microbiologist, Marcus de Goffau. The idea that of the sterile womb has been around for a century but recently researchers have started to challenge this dogma and not everyone's on board.

Interviewee: Marcus de Goffau
Well I would say that the current understanding is quite in flux, so people saying one thing and other people saying another.

Interviewer: Adam Levy
One of the researchers arguing that the womb may not be sterile is obstetrician, Kjersti Aagaard.

Interviewee: Kjersti Aagaard

Our work published in 2014 certainly challenged in a very formal sense, this notion of, quote unquote, how sterile the uterus environment is.

Interviewer: Adam Levy
Kjersti's 2014 work investigated the placenta, the link from the developing baby to the mother that feeds the foetus while protecting it from infection. Kjersti tested hundreds of placentas and, surprisingly, gene sequencing detected bacteria in many of the samples. Finding bacteria in the placenta had long been seen as a sign of problems with a pregnancy but Kjersti was finding DNA even in placentas from healthy pregnancies. This suggested to her that these bacteria may not be harmful but actually an important part of development. And, if the womb is not in fact a sanctuary from bacteria, this raises all sorts of questions as to what they're actually doing there. Kjersti wonders if they might have a role to play in everything from our developing digestion to our early immune system.

Interviewee: Kjersti Aagaard
How does a foetus' developing immune system become educated to what is potentially pathogenic or dangerous microbes? And which ones are commensal and friendly? It's important for us to understand where those microbes come from and what they do, not just kind of trace the lineage but to really understand that function of a mum and a baby being in some level of communication.

Interviewer: Adam Levy
Other researchers are also fascinated by the possibility that the placenta may have its own community of bacteria – a microbiome. There's been a wealth of work to characterise what role these placental microbes could play. This body of research gives Kjersti confidence in her findings.

Interviewee: Kjersti Aagaard
There are literally dozens and dozens of labs that have been able to replicate our findings from different corners of the globes and using different techniques. There's certainly one paper that couldn't replicate our findings but they used very different techniques in doing so.

Interviewer: Adam Levy
But to some, this one paper's failure to replicate is more than an anomaly. One researcher with serious doubts is Marcus who we heard from earlier.

Interviewee: Marcus de Goffau
I'm currently working at the Sanger Institute as a Postdoctoral fellow on the supposed placental microbiome.

Interviewer: Adam Levy
This study, Lauder et al., couldn't differentiate between the DNA extracted from placentas and DNA found on lab equipment. To Marcus this implies that researchers haven't found some kind of placental microbiome. Instead, he thinks they have just been inadvertently detecting sequences from their labs.

Interviewee: Marcus de Goffau
From their DNA isolation kits or their PCR kits and all we're seeing is basically rubbish and contamination.

Interviewer: Adam Levy
What's more, is Marcus says he has conducted similar research, as yet unpublished, that also failed to differentiate placental bacterial DNA from the DNA found on lab kit. But Kjersti isn't ready to throw away the dozens of studies on placental bacteria just yet. After all, her own study tested empty vials to compare placental samples to and detected differences. Plus, her study showed differences between placentas from mothers that had given birth early, or at full term, as well as between mothers who had had or hadn't had infections during pregnancy.

Interviewee: Kjersti Aagaard
So it's not that every single placenta that we analysed looked the same. They actually differed based upon discrete pregnancy characteristics, again arguing against the notion that this was simply contaminant out of the built environment in which we were working.

Interviewer: Adam Levy
Marcus, and others, remains deeply sceptical. He not only feels that these differences could be explained by contamination but that a great deal of microbiome research might have similar issues.

Interviewee: Marcus de Goffau
It's not just the placenta that has this problem. There are lots of studies out there looking at human tissues and they report all these different types of bugs in there and all of these papers basically they are producing nothing.

Interviewer: Adam Levy
So then, when do we first encounter bacteria? Do healthy placentas contain bacteria that play some role in our development in the womb? It seems more work is needed before consensus is reached. For Kjersti this means developing a better understanding of what roles such bacteria would have.

Interviewee: Kjersti Aagaard
I really think it's going to be continuing to describe what that function of these placental microbes must be. Being able to show that there's a translatable step between what a pregnancy exposure is and the end result on an offspring's microbiome.

Interviewer: Adam Levy
But for Marcus, seeing is believing and nothing he's seen so far has convinced him.

Interviewee: Marcus de Goffau
You would need multiple different study approaches, so not only sequencing but also microscopy, and on the sufficient magnification that you can actually see the bacteria.

Interviewer: Adam Levy

That was Marcus de Goffau. You also heard from Kjersti Aagaard who's at the Baylor College of Medicine in Houston, Texas. Studies are now getting under way that could answer the question of baby bacteria once and for all. To find out about them, and more on the divides between some researchers, read the feature in this week's *Nature*.

