

Kate Jeffery on the cognitive map and memory

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SPEAKERS

Steve Flemming, Caswell Barry, Kate Jeffery

Steve Flemming 00:01

Hello, and welcome to brain stories. I'm Steve Fleming and I'm here with my co host Caswell Barrett,

Caswell Barry 00:07

on brain stories, we aim to provide a behind the scenes profile of the latest and greatest work in neuroscience, highlighting the stories and the scientists who are making this field tick.

Steve Flemming 00:19

We don't just ask about the science, we ask how the scientists got to where they are today, and where they think their field is going in the future.

Caswell Barry 00:26

So today, we're very excited because we're joined by Professor Kate Jeffery, who until very recently was a professor of neuroscience at UCL, but she's left us and now she's the head of the School of Psychology and Neuroscience at Glasgow University. Kate's worked in many places, and has had indeed several careers. Originally, she was from New Zealand, she trained as a doctor before switching full time to research science. She completed her PhD in Edinburgh with Richard Morris, before moving to London to work with John OKeefe. Broadly speaking, she works on spatial memory, mainly working with rodents, and is interested in the factors that make place cells fire where they do questions such as what constitutes environmental context, her work recently has sort of focused on three dimensional space and its representations, how we know which direction we're facing. And she's also involved in a number of projects linking science and art. Welcome, Kate, it's fantastic to have you here. Thank you for joining us.

Kate Jeffery 01:25

Well, thank you for the invitation. It's a pleasure to be here.

Caswell Barry 01:28

It's also there's two things that are noteworthy about this as well, I believe you're our first guest who isn't actually at UCL. Now, it's something we always meant to do, but you are a branch leading outside. There's also another connection, I don't know whether you remember this. So Kate was my PhD supervisor. But actually, while I was a PhD students, Steve did a rotation in your lab. And I tried to convince him that he wanted to work on grid cells and things like that, and evidently didn't do very well. So we've got the full, we've got the the full family tree here.

Steve Flemming 01:59

Like it's a it's like a family reunion in some ways.

Kate Jeffery 02:04

Yeah, I remember that I consider that one of my great failures is not to be able to persuade you to come work on placing grids hills. For you, I thought

Caswell Barry 02:11

you're about to say having mean.

Steve Flemming 02:16

I was just saying to Cosmo, before we started recording that we might be starting a foray into rodent work in the lab. So it perhaps is coming full circle. And finally, it's taken fantastic teen years, but maybe I'm now becoming convinced. We'll see. Anyway, it's not about me today.

Caswell Barry 02:30

We play the long game. No, don't worry. So Kate, we should we should focus on you. So maybe a good place to start is if you could just tell us about what you're working on the moment or what you think is interesting this field and what you know, what the questions are that you are focused on?

Kate Jeffery 02:46

So yeah, there are there are so many questions. So began with place cells. Because when I was starting to do my PhD, I started learning about place cells. And I got very, very interested in this idea that these are kind of a kind of represent the assembling of a thought in the brain of the rat. And therefore, you know, it seemed to me if we could understand them, and understand how they create their representation that we would understand how thoughts are made, you know, or at least one type of thinking.

Steve Flemming 03:20

Perhaps we could just start to just by defining, giving, giving the listener a brief definition of a place or what, what does,

Kate Jeffery 03:30

sure, so place cells, single cells in the brains of rats that become active when the rat goes to a place. And so when I discovered that these things existed, and they exist in hippocampus, which has been very interesting for a long time, because it's of its involvement and memory, and they were discovered by John O'Keefe. So, so I actually when I was a PhD student went to visit O'Keefe's lab, and he

showed me a place cell for the first time and I thought, wow, this is amazing. So like, how does that cell know whether it is a type of thing? So then the question became how does the cell know? And that's really the question that's driven me and a lot of other people will ever since and, and there's sort of two levels to the question. One is just the kind of anatomical physiological one of where does the information flow through the brain on its way to the place cells? And then there's the more psychological question of what is the nature of the information that was telling place cells where to fire? And so I've been kind of working on both of those levels, both the kind of the physiological and the psychological level. And for me, that that kind of interplay between physiology and psychology is just a really interesting place to be in. It's where I've stayed ever since.

Caswell Barry 04:49

And, practically, what do we know about what makes these things fire where they do? I mean, I guess, would it be fair to say this is sort of the this is the cell level representation of you knowing where you are in the world are indeed rattling where it is in the world, or is there? Was there more to it?

Kate Jeffery 05:06

Well, that's one of the big unsolved questions. Is there more? Or is that how you know where you are? Or is there some other part of the brain? That's, that's really where you know where you are? Or even, is that a sensible question to ask? Is there anywhere in the brain that knows for sure. So sorry, I've forgotten the question.

Caswell Barry 05:26

What do we know about the things that actually tell the cells where to fire?

