



## Futures in Biotech, 43: Temporal Alien Mammoth Overlords

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Futures in Biotech, Episode 43: Temporal Alien Mammoth Overlords

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[Music]

### Marc Pelletier

This is our second edition of FiB Live, right? We have – we decided to do something a little different because of the fact that we are going live and what I thought it would be really fun at this stage of the game, since there's been 42 episodes, pretty much using the same format except for one, which is about two years ago, we wanted to do a panel show.

And I've brought on four people that I think are really, really interesting, one in part for the work that they do, but also they are very interesting characters. So – and many of them are podcasters, and/or involved in new media and they have done a dual life kind of situation.

So to quickly introduce, around the table we have Andre Nantel who's a senior research officer and adjunct professor at the National Research Council of Canada and he's a project manager of the DNA micro-array lab for the NRC. Welcome, Andre.

### Andre Nantel

Hey dudes.

### Marc Pelletier

By the way, Andre was – I should mention it here, he was on Episode 5 and he had a great episode on DNA micro-arrays and I learned a lot from that episode. So if anybody wants to know anything about how one can probe the function, the live function of thousands and thousands of genes, then you can go back to one of the early episodes with Andre.

### Andre Nantel

Very early.

### Marc Pelletier

Very, very early. He was also my mentor and taught me most of what I know in the lab. Him and Daniele Tesse [ph] really twisted my arms and showed me how to clone a [indiscernible].

### Andre Nantel

That explains an awful lot suddenly.

### Justin Sanchez

Lots of arm twisting there.

**Marc Pelletier**

Well arm twisting – they were shaking me into doing it right.

**Andre Nantel**

I wasn't even his boss, I was just a lab mate.

**Marc Pelletier**

Yes, but our boss was a very, very busy man and a very thoughtful and intelligent man. But you were the one who's bench was right beside mine. So you were the first person I'd ask 'how do I do this how do I do that, how do I do this?' And it was pretty constant for five years. So you managed to survive that.

**Andre Nantel**

Me at the bench, that was a while ago.

**Marc Pelletier**

Exactly. Next we have Vincent Racaniello who's a professor of microbiology at Columbia University Medical Center.

**Vincent Racaniello**

Hello, everybody.

**Marc Pelletier**

Hello. And he's the host of This Week in Virology, which is twiv.tv. So we've recently done a couple of episodes with Vincent. We did an episode with Peter Palese on influenza virus, which is the history of the – we did the Spanish Flu and we talked about Dr. Peter Palese's work. And he was involved in bringing back the Spanish Flu of 1918 that killed 50 million people in three months. So, and that –

**Vincent Racaniello**

We should clarify that he didn't bring back the one that killed 50 million people.

**Marc Pelletier**

No, no sorry. He cloned it in to his lab to study it, thank you very much, Vincent. He didn't bring it back to infect the world, he brought it back to do an incredible level of research on it and he's an amazing scientist and so Vincent helped produce that show and co-host it, which was a lot of fun.

And then we did a show, it was the last show, last episode on influenza, so welcome to the show, Vincent.

**Vincent Racaniello**

Yeah it was great, yeah. Thanks for having me back so soon. Great.

**Marc Pelletier**

We'll have you on again too, we've got plans. So –

**Vincent Racaniello**

You might want to say that we had you on TWiV not too long ago right? It was a great episode too.

**Marc Pelletier**

It was a lot of fun. Definitely a lot of fun. Viruses are scary, by the way, in a cool way. So let me get to Justin Sanchez. He's an assistant professor of pediatrics, neuroscience and biomedical engineering and part of the Neuroprosthetics Research Group.

**Justin Sanchez**

Hello world.

**Marc Pelletier**

Head of the Neuroprosthetics Research Group. And he is at the University of Florida in Gainesville, Florida. Welcome.

**Justin Sanchez**

Thank you so much for having me. I was meaning to tell you that we're already working on a brain implant for the next round of FiB, so we won't be using microphones anymore, we're just going plant right into your brain and mind control right there.

**Marc Pelletier**

Will we have to move our lips? Can we just think about what we're going to say?

**Justin Sanchez**

You're just going to be able to think about it.

**Marc Pelletier**

That's pretty wild. Yes, Justin has invented a new form of wireless mouse. We are going to talk a little bit about your work. I just want go round the table and then we are going to get a little, have you guys tell us a little bit about what you do and then we are going to get to the stories of the day, which aren't necessarily the stories of the day but the stories that interest us and we think are really fun stories. So they are not necessarily this week in biotech but more – wow, these things are just unbelievable.

So I'd like to also welcome Dave Brodbeck who's an associate professor and Chair of the Department of Psychology at Algoma University in Sault Ste. Marie, Ontario, Canada. Hello.

**Dave Brodbeck**

How is it going?

**Marc Pelletier**

Pretty good.

**Dave Brodbeck**

Or as we say in the Sault, how is it going, eh?

**Marc Pelletier**

It's going great, eh. It's excellent, eh. So yes, we are doing an upcoming show on June 5. I might just as well mention it now. At 1 pm Pacific Time or 4 pm Eastern Time on June 5, we are interviewing Dr. Gabriele from MIT who images emotion. He does MRI on human emotion and all kinds of weird stuff. Pretty groundbreaking.

**Dave Brodbeck**

It is cool. Very cool.

**Marc Pelletier**

Yes. It'll be a lot of fun. And Dave has a podcast called thunderbird six, which is a ...

**Dave Brodbeck**

And I have five other podcasts too, but you know, whatever.

**Marc Pelletier**

That's the flagship one right?

**Dave Brodbeck**

Yes, that's right.

**Marc Pelletier**

Thunderbirssix.org. Okay. Now that we've gone around the table let's just say hello to Andre. I've got to keep remembering we're on video, I'm not getting the video here. But so, Andre, tell us a little bit about what you do in the micro-array lab and what you're doing at NRC.

**Andre Nantel**

[7:54] Well, mostly what I work on is on fungal genomics. So essentially I study a yeast pathogen. It's called *Candida albicans*. So it's the main cause of yeast infections, both the kind that just cause you to itch a lot, as well as the kind the kind that can kill you if you catch them in your blood stream.

The other things that I do mostly is systems biology work in mammalian signal transduction, cancer, heart disease. It's very, very varied. I have never been able to concentrate on one thing in my entire life anyway. So that's pretty much it in a short term.

**Marc Pelletier**

So what do you mean by systems biology. Maybe if you could introduce the term and sort of describe how DNA micro-array fits into the bigger picture of systems biology?

**Andre Nantel**

Well, in systems biology, essentially the goal is to try to visualize the human cell more like a very complex system rather than the oversimplified version that biologists have been trying to imagine it to date. Just imagine it – essentially you are cave man and you've been given a laptop computer and told 'how does it work?' So what you do is you stack a bigger stick and you starting smashing things and if you smash things, things stop working. And you haven't even realized that electricity and software exist.

So what systems biology does is essentially to try to get into the complexity of a living cell and use that. And where micro-arrays come in, is that micro-arrays are great for measuring very complex data set and we're using that not just to measure, for example gene expression level, but using protein micro-arrays to measure the expression levels of many proteins and the phosphorylation levels of many proteins simultaneously. We are just starting on that, so.

**Marc Pelletier**

So you're printing protein chips as well?

**Andre Nantel**

Yes, the printing of DNA chips by academic labs is something that is becoming more and more – let's just say it's not competitive with big companies anymore. So we've realized a couple of years ago that we had to evolve or die.

**Vincent Racaniello**

Hey, Andre, how many proteins can you put on a chip?

**Andre Nantel**

Right now we have antibody proteins that we're making ourselves. So they have maybe about just 20 or so. But the biggest one we are about to do is a sprinting plasma. That's a project to screen cancer markers that are in the blood. And we have obtained several hundred – I think we are close to a thousand different plasma samples from cancer patients. We're going to try to spot

all of these on a single micro-array, so you can measure tumor markers simultaneously in all of these patients. But that's still an ongoing project.

**Marc Pelletier**

So you're replacing a hundred test tubes to a silicon chip that's an inch by an inch, or an inch by two inches?

**Andre Nantel**

Well it's not a silicon chip, it's a glass microscope slide essentially but, yup.

**Marc Pelletier**

What's glass made out of?

**Andre Nantel**

Oh. Touché.

**Marc Pelletier**

So, yeah, what I really think is amazing about that whole new level of technology is you can watch the genome in action. It's not a 'here, one gene is turned on, the other gene is turned off' it's the complete network of the genome on and off. And it tells you a living state of – genetics isn't 'do you have that gene or not' it's 'wow, what genes are turned on and off at the same time?' Right?

**Andre Nantel**

And it's really in cancer that this kind of technology completely changes, or confirm initial impressions that we had about cancer in which that – when you have cancer you don't have, every cancer is a different disease, every cancer came from its own different set of DNA mutations. So that it's such a complex cell that's different from any other cell that you've ever studied. That's one reason it makes cancer research so challenging, especially when you look at it on such a global level. you have to pick what's significant out of hundreds of other mutations that have nothing to do with the final disease. But you still have to swim through them to find out what's going on. So it's...