Interviewer: Shamini Bundell
Still to come, wild sex turns explosive.

Interviewer: Adam Levy
That is and incredibly clickbait-y way of describing it.

Interviewer: Shamini Bundell
It is technically accurate though, right?

Interviewer: Adam Levy
Technically – yes, technically it is accurate.

Interviewer: Shamini Bundell
Well, listeners, you can judge for yourselves in the News Chat at the end of the show. But before we get to that, Benjamin Thompson is here with this week's Research Highlights.

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Interviewer: Benjamin Thompson
Atoms are running out of places to hide. Powerful X-ray pulses can now see right through molecules in a matter of femtoseconds. Physicists use a particle accelerator to agitate electrons until they emit bright bursts of x-rays, squishing the electrons tightly together, just before release the x-rays, stops them from repelling each other. This generated a laser beam that lasted just ten quadrillionths of a second. Such snappy snaps can reveal the atomic structure of a molecule before the x-rays cause any damage. The flashy technology could help scientists study individual viruses in high definition. Shine a light on that story over at *Physical Review Letters*.

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Interviewer: Benjamin Thompson
I knew I wasn't the only one who enjoyed a late night snack. It turns out that paternal penguins also enjoy eating after dark. Emperor penguins often go several months without eating while they make their way in land to mate and then sit on their eggs throughout the long, dark, winter. However, males in a colony in Southern Antarctica found a way around this long fast. Satellite tags on four males caught the birds shuffling off the ice for a furtive fish supper at night. They did this during the mating season but before being landed with egg sitting duty and it was only possible as their colony was unusually close to the water. This sneaky snack would give them an energy boost and reduce their time spent fasting. But diving into the dark is risky business. More penguins may have to do this as the colonies are forced further south by thinning ice. Devour more of this research over at the Journal of Experimental Biology.

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Interviewer: Adam Levy
Next up, Benjamin's back and he's brought a story about climate change.

Interviewer: Benjamin Thompson
Last week on the *Nature Podcast* we did some future gazing, trying to predict what the big science stories might be for 2018. One of these predictions was that countries that signed up for the 2015 Paris Climate Agreement would be outlining their progress towards meeting their climate change targets. The agreement aims to stop the world warming by more than two degrees Celsius and ideally keep the warming under 1.5 degrees. But how much more might the temperature rise? This depends first and foremost on how much carbon dioxide we emit. But even if we knew this, there's a great deal of uncertainty about what might happen. In the past few weeks, two papers have been published in *Nature* that use different methods to try and constrain this uncertainty. But why is this something that needs to be done? Here's Patrick Brown from Stanford University, the author of one of the papers.

Interviewee: Patrick Brown
Well, just from a scientific perspective we always want to narrow the ranges of uncertainty around various things. As a physical climate scientist, I want to understand the physical climate system as best that I can. From a more practical perspective, if we're interested in, say, limiting global warming to below two degrees Celsius, it's useful to know exactly how much emissions we can put into the atmosphere before we're very likely to exceed that threshold.

Interviewer: Benjamin Thompson
In a paper published this week, another climate scientist, Peter Cox from the University of Exeter, is looking at how sensitive the climate is to carbon dioxide. The more sensitive our planet, the higher temperature will rise for a given amount of emissions. A common measure of this is the equilibrium climate sensitivity. It's a bit of an abstract concept though, as Peter explains.

Interviewee: Peter Cox
Imagine that you just did a very crude experiment on the climate system, which is to double the carbon dioxide level in the atmosphere, and then you waited for the climate to come to equilibrium. And by equilibrium we mean for the temperature to stop going up. The equilibrium climate sensitivity is how much the globe will have warmed so in some ways it's the simplest possible metric of how the climate will change in response to CO2 increases.

Interviewer: Benjamin Thompson
So a climate sensitivity of two degrees means that if all we do is double the world's CO2, we could eventually expect a two degree rise in temperature but even for this simple measure, there's a great deal of uncertainty as to what the sensitivity might be. The United Nations' Intergovernmental Panel on Climate Change, known as the IPCC have put a range on sensitive as being between 1.5 and 4.5 degrees based on a wealth of available data. What's more, this range of uncertainty hasn't shrunk substantially in over 20 years. One way of

understanding how temperature depends on CO2 is to see how temperature has varied with carbon dioxide levels over the recent past. Using this historical trend in temperatures is a common way of estimating equilibrium climate sensitivity but there are many confounding factors. Peter's team did use historical temperature records, but actually they ignored the overall upward trend in these temperatures. Instead they looked at the noisy fluctuations in temperature that can be seen in the historical record. They showed that the size of these fluctuations can be linked to the climate sensitivity and so measuring these fluctuations accurately provided a more precise measure of the equilibrium climate sensitivity.