Kate Jeffery 05:32

So there's lots of also levels to the answer to that question. So we know what the inputs are to the hippocampus. And we know where they come from in the brain. So a lot of the inputs come from primary sensory areas of the brain. So we know that the cells are using vision, and olfaction. and to a lesser extent, they can use sound and touch. And so they're using all the senses. So once it's we can say, well, the place cells know where they're at is because the sense organs tell it where it is. But that's not really a full answer to the question. But the question really is, how is that sensory information turned into spatial, spatial representation. And the thing that's important about space, that makes it different from other kinds of, of information is that there's, you kind of go through space, like you move through space. So you translate, and you rotate, and you translate and rotate by certain amounts, quantities that we call distances and directions. So that's kind of quite an abstract conceptual idea. So so the question for the brain is, how do you represent distances and directions in the brain? So turn this into a kind of pattern of pixels that are coming into the eyes and so on? How do you turn that into something special, that's got distance and direction. So we, we know that the place cells do get information about the distance that the rat has travelled and the direction in which it's travelled a lot of work, some of it from a keeps lab and colleagues, many colleagues at UCL, including you, and me, and many others, and lots of people, all over the world, really, it's been a very big enterprise, to try and pull all of this apart. We know that the boundaries, certainly in rats and mice, the boundaries of the environment are really important for helping to anchor place cells. So in other words, it looks like a particular cell will get some type of information about how far the animal is away from the east wall of its environment, let's

say, or something like that. So. So we know that the cells are getting this kind of spatial information that's got distances and directions and these metric quantities. So then we sort of step back and go, Well, what's the form that that information comes in, and it seems to be coming in from the parts of the brain that are, again, taking in sensory information, and extracting the spatial information so that I can pass it to the place cells. And one of the big discoveries that came along, in fact, when you were in my lab was the discovery of grid cells by the Moser lab in Norway. And these are cells that track how far the rat has walked, essentially, to put it crudely. And that was a very, very exciting discovery, because that was the first one of the first really explicitly spatial signals that was found in the brain. And then the other really big spatial signal that's been tremendously important, which is thing that I'm really interested in at the moment is the sense of direction, like, how does the system the brain and the rat, and everything, have, they know which way it's facing? So if you want to go somewhere else, and you know that that location is north of here, which way is that? And how do you know? How does your place know? And so? So those are the kind of questions that that I've been working on a lot, you know, they're sort of where are you? And how do you know which way you're facing and where do you want to go?

Steve Flemming 08:59

And I find one thing that is just so fascinating about this area is that the cells when you see them, they are almost by definition, abstract, because they're picking out points in a, in a in a spatial environment that is formed by three dimensions that we move through, but there's nothing necessarily driving them as a stimulus feature. And perhaps we can talk a bit about how they interact with the feature the environment. But I wonder how this then interfaces with this notion that we have some kind of metric space. And I'm thinking here about the work you've done in three dimensions. They sort of anchor to what we need for navigation, which I guess for a rats and for human is largely two dimensional, or are they somehow tracking the three dimensional metric space is kind of given to us by physics? Yeah, that's,

Kate Jeffery 09:53

that's a good question. And that's one that I've been interested in for quite a long time because you could imagine that could be either of those sense. So from the point of view of certainly a terrestrial animal, like a rat, you know, or human, versus walking over the surface of the environment, you might not necessarily need a really fully three dimensional map of space, you really only need to know about the ground that you have to cover. So it could be a two dimensional map, or it could be kind of a, a folded three dimensional map if you like. So it's still still kind of a plane, but the plane does have hills and valleys. So there is some limited information about up and down. Or maybe there's a fully three dimensional map, in which, in which case, you're tracking distances and directions in up and down as well as sideways. But there's a sort of, there's more fundamental questions, and then that's the extent to which the signal has what we call relational information in it. So if you just look at a single place cell, the place cell tells you where you are. So if you're recording from the brain of a rat, and you've got a particular cell at the end of your electrode, every time the rat goes into that place environment, you can go, Aha, I know where the rat is, without even looking at it. Because I can hear that that cell is active, it's quite, it's quite spooky, actually, it does feel a bit like mind reading. But, and you can imagine that, you know, the rat walks all over the place, and all of these different place cells are active. But if you were just listening to those cells, and you didn't have any other information, you wouldn't yourself be able to

build up a picture of the space that the rat is walking around. And you would just know that cell A was sometimes active, and then Selbyville, sometimes active in cell C, but sometimes active and so on. And it's not until you've listened to the cells for a very, very long, long time that maybe you discover that when cell a is active, often B is active shortly afterwards, and that C is active shortly after that. And so you starting to understand that these places are connected, so they have a relationship to each other. So I think the you know, the picture that's kind of emerging, is that the maybe the function of the hippocampus is to understand these relationships between places. And it does that by experiencing the kind of sequences that that the rat walks through, and it's walking through space, and you get sequences of play cells active. So So you know, the picture of the, the internal map is very much one of not just knowing where you are at the moment, but of knowing where are the other places? And how do you what's the best way to get to them from here. And that's where we're still relatively limited in our understanding. So we don't know whether the large scale map is whether it's also in the hippocampus, where the play cells are or whether it's in other parts of the brain and hippocampus kind of teaches those other parts of the brain. We're still trying to answer that question.

