Maths + Cancer

Episode 1: The relevance of maths to cancer with Professor Philip Maini

Transcript

Vicky Neale:

My name is Vicky Neale, and I'm a mathematician at the University of Oxford. Since March 2021, I've also been having treatment, on and off, for a rare form of cancer. That's been very educational, I've been learning lots about cancer and the various treatments available. While I wish it was less personally relevant to me, I also find it fascinating. I take comfort and have great pride in knowing that I have colleagues in the mathematical community whose research helps to tackle cancer from prevention through diagnosis to treatment. In this podcast series, Maths + Cancer, I'm going to sit down with some of them to find out more about their research, and about the people behind the research. I'd love you to join me for our conversations to learn more about how mathematics and mathematicians are helping to combat cancer.

I'm joined today by Philip Maini. Philip is Statutory Professor of Mathematical Biology and Director of the Wolfson Centre for Mathematical Biology at the Mathematical Institute, University of Oxford, and Professorial Fellow of St John's College, Oxford. He's been awarded the Nayler Prize and Lectureship by the London Mathematical Society, the Arthur T Winfrey Prize by the Society of Mathematical Biology, and he's a Fellow of the Royal Society, to mention just a few of his many prizes and fellowships. And today we are talking in the Oxford Mathematical Institute, in the boardroom, with this magnificent view over Oxford. It's a perfect place to discuss maths and cancer. Philip, thank you so much for joining me today.

Philip Maini:

Thank you, Vicky.

Vicky Neale:

I think people might be surprised at how important maths is in understanding cancer. Before we talk about kind of more details of your own work, I wondered whether you could give us a bit of an overview of some of the ways in which maths is relevant to understanding cancer.

Philip Maini:

OK, well there are really two aspects of it. One is the statistical aspect of it, where one can look at correlations and find out by looking at data, maybe find out that certain families are more prone to cancer, certain genetic backgrounds are more prone to cancer. And that simply comes from looking at a lot of data and doing data analysis using statistical methods, and then finding out that there are these relations.

Vicky Neale:

And in this podcast series, we're going to be looking at some of the statistical tools that go into that.

Philip Maini:

Oh good.

Vicky Neale:

Because it's really interesting, that kind of mathematical, statistical techniques for these big datasets. But anyway, I interrupted you, you said two ways. Let's have the second.

Philip Maini:

It's really good you said that because I don't know anything about statistics, so that's fantastic. So the other aspect is to look at more mechanistic aspects of cancer, and if I could give an analogy, most people will have heard of Kepler's laws of planetary motion.

Vicky Neale:

So these describe how the planets move around the Sun. There's mathematical equations that predict that motion.

Philip Maini:

Yeah, well, first of all Kepler, he was a data scientist, and he looked at data and he concluded that there was a relationship between the distance that a planet is from the Sun and the time it takes to evolve around the Sun. But then if a new planet was discovered then we would not know necessarily that it followed the different laws. But then along came Newton, and Newton came up with a mechanistic understanding of gravity. With gravity, and then he was able to prove mathematically that any planet that orbits around the Sun will obey this law. So he took what was a correlation, and he put a mechanism behind it.

Vicky Neale:

So to check I've understood, so Kepler was looking at the data and saying, well based on this data I think this is what's going on. Newton was able to look at, for example, gravity and give an explanation for why that was going on, to give confidence that that was the right way to understand the system.

Philip Maini:

Yeah, that's right. And then not only through Newton's approach could we understand how planets revolve around the Sun, we could calculate how much time we had to run away before the big apple fell on your head. We could do all sorts of things with this, so it was very, very powerful.

Vicky Neale:

OK, so once you've got this model, you've got this understanding, then you can apply that to other situations, not only planets moving around the Sun. That's immensely powerful actually, isn't it?

Philip Maini:

Yes, that's right, but it takes a lot longer to get to that stage. That's the drawback of it. So this is then where mathematical modelling comes in. So Newton's laws of motion are actually a mathematical model of motion. And so what we do is use mathematical models to try and understand how tumours evolve and how they grow, with the view that if we can understand the mechanisms by

how they grow, then those would automatically provide targets for drugs. So that's the role that mathematics plays in in this field.