Interviewee: Peter Cox
Whereas the IPCC typically quote a range of 1.5 to 4.5 degrees Celsius for equilibrium climate sensitivity, our likely range is 2.2 to 3.4, so the central estimate is not so different from the IPCC; it's slightly on the low side. It's about 2.8, but the range of likely ECS values is hugely reduced by about 60%.

Interviewer: Benjamin Thompson
Of course, very little in this world is straight forward and there's some uncertainty about how to reduce the uncertainty in equilibrium climate sensitivity. Indeed, only a few weeks ago, Patrick Brown, who we heard from earlier, published a study which used a different method for estimating the climate sensitivity. This work looks at models – the complex software that simulates the physical processes of the climate – and tries to pick out the ones that would estimate the sensitivity most accurately. To do this, Patrick focuses on the energy budget in the upper atmosphere and that's the relationship between the energy coming in from the sun and that radiated up by the earth.

Interviewee: Patrick Brown
If there's a relationship between how skilful a model is at simulating the recent past where we have observations, if there's a relationship between that and how much warming they produce in the future, then we can use observations to essentially shift the projections of the future warming, such that they're emphasising the models that are most skilful over this time period when we have observations.

Interviewer: Benjamin Thompson
And it turns out that the most skilful models at simulating the recent past, tended to be the ones that predicted the highest warming in the future. But how do these two studies compare? Patrick's estimate of the equilibrium climate sensitivity range is between 3.0 and 4.2 degrees, while Peter's is between 2.2 and 3.4. Although it's important to note that they use different confidence limits, there are clearly differences between the two ranges and these sit alongside many other estimates derived from different methods. So if two new efforts to produce uncertainty are giving different results, are things just as uncertain as when we started? Do we risk presenting policy makers and those planning for the future with an information overload?

Interviewee: Patrick Brown
Yeah, I mean I think that's a legitimate risk from the perception of the public which I think is why it's important to have assessment reports like the IPCC or the Royal Society or National Academy of Sciences to really say, okay, let's not take any individual study too seriously. No-

one should take our estimate as gospel and no-one should take this new estimate as gospel. You should take into account the full range in the literature and I think over time as studies come out and progress over years and decades, that kind of central estimate can change and I believe that our estimate will stand the test of time but we will see. That's not for me to say at this point.

Interviewee: Peter Cox
I think there is a responsibility for climate science to reduce the uncertainty, the things that matter most. A colleague of mine recently said that you don't get to decide whether your work is worthwhile, it's for the community to decide if it's worthwhile. I hope this is part of a way to say let's use everything we've got and the data we've got which is increasing by the minute to get a handle on these things by combining models and observations and theory together in a way that surprisingly doesn't happen very often.

Interviewer: Shamini Bundell
That was Peter Cox. You can read his paper, and a News and Views article over at Nature.com/nature. You also heard from Patrick Brown. His paper's available at the same address.

Interviewer: Adam Levy
Time now for this week's News Chat, and reporter Ewen Callaway joins us in the studio. Hi Ewen.

Interviewee: Ewen Callaway
Hello there.

Interviewer: Adam Levy
Now, first up, China has been trying for some time to build AI research. What's the status of things as they are right now in China?

Interviewee: Ewen Callaway
Well the news we're reporting this week is, my colleague, David Cyranoski who's based in Shanghai has reported that a mountainous district in western Beijing is likely to be the seat of a new kind of AI, Artificial Intelligence Business Park. The Chinese government is interested in investing about 2.1 billion in creating this industrial park in hopes of luring AI start-ups and companies to plant themselves there.

Interviewer: Adam Levy
And hope seems to be to some extent the operative word because at the moment China seems to be finding it somewhat difficult to attract the researchers they want.

Interviewee: Ewen Callaway
I think that's the theme in the story, is that it's an open question. If you build it, will they come? I think is what the story is asking. And there's some sources quoted including people from Microsoft's AI outfit in China that aren't sure if researchers want to move to a, what sound like a rural area known for its temples and mushroom production. So that seems to

be the real open question, you know. China's government can invest all this money but are they going to get the talent, are they going to get the companies?

Interviewer: Adam Levy
But this isn't a new issue for China. It seems like China to some extent has been struggling to get the talent for a little while.

Interviewee: Ewen Callaway
Yeah I think that's what seems to be the case. I think Chinese universities are training lots of students who are highly coveted for their skills in machine learning and other techniques that comprise AI. But it sounds like a lot of them are being lured overseas to the US, to Canada, to Israel where you've got companies flush with cash there and universities with a lot of expertise. So, yeah, China's having some trouble retaining its students.

Interviewer: Adam Levy
Is money just the problem? Are researchers just being offered more in countries like the US?