**Marc Pelletier**

Is that computationally challenging?

**Andre Nantel**

Very computationally challenging. Although hopefully in the end we are going to be able to take a cancer patient and essentially profile his tumor and says 'all right people that this exact profile are more likely to respond to this drug or that drug instead of the current method', which is essential based on statistics. 'Let's try this, not working, let's try that, not working, oh damn the patient's dead.'

So being able to essentially go through personalized medicine to really define what is the cancer, what type of cancer you have is probably going to be the first really broadly available output for micro-arrays studies in that field.

**Justin Sanchez**

So, Andre, how does this in your opinion scale up? So you are looking at single cells right now?

**Andre Nantel**

No, you're looking essentially at – well, you can look at single cells when you're studying cancer but you can also take a tumor sample, at least get enough profiles to know what's going on. As for scaling up, it doesn't scale up very well, you won't be able to do micro-array studies in a

clinic. But what the micro-arrays do is they tell you 'all right you are going to concentrate on that set of 70 to 100 genes and these are the ones that you need to assay to be able to classify that cancer tumor properly.'

**Justin Sanchez**

I see.

**Andre Nantel**

And then you can use other methods like QCPR that are more scalable to develop the actual clinical assay.

**Justin Sanchez**

I see. Interesting, very interesting.

**Marc Pelletier**

Are you working on – not everybody has micro-array facilities, are you working with a hospital right now?

**Andre Nantel**

We work with a variety of different collaborators. They come to us, especially those that don't have expertise in that technology and we help them, we provide them with the expertise. Sometime we just sell them micro-arrays, I mean, we do pretty much all kind of things. Officially this lab was built as a service lab. I've kind of transformed it into a research lab at the same time. But the service part is still very convenient because it brings in money.

**Marc Pelletier**

How many thermal cyclers do you have, PCR machines?

**Andre Nantel**

Oh, we had 10; we are giving some of those away because we don't do as much PCR as we have. We have three micro-arrays spotters right now in the lab. And these are very expensive robots. I actually had to fly to England on three hours' notice to essentially claim one that we've bought because the deadline was getting so close with the end of the fiscal year.

**Marc Pelletier**

You got to plan ahead I suppose. You don't want to – it won't look like you're budget dumping, right? No wait, that's another show.

**Vincent Racaniello**

Nobody has ever done that.

**Marc Pelletier**

Yes, well let's ask Vincent. So, tell us a little bit about your work, Vincent? You're a virologist. You have been at Columbia for a number of years.

**Vincent Racaniello**

[14:27] Yeah I've been here since 1982. I study RNA viruses. Not the same family as influenza but it's a family called picornaviruses and it includes polio virus and rhinoviruses which cause common colds. And if you wanted to put all the work that we have done into two general areas, we are interested – well first of all, we made it possible for Peter Palese to rescue to 1918 virus. We developed a technology for making a virus from a sequence if you will and it was done way back in 1980 and I did that first with polio and then I took that here and used it to study bunch of questions about polio including how it causes disease. And the problem with doing that, at least with polio, is that there isn't good animal to study disease in; polio is a human-specific virus. So we made a transgenic mouse that could be infected with polio. We took the receptor for the virus,

which is a human protein. We made a transgenic mouse with that and those mice can now be infected with polio virus, so we use it.

**Marc Pelletier**

When did you make that?

**Vincent Racaniello**

So, that was done in around 1989. One of my first students –

**Marc Pelletier**

'89? You had a transgenic mouse in 1989?

**Vincent Racaniello**

Right. So, here at Columbia in fact some of the first transgenic people were working and I was lucky enough to collaborate with them and we got in on the technology early, right?

**Marc Pelletier**

Very early. That's about 12 years before everybody else.

**Vincent Racaniello**

Yes, it was already an established technique, but one of those things where it's not for everyone yet. It's a specialized technique. So, it's always about being in the right place at the same time with science. You have people who are doing things at your institutions. Things move faster much more quickly, as you know.

**Marc Pelletier**

So, how does the mouse respond to the human polio?

**Vincent Racaniello**

So, you inject them in any way you want. You can put it in IP, intraperitoneally, you can put it intramuscularly. The virus makes it way to the spinal cord and it grows in neurons, the virus multiplies in neurons. It destroys neurons and the mice get paralyzed. So initially, a few days after injection, the legs begin to get paralyzed and then the arms and then eventually they succumb because they basically, they –

**Marc Pelletier**

Is this the same situation for humans? Is it like – because mice have a tendency to be robust, right? But I suppose it's...

**Vincent Racaniello**

It's interesting. It is – I mean if you look clinically and histopathologically, the disease is very similar to human disease. There are a couple of exceptions, one of which is the disease is always fatal in mice, whereas in humans it is not always fatal. And we're not sure why that is. And the other is that our mice as we made them initially, if you fed the virus to them, which is how humans get polio, you ingest it, the mice didn't get infected. And there's some difference between mice and humans that prevent us studying that the natural route of infection, if you will.

**Marc Pelletier**

Do you have to watch out if the mouse escapes? I mean I guess the mouse is not going to get very far.

**Vincent Racaniello**

This is a really good – so, when I first made these mice, the animal people here were freaking out and they made me buy a special plastic container to put all the animal cages in, in case one of the mice got out. They didn't want to spread this susceptibility gene into the wild mouse population. Now in reality it is not likely the lab mouse could survive in the wild. Here in New York

we have very vicious mice and a white lab mouse running around wouldn't survive I think more than a day.

**Marc Pelletier**

Mickey in the Bronx.

**Vincent Racaniello**

You could see they are slower than the wild mice, because sometimes the wild mice come in our floor here and they are very fast and our lab mice can't even keep up with them. So, I mean we were careful in the beginning, but I think now there is no way this mouse is going to get out. And any way if it did and this susceptibility gene got into the wild mouse population, the mice are not susceptible by oral infection anyway. So it wouldn't matter.

**Marc Pelletier**

Exactly. No, I am not raising any concerns here. I just think it's an interesting thing that you have to deal with when you work in a lab. I used to drop frogs all the time, right. And the frog would end up under your bench somewhere and I'd have to crawl underneath the bench and grab a frog and bring it back.

Yes. So, let's talk a little bit to Justin about his stuff. He is doing some pretty – talking about mice, some pretty amazing stuff, right. It's – tell us a little bit about it. I don't want to put it in the wrong context.

**Justin Sanchez**

[19:02] Sure. Sure, sure, sure. So, neuroprosthesis. This is a real cutting edge area of neuroscience and neural engineering research where we're trying to restore communication and control in patients that have debilitating diseases of the nervous system. So, for example, if let's say you had somebody who had a spinal cord injury, you would like to implant a device into their brain that enable them to think about moving and this device would decode that information from their brain and control something useful, could be a computer, could be a prosthetic arm, could be a variety of things.

So, to put it in real simple terms, we are trying to build bionic technologies like the \$6 million man or \$6 million woman. So there's lots of interesting questions in terms of neural coding and how do you build the computer hardware and systems that directly interface with the nervous system? So we have a lot of challenges ahead of us.

**Marc Pelletier**

Is it for an arm that can respond to the signal of a neuron? So there is an amputee, then you put a prosthetic arm and you connect the central nervous system interface to that...

**Justin Sanchez**

Directly.

**Marc Pelletier**

...using your USB device, right? USB is universal.

**Justin Sanchez**

Yes. So, we have this electrode array, right, that can be implanted directly into the neural tissue and you can sense the firing properties of all of these neurons. So, we have this ensembles of neurons is what call them. And a lot of people refer to this kind of as "the symphony of the brain" that's telling us what the person is intending to do and our job as a computational neuroscientists and neural engineers is to crack that code and decipher what the person is intending and translate it into a command signal.

**Marc Pelletier**

Do you do it in the brain and would you ever need to do it in a limb? I mean if the brain is sending a signal to the limb to move, why would you ever even bother putting an electrode in the arm if you had the central..?

**Justin Sanchez**

It depends upon the disease that you are trying to target. So, somebody who has a high cervical spinal lesion, right, all the signals are still on the brain but they can't get out. You have a disconnect in the system. So, you would have to naturally just go to the brain. Now somebody who is an amputee, you may be able to, let's say, remap some of the nerves that were running to the arm to, let's say, the pectoral muscle and then you could decode the information from there and use it to drive a prosthetic arm.

Another really interesting aspect of all of this is, let's say you had somebody who had a stroke and you lost the ability to control a certain aspect of your brain. There is a possibility that you could build in silico, in a computer, biologically realistic cortex that that person could communicate with and use it to augment some sort of missing neural function that they have.

So our goals really are to blend biological systems, computational, computing systems in a way that enhances or restores communication and control. So we really think about this as a whole new way of expressing your intent, right? Like right now, we are discussing things –

**Marc Pelletier**

Are you saying telekinesis basically?

**Justin Sanchez**

Well, I wouldn't go as far as telekinesis at this point I don't want to make any...

