Predictive mathematical models are a useful tool for just about any type of research in science. But how useful can they be in helping us to understand nature of evolution? One Western researcher Dr. Lindi Wahl from the Department of Applied Mathematics at Western University uses models to understand the evolution of viruses and bacteria. We sat down to talk about her research and the mechanisms viruses have in order to evade extinction.

Henry Standage 0:15
Predictive mathematical models are a useful tool for just about any type of research in the domain of science. But how useful can they be in respect to the unpredictable nature of evolution? One Western researcher Dr. Lindi Wahl from the Department of Applied Mathematics uses models to understand the evolution of viruses. We sat down to talk about her research and the mechanisms viruses have in order to evade extinction. Here it is.

Henry Standage 0:45
What do you look at here?

Lindi Wahl 0:47
So, I study the evolution of microbes - so generally bacteria and viruses. And I study them using mathematical models. So, the main idea is to get a better handle on how they evolve using predictive models so that we can figure out how to prepare for and/or change the future in ways that we want to.

Henry Standage 1:11
And as you just said, you're turning this microbial evolution into a game of analytics. So, let's start with talking about some of the mutations that arose that helped bacteria adapt and survive throughout the years.

Lindi Wahl 1:22
So, like any organism, bacteria, have experienced huge numbers of mutations and adaptations over their history. One of the ways that makes them really particularly interesting and challenging to study is that they exchange genes with each other rather frequently. So, bacteria have several mechanisms for what's called horizontal gene transfer, which means they can share genes between organisms. And so this means that genes for instance, for antibiotic resistance can spread really rapidly because bacteria can essentially hand them to each other and the receiving bacteria just takes that gene and puts it right into their genome and it becomes part of them. And they can even pass these across species boundaries. I don't think they look at each other and say, oh, they're sick - you need this, but they can share genes, for instance, a gene that would fight against a drug.

Henry Standage 2:18
How do they communicate that?

Lindi Wahl 2:20
So, there are a bunch of different mechanisms. One is by actually making this little pilis, which is like a little tube that goes from one bacterium to the other, and genetic material gets shot through the tube into the recipient bacteria.

**Henry Standage** 2:36  
What are the various ways in which a microbe has to learn to adapt?

**Lindi Wahl** 2:42  
So, I guess, there are many ways but the ways that are new now is that microbes have to adapt to all these changes that humans are causing. So, they need to adapt to climate change - just like everything else on our planet. They need to adapt to antibiotics, as I mentioned or antivirals for viruses. They're also adapting all the time to new host species. So, you've probably heard of swine flu or avian influenza. These are examples where a pathogenic microbe has jumped from one species into another species, in this case, humans, and that can cause really dangerous outbreaks.

**Henry Standage** 3:24  
It's interesting to me that it's humans who are causing the most problems, because bacteria is something that affects every species on the planet. And, you know, I guess it's our brains, but we're the first to kind of adapt to counter it.

**Lindi Wahl** 3:36  
Well, I guess there's been kind of an arms race over evolutionary history. All the species on the planet have been adapting to each other and keeping pace with each other. And then humans have suddenly accelerated this pace of change, and that's hard for everyone else to deal with.

**Henry Standage** 3:53  
Can you talk to us about experimental evolution and the tools you use in order to study it?

**Lindi Wahl** 4:02  
Sure. So experimental evolution means evolution that happens in a laboratory setting. And researchers are able to keep populations of bacteria or viruses or other microbes, or bigger organisms (fruit flies) alive for many, many generations and watch evolution unfold.

