Maths + Cancer

Episode 5: Modelling Cancer with Helen Byrne

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 delighted to be joined today by Helen Byrne. Helen is Professor of Mathematical Biology at the Oxford Mathematical Institute's Wolfson Centre for Mathematical Biology, Professorial Fellow at Keble College, and a Senior Group Leader at the Oxford branch of the Ludwig Institute for Cancer Research in the Nuffield Department of Medicine. Her extensive list of publications across a range of topics in mathematical modelling in biology, and outstanding scientific achievements, led to her being awarded the senior Leah Edelstein-Keshet Prize and Fellowship of the Society for Mathematical Biology. Helen also has a long-standing commitment to improving equality and diversity in mathematics, and has supervised and mentored numerous early career mathematicians. Helen, thank you so much for joining me today.

Helen Byrne:

Thank you, my pleasure.

Vicky Neale:

Helen, you studied maths in Cambridge as an undergraduate and then came to Oxford for a Masters and a DPhil, I think with the title “Modelling combustion zones with porous media”. So at what point did you get excited about applying maths to biology?

Helen Byrne:

So in fact it was sort of a bit accidental, so I'd just finished my PhD, and in Oxford, as you may know, on Friday mornings the applied maths group have these industrial workshops. And I actually didn't go to the workshop, but some of my colleagues did, and it was some medics from Hammersmith Hospital in London, and they had just set up positron emission tomography for oncology, and they were basically looking for an applied mathematician to come and work with them, to kind of just look at the sort of data that they were generating with fresh eyes. And so during this first workshop, it was decided that there was a very strong analogy with what they were seeing, and, I guess flow of tracers through porous media, and therefore that that what I had done in my PhD would be sort of a natural sort of extension to use that sort of modelling approach, so I was then found and wheeled in.

Vicky Neale:

I love this idea of your colleagues tracking you down.

Helen Byrne:

Yeah! It was most weird. And so then we chatted, and they basically offered me a postdoc, and I started working at the hospital, and it was brilliant. So what I ended up doing, I think at the time I guess it was very early days. The resolution of the data that they were collecting, this was like not quite, about 30 years ago, so that's quite a while, and the data was quite noisy. And what I wanted to do, which was sort of fitting reaction diffusion equations to the spatiotemporal distribution of radio labels, markers for say oxygen, glucose utilisation.

Vicky Neale:

So let me check I've understood. So the idea here is that the patient is injected with something and then you're using equations to describe how that's spreading through the body. Is that the kind of idea?

Helen Byrne:

Yes, that's exactly right. So they inject into the blood some sort of radiolabelled tracer, which tags say oxygen, or glucose, or different drugs. And then so they can monitor the distribution of the label in the blood. So that's one input signal if you like. And then they scan the patient and then they can see the spatial distribution of this tracer over the organs of interest. And so the idea would be, where they were typically. The sorts of models that they were fitting were essentially just systems of coupled ODEs, where they would take a spatially averaged signature, signal, from across a region of interest, but in doing so they're losing a lot of the spatial resolution.

Vicky Neale:

So they're using these differential equations, but it's rather crude way of doing that.

Helen Byrne:

Yes, yes. So they were fitting. They were say drawing a region of interest around say the tumour tissue, and then potentially over healthy tissue, and trying to model the kinetics, which would be say the delivery of oxygen and then its utilisation, or glucose or whatever it was. But they were just as I said averaging or summing signals over spatial regions, rather than say looking at the spatial distribution as well. And so the plan was that I could do some slightly more sophisticated models which would also take into account the spatial distribution and how that changed over time. And this was why this was so similar to what I'd been doing in my PhD. But as it turned out, there was a good reason why they were averaging the data, because it was quite noisy, and I think this was the increasing realisation that I think at that time, the sort of accuracy of those scanners probably wasn't good enough to do that sort of modelling. Fortunately I think over the last 30 years things have improved, and but I mean, it was for me and I think for also my colleagues, it was a really interesting and useful experience because I'd come very much from I guess a mathematical background. And to actually have to go and present at group meetings and tell them about the sorts of approaches that I was using, when they could just about cope with differential equations, it was I think a very good education for both sides in terms of communication. I had to really get my concepts across in a very simple way. And then also I was pushing them mathematically about the biology, asking questions because of how I was seeing the system that were probably a bit different to what they were doing, so in that sense it was challenging but rewarding.

