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Oral History: Ernst Stelzer / 2017/06/26

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File name: 2017_06_26_ErnstStelzer transcript

Key

AFL: = Interviewer, Anne-Flore Laloë

ES: = Participant, Ernst Stelzer

[??? at XX:XX] = inaudible word or section at this time

AFL: So, we're here today, it's the 26th of June 2017, we're at EMBL Heidelberg, Germany, and this interview is part of the oral histories programme of the EMBL archive. My name is Anne-Flore Laloë, I'm the archivist at the European Molecular Biology Laboratory. Please would you introduce yourself?

ES: Well, my name is Ernst Stelzer, I was at EMBL from 1983 until 2011 and I worked originally in the physical instrumentation programme, then in the biophysics programme and then finally in the cell biology and biophysics unit.

AFL: So could you tell us a bit what you were doing before you arrived at EMBL?

ES: So I had studied physics in Frankfurt and I'd just finished my diploma thesis in the Max Plank Institute for Biophysics, and there I was working on dynamic light scattering, so … and essentially the whole department or the whole Max Plank Institute at that time was somehow concerned with thermodynamics and some of the techniques that we used during my diploma thesis were of interest to Roel Wijnaendts van Resandt who worked on lifetimes of proteins. And that's why I actually started to work here at EMBL as one of the first six PhD students from this PhD programme.

AFL: So you did your PhD at EMBL?

ES: And then I did my PhD here at EMBL and the degree was granted by the University of Heidelberg in the physics department, that's right. And I started off working on the laser because we had a huge laser, and then I gradually actually moved into microscopy and into confocal microscopy and during that period also into confocal fluorescence microscopy because that did not exist when I started, so that was actually the big thing. And then I wanted to leave <chuckles> so I actually had contracts from several companies, got one offer, from a guy in the US, and Carnegie Mellon University, and then I also got an offer from EMBL to stay here, and that was Lennart Phillipson, and then I accepted that offer, and that's why I then stayed at EMBL as a project leader. I was so young <chuckles>, I must have been … I was only, hm, that was in … 1987 I handed in my PhD thesis, and then I

was 27, exactly, and then they thought I was too young, I didn't have enough experience, and that's why they made me this project leader. And before that actually I was sent by Lennart Philipson on a tour through the United States, so he really … EMBL paid a three-weeks tour through US, which was then organised by various people, I can't recall exactly, and I really went from lab to lab, gave talks, introduced my work, and made a lot of contacts, which many of them still last until today. It was really nice, I have to say! Just unimaginable probably nowadays, but Phillipson thought well, you should do it! <Laughs> And then his secretary actually organised the whole trip, so she booked all the flights and hotels and god knows what. So it was quite nice.

AFL: So that was between finishing your PhD and becoming a project leader?

ES: Exactly, yeah.

AFL: And so what were the first priorities of your project, as a project leader?

ES: Well the first thing that I did is that I killed all the other projects, we continued just with confocal fluorescence microscopy. And we had at that time an instrument which we called the confocal beam scanning … microscope, and that was very complicated. It was really, really complicated I have to say, it was too big, so we could make some pictures too slow, and then we actually immediately built a much, much simpler system based on a beam scanning rather than a stage scanning device. And yeah … then we also put that to use. I mean just to give you a perspective, I think with this original device, the CB confocal beam stage scanning microscope, <5:00> we in total probably produced about 3,000 pictures. And with the beam scanning device we probably produced about 30,000 pictures in the first year. So it was a huge increase at that time. Don't forget we're talking about here 1987/1988, something like this. So that was a huge effort.

AFL: And these of course are analogue?

ES: No, that was already, so that was at the transition from analogue to digital.

AFL: So what was the work that was then carried out on the photographs? What did that consist of?

ES: You mean with the data that we recorded? So that, at the very beginning we looked a lot at microtubules, microtubule organisation in PDK2 cells and MDCK cells, probably also in HeLa cells. So that played a certain role, not everything was published of course. And then what is also probably interesting from a point nowadays, from a current point of view, is that everything was live 'cause we had no way to fix the specimens, which didn't really mean that the … I don't think they were really very much alive, but at least they were alive for the first ten minutes of their observation or something like this. But we didn't fix the specimens so we just prepared them from the petri dish, looked at them immediately and so on.