Caswell Barry 12:47

I guess I'm using the sort of backbone that you just described, if you think of play cells as things that just sort of associated locations together, I guess that naturally feeds into a lot of the work you've been doing, where you've sort of extended, extending the typical experiment from two dimensions to three dimensions. And you've done I guess, over it's probably over the last 10 years now a whole array of beautiful experiments sort of making rats do increasingly interesting things like I remember seeing you talking about rats that are climbing through a helical staircases, then climbing walls. And then finally, there was a very what actually went fully 3d and sort of, were able to get through or maybe was mice but get through this sort of three dimensional cube. Do you see that sort of thing as just sort of the the natural sort of endpoint of play cells as in, you know, if you can associate places in 2d, then you should definitely be able to do 3d. And I guess more? More importantly, do you think there's a limit on that, like, if we could design a task with animal moves in 4d, whatever that looks like, with this system? Just adapt? Or what would happen? Yeah, it's

Kate Jeffery 13:47

an intriguing question. Yeah. So the so the results that we've got from these explorations into three dimensions have been not completely straightforward to interpret. I think the starting point was, yes, the map, the internal map is probably three dimensional. And three dimensions is a bit like too, but there's more of it type of thing. So and when people I think, weren't really interested in these experiments at the beginning, because the assumption was, it was just like fleshing out a bit more of what we already know. But then when we started to dig into it, we realised that when you add another dimension, suddenly, things get a lot more complicated, because it's quite tricky to create a three dimensional compass, because you can, when you're rotating in space, it's very, very complicated to track how you've ended up when you've rotated in three degrees of freedom instead of just the usual two. So to create a three dimensional compass would be a really big job for the brain, you'd need a lot more neurons, for example, so whereas we know that the compass for two dimensions just needs to be able to represent the 360 degrees that you might be facing. If you were going to have Three dimensional compass and it's 316 times 360, if you'd like to, that's a very large number. And there's all sorts of other kinds of weird properties that three dimensional space has like a few make a series of rotations. It

depends which order you do those rotations in which way you end up facing. So the brain needs to be really careful about how it assembles all of that information about the different rotations that you make. So the more we thought about that theoretical kind of basis of what it would take to make a three dimensional map, the more we realised it was, it was quite a complex task. And so then we started to do the experiments. And we were hampered by the fact that rats don't swim or fly very easily and three dimensions, and it's quite difficult to record them

Caswell Barry 15:45

to see flying and

Kate Jeffery 15:48

we've got, we've now got bats. So there's offski lab in Israel has been studying bats, which really do seem like rats with wings in many ways. And gratifyingly, they've been finding quite similar some results to some extent. And of course, when we think about it, we all have the vertebrates evolved from fish, which have a fully three dimensional movement space. So it actually makes quite a lot of sense that the brain would be able to represent three dimensions, but but then thinking about how the place and the head direction cells, and then these other distance tracking cells, these grid cells, you know, in terms of how they do that, we just have to do the experiments and see. So the very first thing was to get rats walking around a kind of a climbing wall. And we found that the place cells seemed to encode locations on the wall, pretty similarly to how they would do on the floor. And that fitted with some of the behavioural experiments that we did, that showed that rat seemed to be able to find food that was located somewhere on the wall. So they seemed to be able to navigate and so on. And that seems sensible to us as well, because we know that rock climbers don't lose their sense of space just because they're climbing a rock instead of walking around. So that was fine. And then we were then we decided to record the grid cells is distance tracking cells. And what grid cells do is they they make this very regular pattern over the surface of the environment. So when the rat is walking around, if you're recording a grid cell, you'll find that there's a place where it's active. And then when the rat walks on a certain distance, suddenly the cell stops being active. And then when the rat goes a bit further, the cell starts again. And then when it goes a bit further, again, it stops, and so on, and so on. So if the rat walks in a straight line, there's this very regular periodic rising and falling of activity. So that's, that's kind of if it's walking in one dimension, if it's walking in two dimensions, the really amazing thing is that this rising, falling occurs and the two dimensions such that you end up with this really beautiful polka dot pattern of hexagonal arranged blobs, if you like. So these blobs are kind of the places where the cell would fire. That's really amazing. It looks like a polka dot a tablecloth, when you actually look at the data. And it was, it was the discovery that the Moza lab made that really electrified the field and made us realise that there's a lot of distance information in the system. So we thought, what are the grid cells going to do on this climbing wall? And we thought, well, I thought, naively, that there might be a polka dot pattern over the wall that's very similar to the polka dot pattern on the floor, that would have made sense because the place cells were doing that thing. And so and then I thought, you know, Knowing my luck, that probably won't happen, what will probably happen is that the cells just won't know what to do on the wall. And it'll all be a huge mess. But actually, what we found was that the grid cells produced this really beautiful pattern of stripes, where if you look at the horizontal component of the of how it's walking on the wall, so the distance that has travelled parallel to the floor, you get this rising and falling this periodic pattern. But if you look at how the rats walking in the vertical dimension, there isn't that