Vicky Neale:

Fantastic, and this idea of mathematical modelling I guess for people not used to kind of the way that mathematics is used for cancer, this idea of modelling seems really interesting. So how do you start to build a mathematical model of something like the growth of a tumour? That feels like an enormous, I mean understanding how the planets move is complicated, but tumour growth feels really complicated.

Philip Maini:

Yeah, well you're absolutely right. So the first thing to bear in mind is that we are all modellers, and mostly the models we have are verbal models. So when I said to you that you can look and you can say that certain gene expressions lead to certain types of cancer, that's a model, but it's a verbal model. So what we do in mathematical modelling is to try to abstract the processes that go on in cancer. And before I go ahead with that, I'll just maybe give an analogy of how mathematics can be used. So suppose we have some chemical A. And it produces chemical B, and chemical B produces chemical C, and suppose chemical C is the one we're interested in. So if we were asked, well, how do we increase the amount of chemical C then we would say, well, A produces B, and B produces C, and I've got loads of A so I'll just add more A.

Vicky Neale:

Makes sense.

Philip Maini:

And now I'll get more C. That makes perfect sense. Biology isn't like that. That's a linear model, and that's a verbal model. Biology isn't like that. The equivalent biology would be A produces B but B inhibits A. It degrades A. B also produces C, but C inhibits A, stimulates B to produce more, but does so after a period of time.

Vicky Neale:

So there's this complex interplay.

Philip Maini:

This complex interaction. So now if you ask the question, how do I get more C? Should I increase A or should I decrease A?

Vicky Neale:

It's really not so obvious is, is it?

Philip Maini:

It's not obvious. But those laws, those processes, you can put in a mathematical model. And once you have them in a mathematical model, it is pretty easy for that simple example I've given to figure out, and what you would find is that depending on the interaction strengths, in some cases adding A would increase C, and in other cases decreasing A would increase C. It's because of the complexity. And you see this a lot in experiments, where you see that somebody does an experiment and gets a certain result, and then somebody does seemingly the same experiment and gets a different result.

Now it could be that one of them made a mistake. But more often than not, both experiments are correct, it's just that they were done under slightly different conditions, so both results are correct, but they're done under different conditions. And then what mathematical modelling can do by writing down, mathematically describing, by taking this verbal description, by converting it into mathematical equations, and then once you convert it into mathematical equations, you can use the power of mathematics to investigate all the different interactions that we simply can't think through in our mind because we can only think linearly, we can't think through very, very complicated interactions.

Vicky Neale:

So having taken your complex biological system, tried to capture the essence of that with some equations, potentially you could then put those into a specialist piece of software, or write a new piece of software, and then maybe you could put in different parameters, and experiment a bit to see what the consequences of those different parameters might be, is that right?

Philip Maini:

Yeah, that's exactly right. And as you mentioned, I mean what we try to do is get to the core issues. So we can't put everything into a mathematical model because to begin with everything isn't known. Plus if we did put what we all know into the mathematical model, we wouldn't actually be able to solve, get insight from the mathematical equations.

Vicky Neale:

The equations would be too complex.

Philip Maini:

The equations would be too complex. So we have to simplify. So now you might say, but then how do you know you're missing? You might be missing the key things. But that's the case with all models, because think of an experiment. In an experiment, in many cases you put cells or a tissue into a dish. And then you do experiments on it, and that's what an experimentalist would call a model. It would be called an in vitro model. You put your tissue into a dish, and you add some chemical, and you say oh, the cells behave in this way. So what have you discovered? You've discovered how cells behave in that dish.

Vicky Neale:

And you hope that that sort of translates to what happens in a human body, for example. But you can't be sure.