**Marc Pelletier**

You think about something and it happens.

**Justin Sanchez**

...promises about – I don't want to inflate what you are trying to do but essentially –

**Marc Pelletier**

Yeah right. I do. It's great for ratings, no?

**Justin Sanchez**

I would say that we are trying to better understand the neural code so that we can deliver therapy to disabled individuals. Now if in the future, that will enable even more extensive communication via directly in your brain, then, I think that that's a great visionary perspective into all of this. But we still have a long way to go. There's still so many unanswered questions that are out there.

**Marc Pelletier**

This is an output device. And let me just – so the audience can picture what are you doing, you would implant a small chip with 50 to 100 electrodes directly into the brain of an animal or a human?

**Justin Sanchez**

That's exactly right. And –

**Marc Pelletier**

And how does that chip communicate to the computer?

**Justin Sanchez**

Yeah so right now, we just have either standalone computers or wearable types of, let's say, DSP processors that would run an algorithm that decodes this type of information from the brain, right.

So, all of these signals that are coming out of the brain, they are just firing patterns. Neuron A fires 100 times a second or neuron B fires 25 times a second. And we have to translate what that means in terms of 'oh, I want to move in this direction or I want to create this trajectory or I want to express this type of intent.'

So on the –

**Marc Pelletier**

So, that's a human – with the chip and the software, you have got like a human DSP, something that translates neuronal physiological responses into a digital signal. Analog, literally analog to digital.

**Justin Sanchez**

Analog to digital and we're trying –

**Marc Pelletier**

Human analog to digital.

**Justin Sanchez**

Yeah, human in vivo analog to digital. And when we say digital we mean command, right, behavior. We're translating thoughts into behavior essentially.

**Vincent Racaniello**

You know Neal Stephenson wrote a book about that once. You know that one?

**Justin Sanchez**

Yes, there has been several books and movies all about this. So it really captures the imagination of the general public. So...

**Marc Pelletier**

Now, are you wireless or do you go wired with these chips?

**Justin Sanchez**

Yeah, so one aspect of the work that we're currently doing is trying to build a fully implantable wireless rechargeable neural implant type of system. So, there are several groups around the world that are really breaking this barrier, right. You can imagine if you're – the amount of information that we're trying to send out of the brain is tremendous. So, trying to have a low-power wireless device that has enough bandwidth to do this is extremely challenging, and we have a great project right now that's attempting to do this.

**Andre Nantel**

So, who would want to get version 1.0 implanted in his brain? I'll wait for 1.1 if you don't mind.

**Justin Sanchez**

You'll want 1.1? So, yes, there's some ongoing human trials that are showing proof concept of all of these and maybe that's the 1.0 but I would anticipate in the very near future that this is really going to be taking off quite fast.

**Marc Pelletier**

The rule of thumb is the first 100,000 units, right? Certainly in a MacBook.

**Justin Sanchez**

That's right.

**Marc Pelletier**

So, you're ahead of the game at least with respect to design than the crew on the Matrix, right? So they had this big jack in their head and it hurt every time they plug it in and plugged it out – pulled it out.

**Justin Sanchez**

That's right.

**Marc Pelletier**

Wouldn't it just be easier just to have what you're designing?

**Justin Sanchez**

Yes, we want the wireless interface. So, our ultimate dream is you see somebody walking down the street that actually has a neural implant and you wouldn't even know that they had a neural implant. It's that inconspicuous for each of these individuals. So yes, that's what we're shooting for.

**Andre Nantel**

It's already weird when we have somebody with the cell phone in his ear and you think he is crazy because he is talking to himself.

**Marc Pelletier**

That's right.

**Andre Nantel**

Now you're going to have somebody walking the street talking to himself and surfing the net simultaneously.

**Justin Sanchez**

Well yeah, so the beauty of it, they wouldn't even have to say anything, right. They are expressing their intent directly through this interface and they may not have any physical movements or any speech associated with that. So just – you start thinking about these ideas very deeply and just the implications are huge, right. Communicating via neural interface is just – I am very interested to see how it's going to turn out in the future.

**Marc Pelletier**

Did we do episode 35? Was it – you were on 35 or what number was FiB?

**Justin Sanchez**

Oh, I don't remember exactly what number. I can look it up here. But it wasn't too long ago. Several months ago?

**Marc Pelletier**

Yes, 35.

**Justin Sanchez**

35?

**Marc Pelletier**

It was 35. Yes, so, I certainly direct the audience to check that out, because there is a lot of implications with respect to possibly doing time shift. You could think about the intent of doing something for later, store it and then the machine or robot or whatever you are trying to control does it in the future, so...

**Justin Sanchez**

That's right.

**Marc Pelletier**

...you're time shifting your function. So you can think about 'I am going to think about getting up and walking down the street' and then two hours later your body gets up and walks you down the street.

**Justin Sanchez**

Yes. So, we think of these devices as intelligent tools. If you look back in the history really of tools use, even from early stages of mankind, tools are really passive instruments, right. You exert your intent on them and they just blindly do whatever you tell them. If you had an intelligent neural interface directly into your brain, this system, could be an assistant to you and it could co-adapt with you and it could evolve as you change your neural representations and your behaviours. So if you think about the implications of that with computers, right, they could be much more assistive in their nature. So this is also the next step that we're trying to build into this, intelligent neural assistance on these type of interfaces.

**Marc Pelletier**

By the way, like every great scientist, right, did you test it on yourself?

**Justin Sanchez**

Yes, so we have tried EEG based types of neural interface, so these are scalp based types of electrodes. And we can use that to communicate and control via the device. And actually one of the stories that we're going to be talking about later today is in direct respect to this.

**Marc Pelletier**

Yes, we'll definitely crack that open after this, the Audible part.

**Justin Sanchez**

Yes, sure.

**Marc Pelletier**

We've got to support the podcast here. Let's finish the round table on people's work, we've got Dave Brodbeck and you are the Chair of Psychology at Algoma.

**Dave Brodbeck**

Yep.

**Marc Pelletier**

I am getting a little bit of echo here. And so you are podcaster first, professor second?

**Dave Brodbeck**

[29:28] Oh please don't say that. Though I have tenure, what are they going to do, fire me?

**Marc Pelletier**

Sorry...

**Dave Brodbeck**

No, I mean, the most important – I teach a course and – because it's a small school, right, so I do a lot of teaching, but also one of the other things I am interested in is the evolution of memory and cognition. So most of my stuff's on differences between different animals in their ability to remember things. So food storing birds is something I have been interested in for a long time, like Chickadees, birds like that and how they remember where they put their food, so that they can go back later because if they don't eat in the morning, they die, because they don't migrate, right. So their specialization is that their memory is really good and they are specialized to remember where it is, not so much what the color is, things like that. So that's something that I have been pretty interested in, and recently have been doing something with a bird species called Pine Siskins, and they are kind of funny because they don't migrate all the time, they only migrate

when the food supply gets really bad. So me and a couple of colleagues, we figured out that what they were probably doing, our guess was that they were detecting fluctuations in the food supply and they'd also be really good at detecting food supply density. And it turns out they really are, and they are doing it the same way the Chickadees do, so they are using the same kind of specialization, which is remembering where things are in space quite precisely, except they are using it for a different function.

So that's some of the stuff that I've been interested in, and I am also interested in doing some research in video game design, but that's a whole 'nother thing. But yes, so that's sort of lot of the stuff that I have been doing, and I also I teach all that stuff here because like I said, it's a small school, so what I do is, because we don't have graduate students, so what I do is I prepare people so that you guys can wreck their minds when they get to graduate school.

**Marc Pelletier**

But you also – you are one of the, probably the pioneers of podcasting your lectures too.

**Dave Brodbeck**

I've been doing – I've just posted my 400th podcasted lecture yesterday, so yes...

**Marc Pelletier**

That's unbelievable.

**Dave Brodbeck**

Yes, it's – it's almost – I almost do it automatically now, I come home, I just download the audio, and there it goes, but – yes, I have been doing that for quite a while now, three years, which gives you an idea, if that's 400 classes, gives you an idea of our teaching load here, ah...

**Justin Sanchez**

So Dave, do students actually – are they just auditing the course or are they participating in the course, or how does this usually work out?

**Dave Brodbeck**

Well what happens with me is that most of my listeners aren't my students, I know my students do listen, and I have data that show that their marks have gone up about 5.5%.

**Justin Sanchez**

Wow!

**Dave Brodbeck**

But – yes, which is, which makes me happy, but most of my listeners aren't – well, ours is really a small school, we have 1,200 undergraduates here, in the whole school, so, like not in the psych department, in the school. So, but I have, oh, hundreds, thousands rather of listeners, and I've – stuff has been downloaded over half a million times, and people from all over the world listen, and to me that's a lot of fun.

I have had a couple of people that have taken courses, in fact, I am doing one right now, where a woman is listening to some old archives of my stuff, and I send her questions by email every – after every class she listens to. And she replies to me and then I mark them and then she listens to the next one. So it's a little bit – that's more just, I am just sort of doing that as a favor to somebody. But I've done that a couple of times.