But it was a huge variety of specimens that we looked at. I mean you shouldn't forget, nobody really had any clue what to do with it. It developed. We had to understand things like optical sectioning. Theory existed but it was very complicated and not really well explained, and also with hindsight I still think there were a lot of mistakes and misunderstandings in it. The instrumentation was not so simple, because it involved electronics and high-speed photomultipliers, and scanners. And then of course you had to do some big data processing. That was also not so mature at that time. And then of course one had to build a lot of the stuff ourselves so we just couldn't purchase it. We couldn't go to a catalogue and purchase some filters and so on. That did not exist. Or you also had a small variety of lasers, so we had to be very, very careful even with the lasers that we purchased, I had to select the wavelength at which they would lase myself. And they had to be adapted for some of the fluorophores and so on. So it was a lot of details one had to take care of. Of course nowadays it's completely different because the optics industry has matured much, much more. There is a much larger variety available.

AFL: So could you just tell me, just take a step back and could you describe what EMBL was like back then? So you arrived in '83 and obviously it was a much younger institution then and it's evolved, so you were at Heidelberg, what was it like?

ES: Well first of all it was half empty, or half full, so there were a lot of floors which were unused at that time. I would say there were also a lot of parties! I'm not joking, seriously there were a lot. I'm not exaggerating, I'd probably say there were one or two or maybe even three parties a week! Because everybody was a foreigner, and so people generally were very interested in meeting. So that made a huge difference. You could really walk into the floors and just occupy a room and nobody would care about it. Then we really also did not have a budget. So I have to say I don't know exactly <laughs> how it was organised, because don't forget I was a PhD student at that time, but if we wanted something, we just ordered it. <Laughs> If it was a very expensive piece of equipment, like some lasers or something that we wanted to purchase then I went to Phillipson, talked to him and he would say yes or no. And I can't recall him ever saying no. Also when someday I thought I would need somebody to work on the software, so I just went to him, told him, he picked up his phone and then I went downstairs to the human resources department, *Personalabteilung* at that time, and then we just employed the guy. So that was very, very <10:00> easy, and also you were really basically in daily contact with the administration. There was no barrier between you and the people who worked in admin. So that was good, I would say it was reasonable.

AFL: And also it was a much smaller organisation, wasn't it?

ES: It was much, much smaller, many fewer people, yeah, and there was a mixture, as nowadays I would say. Probably as everywhere. So there were people who were, let's put it frankly, totally useless … and then there were people with whom one got along and you could really do something and achieve something.

AFL: So that facilitated the work that you then carried out.

ES: Yeah, then also I mean we had these huge workshops, but I'm not quite sure if we could … if everybody knew how to use them. And then of course there was also the workshops here at EMBL worked also a lot for other facilities. That was also a difference.

AFL: So about the workshops, could you describe for us the relationship that you'd have between having an idea for an instrument and the development of the idea, and what the back and forth would be there?

ES: Well at that time I actually had … so my group at the very beginning was very small, so we had a programmer, and then we had an electronics engineer and the term did not exist but electronics engineer was also very interested in mechanical designs, Reiner Stricker, and he was actually a wheelchair driver, so he sat in a wheelchair, and he was probably also for that reason very interested in sensors, motors, making sure … I think he even designed more or less his own wheelchair, and now he has a company for the cycling equipment that is attached to a wheelchair. That's what he founded later when he left EMBL. So together with him we did a lot of the designs for these microscopes and then I did all the calculations because of course we didn't have any software to know where to place the equipment, and then we worked on building the various different parts and then of course all these parts had to be drawn, so they had to be really designed and that we did together with the design department or drawing department which existed at that time. But I would say we did the design and they did the drawing. That was really the order. And then with those you could go to the mechanical workshop and then … have the parts built. And then assemble them and check them and so on. And the electronic parts we did ourselves and then we also wrote part of the software … or everything actually!

AFL: So it was a multiphase approach.