Philip Maini:

That's right. You can't be sure. Because when you've taken the cells out of the body, you've changed all their mechanical properties, and due to the process of mechanotransduction you've changed all their chemical properties. So what you've determined is how do cells behave in the dish when I apply this chemical at this time. If I was to do this experiment later on today, I'd get a different result because of circadian rhythm. So that's a mathematical model. I mean, that is a model. It's a huge abstraction to say how cells behave in the dish is how they behave in the human.

Vicky Neale:

But we know that that can be informative, and I guess, analogously with mathematical models, even though they are simplifications necessarily, they can still be really informative for predicting what happens in a human, for example.

Philip Maini:

That's right. And the bottom line is: what else can we do? We can't experiment in humans, so that's all we can do. It's the best that we can do, and therefore the key thing is that once you've done these experiments in the dish, they give you ideas as to what might be happening, and then you test that out on the human. And the same thing with mathematical modelling. Mathematical modelling, which actually is cheaper than doing experiments in the dish. Plus with mathematical modelling you can do many more different things. You can manipulate all sorts of things. So things that might literally take years for you to do in a dish, you can do in an afternoon on a mathematical model. So you can use the mathematical model to go through all sorts of different hypotheses, generate new ideas for what might be happening, and then provide the clinician or the experimentalist with a number of scenarios of, you clinician told me that you think this is happening, so if that was happening then if you did this experiment, you should see this result. And then they can do that experiment. And then if they don't get that result, that means they were missing something. It doesn't mean the mathematical model is wrong, it means the hypotheses that went into the mathematical modelling, in other words, the biological understanding that went into the model is lacking something. And that's where the model is really useful. It can point out where something is lacking. But moreover, the mathematician can then say, well, the model said you should have got this result. You got this different result, but if I was to change the model in this way, then it would agree with that result. So if I change the model in this way, that means I'm saying that there's this other biological process going on. Is that true? Is that what's happening?

Vicky Neale:

So it sounds to me as though these. I was picturing what does this collaboration look like? And I was picturing maybe a clinician or somebody, an experimentalist, coming along and say, well, we're looking at this process and we think these are the important factors, and Philip can you and your team kind of come up with some equations that build on those factors, describe what's going on. Crunch the numbers then, using those equations, and tell us what you think will happen, and then you go back to the clinician or the experimentalist and say, well, this is what I think will happen. But actually, it sounds as though it's much more iterative than that, that you're going back to the experimentalist or the clinician, they're testing out what the mathematical model has predicted. They're going well, actually in reality that's a really good fit. Or actually, that doesn't seem quite right, can we go back and see? Can we tweak the model a bit so that the data does match up and it sounds as though there's a lot of backwards and forwards between you and the scientists in the lab.

Philip Maini:

Well, typically what happens is that, well, if I go to a collaborator and say, could you work with me? I've got this mathematical model, I've predicted these results. That by and large hasn't worked because they've got their own stuff to do.

Vicky Neale:

They've got constraints on their lab time.

Philip Maini:

Exactly. What has worked is that when people have come to me and asked me the questions, and as it's turned out, the two or three of the best collaborations I've had are people that have come with who actually were mathematicians or physicists or engineers who then converted to becoming biologists or clinicians. And they then can spot when they have a problem where they see, oh, this is amenable to mathematical analysis, and I can do the experiments, but I don't have time to do the mathematics. And now here's where we can ask a mathematical modeller.

Vicky Neale:

And I guess they speak both languages, so they can be a bit of an interface between the experimental and the mathematical.

Philip Maini:

That's right, and in fact one thing I should add to that then, is that this is now being recognised throughout the scientific community, that really the forefront of a lot of science now requires us to move away from these artificial boundaries we have of mathematician, physicist, biologist, etc, and to blur those boundaries. And so we do now have doctoral training courses where people are given a background in a lot of different scientific areas. Now really to ask somebody to be an expert in one area is a big ask. So to ask them to be experts in more than one area, you know, typically that doesn't happen. But training people to have expertise in one area but to be able to speak the language of the other areas is I think very, very important. So it's not that you have to be a trained mathematician who then became a biologist, and only then can you collaborate with a mathematical biologist, but you could be a biologist who sort of knows some aspects of mathematics, and then can pinpoint when your problem would benefit from a mathematical approach and then go and talk to a mathematician.