But for the most part, it's for my students, but other people listen, and it's a lot of fun. It's something different.

**Marc Pelletier**

Yes, it's kind of like you are Leo of academia.

**Dave Brodbeck**

I don't even know what that means, so I'll just leave that where it is, yes.

**Marc Pelletier**

And then I – you've helped me out quite a bit on FiB, and I really appreciate it...

**Dave Brodbeck**

Thanks. Oh, it's been fun.

**Marc Pelletier**

...and you're scheduled to do it again, so...

**Dave Brodbeck**

Yes.

**Marc Pelletier**

...it really – it helps me because I don't have the expertise in the area of psychology, and I think that there is an incredible history of psychology and an incredible future, so...

**Dave Brodbeck**

Sure. I don't have any expertise either, I am making most of this stuff up. But like I said, I am tenured, what are they going to do, fire me? So.

**Andre Nantel**

Give you a smaller office?

**Vincent Racaniello**

Yes, right.

**Marc Pelletier**

Well, you're the Chair, right? You're the boss.

**Dave Brodbeck**

Yes, I am, actually.

**Marc Pelletier**

Before we get on, move, why don't we stay with you Dave and let's do a – we have to do an Audible spot.

**Dave Brodbeck**

Right.

**Marc Pelletier**

So, I'd certainly like to thank Audible for sponsoring Futures in Biotech, right? They have, I think, over 50,000 titles right now, and there is a free download as – if you'd like to try it out a subscription, you get a free download, a free credit towards a download, and then, if you like it, you can stay with it, and if you don't, well, you just cancel the subscription, you get to keep the free book, so it's like win-win situation, so it gives you the chance to try out Audible books, which are a lot of fun, by the way, especially if you're travelling, and doing a long road trip. I – I probably listen to about ten a year, Audible books, and it's – they just get you through that road trip, so Dave, do you want to be the honorary Audible pick?

**Dave Brodbeck**

I have always wanted to do this. Often when I am listening to TWiT, I am yelling, what about this book?

**Justin Sanchez**

'I love Audible.'

**Dave Brodbeck**

Okay, Calacanis. To me the book that, I was thinking about is one that has some personal meaning to me, but it's also one that – it's a great popular science book, and it's by Steven Pinker, *The Stuff of Thought*, and the thing about Pinker is that he's one of these guys he's kind of like Richard Dawkins in the way that he writes, he writes about really complicated stuff, but you feel like a genius when you read it, because it's so easy to understand. And – so that's something that I have really found – like the book is great, it's about how language affects thought and thought affects language, but it – and it's written – if you're really an expert in this kind of stuff, if like let's say you are a psychologist or a neuroscientist or a linguist, you will read it and you will not be disappointed, but if it's for a general audience, it also is, really, I think, pretty easy to understand, and it's written – all it does is assume you have a brain, it doesn't assume you have a – you've taken a major in psych or linguistics or something, and I actually have the paper – the hard cover version of this book which was given to me by one of my honors thesis student last year, Shauna Barrett [ph], and Shauna gave me this book because she had based her honors thesis on some of Pinker's work, she gave me that and a bottle of gin, which all my students are required to give me.

But it really – the book itself is so good, and like I said, you feel like a genius, you are reading this stuff and just like, like I said, just like Dawkins, just like when you read something like *The Selfish Gene*, it sort of changes the way you look at stuff and that's what *The Stuff of Thought* and a lot of other Pinker's work does.

**Marc Pelletier**

So that's Steven Pinker?

**Dave Brodbeck**

Yes.

**Justin Sanchez**

How do you spell his last name?

**Dave Brodbeck**

Like P-I-N-K-E-R. Just like Pinker. I know they have it because I checked.

**Justin Sanchez**

All right. I am looking right now.

**Marc Pelletier**

He's at Harvard.

**Dave Brodbeck**

And he is originally from Montreal, so...

**Marc Pelletier**

He was on the Colbert Report.

**Dave Brodbeck**

Yes, he has been on the Colbert Report. And he's got insane hair. But at least he has hair, so let's give him some credit there.

**Marc Pelletier**

Thank you for the pick.

**Dave Brodbeck**

I do what I can.

**Marc Pelletier**

I guess I always wonder, the slip of the tongue, does it really mean something?

**Dave Brodbeck**

Oh, I don't know.

**Marc Pelletier**

There was someone who did a lot of mis-speaking over the past eight years. I wonder what it all means.

**Dave Brodbeck**

Get in line, pal.

**Marc Pelletier**

Okay, so why don't we get on to the stories? I thought we'd talk, we'd have Andre first, because Andre actually has to head out at 5.30 Eastern Time. Is that okay, Andre?

**Andre Nantel**

Yes, that's fine. I mean, I figured, we are going to do one story each first, right? Depending on how much time we have after everybody's gone through one.

**Marc Pelletier**

That makes sense. Yes, let's do that. Yes, that sounds like a great idea.

**Andre Nantel**

[38:03] Okay, so, the – so initially we were talking about getting essentially our favourite stories of 2008, right? And I figured I would choose my favourite essentially genomics story of 2008, although it may not be the most scientifically relevant or important story of the year, it was certainly the one that captured most of our imagination during that year. And one of the reason is that the field of genomics is going through what can be described almost like their fourth revolution. I was – suppose you are all familiar with Moore's law, which essentially says, in the computer field, that everything is going to get twice as fast and twice as cheap every 18 months.

Well, in genomics, it's the same thing, what's really fun is we're in the exponential curve, we're really in a point where it's getting so easy to get so much genomic information, that we're simply swimming in data, and we can afford to really sequence things that we would not have thought of sequencing in the old days. So the paper I chose was published in Nature last November and essentially the title was sequencing the nuclear genome of the extinct woolly mammoth, so we're taking our first little dip into Jurassic park territory and sequencing an extinct species.

The study was pub – as I said, the study was published in Nature, it was essentially set – put together by a team from Penn State University, the Russian Academy of Sciences, as well as the people who make the 454 high-capacity Sequencer. And, as you all know, the woolly mammoth, they died out or they were hunted out in extinction about 10,000 years ago. So the goal of this project was to sequence the mitochondrial and genomic DNA of two individual mammoths that were thawed out from Siberia, and they gave them the very Walt Disney-esque names of M4 and M25.

M4 is the only one that you'd know how old it was, it was carbon dated to about 18,545 years, so plus or minus 70 years, and the source of the DNA is not muscle or tissue, they actually use hair, and it was actually quite intelligent why they decided to do that, it's because the – hair shaft especially, the DNA in hair shaft is wrapped in keratin which is what you make hair and nails, it's

very hard, it's very resistant, and that essentially sealed the DNA so that bacteria and fungi would not be able to go in and degrade it. The other advantage of using hair is that I have talked with people who work with very, very old DNA whether it's archaeological samples or fossil and their biggest problem is contamination. These are samples that there is a lot of fungi, there is a lot of bacterias around them not to mention there is very little DNA that you are interested in, so there is always problems contaminating from the researchers themselves. You would be amazed the amount of skin cells that we're shedding at all time. So, working with hair shaft allowed them to be very, very stringent in their purification methods, to really eliminate as much contamination as they could, but even then once they finally got the sequence data 10%, 9.5% of the M4 sequence was contamination, 42% of the M25 sequence was contamination, most of it was bacterial or unknown origins, very, actually none of it was human origin, so that's very encouraging, tells you that they were being very, very careful with their samples.

**Marc Pelletier**

It wasn't degraded, was it?

**Andre Nantel**

It was massively degraded in a sense that when you do a 454 sequencing run you can expect to read 4, 500 base pairs for every reaction. The average sequence read in that paper for what I could tell was about 130, 140 bases. So there was still significant levels of degradation in there. Nevertheless, they managed to produce 3.3 gigabase of sequences which is very impressive and it was aligned and assembled on what's currently known of the African elephant genome. Now, elephants aren't only big, they also have the biggest genome of all placental mammals. For example, right now it is estimated that the African elephant its genome is like 4.4 gigabase so that's about four times the human genome if I am not obscenely mistaken.

Nevertheless, they were able to get the sequence from the mammoths aligned over the sequence of the elephants and they say that they have about 63 to 70% of all the mammoth sequence at least once. And I have to say as a guy who has assembled genomes that's really crappy coverage. It's borderline, it's barely sufficient but considering the source that's pretty much as much as you can hope for the moment. That also explains why the original paper has very little in detailed genomic analysis of what they could get. Pretty much all that they were able to say is 'so how different was the mammoth genome from the elephant?' and this is where they had the first very interesting observation.

The mammoths and the elephants diverged about six million years ago and that's about the same time as the human diverged by chimpanzee. It's a very interesting coincidence. But the differences in genomes between the mammoth and the elephants is like 0.6% of all nucleotides and it's only half of what you're seeing between us and chimps. And that was the first indication that there's not – there was not as much evolutionary pressure on large pachyderms as there are on small yummy primates.