ES: Yeah, yeah. Correct. But there was a real plan behind it so I know there's always a booklet that I always wrote, so there was … that's why we have a lot of these little documents, because I really wrote down everything from beginning to end what it should look like and what would be special and made some notes on how to do certain things and how to program them or filter designs probably paid a huge role at that time.

AFL: And then of course using the machines, so …

ES: Using the machines was always a hassle, let's put it this way, because … so you see on one hand it was obvious that confocal fluorescence microscopy was useful, but it was not so obvious how to take advantage of it. So at the very beginning a lot of people came and they had prepared the specimens as they had prepared them before for fluorescence microscopy, which usually meant that the specimens were completely flat and then in the confocal microscope, which has this optical

sectioning property, it only makes real sense if you have some depth to the specimen, so it had a certain thickness. And then people had to change the way they prepared the specimens. That's where these collaborations come in quite handy and that's where I would say we were really lucky, like for example guys like Robert Bacallao who at that time was <15:00> a post-doc with Kai Simons … or with Eric Karsenti actually, he really put his career into using these confocal microscopes, so he would really adapt the applications, so I really have these … there's really something like Bob Bacallao, he had prepared something, we looked at it in the microscope and I would tell him, 'Well, tell him well, you only label let's say the apical side of these MDCK cells, and then he would go back <chuckles>, seriously, we'd just go back to his fridge and pick the specimen that looked completely lousy in a conventional microscope, and it turned out that actually in this specimen he had labelled everything in there, all the microtubules. So suddenly we could see the microtubules from the apical to the basal side. But as I said, that was really his main project. He really … his projects would not have worked if he hadn't had the confocal presence microscope and we had several of those cases, so Morgane Bomsel was another person, and many others. But they really invested their career in this and that's how we further developed it. And that was the kind of information, so he could tell other people, or Bob could tell other people how to prepare the specimens and in this way we could somehow understand and learn what could make sense with the confocal fluorescence microscope, which dyes would work, which lasers might be useful in the future, which filters do we need and so on and so on. So that actually then gave us an idea of what the next design could look like, and then we also changed things a little bit and so on. So this is really I would say the general principle in which we approached the different designs.

But as I said before, the really important thing is that we … I've lost it! <Laughs>

AFL: It worked as a collaboration –

ES: It was a collaborative effort, that was really important.

AFL: I think that was what was coming out of that.

ES: Exactly. And the designs of the instruments were really driven by an interest in certain applications.

AFL: So just to get an idea of the timeframe between one machine and the refinement and the processes and the next machine, how fast does it go?

ES: So I have to say that's a really good question. So I assume that the first machine was really started in '81, that was before I came to EMBL. Then it was functioning while I was here in '83 or started to function, but it didn't produce any useful pictures, and then we completely remodelled the instrument to make it useful for confocal fluorescence microscopy, so that was probably … and then we published a paper with Gerrit Van Meer, that was in '87, the *Journal of Cell Biology,* and that

really was a kind of breakthrough at that time. And then the next instrument was probably built 1990, and then we continued building instruments probably until 1995, confocal fluorescence microscopes, and somehow I think in '94 or '95, I really can't recall it exactly, I'd have to look it up, we started collaborating in earnest with Carl Zeiss, because I was really sick of building all these instruments. By that time I'd probably been through four or five generations so we really changed them every 12-18 months, because there was a huge need, and until 1996 there was not a single microscope from a company or a vender. All the confocal microscopes actually came from my group, and don't forget we had been doing this now for more than ten years by that time, so we collaborated with Zeiss, and then I also wrote a little booklet, how to build a modern confocal florescence microscope and that was then the LSM 510 which was then later the LSM 710 or 810 or now it's the LSM 800 series, so that actually a lot of the stuff that we built at that time actually then made it into what is the confocal fluorescence microscope nowadays. And that's the way that we did it.

That was also, this development with Zeiss also took us probably 12 months, and then we transferred all the software and hardware and whatever to Zeiss. So people actually moved to Jena, two people from my group, to <20:00> make sure that the transfer actually worked. So they were there for two or three months or four months even, I can't remember.

AFL: To set it up.

ES: To set it up and make sure that the software worked and so on, and make a real product out of it.