Vicky Neale:

That's really interesting. It's definitely highly interdisciplinary, isn't it?

I'm just going to interrupt briefly to let you know that if you're enjoying this episode of Maths + Cancer, then please do head to ox.ac.uk/cancer to find the other episodes in the series, in which my amazing guests tell us about some of the many intriguing ways in which maths and stats are helping us to understand and tackle cancer.

One of the things I wondered was how much you see a direct impact for patients of your work and to what extent your work is more fundamental and then there need to be subsequent stages before that has an impact for, for example, cancer patients.

Philip Maini:

Yeah, at the moment it's more fundamental, and it's more sort of suggesting ideas, because my view's that eventually the person who's really going to solve the problem is going to be the clinicians and the experimentalists. What the mathematicians can do with mathematical modelling is to give ideas that may be counterintuitive to the clinicians. That they could maybe test and then find that that it works. Certainly there are some clinical trials going on that are in early stages that are based on some mathematical models, but as you know a clinical trial, whether it's based on mathematical model or on experimental models, has to go through many different rounds before it would eventually get approved in the hospital.

Vicky Neale:

I guess anybody doing research in cancer in any way knows that this is a long game. This is not about quick results.

Philip Maini:

That's right, yeah. And of course, although we're talking about cancer, I mean cancer is a series of diseases, and so some approaches that might be appropriate for one type of cancer may be not appropriate at all for another type of cancer. So that makes it even more difficult in terms of getting the appropriate data and the appropriate amounts of data. There's a whole series of diseases.

Vicky Neale:

Yeah, absolutely. And yes, rare cancers don't have very much data because there aren't very many people who have them.

Philip Maini:

Yeah, that's right.

Vicky Neale:

You mentioned that sometimes the models can produce counterintuitive predictions. Do you have any kind of favourite specific examples from your own work?

Philip Maini:

Well, there's one example where we were working with somebody called Bob Gatenby, who's a physicist who became a radiologist, and now he's chair of radiology and he works at the Moffitt Cancer Centre. And they were looking at a model of, they had a verbal model of ductal carcinoma, so breast cancer. And they were talking about evolution and the idea that the cells would evolve from one type to another type. So basically what happens is cells have to be attached to a surface, and if they fall off that surface they die. So the first thing that the cell has to do is if a cell is going to invade in the duct, for example, it needs to have a mutation that will allow it to survive once it's come off the membrane. And then it'll start to grow into the domain, but the nutrient is only coming from the outside of the domain, so pretty soon it's going to run out of oxygen.

Vicky Neale:

So this is the scenario where you've got this cancer cell. It's got the mutation, but in order for it actually to turn into a tumour that's going to cause a problem to the patient, you need the circumstances to be right, and in particular it has to get its supply of nutrients in order to be able to grow and expand uncontrollably.

Philip Maini:

Yeah, exactly. So if you think of it being a ball, and you start growing from the surface of the ball on the inside, but you only get in nutrient from the outside of the ball, the nutrient can only penetrate a certain amount.

Vicky Neale:

So the cells in the middle are not getting any nutrients.

Philip Maini:

Yeah. So they have to mutate to use different mechanisms of growth anamaybe in order to survive. So what Gatenby and Gillies and various people had in their model, verbal model, was that you had this progression from one type to another type to another type.

Vicky Neale:

As these cells are mutating, evolving, right.

Philip Maini:

And then eventually you would get a sort of super cell that could do everything and then it would invade. So we decided, OK working with them, that we would test this by using a mathematical model. So we used a mathematical model for this which basically just said let's consider cells as little discs, and then when they divide there's a certain probability that they get a mutation, and then based on that they have certain properties, and then let's go through and do all this. And what we found was that instead of having this evolution from one type to another to another, we find that there would be a coexistence. In other words that you wouldn't get one type and then that get replaced by another and then replaced by another. There'd be a mixture.