Interviewee: Ewen Callaway
I'm not sure if that's entirely the case because as the story reports, some Chinese companies take advantage of AI including Tencent and Baidu who are offering people a million dollars per year in salary so I don't think that can be the only part of the story.

Interviewer: Adam Levy
Is this an issue that is specific to universities and companies in China. I mean, Artificial Intelligence is quite a big field worldwide.

Interviewee: Ewen Callaway
Yeah, I don't think so. I think this is a global trend. Companies are really, really competing for what they perceive as a dearth in talent, in people who have the skills to develop these systems. We hear about companies like Deepmind and others establishing labs in Canada. I think Deepmind opened a facility in Alberta and that's because there's a pipeline of talent coming out of universities there. So the same thing that's happening in China is happening all over the world.

Interviewer: Adam Levy
Let's move on from Artificial Intelligence to a story that you wrote on artificial sex. Researchers are trying to make species unable to reproduce. Why is that something that you'd want to be able to do?

Interviewee: Ewen Callaway
Well, the sex isn't artificial. At least they're trying. So, this research is about establishing reproductive barriers. So two populations, two organisms can't interbreed which, by some definitions, you could say that makes them separate species. I'm not a systematist; I'm not going to get involved in that. The goal in doing this – I mean, you can think of a lot of reasons why you might not want one organism to interbreed with another. If you've got a GM crop that has pesticide resistance or makes a really valuable pharmaceutical, you don't want it mixing genes with either regular domestic crops, unmodified crops, or with weedy

relatives that it's inter-fertile with. So you can imagine that as being one of many reasons why you might want to prevent sex.

Interviewer: Adam Levy
So is that what the researchers are aiming to do, to stop some kind of artificial variant breeding with potentially natural species?

Interviewee: Ewen Callaway
The definite goal here is to prevent a genetically modified organism from breeding with an unmodified organism, be it wild or domestic. But it's not just bio-containment that this would be useful for. My reporting suggested that this technology, this way of keeping populations from breeding, could actually be used to control pests and invasive species. So if you can have a GM species or a GM population that can't interbreed with, say, a mosquito that's transmitting some sort of disease, you can actually, by deploying large numbers of your GMO mosquito you can actually tilt the population so that one is favoured and the wild mosquitos eventually can't find anyone to breed with because their offspring aren't fertile.

Interviewer: Adam Levy
It seems like whenever we cover stories like this it often comes down to trying to eliminate malaria carrying mosquitos.

Interviewee: Ewen Callaway
That's an easy target. I mean, malaria is one of the world's leading killers and I think there's a reason people are looking to apply genetic technologies to control malaria carrying mosquitos, though the mosquito, I believe, that these researchers are interested in is the one that carries dengue and Zika and chikungunya, not malaria – at least not yet.

Interviewer: Adam Levy
And in terms of how it actually works, what have the researchers done?

Interviewee: Ewen Callaway
It's kind of a tricky but quite ingenious system and when I wrote about it, I made it analogous to a poisoned antidote and the poison in the system is based on, basically, cranking up the expression of a gene, any gene whose expression, when you turn it all the way up, is toxic, so, in their proof of principle experiments in yeast, they found that they could turn up the expression of this cytoskeletal protein called actin and if you do that, yeast cells pop. Now, the antidote is basically a kind of a mutated sequence next to this gene that makes it impossible for the mechanism they use to crank up expression. So if you have two yeast cells and they breathe and they carry both the poison and the antidote, they're fine. The sex is all good. But if you have a yeast cell that has both the poison and the antidote so it's fine and breed it with a yeast cell that has neither, that lacks the antidote, then a lot of its offspring are popping like balloons in their experiments.

Interviewer: Adam Levy
Now does this always work or could life find a way around this?

Interviewee: Ewen Callaway

Of course life could find a way around this. I think resistance to something like this is inevitable. You can think up some smart ways to overcome it. Some researchers I spoke with, they weren't completely convinced that the system itself was evolutionarily stable. They thought that an organism carrying both this poison and antidote, that it might be at a competitive disadvantage, compared to wild organisms, making it hard to replace them, so a lot of work needs to be done. These are only proof of principle experiments but they have high hopes for this and, you know, I think time will tell whether this approach is successful.

Interviewer: Adam Levy
Thank you, Ewen. For more on that explosive sex story – and other less raunchy science news – head to nature.com/news.

Interviewer: Shamini Bundell
That's it for this week but for more ways scientists are taking a swipe at mosquitos, check out the Ewen's podcast piece from the 5th October 2017 episode, where he found out about breeding malaria-free mozzies.

Interviewer: Adam Levy
We'll be back next week with all the latest and greatest research. Until then, I'm Adam Levy.

Interviewer: Shamini Bundell
And I'm Shamini Bundell.

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