**Marc Pelletier**

Such as humans.

**Andre Nantel**

Yes. Essentially we were obviously tiger and lion foods for a very long time and that kind of forced us to evolve or die. And elephants until people with guns and arrows showed up, they really had it made. Now, they also looked at the differences between the sequence of the two individual mammoths and they found out that they were markedly similar genetically and that led to the hypothesis that that made them especially susceptible to any changes in environmental conditions like probably human with arrows and guns. Although it should be noted that there are differences between the two, while first of all it's just two individuals is not that big, although according to mitochondrial DNA they were from different strains of mammoths. The differences are similar to what you see within the human population. It's something that not too many people would realize but as a species we are remarkably homogenous in our genome sequences

probably because several thousand of years ago our population got reduced to just a few, a very small number of individuals.

So just to finish, almost every mention of this study in the press then speculated about the possibility of using that information to rescue the mammoth from extinction. So the big question is do Bill Gates or Warren Buffett have enough money to surprise their kids by giving them a hairy elephant as a pet?

**Marc Pelletier**

Sure they do.

**Andre Nantel**

Yeah, of course, they have nothing else to spend their money on irrespectively of malaria or other things like that. And, so I have, I have looked a little bit of the speculation on that aspect and can we go Jurassic Park on the woolly mammoth and theoretically it is possible but the task is monumental. A 0.6% difference in DNA sequence between elephant, it looks – man, you are quick on that Google thing. It looks small but it means that you would have to go in and make upwards of 25 million individual mutation in the genome of an elephant embryo. And I am not even talking about differences in DNA packaging and genomic imprinting, there was a paper today in Science explaining how we always thought that there was four nucleotides, turns out there are six. There is also methylcytosine and hydroxymethylcytosine and we are not even close to figuring out – and this is very important for brain development essentially and just how we would integrate that into creating a new species is so far from being addressed, it's the equivalent of, well knowing that there are planets in another solar system and actually building a spaceship and going there, the work to do that is simply huge and enormous.

**Marc Pelletier**

At the moment, right, Andre, I would like to say that we had Drew Endy, synthetic biologist from Stanford at the time he was at MIT on the show and – we were talking about having the entire human sequence and then using it to create a synthetic genome and he said – at the moment it would cost tens of millions of dollars, but – if you look at the time of George Church, right, when he first started sequencing DNA using crystallography, he would crystallized DNA and then sequence it, I think he did this as a high school student generating DNA crystals and then counting their bases, then you take, that was in the '70s and then in the '80s well you could get an entire Ph.D. for sequencing a thousand bases and reporting the gene. And in the '90s you and I sitting at the bench sequencing 300, 400 bases at a time, we could get through a couple of kb. Now, it's a genome in a day with the right set of robots...

**Andre Nantel**

About a week, yes.

**Marc Pelletier**

...and so the same thing goes with synthesizing DNA, right. Making a little 30 bases of DNA used to take a long time but now we have got machines cranking the stuff out.

**Andre Nantel**

Yeah. I was actually thinking about graphing how much the improvement in sequencing and essentially synthetic genome creation, would essentially put them on the graph and see can I estimate how long it would take to get a 4.4. gigabase genome done. But you are going to have to practice on a lot of other critters before you go and make an elephant, especially because something with a generation time of 25 years, it's kind of hard to get a grant that's going to last that long.

**Vincent Racaniello**

You know, mostly the difference between chimp and human DNA is the endogenous retroviruses that are present in the genome, so that 5% or whatever it is. So do you know if the difference between the mammoth and the elephant genome has to do with retroviruses as well?

**Andre Nantel**

There is no mention of that in the publication and I was actually, I unfortunately didn't have the time to actually download the genome and start to do my own comparison. That's an excellent question, what they were mentioning at the end of the paper is that, what they wanted to have is they want to have at least, they are calling it a 30-fold sequencing density. So essentially, every region would be sequenced at least 30 times to really get sequences of high quality before they would go in and do further studies. The other difficulty that they had is that even the elephant genome is not completed. So, they would have to at least finish that before they would move in and get more information on how the mammoth genome looks like.

**Vincent Racaniello**

I would be very surprised if there were not retroviruses in that genome and if we found them there would really add to the historical tracking that we could do using those, I mean those are really good measures of evolution.

**Andre Nantel**

Well, I mean that kind of stuff fascinates me, I mean I had to essentially to choose between the mammoth genome and they actually, there's sequencing data coming from Neanderthal tissue now. So you were talking about making a new mammoth, how about – while you're at it why not make another class of humans?

**Marc Pelletier**

We talked about that with Svante in episode 11, right. And literally we could be synthesizing the Neanderthal genome for injection into a human oocyte at a reasonable cost in about 15 to 20 years.

**Andre Nantel**

I would love to see the ethical panel that's going to review that grant.

**Justin Sanchez**

So, I was going to play the devil's advocate here, what would we be doing with a woolly mammoth or a new Neanderthal or species of human?

**Marc Pelletier**

A teen movie?

**Vincent Racaniello**

Well remember we brought back a dead virus. So the principle was there, right?

**Marc Pelletier**

That's true.

**Andre Nantel**

There's a good reason to bring back a dead virus for studies, but for these, for something that big and it's such a monumental task that I don't see that happening in my lifetime.

**Marc Pelletier**

Okay, so those organisms are fairly large and would impact our community in – you know not just put them in a zoo, but what about ancient DNA from plants that have entirely different lines of secondary metabolites, being chemicals that could be used to treat cancer that are no longer in existence. Taking CO<sub>2</sub>, water, producing oxygen.

**Andre Nantel**

Yeah, but you talk about alien species invading new environment that's, now you have temporal alien species, you have no idea what these will do. You could be creating a new version – you could be having a worse version of kudzu and really regretting it afterwards.

**Marc Pelletier**

Absolutely. I guess we should try to preserve the ones that are around. Go ahead, Dave.

**Dave Brodbeck**

I just said I for one welcome our mammoth overlords.

**Andre Nantel**

Yes, as a very famous photoblogger I can easily tell them which ones, which people should be put into sandwiches and which ones should be just left alone. I love that show.

**Marc Pelletier**

Well that's a great story. The whole concept of ancient DNA, it's not just about, wow, wouldn't it be cool to bring back a mammoth, but what we can learn from the history. This is archaeology – more than archaeology it's...

**Andre Nantel**

Molecular archaeology.

**Marc Pelletier**

Molecular archaeology. It really tells us about who we are and – because this is, what's being done on the mammoth is being done on the Neanderthal and every individual we can get. By the way just a little interjection here, when Svante did it on – first on the Neanderthal, it was at the same time, but he practiced – the DNA he was working on was degraded. He took bone samples from museums in Western Europe, Eastern Europe sorry, I am pretty sure it was. And these bone samples of DNA was 70 bases long. And to practice, before using that he used salami from New York. Beef genes were cut up into 70-mers while he was – so these salami from New York City. Anyway...

**Andre Nantel**

Although, I think he was mostly doing it on mitochondrial DNA, which is a lot easier to work than genomic DNA, because there's so many copies of it in every cells.

**Marc Pelletier**

Possibly at the start but they are going after the entire genome.

**Andre Nantel**

Now he is going with the whole thing, yes.

**Marc Pelletier**

It's wild. Crazy. Thank you for bringing up the story. Let's go over to Vincent. He's got a couple of really interesting stories. Which one do you want to present?

**Vincent Racaniello**

[53:15] Well let's start with the oceans. So I have two virus stories and they are both in my view amazing. I mean there are many amazing virus stories. Right now we're in the midst of one with influenza. But I thought I would focus on viruses that people really don't think about much. And the first one has to do with viruses in the sea. And it turns out there are an enormous number of viruses in the ocean. Wherever you look to about a million virions, or virus particles, per millilitre of ocean water. So, that adds up to  $10^{30}$  total virus particles in all the oceans of the earth. And if you took all those viruses and lined them up end to end they would go for 200 light years into space. That's how many of them there are,  $10^{30}$ .

**Justin Sanchez**

So, Vincent, how does that compare to what you'd find just in terrestrial situations?

**Vincent Racaniello**

It's probably far more abundant, because there is so much life in the ocean. And there is just such a volume of it. It's much more. I mean they're certainly more abundant than anything else that has nucleic acids in the oceans.

**Justin Sanchez**

I see.

**Vincent Racaniello**

I think there are 94% of all nucleic acid containing particles in the ocean and more abundant than bacteria and Archaea that are in the ocean as well. So there is incredible diversity. Most – many of these viruses are actually viruses of bacteria. So the oceans are full of bacteria. And so there are many viruses of those. But there are also algae of various sorts and there are viruses of the algae. And then there are viruses that infect fish and there are viruses that infect mammalian species, whales and dolphins and seals and so forth.