Vicky Neale:

So cells with these different mutations are happening at the same time.

Philip Maini:

Yes, that's right. And so you'd still get evolution to this very damaging cell, but there'd still be these other cells left around. So then we went back, we were working with Bob, and we went back and said, you know, this is our prediction, that actually what you should see is pockets of these sort of super cells for want of a better word, but then you'll see other cells still hanging around. So then they did a experiment. They had some cancers there that they could actually analyse to see. And that's precisely what they found. And of course, this is one of the many things that makes cancer very, very difficult to analyse. The fact that it's not one cell type.

Vicky Neale:

So even in a single patient with a single tumour there's different types of cell.

Philip Maini:

That's right, loads of different types of cells. And then drugs tend to target certain types of cells. And one of the things we're doing at the minute, actually with the Moffitt Cancer Centre, is this idea that. So if you've got all these different types of cells and they're competing with each other because they're competing for nutrient, for resource, and you can kill one of those cell types, then if you kill that cell type, you've removed the competition from the other cells. So the cells can grow now without any competition, and you don't have a drug to target those cells.

Vicky Neale:

I'm picturing weeds in my garden now, and sort of different types of weed. I guess there's a limited amount of water and nutrients in my soil. If I if I take out one type of weed that I've got a particular dislike to, that just means there's more opportunity for the others to flourish.

Philip Maini:

That's right. And in fact you pick a very good analogy there, because Gatenby and his group have been developing the idea of think of cancer as an ecology. And as soon as you think of cancers and ecological things. So you think of cancer cells as an invader. So a weed that's invading your beautiful lawn. Well, modelling has been going on to look at invasion. Or think of the grey squirrels that invaded the indigenous red squirrels of the UK in the last century. There have been models developed for that since the beginning of the last century. Moreover, they've been in terms of plants and things like this. People have developed strategies to control. So how can we learn from those? And that becomes very important. The idea then, is well, should we kill some of the cells that we can kill, but leave enough of them so they can compete with the ones we can't kill and stop them from growing? But then how do we do that? How do we know how many cells to kill? If we kill too many of them, the resistant cells will grow. If we don't kill enough of them, the sensitive cells will grow.

Vicky Neale:

This sounds like an ideal opportunity for you with your computer to use your mathematical model and test out scenarios.

Philip Maini:

That's right. So what you can do with the mathematical model is you can test out things like you can say if I was to give what's called adaptive therapy. So I give therapy, and then until the cell decides the tumour gets to a certain volume and then I leave it to grow again.

Vicky Neale:

OK, so you want to shrink the tumour to a certain amount, but then kind of back off.

Philip Maini:

Let it grow.

Vicky Neale:

And see what happens.

Philip Maini:

And then give the drug again and then it contracts and then grows again. Of course at the same time this is happening, and your analogy is fantastic because we know that plants become resistant to what you're treating them with. Same thing with tumour cells. So slowly these sensitive cells will become resistant. So eventually you're going to get this population that will just grow to infinity. The question then is: could you, by giving this adaptive therapy, could you make that push the time back for that. And so what we can do with the mathematical model is we can say right, the standard of care which is called maximum tolerated dose, which you just hit the tumour with as much drug as you can that the patient can tolerate, versus this fluctuating drug dosage. Can we see under what conditions that fluctuated drug dosage would give more time than the maximum tolerated dose? And that's an ideal problem for mathematics, where, like you say, you can ask questions like what should the limit be? At what point should we decide to give our drug again? How much drug should we give? And we also then have to bear in mind the practicalities of this. Like maybe practically it might be that your model predicts you should give the drug at the weekend, but there's nobody in at the weekend to give the drugs. So that's the sort of way in which you can then have what's called a constrained optimization problem. Which again is a very mathematical problem, has been looked at in all different contexts.