AFL: And that was a successful collaboration?

ES: That was a very successful collaboration. I mean we cannot claim that we made hundreds of millions on it, but for a company like Zeiss, and probably they probably sold equipment worth somewhere in the range of a billion euros or something, or a billion D-marks, so that's the scale.

AFL: So you said that at the beginning your group was very little. Did it grow?

ES: Actually it grew, yeah. <Laughs> So in fact the very, very beginning we were not allowed to apply for grants. So that really changed only after a few years. And then we were really asked to apply for grants from the DFG and we did that, and they were then granted, and then suddenly we had money to pay for extra people. So until then we hadn't done that. So we had these diploma students, and later I had of course PhD students, but at the very beginning we didn't have any external funds, and we were very successful with that. The grants covered all sorts of equipment. Maybe I shouldn't go into all the details but one of them was a huge EU grant, an FP4, so that was really a long time ago, and suddenly we had 12 people in the group instead of 8 or 6 or 7 as we had until then, and then we really expanded and also used other rooms and other places here in the lab, so that was

no problem at that time. And then when the grants were finished we just returned the rooms and the people left! But usually the group was never really much larger than eight people and since then we always had grants from BMBF and DFG and also to a certain extent from other funding bodies. And with this we paid … it usually paid for post-docs. So the group certainly was post-doc heavy, which of course is really important when you want to get along very quickly.

AFL: And the different areas of interest in the group, I guess. What kind of people did you have? Because you have physics, there's biology, was it a very diverse group in terms of interests?

ES: Yeah, that's true. I mean we never only worked on confocal microscopy so that was important. But beginning in the early nineties we worked on optical tweezers, so that played an important role, optical levitation, then we also worked on trying to use collimated laser beams to push particles along, so that we still did until the early two-thousands, so that was really a big project. Laser cutters have played a huge role for many, many years so we also worked on that.

I would say that we probably did everything that you could do with a microscope and a laser. That's probably true. And a lot of things are still used up to now. I mean the way that we built the laser cutter is exactly the way that most laser cutters are still built nowadays, so that worked really well, I have to say. And then the people, they were usually physicists, so we always had biologists and chemists in the group, like Emmanuel Reynaud, he's a biologist, or Francesco Pampaloni who's a chemist. So these people were always there, or Ernst-Ludwig Florin, he was a biophysicists from the LMU in Munich. He was more interested in working more in a biophysics area. And the projects that we were interested in varied a lot. So at the very beginning I have to say we really worked in intracellular trafficking a lot. That played a huge role. And then we also worked on bleaching in order to investigate this, so that is something that we picked up, <25:00> where we also published quite nicely, together with Jamie White, who was a student of mine, an American who later got his degree from Stanford. And then what I always tried to do is tried to push the physicists who worked in my group also to work on more biological projects, like Jan Huisken, for example. He started working on what we at that time called a tetrahedral microscope, or an optical levitation, actually at the very beginning, and later on I tried to make sure that he would work, collaborate with Jochen Wittbrodt on the zebrafish project and Philipp Keller, who was actually also working more on microtubule dynamics at the very beginning, so we looked at microtubule dynamics in 3D. That was a project that we more or less did in collaboration with Eric Karsenti, and then that was for his diploma thesis, and then later for his PhD thesis he worked also on zebrafish, medaka and so on.

So we had to do it this way because the instrument was complicated. And they were not so easy to use in many cases. So it was very important that you had a kind of technology background in order to be able to use the instruments.

AFL: And it sounds a very results-oriented group.

ES: It was, definitely. Usually I would say we always tried to … it wasn't always possible because the people were always not always ready for that <chuckles> but in principle we always tried to go for projects and publications.

AFL: And applications.