Vicky Neale:

So it seems really interesting that the kind of equations, the modelling techniques that you were using in your PhD, then it turns out transferred so nicely to this kind of other application. I guess this is this is part of the power of mathematical modelling, that we can describe the same kind of phenomena using the same sorts of equations, but they might be applied in really different ways.

Helen Byrne:

Yeah, and I think that's one of the, for me one of the lovely things about the sorts of mathematical modelling that I do, that again we can. Once you understand the physical principles of certain types of equation, then they can be quite widely applied. The way in which I guess ink diffuses on a piece of blotting paper is the same in which heat is conducted down a metal bar is the same as the way in which oxygen or drugs will diffuse through a tissue, and so if you understand the mathematics of one of those and you can see the analogies then you can specialise it to the application, and I think that's a real strength of maths and one of the things I think that I really enjoy about spotting those connections.

Vicky Neale:

Yeah, you and me both. I love this power of maths to, you understand a problem in one context and then suddenly that gives you access to all of these other kind of settings. So this seems kind of completely serendipity, that this workshop that you weren't even at, somebody said we need Helen here, you know, Helen talk to these people from the hospital, and there you are with this postdoc. How unusual was it at that point for there to be a mathematician in the team? Was that quite unusual? Were there lots of places also having mathematicians in the team in the hospital?

Helen Byrne:

Oh, it was quite unusual, and I would say quite experimental. I must say I was very lucky, so I shared an office with a guy who was a biochemist, but he'd done a maths degree on the Open University in his spare time. Really clever guy. And there were I guess engineers because I guess, and physicists, because I guess the technology underpinning the PET scanners, there's a lot of physics, maths, needed to kind of reconstruct the images. So they weren't averse to I guess engineering concepts and physics, but I think it was more the modelling approach that it was kind of pushing the boundaries of what they were doing. But again, I guess the reason why they came to the workshop in the first place was because they recognised, I think, that they weren't perhaps getting all they could out of the data. And that's why they wanted fresh eyes to look at it, to see whether what they were doing was the right thing to do. And I would say that at that time, given the resolution of the data, given the noise levels, etc, it was the right thing to do.

Vicky Neale:

You've subsequently built a very successful career in mathematical biology, so I'm guessing that you enjoyed the experience in that postdoc. What was it about that kind of move to mathematical biology that has kept your interest throughout your career?

Helen Byrne:

I don't know. I think I just very much more motivated by the application. I love learning about the biology, and there's so much to learn. At that stage it was a very sort of uncharted territory, and like with the application to modelling and the positron emission tomography imaging data, I could see how a lot of the maths that I'd learnt could be repurposed, and there was just lots and lots of

opportunities for using maths in creative ways, and actually generating some insight. And I think yeah, just more motivated by the applications and learning the biology. Sort of the intellectual challenge of talking to people who weren't necessarily so used to talking to mathematicians, trying to pull out an interesting problem where you can say something useful. And that might be something useful in terms of insight into the biology, or equally oftentimes as well, by virtue of developing a model, then that will generate sort of nonstandard systems of equations that the mathematical part of my brain also enjoys. So it was for me in I guess, a slightly selfish way, it was a win win situation. On the one hand, you hope you're helping to increase understanding and insight, but on the other hand, you're also doing sort of interesting maths as well.

Vicky Neale:

That doesn't strike me as selfish at all. I think it's important that you have that intellectual stimulation because that's what gives you the kind of drive to keep going, to be curious about these equations, and to keep exploring. One prominent theme in your research is about modelling tumours in in various different ways. Can you tell us a bit about the role of maths in understanding tumours?