Vicky Neale:

I think this is a really interesting example because you talked a little bit about kind of mathematical modelling, maybe thinking about how tumours grow, for example, but I think also using a mathematical model to test out different treatment scenarios, I think that seems really interesting. And also the limits of that, that actually there's a patient behind all of this with their quality of life and the practical realities of a health system managing this patient's treatment and all of those kind of things. But the ability to use the mathematics to explore different scenarios and say, well, if we had this treatment regime or that treatment regime, what might that look like for the tumour? And then to be able to discuss that with the clinicians and think about well, from a patient perspective and from a clinician perspective, how does this work in reality? That seems like a really interesting example of the power of mathematical modelling.

Philip Maini:

Absolutely. And another example of where the mathematical modelling can be helpful, and again, people have done this. I mean it's not our work, it's work of other people like Kristin Swanson and and in fact Jim Murray who started this, who used to be Professor of Mathematical Biology here, is the idea that if you look at when you visualise a tumour using whatever machines you use, you only see part of it, because you can't see all of it because you don't have the technology. And this is a bit like an iceberg where you see the top of an iceberg and you know that in fact there's a lot of it you can't see. So as a clinician, you have to decide well, I've seen this tumour, so how much extra do I need to cut out?

Vicky Neale:

These are the surgical margins, is that the phrase?

Philip Maini:

Yeah. And what a mathematical model can do is, because a mathematical model doesn't have any limits in terms of I can't see my solution if it's below a certain value. The mathematical model will give you the prediction of the cancer cell density from zero to whatever.

Vicky Neale:

So even when there are tiny, tiny numbers of cancer cells.

Philip Maini:

Yeah. So therefore you can use the mathematical model to say that if you see this amount of cancer, then there may be this extra amount. It can give you an idea of, as you mentioned, the surgical limit.

Vicky Neale:

So a surgeon in an operating theatre. I guess removing a tumour is not like removing a golf ball or something with nice, clean edges, it's got these fuzzy edges and the model is helping the surgeon say well, if this is what I can see that's going on with cancer cells, I know I need this much extra margin to try to catch the cancer cells that I can't see.

Philip Maini:

That's right. And at the moment the surgeon is using a model, and the model is well, in the past when I saw something that looked like this, I removed this extra bit, and that helped, so I'll remove

that extra bit. And we are providing a different mathematical model which then actually means that it could actually inform. So for that model to work where the surgeon says, well in the past I've seen this, I can remove that. That requires you to have done a lot of this. So what about the surgeon starting out for the first time, who doesn't have that experience? Well, of course you can work with someone who's got a lot of experience. But this could be a way of giving independence right from the start.

Vicky Neale:

And from a patient point of view, you don't want to have more tissue removed than necessary because that can have a real impact on somebody's life.

Philip Maini:

Absolutely, because particularly this particular cancer we're talking about is glioblastoma, which is in the brain. And of course, there in particular you really don't want to remove more than you have to remove.

Vicky Neale:

Such interesting work. So you clearly are working in collaboration with people in lots of different fields. How do these collaborations start? Do people come to you and say, Philip, we've got this idea, can you build us a model? Do you have an interesting mathematical idea and go and find clinicians and talk to them? How does it happen?

Philip Maini:

Well, what I found. So one of the aspects about it, I mean, typically you find more mathematicians or engineers or physicists going into biology than vice versa. And the reason for that to some extent is that mathematics is sort of like building a pyramid. You have to start off with a lot of groundwork theory that you need to know, and then as you specialise, you sort of narrow and build up. And so even though for example you mentioned I work in differential equations, I need to do stuff about linear algebra and things like that. And if I apply my equations in some contexts, I might need to know geometry and things like this. But biology tends to be built more as pillars, so that you can take, I mean not all biology, but a lot of it, you can focus in on one aspect of the biology. Learn that without having to know all the other aspects, and of course the key thing with all of this is not be scared to ask silly questions. OK, there's no such thing as a silly question. There's only silly answers. And working with biologists you can say look, I don't understand this and they'll very quickly be able to tell you the answer. In fact, in most cases, if you don't understand something, it's probably because it isn't understood. So there are many, many examples of mathematicians, physicists, engineers, going into mathematical biology. There are some examples of people going in the other direction, but not as many. And my approach is that a good mathematical modeller should be a lazy mathematical modeller, and that is someone who will first of all say well, why can't you do more experiments? Why can't you just think this through and get the result? What is the issue you're having here that defies your logic?