rising and following. And so the consequence of that is that you get strikes. So if there's a place in the horizontal space where the cell is supposed to be firing, then it will keep firing, as the rat climbs up the wall at that location. And if there was a place where themselves supposed to be quiet, it continues to be quiet. So the consequences as the rats walking over this wall, there are all of these vertical stripes. So it looks very much as though the grid cells were interested in the distance that the rat walks on the horizontal plane, but not in the vertical plane. So So then we started thinking, does this mean that the map is not really three dimensional? That actually, it doesn't have a good representation of height above ground? But then how do you explain how the play cells know what to do? And just, it was just all very confusing and puzzling. So then we thought, well, maybe there's something about the way that the rats are climbing on the wall that's restraining the ability of the cells to track distances, because the rats were standing on little footholds. Very much like a rock climb aboard. So so they were holding on to these footholds and because rats are quite small, they were actually able to stand so that the body was horizontal. So not not flat against the wall like a human would be, but actually horizontal. And we thought maybe, maybe that's affecting how the cells are able to track the vertical distance and it messes them up so so then we change the environment, and put chicken wire over the wall so that now the rats could climb very much more like a human rock climb aboard with their body flat against the wall and all four limbs on the wall. And suddenly, we got the blobby pattern back, so they were no longer stripes, we now got blobs again, so that was cool. But the regular polka dot pattern wasn't discernible. And the size of the blobs was far too big, relative to horizontal. So it sort of looked like the system was trying to track distances, but its scale was kind of messed up. So that was also quite puzzling. And then finally, we thought, okay, let's really put this to the test and create a situation where the rat can really fully explore the three dimensional space. And it took a long time to get that set up, we needed to have a way of tracking the rats in three dimensions, we needed to have an apparatus that they could move through in three dimensions, which was, you know, turned out to be this big kind of jungle gym kind of apparatus like, like those used to get in children's playgrounds. And before they decided it was too dangerous, you know, sort of criss crossing bars. And so the rats could climb through these. And we also developed wireless tracking, so that we could record sorry, wireless recording so that we could record the the neurons. So now the rats could climb through this space. And they weren't encumbered by recording cables and, and the camera could see them and all of that kind of stuff. So when we recorded in this space, we weren't really sure what we were going to find. So we thought we might see a nice, regular packed lattice of these nice round kind of firing fields is locations where the cell is active, we might see strikes, like we saw in one version of the of the wall, we might see big blobs, like we saw on the other version of the wall might just see a huge mess. And what we actually found was, we saw blobs, so these focal regions of space where a cell would be be active surrounded by a region where it wouldn't be so. So it kind of looks like the cells are very much trying to identify locations in the space where they should be active. And then they want us around that by locations just beyond that, where they're not active, it sort of looks like the system was trying to do that. But there was no regularity to the pattern that we could discern. And there's quite a lot of variability in the size of the blobs. And a pretty similar finding came out from the bat lab, as we call it. So loskis team in Israel who was studying bats, they also found that the grid cells in the bats even though the bats can fly smoothly through the space, also produced irregular blobs, they actually found a slight difference, which was that the distance between the blobs was not completely random, it was it was more uniform, than you would expect, the chances of the system was trying to preserve those distances, but it was pretty irregular, and ours was just as far as we can tell, completely irregular. So that made us do a lot of rethinking about what the

system is trying to do. Because I don't really think that rats or bats are completely confused in a three dimensional space. I think very much like humans moving through, you know, a scuba diver moving through space or rock climbing, climbing over a wall or, you know, a gymnast, or whatever, I think we are quite good at localising ourselves to three dimensional space. But I think that the function of the grid cells is not. And this is a personal view. And I'm not sure if anybody but me agrees I should say that. This is not what the field thinks this is what I think. But I don't think that the function of grid cells is to produce these evenly spaced firing fields. I feel that the even spacing is a kind of a happenstance that arises from the somewhat artificial environment that we record the cells and where the rats are able to move very homogeneously through a wide open space, which doesn't have any obstacles and doesn't interrupt its path at all. That's kind of an unnatural thing for a rat to do. So I feel that the even spacing that we see, although it's really beautiful, is not essential for the system to work. I think what the system was trying to do is to sort of discretize the space in other words to break it up into chunks that are roughly evenly spaced, but the precise characteristics don't matter.