Helen Byrne:

OK, so one of the ways in which the mathematics can help is by providing what I would call mechanistic insight. So we're trying to propose physical mechanisms for why particular phenomena are observed. And oftentimes experimentalists and clinicians will have hypotheses about why they observe particular phenomena. Why if they grow a bunch of cells in a test tube, initially they grow very rapidly exponentially, and then over time, the growth saturates, and eventually the cells will reach some sort of equilibrium size at which there is, say, a balance between the number of cells that are proliferating and the number of cells that are dying. And so very simply one thing that we can do is try and sort of articulate those hypotheses of why they think they're observing what they're observing, with equations in mathematics, and in a sense, that's a sort of way of testing whether those hypotheses are consistent. So we can embody their assumptions, their hypotheses, in the language of maths. We can then solve those equations. Are they consistent with what they observe? In simple settings, then everything is consistent and everyone is happy. Oftentimes, though, there's a mismatch, and that's I think where it becomes interesting, because then you need to kind of explore what might be missing, or what they not told me that might explain why their sort of seemingly logical understanding of what they see, why it's not quite gelling with the sort of mathematical representation of that description.

Vicky Neale:

You're gathering these assumptions from the experimentalists. You're writing down some equations that capture those, solving those, presumably with the help of a computer, and then I guess the idea is that you can kind of run like a simulation almost of the experiment that they're doing in the lab. You can say, well, OK, if I if I start with these cells then the equations predict that it will unfold in the following way, and then you can compare your sort of virtual test tube with the real test tube and go oh, hang on a minute, that doesn't match up. That means that somewhere there must be some misunderstanding, or the assumptions weren't quite right, or something.

Helen Byrne:

Yes. And that's I think where it becomes most interesting because they've told you their understanding, and clearly that sort of logic, there was something missing, because it doesn't all

hang together. And then it's a question of trying to troubleshoot and maybe then they say Oh well, it could be this or that or the other. And then you try and say incorporate that into your model, and iterate, until you kind of get good agreement between them, the observations and the model. So I guess you're iterating until you can kind of validate their assumptions, and I guess that's probably the first level with mathematical modelling. Once you've got that, then I guess the next step would be, because in a sense, oftentimes that validation step is just confirming what they think. Admittedly, sometimes that requires a few iterations to kind of add in some extra detail, but in a sense that's often just confirming. The real power that can go beyond that is then using your validated model as a predictive tool to say: what would happen if I make some perturbation: What would happen if I added a treatment that worked like this? What would happen if I took another population of cells which behave slightly differently? Can I predict what they would do? And so then you're adding value, and you're making predictions that they can then go and test in the lab as appropriate, and I think that's an additional sort of insight and value that the modelling can bring.

Vicky Neale:

And I guess it's potentially much quicker and much cheaper to run those kind of simulations on the computer than it would be to carry them out in the lab with actual cells and test tubes.

Helen Byrne:

Yes, absolutely. I mean even you know, running series of experiments to test lots of different sort of drug concentrations or using different cells lines, the I guess the theoretical or in silico experiment is clean. It's not intentionally noisy in the same way as things can be in the lab, and much much quicker and cheaper to do.

Vicky Neale:

Noisy in the sense of kind of the data not being quite accurate.

Helen Byrne:

Yeah, and I guess cells don't all behave exactly the same. You know, you could take a cell line which you buy from a manufacturer, put it in one lab or in one fridge, the conditions may not be exactly the same. The culture medium may not be exactly the same. So the cells may not behave in exactly the same way. So there's lots of sort of confounding effects that can kind of mess with your experiment, but I guess with mathematics, your equations are what they are. OK we can put in noise and stochastic effects if we want to, in an attempt to mimic the real world but at least we have control over noise, etc. And we control where we add it.

Vicky Neale:

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.