**Henry Standage** 4:26  
A hypothetical timeline of adaption.

**Lindi Wahl** 4:29  
Yeah, so instead of just studying the fossil record, we have a fossil record in the freezer from the last few months of adaptation that happened in the lab. And because generation times are very short for bacterian viruses, people have studied thousands upon thousands of generations of bacterial evolution. So, more generations than homosapiens has had, for instance, have been studied in laboratory settings for bacteria. So, all kinds of cool changes have happened. The bacteria look different. Their cells are shaped differently, they exist at a different place on the plate. So, they learn to live on the surface or look deep. In the experimental flask, they learn to process different sugar sources, so they eat a completely different type of food than they did at the beginning of the experiment. So, in my work, we study experimental evolution using mathematical models. And the idea with a mathematical model is to distil the essence of the problem into something that we can write down with pencil and paper, and then we can manipulate it. And an analogy I can give you is that when you have a mental model of a teeter totter, it's really easy to see if I push down on A then Part B will go up. But if you have a mental model of a much more complicated system, so you have a teeter totter, but on one end of the teeter totter, has a rope which is attached to a wheel which is attached to a gear which links back to the first side of the teeter totter, which attaches to something else. And then I asked you what happens if I push down on this end of the teeter totter, it's very difficult or sometimes impossible to figure out what you would predict to be the outcome. And so biologists have very, very complicated mental models of the systems that they studied because they understand them in
such incredible detail. And so, the goal of a mathematical model is to write down the essential features of that in some very clear way, if possible, and in a way that we can then manipulate and see what their model predicts.

**Henry Standage  6:41**
What organisms do you look at when you’re studying experimental evolution?

**Lindi Wahl  6:46**
Mostly bacteria and viruses and within those there are certain bacteria that are well studied like E. coli, or viruses like HIV.

**Henry Standage  6:59**
Are infectious microbes an inevitable part of the human experience? Is it rational to imagine that one day, we will have the systems developed in place to study their evolution, or just to stay safe from them?

**Lindi Wahl  7:12**
So, I think in a bigger picture, parasites are an inevitable part of life. So, at every level of life, there are parasites, there are even parasites in your genome. So, I think we'll never have a world without parasites where there's life, there will be parasites, microbes are particularly effective parasites. And I also believe that where there's life, there will be evolution, it's just fundamental to the way life works on this planet. So, all that we can do, I think, is try to understand evolution better so that we can predict it better. And one thing we've learned from experimental evolution is that we are able to direct evolution, we're able to accelerate it, we're able to slow it down. And so, we want to use those tools for instance, to slow down the evolution of antibiotic resistance.

**Henry Standage  8:03**
So, you think that it's possible that we could put better systems in place to stay safe?

**Lindi Wahl  8:09**
Yes, to stay safer. Yeah, we can, like get one step ahead in the arms race, right?

**Henry Standage  8:15**
Can your models apply to more personable organisms such as humans?

**Lindi Wahl  8:19**
Yes, I would say, I don't study human evolution. But one thing that I do study quite a bit is the human immune system, because this is our first defence against bacterial invaders or viral invaders. So for instance, in HIV, we have detailed models of the virus inside an infected individual. And as you may know, HIV is particularly mutable and adaptable, it changes all the time. And then the human immune system is adapting all the time trying to fight back and ultimately what happens when AIDS progresses is that the human immune system has lost that battle. We're trying to understand it better to understand how we might slow that down.

**Henry Standage  9:06**
So, in the context of you looking at viruses and your experimental evolution, can you give me an example of something you look at and how A effects B there?

**Lindi Wahl  9:16**
Sure, in one project that I have, I'm modelling a virus that usually infects a bacterium, and when it infects, it explodes the bacterial cell and releases a huge number of baby viruses. And those viruses go on to infect other bacteria. So, the virus is a predator that's killing the bacterial prey. But these viruses have another option where they can go into a bacterial cell and then put their own genome into the bacterial genome and sort of become one with the bacterium. And this is an incredibly complicated system because the predator can either eat the prey or become part of the prey. Then it's not clear, even where I should draw the species boundary here, right? It blurs a lot of really important lines. And so, this mathematical model, we're trying to predict what is the effect of this
strategy? Why did viruses pick up this strategy? How is it affecting bacterial populations? And all these are questions that we can start to approach with a mathematical model?

**Henry Standage 10:24**
Is it a fight or flight mechanism when this happens?

**Lindi Wahl 10:28**
No, it's more like if there aren't very many other bacteria to infect. Maybe it's a good idea to hide out in the bacterial genome and be replicated when the bacterium replicates and then later they can come out.

**Henry Standage 10:47**
As Lindi said, viruses will always be a part of the human experience. However, by using the analytical tools available to us, we can stay one step ahead in the arms race of adaption. Look at HIV for example, a disease that when diagnosed to someone in the 20th century, signalled an almost certain demise. Yet it's now treatable thanks to a better understanding of the functions it exerts on our body. For the first time in human history, we have the leg up on viruses. Let's keep it that way. I'm Henry Standage, signing out. Thanks for listening.