Just enormous diversity and people are beginning to sequence these very much as we've just talked about the power of sequence analysis, what people do is go into the oceans and get a couple of liters of sea water, extract the DNA or the RNA and sequence it. And the results are just astounding. First of all, 90% of all the genes that you find in the viruses in the ocean are brand new. You can't find them in GenBank. If you try and search for them you don't find anything that resembles them. So there could be amazing new proteins for example, that we could use some data to do things, enzymes or therapeutic uses, structural uses, who knows? So it's incredible. We thought we knew a lot of biome of the world, if you will, but the ocean is just incredible.

So, the other question is – there are two interesting aspects more I'd like to just touch on. First of all, it turns out that these viruses have a huge role in the geo-thermo cycle of the earth. And I don't know a lot about this, I'm a virologist. But it turns out that there are  $10^{23}$  virus infections every second in the ocean, right. Huge number. And it turns that they eliminate daily about 20 to 40% of all the bacteria that are in the ocean.

**Marc Pelletier**

Holy moly.

**Vincent Racaniello**

So there's this huge turnover of bacteria. So what this does, is liberates carbon in the end. And it plays a huge role in the carbon cycle of the ocean, which had never even thought of. I think of viruses is making you sick, right. And here it is in the ocean, they are incredibly important than in the geo-thermo cycle. And then of course the other thing is do these viruses pose a threat to us? You know, I go swimming in the ocean and I'm always pulling water in and spitting it at my kids you know. And it's a million – there are a virus million particles in that stuff that I'm taking in.

**Marc Pelletier**

Really. It's a lot.

**Vincent Racaniello**

Well, it turns out that a lot of them do. Whales for example get these virus infections and they excrete  $10^{13}$  viruses per gram of feces and those viruses –

**Andre Nantel**

That's a lot of feces.

**Vincent Racaniello**

They have that – they have a lot of feces and these –

**Andre Nantel**

I've been shat on by a dolphin once. It's not pleasant.

**Vincent Racaniello**

And they – it's been shown that they can make you sick. So if there's really – we call – there is a big pool of viruses out there that can infect people and the ocean just adds to it. And also –

**Marc Pelletier**

I'd similarly like to welcome our new viral overlords.

**Vincent Racaniello**

So if anything I just want you to realize the enormity of this pool of viruses out there that could contribute to illness. They infect fish. They infect salt water fish and then they jump into fresh water lakes. They get transported into fresh water lakes in the bilge water of ships and then they infect fresh water fish and you might have heard in the Great Lakes for example, there are all kinds of problems with viruses infecting game fish. And they are brought in there from the ocean. So they can cross species really easily. So this is a totally fascinating area. I wish I could work on this. But you can't do everything. Viruses of the ocean. So that's my story.

**Marc Pelletier**

How many light years again if you put them side by side?

**Vincent Racaniello**

You put them end to end they would go 200 light years into space.  $10^{30}$  particles. And it's a long way.

**Marc Pelletier**

So what's the biomass for that? How much do they actually weigh compared to the rest of the biosphere?

**Vincent Racaniello**

Oh, that's a good – I have a number for that too. They are like a thousand more times biomass than all the elephants on the earth.

**Marc Pelletier**

Wow.

**Vincent Racaniello**

So it's a lot. It's a lot of biomass. So it's huge. I mean you go, just look at the – I'm looking here at the Hudson River and you just don't suspect this obviously. But it's teeming and this is going to be a big deal in the next ten years, because people are just starting to study it.

**Marc Pelletier**

But they're mostly for bacteria, so...

**Vincent Racaniello**

The vast majority is bacterial. But there are still mammalian and fish viruses as well.

**Marc Pelletier**

How does the bacterial ecosystem compare to the – in the ocean – to the one that's on the human microbiome, right. We are 10%, or there are 10 ten times more bacterial cells than human cells on the human body.

**Vincent Racaniello**

Yeah the – I think bacteria make up about 15% of the volume of the ocean. It's huge.

**Marc Pelletier**

That's amazing. Is there any chance that we can harvest them for very specific phage therapies? What are your thoughts on phage – this is a sidetrack, by the way. I'm just really curious about mining the environment for potential medical uses, right. Do you think there could be some viruses in there that could be used for medical purposes?

**Vincent Racaniello**

Well, you know we already have phages that will kill some of the bacteria that trouble us. The problem with using these is that if you give them to a person, if you inject them to a person you make antibodies to these phages and you clear them pretty rapidly. So I think unless we can get over that obstacle, we can have phages that will be great for killing many bacteria, but if we clear them right away it's not going to be a viable treatment. But you know, you never say never in science. That's the one thing I've learned. You can always figure out some way around a problem. So right now we don't know, but maybe 10 years down the road we might have it.

**Marc Pelletier**

I'm about four miles away from Lake Erie. So would you recommend swimming?

**Vincent Racaniello**

Sure, I wouldn't stay away from it. I mean obviously we've been swimming all our lives and we're okay. You guys look all right. So don't worry about it. It's just –

**Justin Sanchez**

Over here in Florida we're surrounded by water so if there's something happening, there's no hope for us.

**Andre Nantel**

So somebody in the chat room suggested dumping billions of gallons of bleach in the ocean to disinfect it. I'm not sure that's not going to work.

**Vincent Racaniello**

No, no, no, it's an important part of the geothermal cycle, you'll screw that up and then you'll have all kinds of problems. That's the point.

**Marc Pelletier**

Pretty cool.

**Vincent Racaniello**

So that's a great story I thought.

**Marc Pelletier**

It is absolutely insane. It really changes our perspectives – go for a swim. But it also – I never thought the viruses in the ocean could control or play a major part CO2 balance in the atmosphere. So let's go to Dave.

**Dave Brodbeck**

Yeah.

**Marc Pelletier**

Dave has an – one particularly interesting story. I'll let you present it, Dave.

**Dave Brodbeck**

[61:26] Well, which one? I think I'll talk about the Kamitani one. The one where they're reading people's brains. To me this is something that actually blew me away and originally, oddly enough was sent to me by one of my undergraduate students in my intro neuroscience class. Just found a link and sent it to me and there – used to always talk in class about how people could one day be able to – using fMRI, actually be able to watch what you're seeing. Because we understand pretty well how visual cortex works, we're really visual animals. So a lot of our brain does vision – but also I think – which makes us really interested in studying vision.

So, back your head, occipital lobe does all of this visual analysis. And it's pretty well understood, as I said, how it works. So what this group I think in Japan did is they had people in fMRI and they presented them with stimuli. And they're just 10 by 10, so it's 100 squares. So it's 100 pixels, right. And they're showing them the letters N E U R O N, excellent. And they were then able to, by looking at the patterns on the fMRI, able to read what people were seeing.

Now the image is fuzzy. But of course, it's going to get less and less fuzzy as time goes on. And I mean, first of all the fascinating thing there is that it does show that we understand pretty well how V1 to V5 work, how the visual cortex works. But it also shows – I mean it's mentioned in the article – well it's in the popular science sort of articles not in the paper in the journal Neuron, how you might be able to watch someone dream. Because the same part of our brain lights up when we're imagining something as when we're seeing it itself.

Like for example, if you have the region that analyses color vision, if that actually gets destroyed, like if there's a lesion there, then people can't even imagine color anymore. Not just see it; they can't even imagine what a color looks like. There was a famous case of an artist that couldn't see color anymore after a stroke. So we know then that when people are thinking they're lighting up the same bits of the brains as when they are sensing something quite often. The same sort of thing like when people would – that know American Sign Language. Their Broca's area lights up when they doing – when they're signing, just like it does when you and I are speaking.

So what – this shows that we're going to be able to actually record at some point, it seems to me, what people are seeing, but even with their eyes closed. So then you'll be able to of course record it and upload it to DreamTube, which I've already registered that URL. No, I haven't. But someone in the chat room probably has by now.

**Andre Nantel**

I'm doing it right now.

**Dave Brodbeck**

The amazing thing about it boggles my mind. It's funny too though, because it – I always imagined this would happen and I've been saying for ever since I was teaching this intro neuroscience course for the last – gee, since 1996 I said someday we'll be able to do this. And that day's coming.

**Andre Nantel**

So, Dave, this –

**Marc Pelletier**

By using an MRI, a functional Magnetic Resonance Imaging system you could translate what's going on in the visual cortex in to an image generated by a computer.

**Dave Brodbeck**

And right now it's one image and it's 100 by 100 – sorry, 10 by 10 pixels. But it's not a –

**Marc Pelletier**

If you look at the video – well not a video, but some photos here that are – it's pretty amazing. I can read it. I can, I can...

**Dave Brodbeck**

Yeah, I know.

**Andre Nantel**

So let me ask the question here, is this – is this image that they're getting from the cortex there, is this read out directly? Like, is this – is it like a – how can I say – is the cortex viewed as like a screen that's displaying the image or are they having to do some kind of translation of the activity coming from the cortex? Do you know?

**Dave Brodbeck**

A computer is doing it, analyzing it. I mean in some respects, in a lot of respects it's almost a one-to-one relationship except the receptive fields of the cells in your cortex or are way bigger than the receptive fields in your retina.

**Andre Nantel**

Right.