I think this idea of being able to have, I'm sort of thinking now of a kind of virtual tumour, and being able to kind of apply different treatments to that virtual tumour and see what happens. That just seems like such an enormously powerful idea. I suspect that it has to be a relatively new thing, because I suspect it involves quite a lot of computing power to be able to do that, and I guess a few decades ago maybe that wasn't available. Am I wrong in that?

Helen Byrne:

You can build models at lots of different levels of complexity. Yes we can sort of take a lot of compute power to build very very sophisticated and detailed models, which I guess 10, 20 years ago would have been sort of computationally infeasible, but that's not to say if I think back 30 or more years ago, people were still developing models, they were just a lot simpler. So I guess it would be a bit like with weather forecasting or something like this. You can sort of have a short range weather forecast which perhaps is just based on very local like you know, red sky at night, sort of very simple things. We can have analogous sort of levels of complexity in our mathematical models, and so if you think back to for example radiotherapy protocols, those would be based on very simple, say tumour growth models, so there's lots of different models at different levels of complexity which require different levels of compute power.

Vicky Neale:

I really like that analogy with the weather forecasting, that feels like a helpful way to think about it.

Helen Byrne:

Yeah, very much so.

Vicky Neale:

And are there aspects of your work that have already had an impact for patients? Or is your work at a more kind of fundamental research level than that?

Helen Byrne:

I would say thus far it's been much more at a fundamental level. I think largely because the sort of data that's been available has been much more at the experimental level. I think going forward now, and this is part of the reason for having my sort of joint position with the Ludwig, is that with increases in imaging technologies, the sorts of data that can now be collected is much more. I think there's a convergence with the level of detail at which you can collect experimental data and the sorts of models that we're developing. So in particular, very detailed sort of imaging where you can resolve different cell types, which is very much at the level of the more complex multiscale models that we develop, which will say resolve individual tumour cells, blood vessels, blood flow infiltration by immune cells. That sort of level of detail. So if you like the more state-of-the-art imaging techniques can give us that level of resolution, and even within, say, a class of, say, one type of immune cells, you may distinguish different subtypes within that. So it really is exquisitely beautiful data and sort of much closer to the more sophisticated models that we develop.

Vicky Neale:

That's really interesting. That level of resolution sounds extraordinary, and in fact, in another episode of the podcast I spoke to Tom Whyntie, who's a medical physicist who talked to us a little bit about the medical imaging, because that's so key in in this whole process, I guess, of kind of gathering that data, but then making sense of the data and doing something useful with it.

Helen Byrne:

So in fact quite a few students and postdocs now are working on projects where we're analysing clinical data, data from clinical trials, and that is very much about trying to essentially quantify some of the spatial patterns that we see in these data. And I guess traditionally what a pathologist would have done is count. They would stain the images for say one cell type, which might be your cancer

cells, it might be one class of immune cells, and they would just count them. And I mean, that is useful, very helpful. But again, you're losing the spatial resolution of which cells are next to which cells. And so what we're trying to do now is use, say, ideas from spatial statistics, or also from topological data analysis, to try and pull out metrics that are interpretable, that kind of go beyond just pure counting cell numbers. So which cells are next to each other? How do those spatial distributions change as a tumour progresses through different stages? How does that change as you go from the healthy tissue to the tumour, the invasive margin to the centre of the tumour? And a lot of that is trying to identify changes in sort of cell-cell interactions, and ultimately to come up with I guess spatial biomarkers that one could use, I guess diagnostically, but also to potentially identify targets. So if you see associations that are abnormal, you might want to disrupt those by targeting one or other of those cells. Equally, if you want those cells to be together, you kind of might want to exploit that to get one of those cell types to, say target, kill off, the other cell, if that was for example a tumour cell or something. So there's lots of really interesting again mathematical and statistical questions about how you quantify these basically quite high-dimensional spatial data in order to pull out interpretable biomarkers that could be useful either for diagnosis, more sophisticated disease classification and then I guess, ultimately to perhaps identify novel targets for new treatments.