ES: And applications, yeah, that's what I meant by projects. So the project was not essentially to build a microscope but to use it for whatever. For example with Stephan Grill, when he did his thesis the idea was to look at microtubule dynamics in early *C. elegans* embryos, first cell division also, that was the project. So can we figure something out; can we see development distribution of certain proteins, and so on? Or Stefan Hell, he was a post-doc in my lab for three years, and that's when we started working on 4Pi microscopy, and that was also carefully planned. So I had been working on this 4Pi microscopy before, so I had an idea of the complications. We tried to do it and we realised that was not so easy, to get the light to interfere, and then we basically sat down, Stefan and I, and made a list and we also had a kind of plan, so we had the different implementations of 4Pi microscopy, A, B, C, and we really tried to figure out how we could get that working. And then later Steffen Lindek also joined on this project and so on. So we really thought about what we could do and we really set milestones where we tried to publish the stuff.

AFL: I find this very interesting, because through what you're saying I'm also hearing how EMBL is changing around what you're doing in the different dynamics that you're able to make most of in working with other people.

ES: Yeah, because that was always embedded. Because I was always a member of two programmes, so when they existed I was a member of the instrumentation programme and the cell biology programme and so I took part in their retreats, I met the guys probably … half of them every day on the corridor. We were maybe 30 metres away on the same floor. I was reviewed whenever the cell biology programme was reviewed, I was reviewed, and when the physical instrumentation programme was reviewed I was reviewed with that! <Laughs>

AFL: That's quite a lot of reviews!

ES: Yeah. I'm not absolutely sure … so I might be wrong but I think I was reviewed about eight times since I was in these two programmes. So I was certainly reviewed all the time with the cell biology programme but at least twice with the physical instrumentation <30:00> programme. So you were really embedded and then there was an open door policy, which you should also not forget, so you could really go to PI and talk to them and the people would just come to me and talk to me, and try to see what we could do; which doesn't always mean that we collaborate with everybody and we've always got a project working, but in many cases we did.

AFL: And I guess it at least meant that there was a conversation about it.

ES: Correct, yeah, and that also helped to understand certain things, and to get an interest. I mean that is … this whole experience with the confocal microscope really made me think that we should do microscopy differently. I mean it's very hard, I couldn't tell you exactly the day when I thought we should do this differently, but we started thinking about 3D cell biology, we started reading those papers in the group, all around the time that we start with this light microscopy, because we really got the idea that we have to do it differently and we have to make sure that the specimen is not so heavily exposed to light, bleaching should be much less, photo damage plays an important role. I mean photo damage plays an important role we knew from our video microscopy, so I knew, because just looking at the specimen, no fluorophores and they still died! <Laughs> So it was obvious we had to do something differently, yeah? Or we noticed that you could do a lot with plant cells, and you could do much, much less with mammalian cells. They obviously did not survive. And the embryos definitely did not survive. And I have to also say, when we started with light sheet microscopy, we looked at *drosophila* embryos and the very first also did not survive. So they did not look as nicely as they looked later on or look nowadays. So we also exposed them to much, much more energy than was necessary but that, of course, is part of the learning experience. That's why it's called science, yeah? That is really the reason. You learn. You see something and you draw conclusions.

AFL: Yeah. I'm interested to hear about this interaction between the instrument and all the practical work behind, and especially in the specimen preparation that you did clearly a lot of thinking about. Otherwise you wouldn't see anything!

ES: Yeah … so when we started, as I said before, we really worked only with live specimens, so we would have c6-NBD ceramide for example, and you would put a little droplet of that into the medium, and then that would somehow distribute an then you could change the temperature and then they would accumulate, as lipid would accumulate in the Golgi apparatus or somewhere close to that, and then we'd take the specimen and put it into the microscope. So that was a clear way of seeing certain things. Later on of course we got to know the … as I mentioned before, Bob Bacallao, we got an idea on how to fix specimens and then also how to add the antibodies or certain dyes to these microtubules. That helped, and then that was really important. And then we started also with GFP, so that's all when Jamie White was here. At that time we really collaborate with Roger Tsien, because you couldn't buy it. I mean we knew it existed, but it was not so popular and certainly Jamie was the very first one to ever use it at EMBL, and then we introduced GFP to EMBL and that of course made a huge difference. And I have to say when we start with light sheet microscopy we were extremely, extremely lucky that Cayetano Gonzáles at that time had just introduced GFP to *drosophila.* So that's why we looked at *drosophila* very early on, because we could take his embryos and then put them into our light sheet microscope. Because the problems, of course, if you have a thick specimen, we're talking about millimetres, in the millimetre range at least, and you have to get the dye into the specimen, and that is a huge effort. This is really something we've had to think about for decades, and really experienced with it. And then of course what we also did, <laughs> <35:00> is we had these EMBO courses, so we've been doing these EMBO courses since, I think, I'm not absolutely sure now but I think we did the first one in '88, 1988, and