**Dave Brodbeck**

So, I mean what's happening is they are analyzing it. There is processing power happening here. It's not like they're watching a drive in movie on the back of somebody's head, but...

**Justin Sanchez**

But the visual system is a little bit different compared to like the motor system or Broca's area, things like that. There is a little bit more one-to-one mapping like you're describing, right?

**Dave Brodbeck**

Yes, oh yes. I mean, I mean there's – some of it's very counter-intuitive as you probably know, right, so we analyze color in motion separate from color, it's very weird, but. And this isn't showing color, of course. This is just showing – all this is doing – and I think they were looking at V1. So all this, which is like the router for the occipital lobe, for visual cortex, so all they are looking at is a picture itself. They're not getting any color, they're not getting depth, they're not getting motion.

But this was the first one, the paper they did it without having to look at – have somebody lie in the MRI for a while and get a sort of a baseline. They didn't use a baseline in this. They just had them lie down and they analyzed what was going on in their software, which is obviously pretty awesome software, was able to do this.

And it just, it blows my mind, I mean it's one of these things like I said, I always said this day would come, but I kind of don't believe it. I mean I believe it because it's in a proper journal and all that stuff, but it's just blow away – because, it's, you know, when you think about it, there's –

**Marc Pelletier**

Where do you see it going? How far do you – where do you see the timeline of development of this sort of thing? I'd certainly like to take notes on my iPhone wirelessly with the – what we're going to talk about next a little bit, but just some of the thoughts, you know. 'Oh I remember what that looked like. Okay, I'll store that memory. I'll close my eyes, picture it and then store it.'

**Dave Brodbeck**

With the way computing power's going and the way that we're – with imaging's going and the fMRIs are getting – they're going – they're getting better and better months at a time, right. If I was to hazard a guess, I would say within ten years they'll be able – will be able to record moving pictures. And I think...

**Marc Pelletier**

That's amazing.

**Dave Brodbeck**

...also you will be able to start to deal with things like depth and color as well. Because that's the next step. These are just black and white images as it's just the stuff that's happening.

**Marc Pelletier**

We need Steve Wozniak to help fix that.

**Dave Brodbeck**

Yes.

**Justin Sanchez**

So what's quite interesting about all of this is that we're taking the environment, right, that exists in a completely different space and then looking at how that environment is represented in the brain, right. You have all of these neurons, right,  $10^{13}$  neurons maybe and they're processing their perception of the world, right. And I think that through these type of research we're going to try to understand more of how the brain really makes that jump, right. This is a big jump at least for us – for understanding how the brain actually works.

**Dave Brodbeck**

Yes, I mean it's that – it's also, if we can start to understand – I mean there is a lot more, as you said, a lot more one to one in the visual system. But if we can understand the visual system like this and using this kind of software I mean – this is clearly going to help in the kind of stuff that you do as well. So, I mean to me it just blows me away and I can't even imagine what the applications are eventually going to be. Because there's the other stuff where they're putting leads into the back of people's occipital lobes that are blind and they're able to see. I mean – so, you put all this stuff together and the singularity's coming, guys.

**Marc Pelletier**

That sounds – it's – that's paradigm shifting to the human existence.

**Dave Brodbeck**

Oh yes.

**Vincent Racaniello**

I wish I was going to be around to see it, that's all.

**Marc Pelletier**

Yes, there's ways of making that happen there, Vincent.

**Vincent Racaniello**

Maybe that'll change too, yes. We're talk going talk about longevity, right?

**Marc Pelletier**

No, I don't know if we're going to have time. We'll have to refer people back to episode 36. Yes, so let's go on to the next story. And thanks, Dave. Freaky story.

**Dave Brodbeck**

Thank you.

**Marc Pelletier**

But there's another freaky story – I don't know we had two stories each, to dig in to here. Which one would you like to present, Justin?

**Justin Sanchez**

[70:22] I think let's talk about the Twitter story yes. That's kind of a light hearted story and I think you'll – it kind of follows along with what we're discussing here...

**Marc Pelletier**

Okay before you're go, I'd like to present the fact that FiB has been the no Twitter zone on the TWiT.tv network. There's been absolutely never a mention of anybody's Twitter handle or the use of Twitter. It is an amazing technology.

**Andre Nantel**

Well let's pop that cherry, Marc. Here it goes.

**Marc Pelletier**

Amazing technology, it may replace email, who knows where it's going, it's important technology. But that's not actually the body of your next story.

**Justin Sanchez**

No, no. Not at all. Let's just use Twitter as an example of all of this. How about that?

**Marc Pelletier**

Good, good.

**Justin Sanchez**

Okay so you want me to set up the story?

**Marc Pelletier**

Sure.

**Justin Sanchez**

Okay, so one of the things that really intrigues me about this story is first of all that we're taking scientific concepts and really seeing them deployed in everyday life. A lot of times in the work that a lot us do, we could be kind far removed from all of that and now we're starting to see the impact of some new technologies in everyday life. So this is great, so here's how the story goes.

There are lots of people working in this area of neural prosthesis as we talked about earlier and using your brain waves or your thoughts to directly communicate and interact with the world. So this group that's in the University of Wisconsin-Madison is doing just that. They have this user who has a set of EEG electrodes, okay. So these are scalp types of electrodes that can sense the activity of very, very large populations of neurons. So we are looking at very gross type brain activity. And they are using this brain activity to control something called a P300 Speller.

So what they can actually do with this P300 Speller is that they flash a series of images on the screen of letters and whenever they see, or whenever the user sees a letter that they are interested in, there's a specific brain response and you can use it to select that letter. And what's really interesting about this kind of paradigm is you can use it to type. And what they actually did with this typing interface that's excited by your brain activity is that they sent messages directly to Twitter via their neural activity. So I think that the message that they wrote was something like 'using EEG to send Tweet' or something like that. So –

**Dave Brodbeck**

And then getting a sandwich, right.

**Justin Sanchez**

Right.

**Marc Pelletier**

So they just basically put on a type of skullcap with electrodes...

**Justin Sanchez**

That's right

**Marc Pelletier**

Thought about what they were going to write using a computer interface and they would think about it, interface with it and then send off their image just by thinking.

**Justin Sanchez**

That's exactly right. So they were using it as a binary – not necessarily binary, but as a character selector, right. They were looking for signatures in the brain that indicated a character that they wanted in and they would choose that and use it in the sentence they were constructing. So –

**Marc Pelletier**

So –

**Justin Sanchez**

Go ahead.

**Marc Pelletier**

Go ahead.

**Justin Sanchez**

No, I was going to say that while this is a very simple kind of spelling device here, it really opens up a lot of interesting questions about how you can use this kind of thought control to interact with other either the other computer or via the internet

**Marc Pelletier**

So it's the new form of – I guess our hundred year old keyboard or mouse – or the mouse is not a hundred years, it's about forty years old, but the idea of using a keyboard to interface with computer is no longer – and I guess this goes a little bit about – along the lines of what you were talking about and your work, right? An entire new level of interaction with the world, right?

**Justin Sanchez**

Yeah. So how do express your intent, right. This is a – we are embodied, right. Our bodies are the primary tools for expressing intent and now we're opening up the possibilities of using other forms of communication and they may enable us to do much – far greater things than our arms and legs our mouths can actually do. So this is what's really interesting. Now the part that has to deal with the science a little bit is what are the speed capabilities of all of this? What kinds of comments can you actually extract from the brain? How detailed can they be? That's really where we need to make great strides in understanding the neural code and that really isn't addressed in this type of article, right, this is just kind of a fun proof of concept and so all of those young investigators that are out there that want to learn more about the brain, this is where I think you should invest your time and your efforts.

**Marc Pelletier**

It's just pretty amazing. I hate to use the Twitter as an example but it is amazing to be able to think about something and then interface with a – to think about it and having your actions your intent applied, right that is just absolutely insane. I would like to take a minute to thank Squarespace, guys, for sponsoring Futures in Biotech. Have you guys used Squarespace at all, squarespace.com?

**Andre Nantel**

No, I've heard of it by listening to Leo but I have been running my own blogs since way before Squarespace so...

**Marc Pelletier**

Well, I have been using it for FiB, right. I gave it a try and the people who run squarespace.com liked what I had done and they said, okay, let's sponsor Pelletier on FiB and what it really is is a really easy way to publish a high quality website or blog, right. It has this really cool, I think it's Ajax that it uses. So, you just go into your browser, from your browser you log in to squarespace.com and then you can design a website. You can keep tweaking it, you can change it. I had been using Blogger for almost three years and no matter what I did and I tried to change the design, the templates, they were just never right. It was always bothering me and I would be grinding my teeth just never getting it right and a little embarrassed right that my site wasn't as I really wanted it. Well, squarespace.com, if you go to squarespace.com/biotech, you can sign up for a free trial and you will also get a 10% discount on it. Just give it a try, it's easy to use, the user interface is really easy. It's optimized both for beginners and CSS experts, right. There are hundreds of designs, templates to choose from. You can do a blog module, you can do forums, photo galleries. You can integrate Google maps, you can do a lot of fun stuff and it's the easiest thing in the world. So if you want to set up a really nice website, go give squarespace.com a try and go to squarespace.com/biotech for the free trial.