Steve Flemming 24:47

Just to pick up on the last point you said there about whether we can localise ourselves in 3d space. I'm wondering whether are there behavioural effects of the perhaps slightly more irregular coding of the third dimension like would the rodents or humans be worse? Do we do we do we have data knowing that they will be worse at localising themselves in the vertical dimension. There's not

Kate Jeffery 25:13

very much data for either either animals or humans. We certainly know that animals and humans can localise themselves quite well in three dimensions. But whether it's as good in the vertical dimension or not, it's been slightly hard to tell because the experiments were, you know, that would be comparable, where humans can move and abstractedly through the space and in all of the different directions have not really been done at the level that that compares the resolution of that map. And where experiments have been done, like, for example, looking in multi storey buildings and how people can localise themselves in that type of three dimensional environment? Yes, people do get confused. They're more likely to make mistakes about which level they're on and so on. But that may be because the, the information that's available on the horizontal is different quality from the information that's available and the vertical. So we don't we haven't really answered that question yet. It's high on my list of tasks is to answer that question, is the resolution the same? Because we might think that the resolution is different based on some of our experiments, but based on others about experiments, we might say it's the same. So it's an open question I get I

Caswell Barry 26:30

guess, it's very hard to, to control for the natural differences in dimension. So it's much easier to sort of transition around in a plane where I can walk around in this room, and I can get pretty much wherever I want. But just, I guess because of our built environment, the way we sort of spend our time is much harder for me to transition to the floor below because I have to go specifically to the stairs and go down them. And I suppose that's the the tricky bit, right? You, you want to separate out, what's the inevitabilities of the network, what experience you've had of the world, and indeed create an experiment where you have like a totally sort of asymmetric ability as symmetric ability to move around. I'm not sure what that even looks like, yeah, it's quite, it's quite an interesting thing to think about. And by the

way, I have a lot of sympathy with this view that you're having about grid cells saying that, you know, we've all been potentially been slightly misled by the fact that spatial experiments typically done in these totally bare 80 centimetre square boxes. And as a result, we have this view of what things look like. And you know, for many good reasons, because we want to sort of, you know, reduce things to their core components and do the experiments in a pure way we've done these things, but as a result, we've come so far away from the sort of ether logically or naturally valid environments. But some of the things we've all become obsessed with might just be terrible artefacts of the wave of Denise has happened. I guess it's

Steve Flemming 27:55

Yeah, I mean, there's a slight outsider to the field that you both are in, you think that's partly due to the fact that there, people have been seduced by the beauty of these patterns, that they are so regular, they look like something. I've kind of fundamental fact of nature. And perhaps people have been sucked into thinking that that must be then something to be explained as fundamental.

Kate Jeffery 28:17

I do. I do think that's possible. I mean, I, I need to be careful about

Caswell Barry 28:23

you don't need to because

Kate Jeffery 28:30

I think we all are scientists, we have a slight tendency, when we find some phenomenon to assume that the phenomenon has a function. So almost the first question that you know, whenever anyone wants something new in a paper is, is what is the function of this thing? And I think we have a slight it's slightly a mental reflex, and I think we need to sometimes think, does it even have a function? Or is it just a byproduct of whatever its function actually is? Maybe not. Maybe artefact is the wrong word. But it's that property that's interested you is not the property that's important about the system, I think, is a question that we we need to keep remembering to ask. But yes, I think the you know, the regularity of the grid cell patterns really beguiled a lot of people because it is so beautiful. And it's, it's generated a lot of really creative kind of models about how this pattern might come into being. A lot of them are based on sort of engineering systems. So we as human engineers, we have a lot of oscillating systems, for example, or, you know, systems that that have periodic signals of one sort or another. And you know, the way that we just measure distances and so on. And we don't necessarily know that those are the same things that come to play generating something like a grid cell pattern. So these are questions, exciting questions to be answered.

Steve Flemming 29:57

Can I ask about when you were mentioning before In your exchange as Caswell about what would happen in higher dimensions, and that got me thinking about time, because in a way the the animals are in a fourth dimension, they're doing these tasks over time. And one way of thinking about going in the third dimension is essentially like, going around a 2d grid, but a bit later in time. I mean, that's, you know, when you climb up the stairs, you're building, you're on the second floor a bit later on, then you

were on the first floor. And on the third floor a bit later on the We're on the second floor. So I'm just wondering how that how that is, I guess accounted for or modelled in

