Conversations with Michael Levitt

Gemma-Louise Davies *

Department of Chemistry, University of Warwick, Coventry, UK
*Correspondence: G-L.Davies@Warwick.ac.uk

Abstract *Professor Michael Levitt (Stanford University, USA) won the 2013 Nobel Prize in Chemistry for the development of multiscale models for complex chemical systems—computational tools which can calculate the course of chemical reactions. Professor Levitt was born in Pretoria, South Africa; he came to the UK on a summer vacation aged 16, where he decided to stay and study for his A-levels. His interest in the physics of living systems drove him to study biophysics at King's College London, before securing a PhD position at the Laboratory of Molecular Biology in Cambridge. In the interim year between his degree and beginning his PhD, Professor Levitt worked at the Weizmann Institute of Science in Israel, where he met his future wife. They married later that year and moved to Cambridge, where their three children were born. After completing his PhD, he spent time working in Israel, Cambridge, the Salk Institute and Stanford (both California). Since 1986, he has split his time between Israel and California. Outside of science, he is a keen hiker and he is well-known to have attended the eclectic 'Burning Man' Festival in California.*[1]

Professor Levitt visited the University of Warwick to speak at the Computational Molecular Science Annual Conference in March 2015. In this interview, Dr Gemma-Louise Davies, an Institute of Advanced Study Global Research Fellow, spoke to Professor Levitt about the importance of Interdisciplinarity in his field, role models in Academia, and his plans for the future.

Keywords: Michael Levitt; 2013 Nobel Prize in Chemistry; Role Models; Interdisciplinarity

---

Introduction

Last month's *Nature Journal* magazine (September 2015) has an eye-catching cover—superheroes sporting distinctive costumes which reflect

[1] 'Burning Man' is a unique annual festival dedicated to community, art, music, self-expression and self-reliance. Tens of thousands of people flock to this temporary metropolis built in the Californian desert.

their superpowers, focusing them in the same direction (**Figure 1**). It is a Special Issue on *Interdisciplinarity*, probing how scientists and social scientists are coming together to solve the grand challenges of energy, food, water, climate and health (**1**). Interdisciplinarity, however, is not simply achieved through gathering a team (large or small) to apply their individual skills to solve a particular problem (that is multi-disciplinarity); it is a distillation of their different approaches into something unique—unsolvable by traditional methods (**1**). General opinion indicates that it is 'more difficult' to gain funding for interdisciplinary research than for single discipline work, however this trend is beginning to shift (**2–4**). With the Global Research Council selecting interdisciplinarity as one of its two annual themes (along with women in science) (**5**), it is coming to the fore-front and is becoming an important driver for success in research.

Figure 1. Cover art for the September 2015 issue of Nature (**1**).

Professor Levitt won the Nobel Prize in Chemistry for his work on the development of computational methods which allow the accurate prediction of how reactions work at the atomic level. In particular, his research focuses on the theoretical analysis of proteins, DNA and RNA, which are the building blocks of life (**6–7**). Understanding their fundamental behaviour using computational methods provides us with unique insight into how they work, which is vital in the design of highly effective and targeted drugs. He shares the 2013 Prize with Professor Martin Karplus (Université de Strasbourg, France and Harvard University, USA) and Professor Arieh Warshel (University of Southern California, USA).

Given Professor Levitt's diverse research and his experience of working in various parts of the world (including the UK, Israel and the US), I was curious to find out his thoughts and experiences of interdisciplinarity in his field and the future of such research, as well as his opinions of the importance of role models in inspiring the next generation of (hopefully interdisciplinary) scientists. A summary of his advice to young researchers has been provided at the end of this interview.

It was clear that Professor Levitt has an open mind with respect to interdisciplinarity before we had even begun. My research involves the design of very small nano-sized structures as medical devices for disease diagnostics and drug delivery. It is quite different from his 'computational molecular biology' research (according to the 'traditional' boundaries that exist even within chemistry and biology). As I described my work, his response, inspirational in its simplicity, emphasised the logic of working with and learning from other disciplines. I began the conversation by discussing with Professor Levitt the impact of his research, which in itself is highly interdisciplinary.

The Interview

Gemma-Louise Davies (GLD): My research is quite different from yours.

Michael Levitt (ML): Well, it's a good idea!

GLD: I work quite a lot with nanomaterials for healthcare applications, so I'm trained as a chemist, but I dabble in the biological fields.

ML: Well biology is a form of nanotechnology. One can learn in both directions [and] what is nice about nanomaterials is that they are often a lot simpler [than complex biological systems]. Therefore you can learn things about them which are important. Colloids, for example, are a very good model for proteins and things like that.