To come back to the twittering by thinking where do we go on that, you know when's this going to happen?

**Justin Sanchez**

So you want a cortical mouse, right?

**Marc Pelletier**

Cortical mouse. I want a wireless beam, right.

**Justin Sanchez**

Yeah.

**Dave Brodbeck**

Marc I don't think that's that far away. I mean I think that's, we have a BCI lab at the university. I mean that, for some of it can be rather depending on what you want to do for moving a pointer around or I mean there are now coming out EEG-type caps that you will be able to wear to control video games. That's coming down the pipeline. Something that so controlling a cursor or something like that. That's within – it's coming out for holiday '09.

**Vincent Racaniello**

Holiday '09...

**Marc Pelletier**

At Apple?

**Dave Brodbeck**

Soon!

**Marc Pelletier**

No Apple waits, right? They're going to wait till someone else develops it and make it ten times better.

**Dave Brodbeck**

But I mean this is something somebody will commercialize big time shortly but I think to me the more interesting aspect is helping people that are – don't have the use of their arms, things like that or even don't have the sort of anything, you know if they are quadriplegic, people like this, helping them to communicate, say through typing, things like that. So to me that's beyond exciting.

**Andre Nantel**

So if you look back – go ahead. What I was going to say is as you look back in the history of, let's say cardiac pacemakers right in the 1960s these were really viewed as really revolutionary types of devices and now they are millions of them implanted every year. I think that we are at the same kind of point in terms of neural interfaces that cardiac pacemakers were. We're kind of rolling out these types of technologies in a way that shows their initial potential but as the technology really scales and our understanding of how the brain processes information, then we will really be able to make them into truly functional devices. This is the thing that really needs to be demonstrated is what added functionality can they really deliver back to the individual. And I think once that's shown it will really explode.

**Marc Pelletier**

[80:14] It's going to be huge. I guess we're really just – we are cavemen right here with the technologies that we have. So I would like to thank everybody for coming on, I think this WEEK in FUN is coming out soon. So it would be a good time to close and since we all have a story that's from last year or you know the recent past we could possibly come back and do this again and this was a lot of fun. Going around the table, I would really like to thank Andre Nantel who is Senior Research Officer at National Research Council of Canada and you can visit his photo blog. He's an outstanding photographer and has a new photo every day and I visit your site probably twice a day sometimes, you know, it's just what do you call, a home page.

**Andre Nantel**

Digital Apoptosis.

**Marc Pelletier**

Digitalapoptosis.com and...

**Andre Nantel**

So my web persona has little to do with my scientific career.

**Marc Pelletier**

But it's outstanding. And it's definitely you have done a nice job, you do a lot of travels in your work and you take us on trips and it's pretty amazing. So thanks again Andre for coming on, I know you actually have to step out so...

**Andre Nantel**

Yes, so it was a pleasure meeting you guys and hopefully we will be back again very, very soon.

**Marc Pelletier**

Say hi to the girls from me.

**Andre Nantel**

Will do. Bye guys.

**Dave Brodbeck**

Bye, bye.

**Vincent Racaniello**

Later.

**Marc Pelletier**

Next we have Vincent Racaniello who is Professor of Microbiology at Columbia University and host of This Week in Virology which is at twiv.tv. Thank you Vincent for coming on.

**Vincent Racaniello**

Pleasure. You know, Marc, I really like being able to talk to people in other scientific fields. You know everybody gets stratified in science unfortunately and so this is good but this kind of format is just perfect for this. So I thank you for putting it together.

**Marc Pelletier**

Well thanks for coming on. I really appreciate it. You guys have a lot of experience in public speaking as well and you guys have a lot of, I hate to say it, you guys are very charismatic. So I appreciate it. This makes the show easy to do. And so we are all – we are staying around the life sciences, right. So this is where there are so many branches to the life sciences. We could do stories on every different topic, worried that we would never be able to do forty stories, forty FiBs but there is a lot of material out there. So thanks, Vincent, for coming on.

**Vincent Racaniello**

You are welcome, pleasure.

**Marc Pelletier**

Thanks Justin, Justin Sanchez, Assistant Professor of Pediatrics, Neuroscience and Biomedical Engineering. That's three departments.

**Justin Sanchez**

Yeah, three departments. So I see under my name there it says University of Gainesville. Just like to, I have to give a shout to the University of Florida there, I need to make a little correction in all of that. So, they have been really supportive in everything that I have done. So and yeah three departments. What we are doing is highly multidisciplinary work and we are making great strides. Also one other thing, you know, we are taking about Andre's photo blog there. When we are not trying to crack the code in the brain and make these implants, I am out trying to be a rock star in a rock band. So, I would like to send another kind of shout out to my band. It's at myspace.com, Black Snake band and try to get a little attention over there. Yeah, so check that also, so check out the lab website, nrg.mbi.ufl.edu and then also check out our MySpace page. There it is, Black Snake, yes. Cool.

**Marc Pelletier**

I will definitely check that out. That's really cool. I didn't know you are in a band.

**Justin Sanchez**

Yes, you know doing great science and then also doing great arts, I think it makes for a great combo in a well-balanced lifestyle. So we try to do the Renaissance man approach to life here. So it's really good.

**Marc Pelletier**

What do you play?

**Justin Sanchez**

I play the drums.

**Marc Pelletier**

Very cool, very cool. That will guarantee you grandchildren, children and grandchildren.

**Justin Sanchez**

I hope so.

**Marc Pelletier**

Many, many, many, many, many, children okay. Thank you for coming on and, Dave.

**Justin Sanchez**

Thanks. It was really a pleasure.

**Dave Brodbeck**

Same here, Marc, always.

**Marc Pelletier**

Yeah this is Dave Brodbeck, Associate Professor and Chair of the Department of Psychology at Algoma University in Sault Ste. Marie. Your flagship podcast is Thunderbird 6.

**Dave Brodbeck**

Thunderbird 6, I also if you want, dot org. If you want to check out the lectures that's people.auc.ca/brodbeck/blog. Now I sound like Dvorak and so if you want to check those on courses as varied as introduction to psychology, to neuropharmacology which I am teaching right now. So you know if you feel like checking that out, feel free and there is all kinds of stuff there like three years' worth of lectures, 400 classes and it was just a real pleasure to be here with all you guys and it is fun just talking science, it makes you, and it also reminds you that there is a whole lot of other stuff out there besides, at least reminds me there is other stuff out there besides memory and food storing birds.

**Justin Sanchez**

Amen.

**Dave Brodbeck**

There's scary viruses.

**Justin Sanchez**

Scary viruses that come from whale poo.

**Vincent Racaniello**

That's what you got from it. That's good.

**Marc Pelletier**

I like to mention that –

**Justin Sanchez**

If there's one take away message, it's that there are scary viruses in whale poo.

**Vincent Racaniello**

Are you going to make that the title of this episode, Marc?

**Justin Sanchez**

It's the obvious title.

**Marc Pelletier**

Yes. Absolutely. I would also like to mention that we are going again live on June 5<sup>th</sup> at 4 p.m. Eastern Time, 1 p.m. Pacific Time and Dave Brodbeck will join me and co-host the episode and it will be an episode with Dr. Gabrieli from MIT and it will be on brain imaging. So a lot of the topics that we covered today will really get some interesting insight into where it's going, what's going on in those labs on the imaging side. We now know a little bit about the interfaces that are gathering those images. Let's get to the other side and see how those images can be interpreted from inside the lab.

So thank you everyone for coming on.

**Andre Nantel**

Yeah, thanks so much. It was really a great time.

**Dave Brodbeck**

Thanks a lot, guys. Good times.

**Marc Pelletier**

Isn't Skypasaurus awesome? I would like to thank Colleen as well for managing...

**Andre Nantel**

Thanks, Colleen.

**Justin Sanchez**

Thanks, Colleen.

**Marc Pelletier**

Thanks, Colleen and thank you everyone at TWiT and the listeners and we're signing out.

**Vincent Racaniello**

So long.

**Dave Brodbeck**

Later everybody, bye.

**Marc Pelletier**

See you soon. Thanks. See you on the 5<sup>th</sup>.

**Marc Pelletier**

Again I would like to thank the four panelists, Andre Nantel from digitalapoptosis.com, Dave Brodbeck from thunderbird6.org, Vincent Racaniello from This Week in Virology and Justin Sanchez. I would also like to thank Leo Laporte and Dane Goldman for co-producing the show and lastly Phil Pelletier and Will Hall for the opening and closing themes.

Transcripts have been available by the kind folks at Pods in Print. If you need transcripts done, these guys are incredible, they can handle any topic, any field no matter how specialized. For those transcripts, you can go to [futuresinbiotech.com](http://futuresinbiotech.com). For comments and suggestions, I can be reached at [marc@twit.tv](mailto:marc@twit.tv). For Futures in Biotech, I am Marc Pelletier.