Kate Jeffery 30:33

I mean, time was a is a funny thing. And I'm not sure that it's in terms of spatial coding, I'm not sure that we can treat it as just a dimension, because, you know, the thing about time is you can only move in one direction in time. And at a fixed speed. And in a straight line, essentially. I mean, it's not true if you're a subatomic particle, but it is true if you're a rat. So, with with the spatial dimensions, you can trade them off against each other. So you know, I can walk east, west, or I can walk north east, which is a bit of, you know, a bit of North and a bit of east or north and a bit of West and so on. And so, so there's some trigonometry to be done to work out how far have you walked in, in the different directions, and therefore, how do these places all relate. So to be able to do that trigonometry, you need some kind of Compass, some kind of reference that that provides fixed points in the plane that against which you can tell which direction you're travelling, and that two dimensional plane. And then when you add a third dimension, as I mentioned before, you in theory wouldn't need to have a three dimensional compass, if you were going to have a completely volumetric map. And we actually don't have good good strong evidence that there's a fully three dimensional compass in the vertebrate brain. Although there's certainly some vertical information in the head direction system that's been reported by quite a few experiments now, but it doesn't seem to have the same resolution or the same representational capacity as for the horizontal space, it sort of looks like the brain is mostly interested in what direction you're facing on the horizontal plane. And then if you go into four dimensions, it's well, what would you need a four dimensional compass if you were going to fully represent four dimensions? And, and how it how would that work? So I feel it's unlikely. But I think it's still an open question whether we could have a four dimensional map like it was really for space, like dimensions. And I have thought about how you might do this in virtual reality. Because virtual reality lets you mess around with things in ways that you can't do in real space. But I haven't really thought quite how this work yet. But it would be really interesting to see whether we had the capacity to learn about a fourth dimension, with experience, understanding, you know, that that same thing of, of learning about sequences of play cells, for example, in four dimensional space, could you learn to understand how those relationships worked? And in four dimensions, I thought it would be a fascinating experiment to try.

Steve Flemming 33:08

Yeah, absolutely fascinating. Just thinking about the vertical compass, I reminded by, I taught my son to watch the red arrows display a few months ago, and I then bought a book about their training regime and and what they go through. And it's absolutely fascinating, like the precision by which they have to align themselves in three dimensional space, essentially. And I'm wondering whether Yeah, taking some red out, or some aerobatic pilots could be one way of thinking about comparing precision on that visit to convention will be fascinating between experts and

Caswell Barry 33:43

next funding stream right here. I can see it coming. This one could be fun. You need to bring your sick back, though, maybe. So Kate, we've heard loads about police are based on head direction, cell based research back. How do you get to this point? I know. Because I've worked with you. You've had a very interesting career and come to this point. I remember you telling me stories about being a junior doctor

and various places and working in different countries. What you know, what were the defining steps along the way to being where you are now?

Kate Jeffery 34:17

Yes, I did. I did start out in a slightly slightly different direction. I started out in medicine, because I knew I was intensely interested in science, particularly biology, but I was growing up in New Zealand, which has a bar at least back then it had a very small scientific community didn't really know that one could be a scientist. As a career, I just thought of new as interested in science. So I studied medicine. And while I was a medical student, I got introduced to the to the discipline of behavioural science. And in fact, part of that introduction was that I was able to do an elective in my first year where I could choose anything I wanted to do and I just chose psychology just kind of randomly And I just had never heard of psychology didn't really know that one could study thinking. And when I discovered that one could do this, I thought, wow, this is kind of cool, you know. And so as I was carrying on through my training, I became more and more interested in the science behind thinking and, you know, how does the brain generate thoughts and consciousness and so on. And I decided at the end of my training, that I wanted to research that and not treat sick people, but to actually dig around and find out how the brain works. So I, I visited the local neuroscience community in the place where I did my training in Geneva and New Zealand. And they were, they had a group of very, very active neuroscientists studying this thing called the hippocampus. And I'd never heard of it, vaguely knew it had something to do with Alzheimer's disease. But they said, come and work with us. So I went to work with them and found myself studying what we now call synaptic plasticity. So the the ability of neurons in the hippocampus and elsewhere to change the strength of their connections between them to form memories. And I thought this was pretty cool. And, you know, memories are the building blocks of, of thoughts and thinking, and so at the end of my master's degree, I decided I wanted to carry on doing that. And so I tried to find a PhD position. And I saw an advertisement in one of the science journals by Richard Morris saying he was looking for a researcher to come and work with him. And that person was supposed to have a PhD, and I didn't have a PhD, I only had a master's degree, but I also had a medical degree. And so I thought maybe that will do. So I wrote to him from the other side of the world and said, You know, I think what you do is really cool, can I come work with you? And And amazingly, he said, Yes, you know, he said, Come on over. So I went over to work with him. And he, he was also working on hippocampus, but he was relating it to behaviour. So, he had invented this very famous test of hippocampal function called the Morris water maze. And he was trying to understand how synaptic plasticity underlies the learning that goes on in the waterways. And so, I learned how to record from freely moving animals in, in challenging situations, serum water and so on, and to study their behaviour. And, and it was while I was there that I encountered John OKeefe and the play cells and decided that after my PhD, I really wanted to, to kind of come and study the play cells and I had actually visited. I keeps lab a couple of times by then, and I mean, I must have been a strange sight the first time I met him because I was on a kind of a gap year that I had a kind of a year I was just doing locums in London and I had it was kind of the post punk era and I had spiky blond hair. And this really quite aggressive looking don't materialise, that I want to find out how the brain works. But he remembered me a few years later when I was in Richards lab. And so when I, you know, got talking with him, and he had space for a postdoc, and so I went to work with him. And yeah, this sort of took off from there.