Vicky Neale:

I think this is such an exciting area, it sounds like there's a lot happening in this area at the moment and I guess this kind of idea of topological data analysis, these tools being used in this area, is relatively new. You just mentioned high-dimensional, and I think that might feel confusing because these cancer cells live in three dimensions. Or I mean, not necessarily cancer cells, all cells. Can you explain a little bit about where are these extra dimensions coming from?

Helen Byrne:

Right, so what I mean by that is if you think about an individual cell, what makes a particular cell a cancer cell? What makes it a particular type of immune cell? So each cell is like a little factory that's producing lots of different genes and proteins, so you might be able to identify your tumour cells because they're expressing certain proteins or genes and those would be different from, say, a particular type of immune cell. I mean, the biology gets more complicated than that because even say one type of immune cell, say a macrophage, can have different phenotypes, behaviours, and so its signature might change depending on what environment it's in. So the multidimensions comes from if you like a cell signature, that these very state-of-the-art imaging technologies can measure lots of different proteins at the level of individual cells and so giving us that level of information means we can distinguish not just a tumour cell from an immune cell, a macrophage, but we can also distinguish subtypes, say of macrophages, etc etc. And so that's where the sort of multi-dimensional nature would come in, rather than they don't live in a 20-dimensional space because that doesn't exist to the best of my knowledge.

Vicky Neale:

This isn't really about the kind of geometry we're looking at. It's more that for a given cell, you record a list of information about this cell, and as mathematicians we might say if you've got 20 features of a cell that you're recording, we might think of that as 20-dimensional data. That's nothing about the kind of real-world geometry of it, it's just a helpful way of thinking about it.

Helen Byrne:

Yeah, we could think of each person as being like a multidimensional object, which is your height, what colour eyes you've got, what colour hair you've got, male, female, whatever, and if you string all of those properties together, that would make each of us a multidimensional object, and one can apply a similar logic to a cell in your body. Which might sound weird, I guess, once it's the same sort of logic, but just the labels that we use to characterise different objects, whether that's a cell or an individual or a plant. Whatever it might be, the same principle would apply..

Vicky Neale:

I'm finding myself picturing like cell Top Trumps. You know those cards with kind of a list of data about different things, so I'm imagining for each cell then you've got this kind of list of properties. And so the sense in which it's multidimensional is that there are all of these different properties, which as mathematicians we think of as giving different dimensions. It's not about kind of the cells living in some 20-dimensional geometric space.

Helen Byrne:

Yes, so I guess with the spatial analysis we've got if you like a sample of that tissue at a particular time point, and we're using that to sort of assess or to describe, quantify, a patient's tissue tumour, and sort of try and learn something about what stage that tumour's at to try and I guess also predict whether or not they might respond to particular types of treatment. And so indeed, one of the studies we're involved in at the moment is indeed focused at trying to take that sort of histology spatial data and try and see if we can pull out spatial features which would indicate whether they're going to respond well or not to radiotherapy. And we've got outcomes, so we can test all of these different spatial markers against the outcomes so that we can come up with sort of candidate biomarkers that then you could use in a future study.

Vicky Neale:

That sounds enormously exciting.

Helen Byrne:

It is, it is, I mean, and it's. So like you were asking before about whether the work, the research that we've done thus far had impact. So I think it's been more about generating mechanistic insight until recently, but now I think we're at the stage where the things are converging, and a large part of that, I think, is meeting the experimentalists and clinicians very much around the sorts of data that they're generating, and it's so complex that I think it's a great opportunity for bringing in these other parts of maths to try and generate. There's so much information and detail in there, and we don't quite know what are the right things to pull out. And that sort of makes it you know, challenging, but I think if we can pull out a few things, new interesting patterns, then it's yeah, that's brill.

Vicky Neale:

Yeah, I like this idea of a kind of detective puzzle. If you've got this massive amount of data and it's like, well, what are the really interesting things here? And this is such a new field that I guess there's a lot to kind of uncover.