Research and Interdisciplinarity

GLD: In terms of simulation based chemistry, or molecular biology, what do you think is the most important development in the field since the work that earned you the Nobel Prize?

ML: I think the most important thing is that these methods can be applied very broadly. They basically worked—this was the big surprise! In some ways we were lucky, because we put forward a model that had no right to work so well. And then we were very lucky because it got popularised and pushed out there, and lots of people started to work with it. The fact is that it actually works remarkably well! I think that it obviously isn't the last word and it needs to be improved and so on. But computers in chemistry and biology, now, it would be unthinkable without them. So I just really like computers… I'm very geeky and I do like computers and my iPhone.

GLD: I know it's incredible what you can do just on a smartphone now!

ML: It's amazing and this for me is just terrifically exciting and important.

GLD: Traditionally [in science], experiment drove theory—somebody had seen something experimentally and then asked a theoretician to help explain or understand it. Do you think that model is still in place?

ML: No, I actually think that simulations can lead. I think you can definitely start to calculate things and predict them quite well. Certainly in chemistry, quantum calculations of reactions are very predictive. I think it's just a question of getting to the right level and we don't know how much computing is needed. I think experimentalists are very important and often I think one of the hardest things about entering a certain field in chemistry or biology is becoming an expert in the field. Theoreticians can just move around, they are much more…

GLD: …flexible?

ML: … Promiscuous I was going to say, but flexible is fine—that's a nice way of saying it! They can do one thing or the other thing. It's just atoms—put this atom in, put that atom in—in some senses that is true, but I think what they lack is the deep experience and feeling for the system. Often, the experimentalists, someone who has been working in [a field] for a long time, has a feeling for the field and I think interactions between the two are very, very important.

GLD: I would certainly agree—interdisciplinarity is important! Obviously what you do is very much at the interface [of different disciplines]. You moved around a lot [throughout your life and career], how supportive were [these places] of interdisciplinary research?

ML: I worked really in three places—in Cambridge, in Israel and in the United States, at least 10 years in each place. The research environment in England was just amazing … it's extremely well done, so it's not really fair [to compare them]. In Israel, I was more in a regular department. The departmental politics were more difficult. Stanford is an extremely benevolent environment—it's a bit like the weather, it's nice and warm and helpful. One thing that [Stanford] did which was a very strong poster for interdisciplinary research is they made it very easy to get internal grants—not much money, maybe £30,000. But you could come along with something really crazy. I had one [internal grant] where I was doing molecular dynamics[2] and someone was doing walking dynamics[3] and we got together and put a proposal together, just for fun! It was one of those things that was just so interesting to us. And things came out of it and there were similarities and differences, but it was something where you took two people who shouldn't be able to talk to each other and give them some money. But it's still going on!

The other thing that Stanford has is one building, which has got forty faculty from twenty-six departments. Everyone thinks, "Oh it was so well designed", but what actually happened was that Stanford can't build as much as it would like, because Stanford is zoned as farmland. They can build barns, as many as they want, they just can't build offices, labs and things like that. At the end of the 90s, they had 2,500 feet left. The President had already promised a building to Engineering and to the Medical School and so on … and so he said, "I'm sorry, I only have enough money and space for one more building, so you'd better share it!" It worked out to be really very powerful.

GLD: I think that's great—that's similar to what I am part of [the Institute of Advanced Study], it's trying to encourage interdisciplinarity. I think it's very important.

ML: There needs to be a real commitment to recognising [interdisciplinarity]. But I'm a great believer in that personally. I think that when you put strange things together, you get combinations which are unexpected and things happen!

Role Models

GLD: What I thought was really interesting when I was looking back over your past is that you had quite a lot of academic influences during your early life—your Aunt and Uncle are scientists and I believe you have a

[2] Molecular dynamics is a computational method which simulates the physical movement of atoms and molecules.
[3] Walking dynamics is the investigation of physical anatomical motion.

mathematician relation who used to work here at Warwick, so a strong family connection. Do you think that moulded you and pushed you towards an academic career?

ML: I grew up in South Africa until I was 16. In South Africa, science just didn't seem like an option. My Uncle and Aunt weren't in the country, they were living in England and I didn't actually know any scientists, mathematicians, or anyone who was actually interested in thinking about things. I knew people who wanted to be doctors, and lawyers and businessmen, particularly businessmen, but I think I must have somehow liked science. There is no doubt in my mind that [the] people that you bump into, just fleetingly, are very important. One of the reasons why I am actually here, dressed properly and giving these talks is that I actually feel that it's important to pass on things that you know, and I don't think it's what you said[4], I think it's being an example, being a poster. I think science is really wonderful and I'm more passionate about the act of doing science than ever. I feel that science needs role models and mentors. But I have been very lucky.