I've been doing, I don't know exactly how many we did but we did that certainly until the 2000s, 2001 or '07, or '06 was the last one. So in total I definitely organised more than 20 courses, and during that, these courses, we also had programmes. I was really well organised and then part of it was what makes sense, how do you prepare your specimens, and so on and so on. So we really worked ourselves through this programme. Every year or every two years, or if we didn't do it here at EMBL I might have gone somewhere else and did it with somebody else, but we constantly thought about all the different steps that are required to take advantage of these microscopies, and we had to think about sample preparation all the time and then of course people came with completely new specimens and then we did a completely new way of sample preparation. But that played a constant role, and the courses certainly involved biologists, and a lot of biologists, probably many more biologists than technically oriented people.

AFL: Do you remember the name of this EMBO-course?

ES: The very first one?

AFL: Yeah.

ES: I probably still have the documents.

AFL: Oh wow!

ES: I can probably have a look.

AFL: So all of this development was very much a reiterative process, you try, you try, you try …

ES: Correct. As I say all the time, that's research. We're not building a car, where we know in advance what it should look like in five years, but it's more like you stumble through the fog. You have an idea in which direction you want to go, but you don't really … you don't really know whether that's the right direction or not and you try to make rational choices as early and as often as possible. I'm absolutely serious about that. 'cause that is another point when I always try to push this a little bit because the fact that we do a lot of maths, or we always did, so we always did a lot of calculations and personally I always think that helps, because you do a calculation and you realise this is not possible, or this takes too long or you have to find another way to solve this and this. I mean you don't just do a design, then hope that it works. That's not the way to do it. Like I showed you before with these microscopes, I mean you realise there are no sliders or something, it's not built from … pieces. It's really pre-calculated and put the parts into the right position, right from the beginning, and you saw that dates back to the 1990s, yeah? So that's the only way you can get this to work at all!

AFL: Trial and error.

ES: No, no, no. Trial and error in the applications but not in the building the instrument.

AFL: Precision in the instrument building.

ES: Yeah, because that you can calculate, that's more an engineering part.

AFL: Truly interdisciplinary approach.

ES: Truly interdisciplinary approach, exactly. Then coming up with new ideas is more the physics direction, or trying to interpret the data, taking advantage of this and that and trying to come up with a model for how this and this works, like this work on microtubule dynamics in 3D. That is a truly mathematical endeavour, or physics endeavour.

AFL: Always trying to find the next solution.

ES: Yeah.

AFL: This is fantastic, Ernst. Maybe just to start finishing off, clearly EMBL changed a lot during your time here. Is there anything that sticks out as being the thing that changed the most for the institution?

ES: Seeing it from the outside … first of all, what really strikes me, and don't forget I'm German, but I still somehow think there are too many Germans here, I'm really surprised. And I also think that a lot of, many people who have been here much, much … I mean maybe I'm not the person who should say this, having been here for 28 years, but somehow I think that it's stalled to a certain extent. So this huge turnover also at the higher levels seems to have <40:00> stopped. And from my feeling, this has been a little bit different in the past.

And then also teaching seems to play a much more important role and the view towards the outside seems to play a much, much more important role, service seems to play a much more important role. Maybe I'm completely wrong, but I doubt it that I'm completely wrong!

<Laughter>

AFL: It looks like it's slipping?

ES: Yeah, that's what one sees from the outside. I'm still sure it's quite active. It's not as if I'm not here, once or twice every year, certainly that has never been different, so I'm also still in contact with a lot of people. I've just spent four days with Phil Avner, because we're on the same council, ERC panel. So it's the second time this

year already, so it's not completely off, and I'm quite sure a lot of people share some of the ideas.

What else is different? It looks much better organised than it did in the very beginning.

AFL: A necessity of size perhaps?