Vicky Neale:

And I guess you have to understand that complexity to know what's going to be important when you build your model, what assumptions you need to make, and so on.

Philip Maini:

Yeah, that's right. Yeah, to really get to the core of why is this an issue? Why can't it be resolved by just doing another experiment? And then when you understand that they say right, this is right for mathematical model. This is where a mathematical model can give added help. Because that's the key thing. You want to be able to enrich the science rather than trying to do something that actually could have been done easier by just thinking through it with a bit of common sense.

Vicky Neale:

I think that's a really interesting point, to understand the limitations of what mathematical modelling can do. And in the same way that the experimentalists have constraints on lab space and time, there's constraints on your time, and where can you have the most impact, I guess, with your modelling?

Philip Maini:

That's right. And another aspect of this is to say, well, if we were to come up with a mathematical model and some understanding of this, what experiments could you do to validate our model? Because you need to validate the model before you take it further into the clinic. And if you can't do those experiments yet, then maybe this is a bit too early to do mathematical modelling.

Vicky Neale:

So it's picking the right time as well as the right problem.

Philip Maini:

That’s right.

Vicky Neale:

I'd love to understand more about how you got into this field. You grew up in Northern Ireland and then you came to study maths here in Oxford as an undergraduate. Was it an easy decision for you to decide that you wanted to do maths at university or were there other competing options?

Philip Maini:

Well, so this is where it's a bit embarrassing, so I decided to do mathematics because of laziness, truth be told.

Vicky Neale:

Well you’ve just said that’s an asset in a mathematical modeller.

Philip Maini:

Because what happened was in physics, I remember, we'd been taught simple harmonic motion and we were shown the pendulum back and forth, back and forth, and then wrote lots of notes on how this works, and all this and all that sort of stuff. And then I remember in mathematics, Mr Irvine said right now we're going to do simple harmonic motion. And I thought Oh no, not another book of notes to write. And then he wrote down one mathematical equation. And that's all you needed.

Vicky Neale:

There's the power of a mathematical model right there. You can understand the motion of a pendulum with one equation.

Philip Maini:

You can understand everything just from that one equation, and having the techniques. And so then I thought, yeah, that that looks like fun.

Philip Maini:

And then in those days you had to do entrance exam. Well you had to take a year out to do entrance exam. You still have to do entrance exam now, but you do it during school time. And luckily our school did have a mathematics teacher who had the ability to supervise for seventh term exam. So I did that, and then and came here. And then in my third year, so I found I really enjoyed differential equations.

Vicky Neale:

Which in fact is exactly what you need for simple harmonic motion?

Philip Maini:

That's right, yeah. And then in my third year I went to a course which is called differential equations, and it was given by Jim Murray, and I didn't know who Jim Murray was at the time. But then he motivated each application through biology or ecology or epidemiology.

Vicky Neale:

Which was absolutely his research expertise.

Philip Maini:

Which was his expertise. I mean, he was one of the founders of mathematical biology, which of course I didn't know at the time, being an ignorant undergraduate. And I just thought, oh, this is really fun. And so I went up to him and said to him, you know. He mentioned that there was a possibility of doing research in mathematical biology within another sort of group, and I asked him. I said I'm interested in that, and he basically said to me Are you going to get a first? And of course, that's always a touchy subject when, as an undergraduate, I mean how do you answer that?

Vicky Neale:

How well are you going to do in your exams?

Philip Maini:

Yeah, that's right. And I said, well, I think so and he said, right, well, then you should come and work with me. Don't do that project, work with me. And then that's how I started it.

Vicky Neale:

And did you suddenly have to learn loads of biology? This is a really kind of maybe a silly question, but it seems like you have to know lots of biology to do mathematical biology.