Helen Byrne:

Yeah, and again in very much the same way when we were talking about building sort of more mechanistic models that would predict, say how a tumour would grow, that the experimentalists, clinicians, would have hypotheses. In the same way, they have sort of hypotheses or ideas about

which cell types should be next to. I mean, they have really brilliant intuition, because they've looked at these images and they're. I mean really what we're trying to do is mimic to some extent what their eyes, their expert eyes, are seeing, but to quantify it. And I guess there's lots of different ways in which you can quantify that data, and the key is trying to pull out some sort of biomarkers that, and then there's, you know, the moment. Yes, of course. And sometimes you can pull out things, I guess, which are unexpected. And then that's also interesting.

Vicky Neale:

One of the things that I find intriguing about topological data analysis is that topology is a very long-standing branch of mathematics, and my background is as a pure mathematician kind of doing, thinking about fundamental maths for the excitement of the maths itself, rather than because of a specific application in mind. And I guess topology historically has been very much in that area. But it seems like this supposedly abstract, pure, kind of area of maths, doing niche things about topology in high dimensions and so on, actually now is suddenly finding this really powerful application.

Helen Byrne:

Yes, so I can probably give you two examples. So one would be: so if you listen on the news, you'll hear a lot of reports around immunotherapy, so targeting the immune system to deliver treatment to cancers. And so we know that immune cells, lots of different types of immune cells, will infiltrate into tumours. What we can do with one of the pieces of work we've been involved with is sort of trying to look at the spatial distribution of different types of immune cells, and some of the questions about why does one patient respond to immunotherapy and another one not, would be around whether or not those immune cells are able to infiltrate into the tumour regions. So sometimes what you'll find is they infiltrate very nicely and then that would be a good candidate say for immunotherapy. In other cases, what you'll find is that the immune cells are excluded. They just can't quite get into the tumour. And that may well be because those tumour cells are not producing the signals that are needed to pull them in. And so what we've done with topological data analysis is you can sort of, say, essentially in sort of 2-D space, you could see imagine loops which would be, say your immune cells are almost forming a loop that surrounds a tumour nest. And if they're forming a loop, and that's sort of outside of your tumour, then that's obviously a way of quantifying exclusion. And in other cases where you don't see sort of large persistent loops, then that would be more indicative of, say, infiltrating. And so what we did with one study was compare the spatial distributions in terms of the sizes of the loops, their persistence across different immune cell types, and how did that correlate with the degree of the oxygen concentrations within the tumour cells? And we found that there were different sort of spatial distributions between different immune cell subtypes. And so that's one example where essentially what we're doing is quantifying, but with a quite sophisticated mathematical toolkit, what the biologists will see, but not be able to quantify. And I guess the point here is if you're going to look at a whole series of studies, you want to be able to come up with: this one is more than that one. And at the moment I think with a lot of the pathology, that's been I guess somewhat subjective and not reproducible. If we can come up with these sort of more quantitative biomarkers, then it doesn't matter what time of the day the computer did that analysis, it will come up with a reproducible number. And so I think this is part of the power of these sorts of methods. I guess one of the other things that we were able also to do was to use similar sorts of techniques to characterise the vessel networks that are inside tumours. So within a tumour, the way that it's able to continue to grow, or one of the ways it's able to continue to grow, is essentially it builds its own blood supply. The cells proliferate very rapidly, they need more nutrients, so they secrete different growth factors which stimulate new blood vessels to grow in. Because the tumour microenvironment is slightly abnormal, those vessels aren't like the best

functioning vessels in the world. They're quite leaky, and tortuous and they don't function very well. And so what we were able to do with topological data analysis is to actually quantify the spatial structure of tumour vascular networks and show how those change when you apply different sorts of treatment that are designed to target particularly the tumour vasculature. And to show that they are indeed doing what we expect that they would do, but again, it comes back to being able to actually quantify the sorts of structures that you're seeing, rather than just saying, Oh yes, that one looks more normal than that one. And I think it just removes some of that sort of subjectivity, and makes the description I guess more reproducible.