GLD: Actually, when I was considering questions for this [conversation], someone suggested I ask "how much luck do you think is involved?"

ML: I was speaking to a colleague of mine, a woman, and she said "You were so lucky, you had all these great mentors and I really wish I had had good mentors like that". I realised that this was particularly bad because an ideal mentor for her would have been a woman, because at least that would have been a different example and therefore I think that you realise that there is an imbalance in numbers. There aren't mentors [or] examples [to guide young scientists], these are lacking. So I think mentoring is really important. I don't think it's important in that people who have been there know 'stuff', it's that they add to the randomness—randomness is very important. Someone can say to you, "have you thought about that?" and maybe if your office-mate said it to you, you might ignore them, but if I said it to you, it could be absolutely nonsensical, but it will make you pause and think. I think that's very good. The trouble with luck is, people say they have no luck and the fact is that none of us choose whom we want to be. I think life is lucky—I think life is what you make of it.

[4] Familial influence

GLD: So coming back to role models, do you encourage your children and your grandchildren to get into the sciences—do you talk to them about what you do?

ML: It turns out that the whole relationship of role models is a very complicated one. It is much easier to influence someone at a distance because one trouble is that it is very easy to cause a reaction. We have three sons, six grandchildren, each of our sons has one, two or three children, and I would say that the nice thing is that they all still speak to us! We are very close to them, we do things together [and] we try very hard to be involved. I think that they realised that science is very hard. Science I think is particularly hard for a spouse of a scientist because a scientist is in some ways married to their work. It's like sharing a relationship, a relationship which is very asymmetric. So our children didn't want to be scientists.

I think it's a good idea to try to influence people in a very light way; it's a great mistake to think you know what is good for people, which you don't. All I feel I'm doing is just talking to people, showing them that scientists can still have a life and so on. If somebody isn't sure if they want to be a scientist, they should not allow themselves to think for a week, just try not to think for a week—you'd run back to science so quickly! It's so interesting, you are trying to make things happen, I think it's a really luxurious thing to do.

The Future

GLD: One of the most eye-catching quotes that I saw from your Nobel Prize lecture was one where you said "getting the Nobel Prize was a real drawback, because you feel that this is the best that you are ever going to do in life and that is a depressing thought".

ML: So what has happened is that I found that the compensation has been that the pleasure I take in science has actually increased. I don't mean the pleasure I take in, "would you like to organise this meeting, or would you like to give out this prize"—those things I don't like at all. But actually just sitting down and doing a calculation, just working with the people that I work with. Just working is so enjoyable! More than it was before. And actually I think I'm more careful. Maybe it comes from more confidence. There is a term in computing called 'np-complete' which means 'non-polynomial complete', which means when a calculation is really, really hard—something that is exponentially hard. So that means that as you increase the size of the problem, the difficulty increases as an exponential; and 'np' is also 'Nobel Prize', so I joke that I am 'np-complete' now, which makes everything exponentially difficult! I think for me the surprise was that I really enjoy work more than ever! It is actually annoying to find time [to research] … now I have three things that draw my time. One is family (we now have six grandchildren, daughter-in-laws, we have a big family now) and my wife, and this was actually hard for her; second is my work; and then there is public outreach. So knowing how to balance these things is very difficult. It's a bit like riding a bike, or [for] me riding a mono-cycle—you've got to keep on worrying about the balance.

GLD: So, what do you think is the next big thing [in research], in the next ten years, what are we going to achieve? Do you see a time when we are going to be moving completely out of the wet lab and everything is going to be simulation-based?

ML: I think predictions like that are very dangerous—I don't want to say all sorts of stupid things! But one thing that I would like, is someone on a kick-starter to propose making a robot to make an omelette. Let's say it costs £500, a general purpose machine like that, I think it could do a lot of lab chemistry! I think that certainly in computing, we are very 'helped'—there are scripting languages, where you can just throw together ideas without even thinking. It's an incredibly empowering thing and I think that experimental work doesn't yet have this … there is a lot of drudgery involved.

GLD: Yes, washing glassware, that is my pet hate!

ML: Well yeah, you shouldn't have to do that. But it is also interesting that for example in the US, people don't know how to cook anymore! There is an interesting book about this, about how the food industry destroyed American nutrition. The basic idea was to stop people learning to cook. They used to teach cooking in high school, 'home economics', [but] the food industry infiltrated that organisation and destroyed it.

GLD: Really, 'home economics' is not taught anymore?

ML: [*Shakes head*] So as a result you go to MacDonalds or something like that. So I think that people should learn how to cook. So [the next big thing could be] maybe a robot that would cook at home for you. I've been in towns in the US where you can buy fast food, but if you want to find a butcher [*shrugs shoulders*] … it's scary!