Philip Maini:

Well, the thing is, what I found was that I just ended up learning what was needed. And the key thing with this is working with biologists, because then you can ask them the questions and then you can learn it.

Vicky Neale:

This sounds like a great way to learn actually, having access to experts who will take pleasure in teaching you.

Philip Maini:

Yeah, that's right, and I think one thing where it's easier to go from mathematics into mathematical biology than the other way, because in mathematics, mathematics is built like a pyramid. There's a lot of groundwork knowledge you need to know, and then you build on that and build on that and build on that.

Vicky Neale:

And as you specialise that pyramid's narrowing, yeah.

Philip Maini:

There's not so much of that in biology.

Vicky Neale:

On your website you list over 60 PhD students whose work you've supervised, as well as mentoring and supervising postdoctoral researchers, and undergraduate and master students. What is it that you enjoy about that aspect of your work?

Philip Maini:

My supervisor was on sabbatical in the US when I was in my final year, and he took me with him, so my thesis is written on the US paper which is smaller. Which means that my thesis, which is also up on these shelves, it's actually smaller, it looks to the other theses, and that is a perfect analogy, because I look up to my graduate students because they have done things that I wouldn't have been able to do. And I just love it that by complete accident that analogy is on my bookshelf that I see every day.

Vicky Neale:

I can see the joy in your face as you describe that. I think that's a wonderful legacy. What advice would you give to somebody starting out in their studies now who has an interest in applying mathematics to cancer, for example.

Philip Maini:

I think one thing important in choosing a doctorate is to choose something that you enjoy. Because enjoyment is the is the big payoff of doing mathematics, or of doing a DPhil I should say. And so when you're choosing a project, I mean of course the enjoyment might be that you really want to solve this scientific problem and therefore you are prepared to use whatever techniques there are to solve that problem. Enjoyment might be that you really enjoy using a certain type of mathematics and you want to try and address the problem using that mathematics. If you do that, I mean certainly there are certain problems that you know that's the right technique to apply. But you may find if you're, I mean this is what I call are you someone who wants to be a problem driven or technique constrained?

Vicky Neale:

So is it the application of it that excites you or is it that you've got this particular tool in your toolkit that you really want to use?

Philip Maini:

That's right. So if you're driven by the problem you want to solve, then you might end up having to do some mathematics that you're not particularly excited about doing, but that's compensated for by the fact that you're really excited to solve the problem. So I think that choosing a problem that you really will enjoy doing is what's important, and getting enjoyment out of your research, that's the important thing.

Vicky Neale:

It definitely sounds as though there are lots of opportunities for students who are interested in this area to do their own little, perhaps small, part of pushing that frontier of knowledge forwards.

Philip Maini:

There certainly is, and so as well as collaborating with colleagues here at the university, we also have collaborations with pharmaceutical companies. I mean, there's a programme, a doctoral training programme, where the pharmaceutical companies then proposed projects in cancer but also in other subject areas, and we then co-supervise students in those. And in fact some of the students so much enjoy working with pharmaceutical companies that they actually then have then begun their career after their doctorate by going and working with the pharmaceutical companies.

Vicky Neale:

Fantastic, so so many different avenues.

Philip Maini:

Yes, that's right.

Vicky Neale:

Philip, thank you so much for your time, the conversation today, which I found fascinating, but also for all of your groundbreaking and inspiring research. Thank you.

Philip Maini:

Thank you Vicky, very enjoyable chatting to you.

Vicky Neale:

Thanks for listening to this episode of Maths Plus Cancer. I hope that you found the conversation as interesting as I did. There are more episodes of Maths Plus Cancer, as well as features about Oxford’s research into cancer, at ox.ac.uk/cancer . If you're enjoying exploring how maths and stats help us to understand and tackle cancer, I'd love it if you’d tell your friends about the podcast. And please do join in on social media using the hashtag #MathsPlusCancer. That's plus the word, not the mathematical symbol...