ES: Yeah, maybe a necessity of size. Also EMBL was very, very open. I mean you would just walk in and out, you didn't think about it and services probably were not as mature as they are right now.

AFL: And just maybe perhaps a last question; if you were to give a piece of advice to a young scientist starting now, how do you encourage them or is there something of your scientific career that you'd like to pass on or try to …

ES: That's a good question … So first of all I'm not sure that my scientific career is a good model!

AFL: <Laughs>

ES: I'm absolutely serious about that, because you see, I really think I have been very, very lucky to be in the right place at the right time, so I mean I did not plan to work on confocal fluorescence microscopy, but it happened and I was here and maybe somebody else could have been here, in my opinion. But it certainly played an important role, there's no doubt about it, 'cause that was really the foundation of a lot of the things that I did in microscopy because I really did it from scratch. I mean basically absolutely everything. And so … and then we could always do the things that were not mainstream, so they did not play such an important role. It was not … seriously, when we published a paper, we did not think about the impact factor because it did not exist. So we published a paper in JCB because it just turned out to be reasonable, or I don't know … <chuckles> or we submitted it to JOSA A or whatever, or to all sorts of optics journals or *Journal of Microscopy*, and it was absolutely fine. Nowadays it would be a disaster. Seriously because the impact factors are so small and people would be very afraid to publish there, but you didn't do that; you published within your community much more than you probably do nowadays. So … I'm quite sure it's much, much harder not to follow the mainstream nowadays than it was in the past. And what I also think in hindsight is what is really, really important, that once you've finished your PhD you work in at least one, maybe even in two different labs as a postdoc. Otherwise you don't get your network together. Otherwise there are not the people out there, who are willing to support you when you apply for money, for grants, for prizes, for positions and so on. And for me that was simply not so important. So that makes a difference.

And another thing where I don't think I'm a role model is, as I said before, my mother's English, 75% of my relatives are British or live in the US or in South Africa, so this exposure to different cultures is different for me than it is for many other people. And so that is another reason why I think you have to work <45:00>, you should work outside, just to get a better feel, and then, at least for me as a German, going regularly to other countries, I think that Germany is quite well organised.

<Laughter>

And its' really relatively easy to live here. You don't have to be afraid of so many things. This is not the case everywhere. That is, of course, part of it. I mean if you don't feel secure, <sighs> then you cannot work in such a field as in science. Don't forget, I did not have a tenured position until I left for the university in 2011. And I did not even think about it. Seriously, it did not occur to me that … I just never worried about it. We still built a house and we had kids, and whatever. It never occurred to me. But I'm not so sure if everybody can do that, everybody has this freedom to do that. So … there are many different aspects one has to take care of. I really find it shocking to see how many people think they cannot manage that. So we'll see what will happen in the future.

AFL: We need to be positive!

<Laughter>

ES: People often ask me what happens next in microscopy? And the real issue is that the people see what is going on now but they have no concept of what will happen in the future, so they think we've got that far, that's it. But the real issue is that I may have worked in science for 30 years – before me, people have worked in science for 30 years and after me people will continue to work, and they will develop all sorts of instruments or microscopes, and if they don't do that, then they do something else. So there's absolutely no reason to believe that this is it. It will continue. But it doesn't necessarily mean that I will be the person who will push it in the future. I have no doubts that I will not be the person!

<Laughter>

So the best I can do is support people who I think could do something in the future. That's the way I see. Maybe we should conclude here, but I really think for example these panels that I am at the ERC, for me personally, what is really important is not so much the project, I have to say. I mean the project should be reasonable, but what I'm really looking for is the good people, and if I have the impression that this is a good person, then I care more about the good person than about the good project. Because … if I look at all the things that we did, they were all done reasonably and they were all planned, but that doesn't mean that the outcome was useful. But I think that's the way you have to work. You try all sorts of things, you think about certain things, you do them, but then you have to learn from

that and then you continue and in the end you will do something reasonable, hopefully! But that's the way it works.

AFL: Those are great closing words.

ES: Good! <Laughs>

AFL: Thank you very much Ernst.

ES: Thank you.

<End of interview>