GLD: Ok, my very last question … have you been back to 'Burning Man'[5]?

ML: We're going to go back this summer—we have got tickets.

GLD: Do you reckon your experience will be the same? Do you know if you are going to be the first Nobel Prize winner [to attend 'Burning Man']?

ML: So I went first as a baby, the next time I went with my wife—that was actually in the August before the Swedish nonsense[6]! That was wonderful and we actually did 'stuff'. I was surprised because I do a lot of hiking and sleeping in the dust, I don't mind not showering for a week! But my wife, she wants to have food that comes out of a refrigerator [and] she wants to have a shower. I was surprised how much she enjoyed 'Burning Man'. We were in an RV and we had those things, but even then it's not the same as a hotel. She enjoyed it, so I was surprised. It's a very special place, everyone is looking into other people's eyes, everyone is very friendly. One of the hardest things about 'Burning Man' is leaving. It's like a kid when you go to camp—you don't want to go home.

I think this time we are going to have a camp, with one of our sons, who has now three children, maybe some babysitting involved, but grandparents are very happy to babysit. The place is interesting because the art is spectacular, quite good music. I'm looking forward to it, we'll see what happens. It will be fun! As long as I'm not recognised! One thing I realised is that people in the news who are recognised … they are actually working quite hard to be recognised. If I dress like this[7] versus wearing shorts and a t-shirt—no one actually thinks it's the same person. That's why I dress up for these things, so no one will recognise me afterwards! People end up dressing in a very characteristic way so they get recognised. It's addictive—[the] media attention that you get is very addictive, so I'm very lucky because my wife thinks it's all complete and total nonsense! She doesn't want to go to any function whatsoever, she refuses! That's actually good. It grounds you.

GLD: Thank you for your time!

[5] 'Burning Man' is a unique annual festival dedicated to community, art, music, self-expression and self-reliance. Tens of thousands of people flock to this temporary metropolis built in the Californian desert.
[6] Being awarded the Nobel Prize in 2013!
[7] Sports jacket, shirt and tie.

Conclusion

The 2013 Nobel Prize in Chemistry recognises how disciplines can work together to provide new tools with massive potential to change how we understand and work on entire fields of research. Levitt, Warshel and Karplus's method is still a popular and widespread technique in computational science, which is ever expanding and overlapping with different research areas. This acknowledgement by the Nobel Prize committee is a massive step forward in interdisciplinary research, which is making an impact and is certainly here to stay.

A Nobel Prize Winner's Advice for Young Researchers:

- Be passionate. Do something you really want to do. It's really important, it doesn't matter what it is.
- Be persistent, don't give up. You have got to believe in yourself. If you don't believe in yourself, how can you expect someone else to? It's logical!
- Be original. By that I mean, each of us are different, we have different backgrounds—even if we are identical twins, we are different. Therefore, do something that suits you, because that is something that is going to be special.
- Finally, be kind and good. I just think that life is much easier if you are kind and good. Even if you are not—act kind and good, because you'll get away with it much more often!

Professor Michael Levitt, Chemistry Nobel Prize Winner 2013

Figure 2. Professor Michael Levitt (left) with Dr Scott Habershon (right), organiser of the 2015 Computational Molecular Science Annual Conference) during his visit to the University of Warwick in March 2015.

References

1. Editorial (2015), 'Mind Meld'. *Nature*, 525, 289–90.

2. Wagner, C. S., Roessner, J. D., Bobb, K., Klein, J. T., Boyack, K.W., Ketyton, J., et al. (2011), 'Approaches to understanding and measuring interdisciplinary scientific research (IDR): A review of the literature', *Journal of Informetrics*, 5 (1), 14–26.

3. Ledford, H. (2015), 'How to solve the world's biggest problems', *Nature*, 525, 308–11.

4. Van Noorden, R. (2015), 'Interdisciplinary research by the numbers', *Nature*, 525, 306–07.

5. Rylance, R. (2015), 'Grant giving: Global funders to focus on interdisciplinarity', *Nature*, 525, 313–15.

6. Warshel, A., Levitt, M. (1976), 'Theoretical studies of enzymatic reactions: dielectric, electrostatic and steric stabilisation of the carbonium ion in the reaction of lysozyme', *Journal of Molecular Biology*, 1976, 103 (2), 227–49.

7. Levitt, M. (1975), 'Computer simulation of protein folding', *Nature*, 253, 694–98.

To cite this article:

Davies (2015), 'Conversations with Michael Levitt', *Exchanges: The Warwick Research Journal*, 3(1), 1–11. Retrieved from: http://exchanges.warwick.ac.uk/index.php/exchanges/article/view/82