Vicky Neale:

This is so exciting. I'm loving all of this. This is just great. You mentioned that that you have these kind of joint positions, you're in the Maths Institute right now, but you also have this position at the Ludwig. How does it work out kind of being between the two? How does that kind of add to what you're able to do with your team?

Helen Byrne:

Yeah, it's really great. So I spend two days of the week up at the Old Road Campus at the Ludwig Institute, and I guess I am the only group leader who is completely a mathematician. So there are bioinformaticians and, but everyone else is pretty much experimentalists. And so it means that you're much closer to the biology and to the experimental work. And so it means you can sort of. By talking to my colleagues, you can start to identify other sort of problems, look at the research that they're involved with, and see how some mathematical modelling, how we can help. And again in the process by understanding more about the biology, the experimental work that they're involved with, then oftentimes that's challenging because it's things perhaps that I don't know about, and so it's what sort of modelling could we do there? How can we actually help? There's no point in doing modelling if it's not going to add value, and so that then I think brings challenges and new sort of modelling projects back into maths. So again, it's this fortunate situation, which is I guess win, win. So hopefully you can bring new insight and then at the same time you identify sort of, just by the nature of the biology, sort of non-standard mathematical equations that are interesting to analyse in in their own right.

Vicky Neale:

I'm mischievously thinking that you were talking earlier about the fact that it's important to know which cells are next to which cells, and it sounds as though you need to spend some of your time next to other mathematicians, and some of your time next to experts in other areas.

Helen Byrne:

Yes, I think so. I think, I guess everyone is different. I think I like to be. I guess I'm a mathematician first and foremost, but I think it's important to spend time with the biologists, because I think if you just have meetings, if you don't embed yourself within their environment, I think you've got to meet them at least halfway.

Vicky Neale:

And it sounds as though you really thrive on this interdisciplinary working, that you really relish that.

Helen Byrne:

Yes, I do. I mean, it's sort of a bit scary because you're not quite sure, you think there should be an interesting problem in there, but it's finding the right language, because oftentimes, especially if you're talking to people who haven't worked with mathematicians before, and sort of getting over this, I'm not a bioinformatician, I'm not this and I'm not that, and trying to get to the mechanistic understanding, trying to shape the research, what they're interested in, to identify a sort of common questions where the maths can actually help. I think that's I think part of the challenge, but I think to be doing that all the time, I think sometimes you need some quiet time to actually work on those equations and then my sanctuary is to come back here to be able to do to fulfil that part of what I enjoy about my job. So it's a nice complement, nice balance to each other.

Vicky Neale:

It sounds as though your work is getting closer to being used in the clinic. The mathematical oncology has done lots of fundamental research and is now getting a step closer to being used to directly impact patients. Are there, is that happening in other areas of mathematical biology as well? Is mathematical oncology following in the footsteps of other areas? How does that work?

Helen Byrne:

I would say that in terms of mathematical biology and where it is in terms of having impact in the clinic, I think if you look at say cardiac modelling, that's I would say probably at the forefront. So in the cardiac world, I think there's drugs that have been identified and they've had FDA approval. That's kind of, I think the best example. So the cardiac models I think have been ahead of the oncology world. And this is Denis Noble. So his work I think they've had FDA approval. It must be FDA approval for their mathematical models. That I would say is the state-of-the-art, FDA approval for their models for drug testing.

Vicky Neale:

Different kind of question. What advice would you give to somebody who's early in their studies now and who's interested in applying maths to cancer?

Helen Byrne:

Go for it. There's loads and loads of really interesting questions. I think probably pretty much. I mean, as we sort of discussed already, I think most branches of maths you will find some application in there. Go and talk to people. Very rewarding, again in many many different levels, whether it just be in terms of analysing interesting equations, generating insight, fitting models to data. There's so many different ways in which I think the maths can help and be rewarding at the same time.

Vicky Neale:

That's really encouraging. Thank you so much Helen for our fascinating conversation today and also for the research that you and your team have done and are doing, which I think gives hope and inspiration for all of us affected by cancer. So thank you.

Helen Byrne:

No problem, take care.

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...