Caswell Barry 38:06

Amazing, was meant to be, it's,

Steve Flemming 38:09

it's amazing how many people we talked to who say that they didn't really know that psychology is a field existed, or the study of the mind as a science existed. And I always think the more we hear this, I always think that psychology must be doing a really bad PR job. I don't know whether that's still the case, but certainly seemed to have been the case a few years ago.

Kate Jeffery 38:30

Yeah, I think it took a while to get going. And one of the I mean, one of the really big instigators of that was Donald Hebb at McGill, and the so you know, Akif had worked with him. And so had Graham Goddard in Otago. Who was the person that I was meant to go and do my Masters with? Actually, tragically, he was he was killed in a hiking accident. And so I went to work with his colleague, Cliff Abraham, when I think he was really kind of, in many ways responsible for the bringing together of psychology and neuroscience and such a strong form, you kind of see seeded this right across the world. And and I think it's certainly those two disciplines have come together a lot now. So I think most psychology departments have some neuroscientists in them, which certainly wasn't the case when I started out. And now we're starting to see, you know, departments like the one that I'm now in where, where they're aiming for a kind of an even balance, like trial and trying to really strongly bring these two things together, which I think is great, because I like to, I like to be able to see the continuity of explanations that goes from molecules all the way up to thinking and consciousness and these really, really ephemeral things that I just think it's really cool if we can explain how to get all the way through those levels from one end to the other. So maybe

Steve Flemming 39:49

we can ask you about the new role case only. You've just been appointed as the Head of School of Psychology and Neuroscience at Glasgow University. And I'm wondering What are your thoughts at this stage just going into that are about the challenges of creating a vision around this intersection?

Kate Jeffery 40:10

Yeah, so it's a really exciting project. It's, it's like a grand version of the one that I undertook in UCL when I created the the Institute of behavioural neuroscience, which is a neuroscience research group within the psychology department, essentially. So this is like that, that same thing, but a much bigger scale. And it's a it's a school that's been formed from the amalgamation of neuroscientists doing you know, pretty biological research a lot of it and spinal cord and like very, very sort of cellular kind of what you might call low level neuroscience, very biological, what wetware is another word for it. I would say, so people, people doing that, and then quite a lot of cognitive neuroscientists who are studying the human brain using various kinds of imaging. So, you know, functional neuro imaging and EEG recording, some electrophysiology, and magnetic stimulation techniques and imagery. So all of these ways of interacting with the human brain, so, so there was that on the one hand, and then a strong community of more pure psychology, you might call it that, so people who really studying behaviour, to do things like language, and, and social cognition, and so on. So these two things been brought together, under the umbrella of the unit of assessment for and the research, excellence framework, where psychology and neuroscience clearly, you know, a treated as a single discipline, so it made

sense to create this unit within the university as well. And they really wanted somebody who could, could speak to both of those communities, the neuroscience community and the psychology community and and fill in the gap in the middle essentially, that's, that's how I kind of see it. So it's quite challenging, because it is a big gap and trying to get people on either side of that gap, to feel that the gap is crossable. And that they want to cross it is kind of the challenge. But everybody is excited about the challenge, I've had huge positive response to, to the idea that we, we would like to recruit it in that gap, to kind of build a community of people who are studying biology, so you know, animal research, but in a way that links to both the neuroscience and the psychology, so really, really spans all of those explanatory gaps and uses a lot of cool technology and all that kind of stuff. So, and at the same time, we're trying to build up the teaching programme to also close that gap so that neuroscience students can learn some psychology if they want and psychology students, because it's neuroscience, perhaps in future will even have a neuroscience and psychology degree programme. possibly in the future, that's still to be decided. But yeah, so it's really challenging, but exciting, and really kind of looking forward to the challenge.

Caswell Barry 43:02

Do you think bringing these things together? Do you think that sort of brings into focus? The challenge of delivering something at the at the sort of far end, I mean, certainly sort of much of sort of the history of the at least the neuroscience I've worked in, it's sort of research for research sake. But I know, people including myself, increasingly thinking about, you know, what, what are the impacts we can make on people's lives like these, these technologies and ways of thinking are now mature. And we should be able to be thinking in terms of translation and what it means and how we can sort offset dementia, whatever, is there. Is that part of the picture here? Or what do you think about that? Is it time for those sorts of realisations?

Kate Jeffery 43:44

Yeah, very, very much. So I think there's always a balance to be struck between trying to solve real world problems and trying to solve what some people call blue sky problems, you know, that they don't seem to have any real world applications, like, you know, the head of the university getting that type of thing. It doesn't seem to have any practical application, because it's understood that that the technological advances that ultimately produce real world applications began with just straight out curiosity, you know, how does this thing work type of thing. And, you know, electricity was discovered, not because we were looking for energy, but because we were trying to understand the structure of matter and so on. So there's always that balance to be struck. But I find myself increasingly as I go on in my career, wanting to feel that the stuff that we've dug up, about how the universe works, you know, how the brain works, and so on, could have some practical application so that the taxpayers have paid for it or getting something back. So you know, you are making a change in real people's lives because we've got this knowledge now and we can use it so we should use it. So in the domain of spatial cognition, we have learned a lot now about how the brain does creating an understanding of space for the animal And I think it's well past time to deploy our knowledge of that, to, to try and create spaces that can be understood better than the spaces that we sometimes create. So my big bugbear is very, very complex, large buildings like hospitals or conference centres or train stations are something that are hopelessly confusing. And even even ordinary buildings just can be confusing for some people. So some people find themselves distressingly disoriented, in normal everyday situations, because they,

they just don't understand they're not able to build a mental map of a space that makes them feel confident that they understand where things are. And I think now that we understand about the, you know, the head direction system, and its importance and the, the grid cell system, and you know, the, the involvement of distances and directions, and the role of boundaries, and how spaces are kind of joined together and our large scale map and so on. Now that we're starting to understand how this has happened, I think we could be using that information to help architects and urban planners and designers, and so I've become increasingly involved with those communities. And I've been talking a lot to architects. Partly, I think, because I developed a love of architecture from building architecture, very strange apparatus for my rats, I always found that one of the, one of the things I loved about doing those experiments is I just really love building these strange things. And there's a there's an aesthetic pleasure and building a structure that has a three dimensional form, you know, sort of on a large scale, you know, structure of a building, I really love buildings, I love architecture, and I would love to be able to help architects create navigable architecture, as well as simply aesthetically pleasing architecture. So that's, that's kind of the mission for me going forward.

Steve Flemming 46:54

Okay, so we're almost out of time, it's been absolutely fantastic discussion, and we wish you all the best in the new role in Glasgow. But before we wrap up, we, as regular listeners will know we'd like to ask each of our guests the same question and we're going to ask you the same question now. So what is your favourite facts that you've encountered about the brain?

Kate Jeffery 47:19

I knew you were going to ask this question. And I actually have 2am. I allowed to Yeah, definitely. There's there have to be one drive to choose.

Steve Flemming 47:25

Okay. No, no. Well, that you have to I feel like it's a bit like that thing at the end of this, but this one more than one it?

Kate Jeffery 47:35

Okay, well, that one's that one's a small scale one on one to large scale. And if you feel it's unfair, you can chop out but so the small scale one is that I, I learned that I did some reading into the evolution of brains, how brains came about from the, you know, the precursor kind of ancient life. And I discovered that all of the proteins that go to make up synapses in neurons, so the specialised connections between neurons are actually present in sponges, even though sponges don't have nervous systems. So you know, the post synaptic density proteins, and all of those things, NMDA receptors, and so on, all of the stuff is present in sponges. So before nervous systems came out. So I think that's an amazing

Caswell Barry 48:19

I want to be doing and responding. That's what I need to know.

Kate Jeffery 48:23

I think that's a really small questions, but we, I mean, we know that evolution, you know, reuses and recycles. It's very, if you've got a complex molecule, then why not use it for something even if it's

different from what you first built it before? I guess. But that's, I think that's cool. My other my life's goal and favourite factors that, that dolphins sleep with one half of their brain at a time. And I think quite a lot of constantly mobile animals do. And I think that's amazing. And what what was the experience of the dolphin be like, and how does that happen? I think that's, that's a cool, interesting fact as well.

Caswell Barry 48:59

That's fantastic. I imagine it feels like me before I had my coffee in the morning is what?

Steve Flemming 49:09

Yeah, we need to check whether Caswell sleeping with it.

Caswell Barry 49:17

So that was fantastic. Thank you so much, Kate, for joining us on this episode of brain stories. And to our listeners. We'll see you next time. In the interim, we'd like to thank Matt Wakelin, Maya Sapir and Trevor smart for their roles in taking brainstorming from an idea to a fully fledged podcast. Patrick Robinson and UCL digital education for editing and mixing. Follow us on Twitter at UCL brain stories for updates and information about forthcoming episodes.